Solvent-Free Organic Synthesis

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I. Introduction

Crushed grapes give wine by fermentation, but dried grapes do not result in wine. Although milk turns sour and shaking of milk gives cheese, dried milk can be kept unaltered. Similarly dried meat can be stored for a long time, whereas meat soup rapidly putrefies on standing.

By observation of these phenomena, one can see that conversion of one material into another one occurs in the liquid state but not in the solid state. One of the most famous ancient philosophers in Greece, Aristotle, summarized these observations by concluding "No Coopora nisi Fluida", which means "No reaction occurs in the absence of solvent". Such philosophies had a big influence on the evolution of the modern sciences in Europe, and this provides one historical reason most organic reactions have been studied in solution.

Nevertheless, it is remarkable that chemists still carry out their reactions in solution, even when a special reason for the use of solvent cannot be found. We have found that many reactions proceed efficiently in the solid state. Indeed, in many cases, solid-state organic reaction occurs more efficiently and more selectively than does its solution counterpart, since molecules in a crystal are arranged tightly and regularly.

Furthermore, the solid-state reaction (or solvent-free reaction) has many advantages: reduced pollution, low costs, and simplicity in process and handling. These factors are especially important in industry.

When greater selectivity is required in the solid-state reaction, host−guest chemistry techniques can be applied efficaciously. Reaction in the solid state of the guest compound as its inclusion complex crystal with a chiral host can give an optically active reaction product. Various host compounds have been designed by us to follow this simple principle. Although both thermal and photochemical reactions can be carried out selectively in inclusion crystals, the selectivity of the latter is usually higher than that of the for-

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Koichi Tanaka received his Bachelor's and Master's degrees from Ehime University in 1976 and 1978, respectively, and Doctor's degrees from Osaka University in 1983. He was appointed an Assistant Professor at Ehime University in 1978 and worked with Professor F. Toda. He was promoted to Associate Professor in 1991. His research interests are in the area of design of novel host molecules, chiral recognition in host–guest inclusion crystals, and solid-state organic reactions.

Fumio Toda received his Bachelor's, Master's, and Doctor's degrees from Osaka University at Osaka City, Japan, in 1956, 1958, and 1960, respectively. After staying at Osaka University for four years as an Instructor and in the United States for two years as a postdoctoral fellow, he obtained an Associate Professorship at Ehime University in 1966. He was promoted to Full Professor in 1972. He has held the Synthetic Organic Chemistry Award in 1988, the Chemical Society of Japan Award in 1993, and the Inoue Harushige Award in 1999, and he moved to Okayama University of Science. His research interests are in the area of strained small-ring compounds, unusual chemical bonds, host–guest inclusion compounds, solid-state organic chemistry, and reaction control in crystals.

mer. However, solvent-free thermal reactions are important for practical synthetic processes in industry.

The occurrence of efficient solid-state reactions shows that the molecules reacting are able to move freely in the solid state. In fact, host−guest inclusion complexation can occur by simply mixing and grinding both crystals in the solid state. These solid-state reactions can be easily monitored by measurement of IR and UV spectra in the solid state. Surprisingly, solid-state complexation even occurs selectively. For example, mixing and grinding racemic guest and optically active host in the solid state gives an inclusion complex involving just one enantiomer of the guest with the host and from which the optically active guest can be obtained. Such efficient chiral recognition has been observed in many inclusion crystals, and efficient optical resolutions have been achieved by using this phenomenon. The most interesting application of chiral recognition in the solid state is resolution of a racemic guest by fractional distillation in the presence of an optically active host. When racemic guest and chirally pure host are mixed in the solid state, one enantiomer of the guest is included by the host, and then when the mixture is heated the uncomplexed guest distills at relatively low temperature. Thereafter the complexed enantiomer is released on distillation at relatively high temperature. In this review, optical resolution by selective inclusion is not discussed. However, optical resolution by the combination of enantioselective solid-state reaction and the distillation technique is described in chapter II.

In an inclusion crystal formed by a prochiral guest and chiral host, molecules of the former are arranged in a chiral form and such chirality becomes permanent on solid-state reaction. This is the basic principle underlying enantioselective reactions in inclusion crystals using chiral hosts. In some special cases, prochiral molecules are arranged in a chiral form within the crystal without using any chiral source. Once again this chirality can also become permanent through solid-state photoreaction. This is absolute asymmetric synthesis and is summarized in chapter IV.

Inclusion crystals are usually prepared by recrystallization of both components. Surprisingly, however, it was discovered that movement and chiral arrangement of achiral molecules can occur by mixing and grinding host and guest crystals in the solid state. In other words, an optically active product results from mixing and grinding an achiral guest with a chiral host followed by irradiation. The chiral arrangement of the achiral guest resulting from mixing and grinding with a chiral host can also be easily monitored by measurement of its CD spectrum in the solid state. This is described in chapter II.

This article covers such solid-state organic reactions including the reactions that start with a solid, at least one solid reactant or solid catalyst, the reactions in the inclusion crystals, and organic solvent-free reactions mainly since 1983 although some review articles and books on these topics have been already published.[1]

II. Molecular Movement in the Solid State

In 1987, it was found that inclusion complexation occurs by simple mixing and grinding of powdered host and guest compounds. For example, when an IR spectrum of a mixture of powdered 1,1,6,6-tetraphenylhexa-2,4-diyne-1,6-diol (**1**) (Chart 1) and an equimolar amount of powdered benzophenone was measured as a Nujol mull, it proved to be identical to that of their 1:1 inclusion complex prepared normally by recrystallization of the two components from solution.[2] This result shows that formation of the complex by solid-state reaction occurs very rapidly. Similar inclusion complexation in the solid state occurs for many other kinds of host and guest combinations.

These solid-state reactions can easily be monitored by measurement of the IR or UV spectrum as a Nujol mull. For example, when IR spectra of a mixture of **1** and two molar amounts of amide **2** were measured

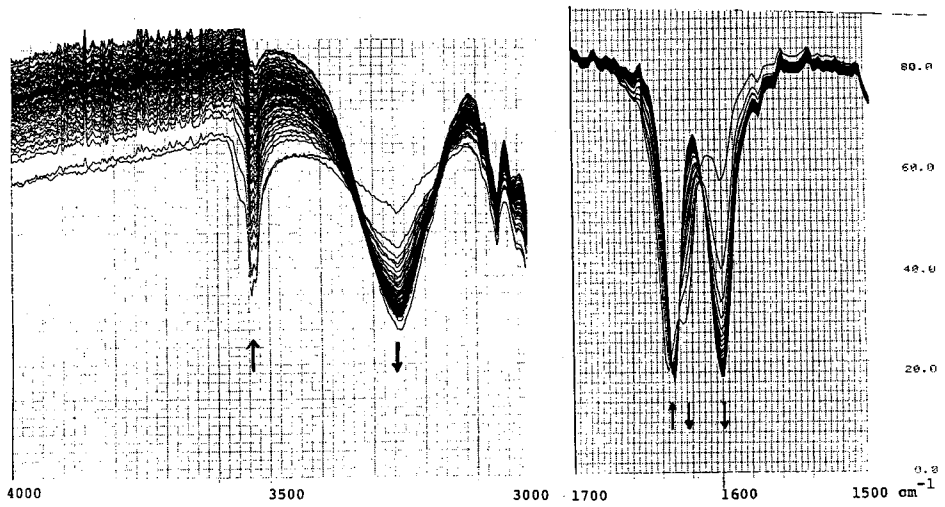
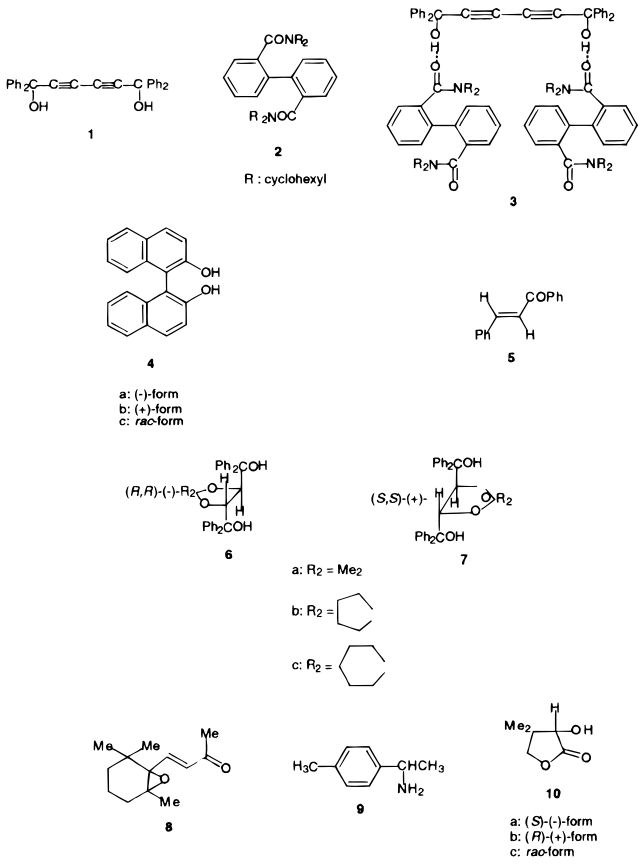


Figure 1. IR spectrum of a mixture of powdered (50 μm) **1** and **2** in the solid state (measured every 10 min for 17 h).

Chart 1



in Nujol every 10 min for 17 h, the ν_{OH} of **1** at 3540 cm^{-1} decreased and finally disappeared and a new hydrogen-bonded ν_{OH} due to a 1:2 complex (**3**) appeared at 3250 cm^{-1} and increased gradually. Concomitantly the $\nu_{C=O}$ of **2** at 1690 cm^{-1} split into two $\nu_{C=O}$ at 1680 and 1600 cm^{-1} as the inclusion complexation proceeded (Figure 1).[3] Formation of racemic 2,2′-dihydroxy-1,1′-binaphthyl (**4c**) by mixing and grinding of powdered (−)-(**4a**) and (+)-enantiomers (**4b**) in 1:1 ratio may also be followed by successive IR measurements in the solid state and in Nujol (Figure 2).[4] As the formation of **4c** by solid-state reaction of **4a**,**b** proceeds, the ν_{OH} absorptions of **4a**,**b** at 3510 and 3435 cm^{-1} decreased and finally disappeared within 1 h, and the new ν_{OH} due to **4c** at 3490 and 3405 cm^{-1} appeared.

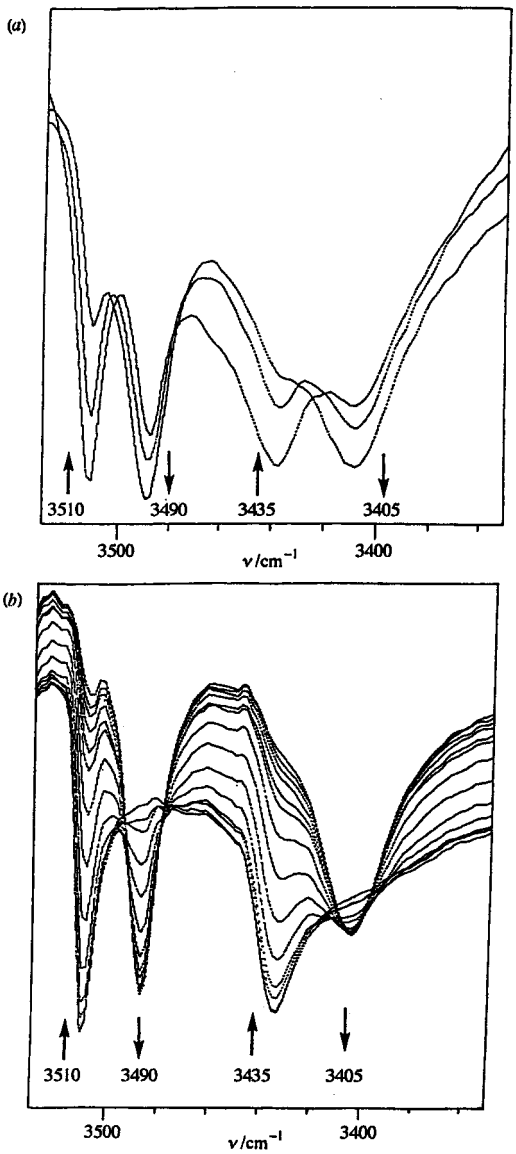


Figure 2. IR spectra of a 1:1 mixture of **4a**,**b** in the absence (a) and presence (b) of liquid paraffin. Samples were measured every 24 h for 48 h (a) and every 5 min for 1 h (b).

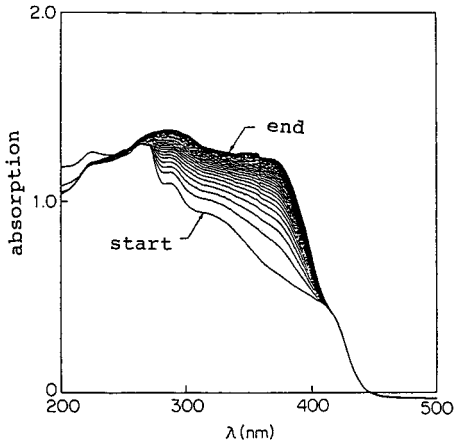


Figure 3. UV spectrum of a mixture of powdered (50 μm) **1** and **5** in the solid state (measured every 10 min for 6 h).

When UV spectra of a 1:2 mixture of **1** and chalcone (**5**) were measured in the solid state every 10 min for 6 h, the absorption increased gradually as shown in Figure 3. As inclusion complexation proceeds, the number of complexed chalcone molecules (which has a coplanar structure) increases and hence the absorption coefficient increases. The coplanar structure of **5** in its complex with **1** has been proven by X-ray analysis.[3,5]

Solid-state reaction occurs even enantioselectively. For example, inclusion complexation of chiral host **6** and *rac*-**8** proceeds enantioselectively and (+)-**8** is included. After a 1:2 mixture of powdered **6b** and powdered *rac*-**8** was kept at room temperature for 2 days, uncomplexed (−)-**8** was extracted with hexane to give a 1:1 complex of **6b** and (+)-**8**, from which (+)-**8** of 88% ee was obtained in 32% yield by distillation in vacuo. From the hexane solution, (−)-**8** of 62% ee was isolated in 60% yield.[6] When **7b** is used instead of **6b** for the resolution of *rac*-**8** in the solid state, (−)-**8** of 88% ee was obtained. The most interesting application of the enantioselective solid-state reaction is the resolution of racemic guest by distillation in the presence of a chiral host.[7] Heating of a 1:2 mixture of **6c** and *rac*-**9** in a Kugelrohr apparatus at 70 °C/2 mmHg gave (+)-**9** of 98% ee in 100% yield by distillation, and then further heating of the residue at 150 °C/2 mmHg gave (−)-**9** of 100% ee in 98% yield. The mechanism of this fascinating resolution by distillation is as follows: first, by mixing and grinding **6c** and *rac*-**9**, inclusion complexation between the host and (+)-**9** occurs by enantioselective solid-state reaction; second, by heating at 70 °C/2 mmHg, uncomplexed (−)-**9** is liberated by distillation; third, by further heating at 150 °C/2 mmHg, the inclusion complex is decomposed and (+)-**9** is liberated by distillation. Since the chiral host is recovered unchanged and can be used again, this simple resolution method is highly economical. This resolution method is applicable to many kinds of *rac*-guest compounds such as alcohols, diols, epoxides, amino alcohols, and cyclic amines.[7]

The enantioselective solid-state reaction can also be followed by measurement of CD spectra in Nujol mulls. It has been reported that cocrystallization of **6b** and *rac*-pantolactone (**10c**) from benzene−hexane (1:1) gives a 1:1 inclusion crystal of **6b** and (*S*)-(−)-pantolactone (**10a**) of 99% ee.[8] The enantioselective inclusion complexation was found to proceed even in the crystalline state, and the enantioselective solid-state reaction was monitored by measurement of CD spectra as Nujol mulls. The CD spectrum of a mixture of powdered **6b** (5 mg) and 2 equiv of **10c** (2.6 mg) in liquid paraffin (100 mg) was measured after 5 min of the preparation of the mull (Figure 4). The spectrum which shows a (+)-Cotton effect is almost identical to that of an authentic inclusion crystal of **6b** and **10a**. An X-ray crystal structure of the complex has been analyzed.[8] The assignment of the CD spectrum to **6b**:**10a** complex is reasonable, since **6b** itself shows only very weak spectrum and uncomplexed **10b** left after the enantioselctive complexation also shows only a weak spectrum (Figure 4). On the other hand, a mixture of **7b** and 2 equiv of **10c** showed a CD spectrum with a (−)-Cotton effect by formation of the **7b**:**10b** complex (Figure 4).

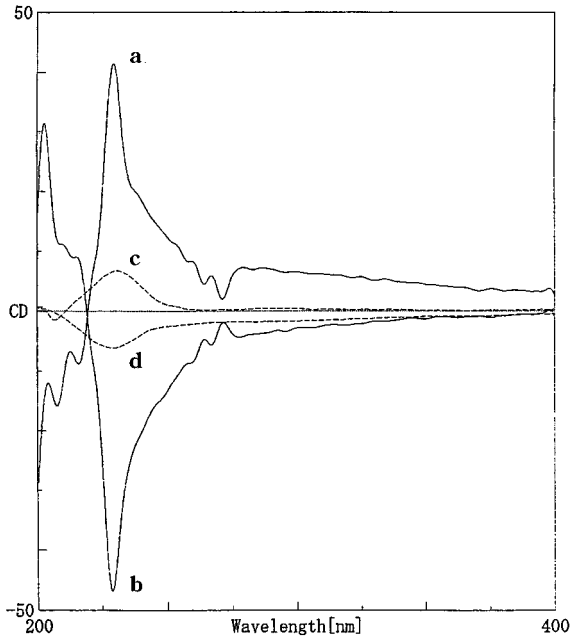


Figure 4. CD spectra of (a) **6b·10a** and (b) **7b·10b** complex prepared by mixing of **10c** with **6b** and **7b**, respectively, and of (c) **10b** and (d)**10a** in Nujol mulls.

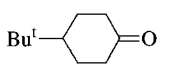
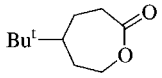
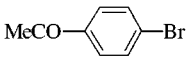
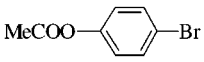
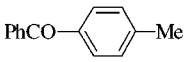
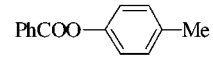
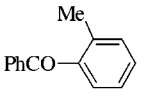
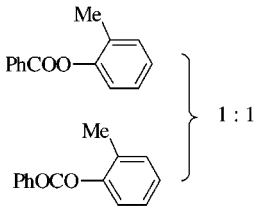
When molecular motion occurs in the solid state between reactant and reagent, then solid-state reaction proceeds. These reactions can be followed by measurement of IR, UV, and CD spectra. The AFM technique is a powerful tool for analysis of solid-state reactions. Many examples of these techniques are used in order to follow solid-state reactions in the text.

III. Thermal Reaction

A. Oxidation

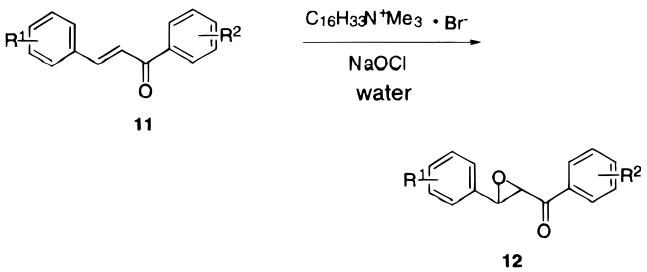
Some Baeyer−Villiger oxidations of ketones with *m*-chloroperbenzoic acid proceed much faster in the solid state than in solution. When a mixture of powdered ketone and 2 mol equiv of *m*-chloroperbenzoic acid was kept at room temperature, the oxidation product was obtained in the yield shown in Table 1.[9]

Table 1. Yields of Baeyer−Villiger Oxidation Products in the Solid State and in $CHCl_3$

ketone	reaction time	product	yield (%)	
			solid state	$CHCl_3$
	30 min		95	94
	5 days		64	50
$PhCOCH_2Ph$	24 h	$PhCOOCH_2Ph$	97	46
PhCOPh	24 h	PhCOOPh	85	13
	24 h		50	12
	4 days	 1 : 1	39	6

Each yield is higher than that obtained by reaction in $CHCl_3$ (Table 1).

Epoxidation of chalcones with NaOCl in a water suspension was found to proceed very efficiently.[10] For example, a mixture of **11a**, hexadecyltrimethylammonium bromide, and commercially available 11% aqueous NaOCl was stirred at room temperature for 24 h. The reaction product was filtered and dried to give **12a** in quantitative yield. This procedure was applied to various kinds of chalcone derivatives, and **11b**−**i** were oxidized efficiently to give the corresponding epoxides **12b**−**i** in good yields (Table 2).



a : $R^1=R^2=H$ **e** : $R^1=p$-Br, $R^2=H$ **i** : $R^1=H$, $R^2=p$-Br
b : $R^1=m$-Me, $R^2=H$ **f** : $R^1=p$-MeO, $R^2=H$ **j** : $R^1=H$, $R^2=p$-MeO
c : $R^1=p$-Me, $R^2=H$ **g** : $R^1=H$, $R^2=p$-Me **k** : $R^1=R^2=p$-Me
d : $R^1=p$-Cl, $R^2=H$ **h** : $R^1=H$, $R^2=p$-Cl **l** : $R^1=R^2=p$-Cl

When a 1:1 inclusion complex of β-ionone **14** (Chart 2) and optically active host compound (−)-**6c** was treated with 2 molar equiv of *m*-chloroperbenzoic acid in the solid state, a 1:1 inclusion complex of (−)-**6c** with (+)-**8** of 66% ee was obtained together with (−)-**15** of 72% ee.[6] This can be interpreted by an enantioselective inclusion complexation in the solid state between the initially formed (±)-**8** and (−)-**6c**, namely

Table 2. Epoxidation Reactions of Chalcones in a Water Suspension Medium

chalcone	product	reaction time (day)	yield (%)
11a	**12a**	1	100
11b	**12b**	2	80
11c	**12c**	2	85
11d	**12d**	4	85
11e	**12e**	2	90
11f	**12f**	1	78
11g	**12g**	2	36
11h	**12h**	0.4	90
11i	**12i**	0.3	99
11j	**12j**	1	93
11k	**12k**	5	43
11l	**12l**	5	30

(−)-**6c** includes (+)-**8** selectively in the solid state to form the 1:1 complex, and the uncomplexed (−)-**8** is oxidized further to (−)-**15** with *m*-chloroperbenzoic acid. Similar solid-state kinetic resolution of dialkyl sulfoxides **16** was achieved by their enantioselective oxidation to dialkyl sulfones **17** with *m*-chloroperbenzoic acid in the presence of (−)-**13**. For example a mixture of sulfoxide **16a** (1 g) and (−)-**13** (1.8 g) was kept at room temperature for 1 day and then mixed with *m*-chloroperbenzoic acid (0.64 g) and kept for a further 1 day. From the reaction mixture, (+)-**16a** of 37% ee (0.38 g, 38% yield) was obtained (Table 3).

Chart 2

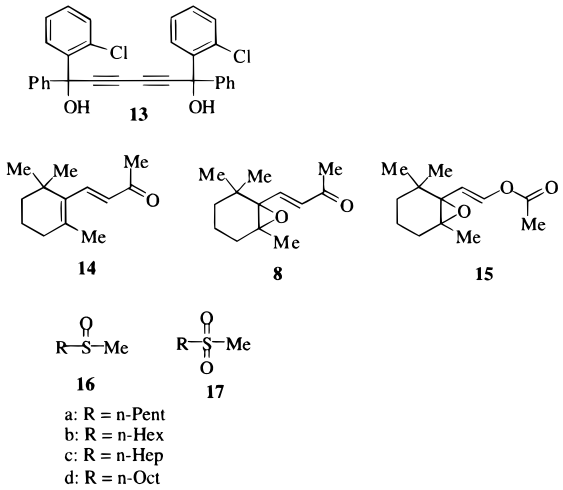
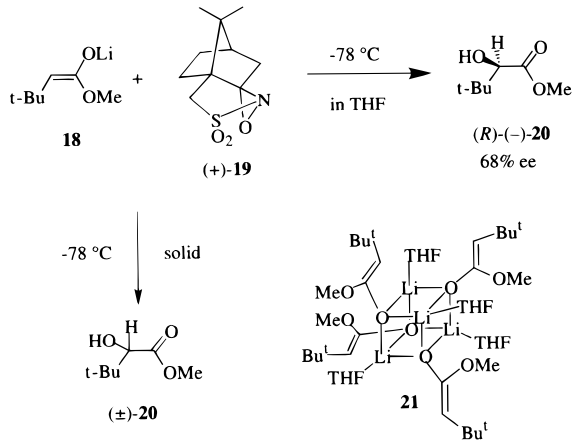


Table 3. Solid-State Kinetic Resolution of 16 by Selective Oxidation with MCPBA in the Presence of (−)-13

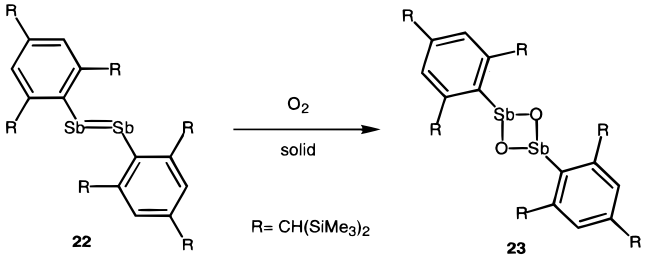
sulfoxide	product		
	yield (%)	$[\alpha]_D$ (EtOH)	% ee
16a	**(+)-16a,** 38	+44.2	37
16b	**(+)-16b,** 51	+51.6	42.7
16c	**(+)-16c,** 40	+25.6	25
16d	**(+)-16d,** 7	+69	100

Oxidation of the lithium enolate of methyl 3,3-dimethylbutanoate **18** by enantio pure (camphoryl-sulfonyl)oxaziridines **19** in THF afforded optically active α-hydroxyester **20**, but the product from the solid-state reactions was racemic.[11]



For example, the oxidation of **18** with (+)-**19** in THF at −78 °C afforded (*R*)-(−)-**20** of 68% ee in 35% yield. However, the treatment of powdered **18** with powdered (+)-**19** in the solid state at −78 °C for 4 h produced (±)-**20** in 17% yield. The solid enolate **18** was found to exist as a tetrameric aggregate **21** by X-ray crystallographic studies.[12] In the solid-state reaction, **21** could not dissociate into the monomer **18** that is necessary to form the coordinated transition state of the enantioselective reaction.

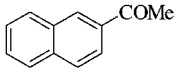
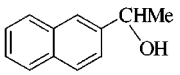
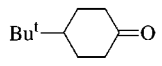
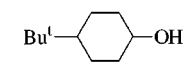
Oxidation reaction of overcrowded distibene **22** with molecular oxygen was found to proceed in a single-crystal-to-single-crystal manner.[13] The green crystals of **22** reacted with atmospheric oxygen to give colorless crystals of **23** quantitatively. Interestingly, the reaction occurred within 10 h after an induction period (ca. 30 h).



B. Reduction

Reduction of ketones with $NaBH_4$ also proceeds in the solid state. When a mixture of the powdered ketones and a 10-fold molar amount of $NaBH_4$ was kept in a drybox at room temperature with occasional mixing and grinding using an agate mortar and pestle for 5 days, the corresponding alcohols were obtained in the yields shown in Table 4.[14]

Table 4. Reduction of Ketones in the Solid State by $NaBH_4$

ketone	alcohol		yield (%)
Ph_2CO	Ph_2CH-OH		100
trans-PhCH=CHCOPh	trans-PhCH=CHCHPh (OH) and $PhCH_2CH_2CHPh$ (OH)	1:1	100
			53
PhCHCOPh (OH)	meso- PhCH-CHPh (OH OH)		62
$PhCH_2COPh$	$PhCH_2CHPh$ (OH)		63
			92

The reduction of benzophenones was studied in detail by in situ X-ray powder diffractometry and by ^1H NMR spectroscopy. The reaction efficiency was found to show a strong dependence on the water content of the mixture and on the type of benzophenone.[15] Under strict water exclusion, the reaction does not occur whereas the presence of small amount of water enhances the reaction. The following order of reactivity of benzophenone derivatives was obtained for the solid-state reduction with $NaBH_4$:

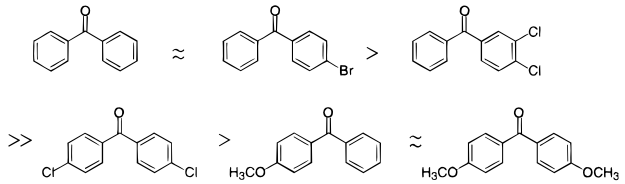
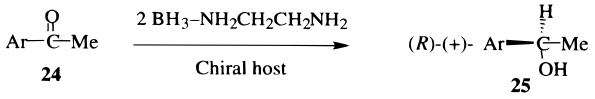


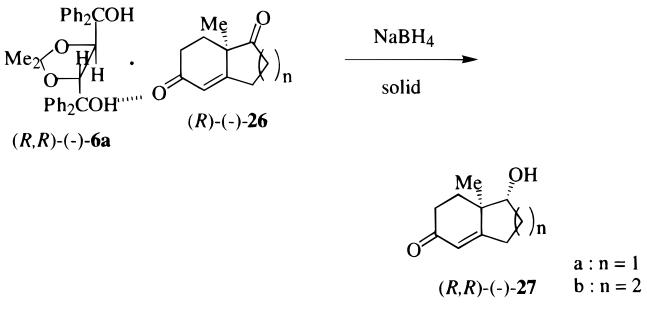
Table 5. Yield, Optical Purity, and Absolute Configuration of the Alcohol Obtained by Solid-State Reduction

host	Ar	alcohol **25**		
		yield (%)	% ee	absolute confign
(–)-**13**	Ph	96	44	*R*
(–)-**13**	*o*-tolyl	57	59	*R*
(–)-**13**	1-naphthyl	20	22	*R*
(–)-**6a**	1-naphthyl	32	22	*R*

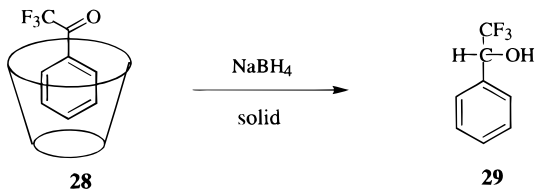
In addition, enantioselective reduction of ketones is also found to proceed efficiently. For example, treatment of inclusion compounds of the ketones **24** in optically active host compounds with a BH_3−ethylenediamine complex in the solid state gave the chiral alcohols (*R*)-(+)-**25** of 20−60% ee as shown in Table 5.[16] With the inclusion compounds of ketones with chiral host compounds, the BH_3−ethylenediamine complex would attack the ketones from the direction which gives the (*R*)-alcohols selectively.



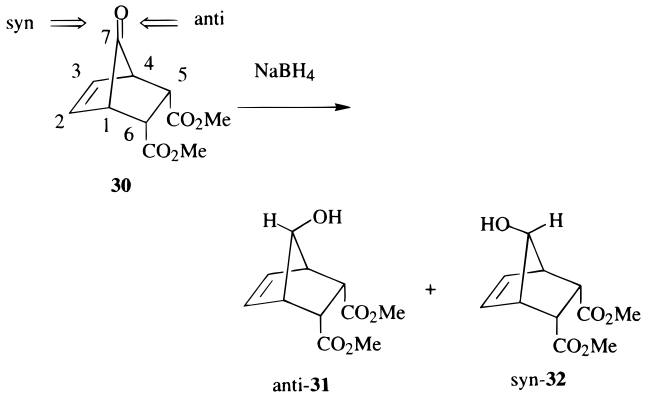
Treatment of a 1:1 inclusion complex[17] of (*R*)-**26a** and (*R*,*R*)-(−)-**6a** with $NaBH_4$ in the solid state for 3 days gave (*R*,*R*)-(−)-**27a** of 100% ee in 54% yield.[14] The corresponding reaction of a 1:1 complex of (*S*)-**26a** and (*S*,*S*)-(+)-**7a** gave (*S*,*S*)-(+)-**27a** of 100% ee. The enone moiety of (*R*)-**26a** is masked by forming a hydrogen bond with the hydroxyl group of (*R*,*R*)-**6a**,[18] so that the other carbonyl group is reduced selectively. Similar reduction of a 1:1 complex of (*R*)-**26b** and (*R*,*R*)-**6a** with $NaBH_4$ in the solid state gave (*S*,*S*)-**27b** of 100% ee in 55% yield.



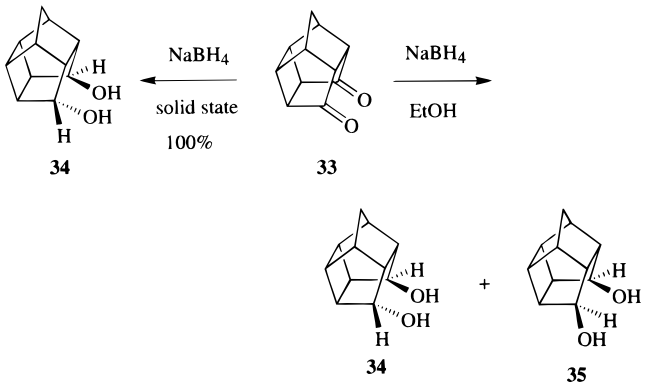
Enantioselective reduction of ketones in inclusion complexes with β-cyclodextrin in the solid state proceeded less selectively. For example, a mixture of the finely powdered β-CD complex of **28** and 10 mol of $NaBH_4$ was kept at room temperature for 5 days to give the corresponding alcohol **29** of 11% ee in 56% yield.[19]



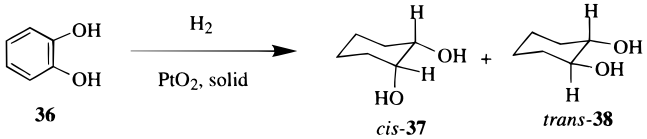
It is also interesting that a reversed selectivity in the reduction of 7-norbenone **30** in the solid state is observed compared to the reaction in MeOH. For example, a 45:55 mixture of *anti*-**31** and *syn*-**32** was obtained on $NaBH_4$ reduction of **30** in MeOH. Treatment of **30** with $NaBH_4$ in the solid state, however, afforded a 87:13 mixture of *anti*-**31** and *syn*-**32** in 80% yield.[20] X-ray structural analysis of **30** showed that its C1−C7−C4 bridge is tilted by 6° toward the C5−C6 bridge in the crystal.



$NaBH_4$ reduction of the a pentacyclic cage diketone **33** in EtOH afforded a 38:62 mixture of *endo*,*endo*-diol **34** and *exo*,*endo*-diol **35**. In contrast to these results, the solid-state $NaBH_4$ reduction of **33** affords exclusively the corresponding *endo*,*endo*-diol, **34**, in quantitative yield.[21] This indicates that the hydride transfer occurs exclusively at the exo face of the carbonyl group.



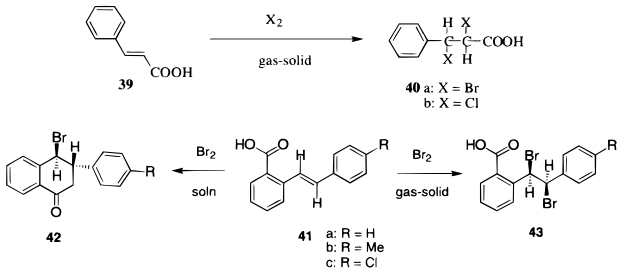
Solid-state hydrogenation of dihydroxybenzene proceeds under milder conditions than under liquid or vapor phase conditions. For example, PtO_2-catalyzed reduction of o-hydroquinone to *trans*-1,2-cyclohexanediol proceeds efficiently in the solid state.[22] When the reaction is carried out by mixing powdered 1,2-dihydroxybenzene (**36**) and PtO_2 catalyst under a hydrogen pressure of 1 bar at 25 °C, a 71:29 mixture of *cis*-**37** and *trans*-**38** is obtained in 68% yield along with cyclohexanol.



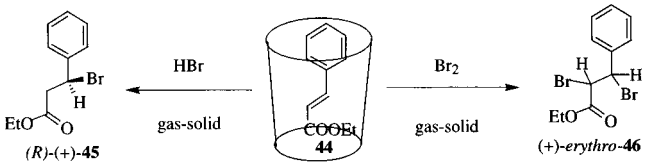
C. Addition Reaction

1. Halogenation and Hydrohalogenation

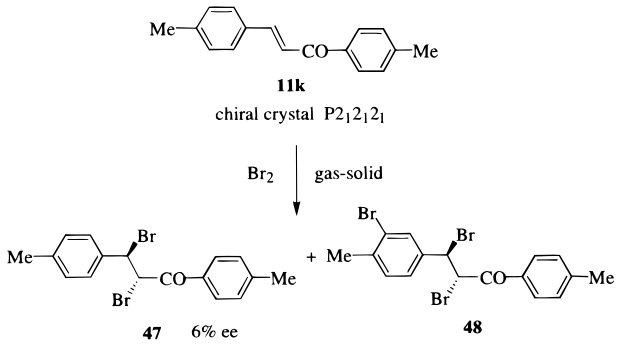
The solid-state bromination of cinnamic acid **39** has been known since 1863[23] and reexamined recently.[24] Bromination of crystalline cinnamic acid **39** gives the erythro-isomer **40a** exclusively and its chlorination gives *threo*- and *erythro*-**40b** in 88 and 12% yields, respectively. Reaction of (*E*)-*o*-stilbenecarboxylic acid (**41**) with bromine in solution gives *trans*-4-bromo-3-phenyl-3,4-dihydroisocoumarin (**42**) as the major product. On the other hand, treatment of powdered **41** with bromine vapor or with powdered pyridine·HBr·Br_2 complex in the solid state at room temperature gave *erythro*-1,2-dibromo-1,2-dihydro-*o*-stilbenecarboxylic acid (**43**) selectively.[25]



On exposure to HBr at 20 °C for 15−20 h, ethyl *trans*-cinnamate (**44**) in solid α- and *β*-cyclodextrin complexes yields ethyl (*R*)-(+)-3-bromo-3-phenylpropanoate (**45**) of 46% ee and (*S*)-(−)-**45** of 31% ee, respectively.[26] Bromination of the *β*-cyclodextrin complex of the cinnamate gives (+)-ethyl *erythro*-2,3-dibromo-3-phenylpropanoate (**46**) of 23% ee.



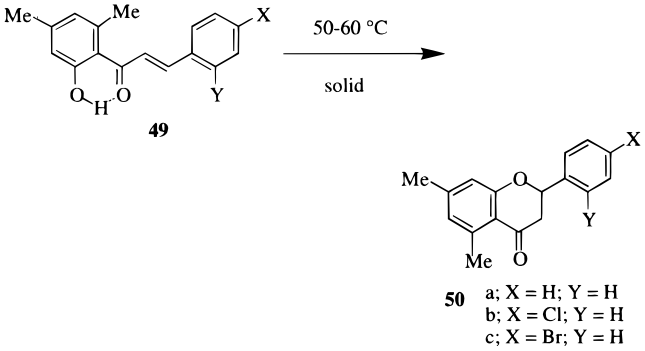
Asymmetric bromination of 4,4′-dimethylchalcone (**11k**) in its chiral crystals was accomplished starting from optically inactive molecules. A powdered crystal of **11k** prepared by recrystallization from ethyl acetate solution was exposed to bromine vapor for 2−3 h to give an optically active *erythro*-dibromide **47** of 6% ee along with byproduct **48**.[27] The X-ray



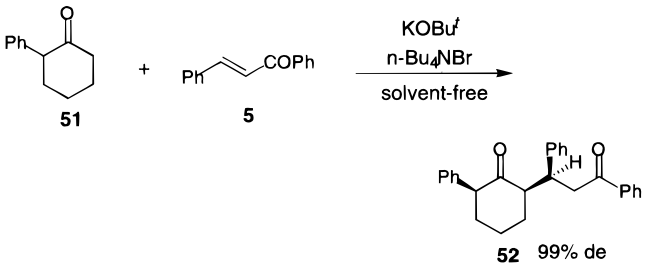
study showed that the molecules of **11k** are arranged in a chiral space group, $P2_12_12_1$, with the molecule distorted from planarity, the angle between the planes of the two phenyl rings being 48.6°. The tilted carbonyl and phenyl groups block access of bromine to the double bond from one side, thus leading to the optically active product.

2. Michael Addition and Aldol Addition

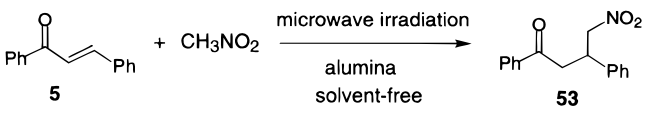
Several substituted 2′-hydroxy-4′,6′-dimethylchalcones **49a**−**c** undergo a solid-state intramolecular Michael-type addition reaction to yield the corresponding flavanones **50a**−**c**, at temperatures below their melting points.[28] Conversions of the chalcones **49** to flavanones **50** could be followed by the orange to pale yellow color change. X-ray studies of the reactant and product indicate that these reactions proceed in a nontopochemical fashion.



Solvent-free solid−liquid Michael addition of 2-phenylcyclohexanone (**51**) to chalcone (**5**) under PTC conditions gave 2,6-disubstituted cyclohexanone derivative **52** in high diastereoselectivity (99% de).[29]

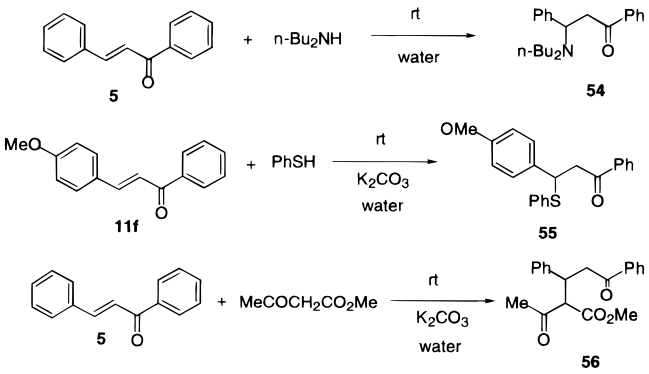


The solvent-free Michael addition reaction of nitromethane to chalcone in the presence of alumina under microwave irradiation proceeded very efficiently.[30] For example, a mixture of nitromethane, alumina, and chalcone (**5**) were irradiated using a commercial microwave oven (2450 MHz) for 18 min to give the corresponding Michael adduct **53** in 90% yield. This reaction takes about 15 days and gave the product only in 43% yield under the conventional conditions.[31]

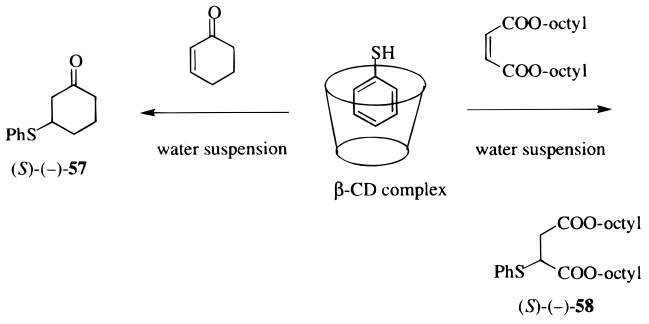


Very efficient Michael addition reactions of amines, thiophenol and methyl acetate to chalcone in a water suspension medium have been developed as completely organic solvent-free reactions.[10] For example,

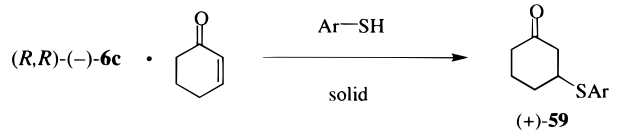
a suspension of powdered chalcone (**5**) in a small amount of water containing n-$BuNH_2$ and surfactant hexadecyltrimethylammonium bromide was stirred at room temperature for 4 h. The reaction product was filtered and air-dried to give the Michael addition product **54** as a colorless powder in 98% yield. By the same procedure, Michael addition reactions of thiophenol to *p*-methoxychalcone (**11f**) in the presence of K_2CO_3 gave **55** in 92% yield. The Michael addition reaction of methyl acetoacetate to **5** also gave the addition product **56** in 98% yield.



Asymmetric Michael addition of benzenethiol to 2-cyclohexenone and maleic acid esters proceeds enantioselectively in their crystalline cyclodextrin complexes. The Michael adducts (*S*)-(−)-**57** and (*S*)-(−)-**58** are obtained in 30% ee in both cases by the reaction of 2-cyclohexenone and octyl maleate with the *β*-cyclodextrin complex of benzenethiol in water suspension.[32]



The high enantioselectivities (∼80% ee) are obtained by using the optically active host compound (−)-**6c** derived from tartaric acid.[33] For example, when a mixture of the powdered 1:1 inclusion complex of 2-cyclohexenone with (−)-**6c**, 2-mercaptopyridine, and a catalytic amount of benzyltrimethylammonium hydroxide was mixed and irradiated with ultrasound for 1 h at room temperature, then (+)-**59a** of 80% ee was obtained in 51% yield (Table 6).



Michael addition of thiols to 3-methyl-3-buten-2-one

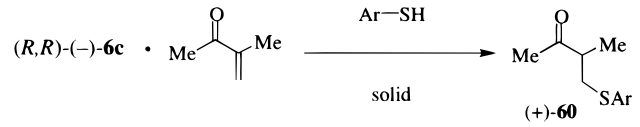
Table 6. Enantioselective Michael Addition of Thiols to 2-Cyclohexenone in Its Inclusion Crystal

Ar	reaction time (h)	product	
		yield	% ee
a	24	51	80
b	36	58	78
c	36	77	74

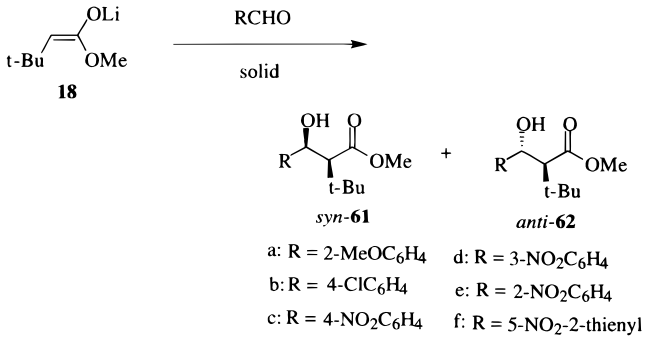
Table 7. Enantioselective Michael Addition of Thiols to 3-Methyl-3-buten-2-one in Its Inclusion Crystal

Ar	product	
	yield	% ee
a	76	49
b	93	9
c	89	4
d	78	53

in its inclusion crystal with (−)-**6c** also occurred enantioselectively (Table 7).

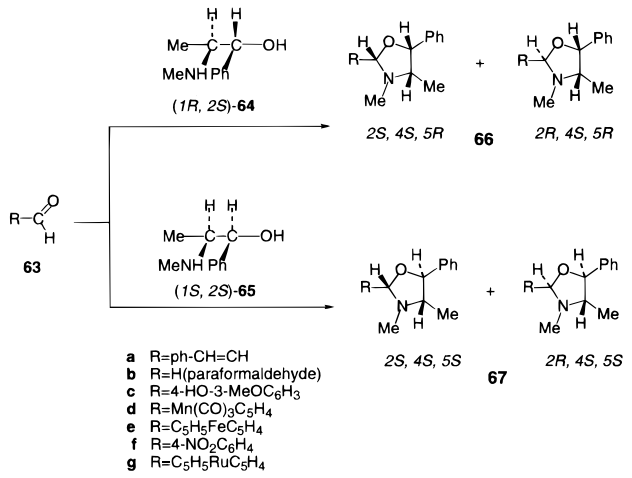


The solid-state aldol addition of the lithium enolate of methyl 3,3-dimethylbutanoate to aromatic aldehydes is also reported.[34] For example, a mixture of freshly ground lithium enolate **18** and powdered *o*-anisaldehyde kept at room temperature under vacuum for 3 days gave a 8:92 mixture of *syn*-**61a** and *anti*-**62a** in 70% yield.[34]



The solid-state synthesis of oxazolidines from aldehydes and (−)-ephedrine or (+)-pseudoephedrine has also been reported.[35] An equimolar mixture of powdered **64** or **65** with one of the aldehydes **63c**−**g**

or **63b** kept at room temperature gives the corresponding oxazolidines **66** or **67** quantitatively.



D. Elimination Reaction

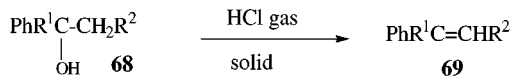
Dehydration reactions of alcohols also proceed efficiently in the solid state.[36] For example, when powdered 1,1-diphenylpropan-1-ol (**68b**) was kept in a desiccator filled with HCl gas for 5.5 h, pure 1,1-diphenylprop-1-ene (**69b**) was obtained in 99% yield. By the same method, **68a**,**c**,**d** gave pure dehydration products, **69a**,**c**,**d**, respectively, in almost quantitative yields (Table 8). The dehydration reaction proceeds much faster by using Cl_3CCO_2H as a catalyst. For example, a mixture of powdered **68b** and an equimolar amount of Cl_3CCO_2H was kept at room temperature for 5 min, and then the reaction mixture was washed with water and dried to give pure **69b** in 99% yield. However, the dehydration reaction in benzene gave **69** in relatively low yield (Table 9).

Table 8. HCl-Catalyzed Dehydration of 68 in the Solid State

	R^1	R^2	reaction time (h)	yield (%)
a	Ph	H	0.5	99
b	Ph	Me	5.5	99
c	Ph	Ph	8	100
d	o-ClC_6H_4	Me	4	97

Table 9. Cl_3CCO_2H-Catalyzed Dehydration of 68

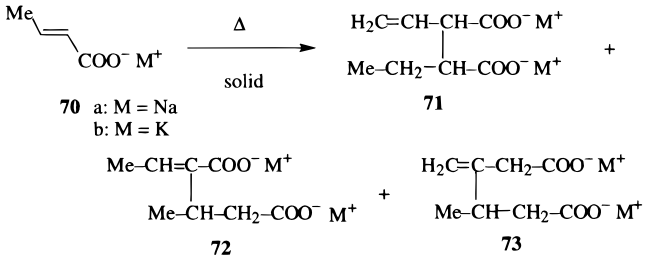
	R^1	R^2	yield (%)	
			solid	benzene
a	Ph	H	99	
b	Ph	Me	99	74
c	Ph	Ph	97	65



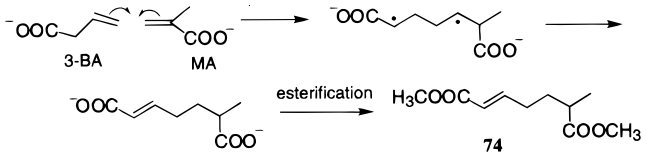
E. C–C Coupling Reaction

1. [2+2], [4+2], and [6+2] Cycloaddition Reaction

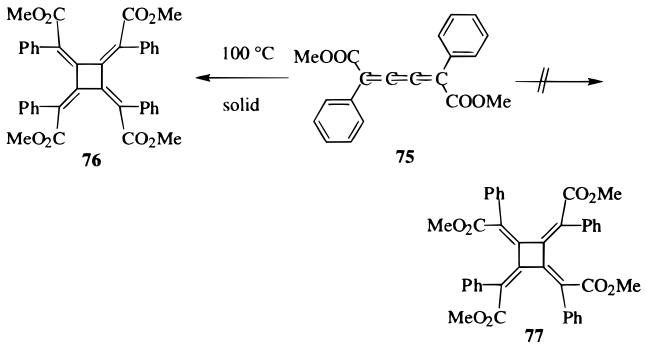
Thermal reaction of sodium crotonate (**70a**) in the solid state gave hex-1-ene-3,4-dicarboxylate (**71a**) in quantitative yield. For example, heating **70a** at 300−320 °C for 4 h in the solid state gave **71a** in 90% yield. On the other hand, potassium crotonate **70b** afforded three isomeric dimers, **71b**, **72b**, and **73b**.[37]



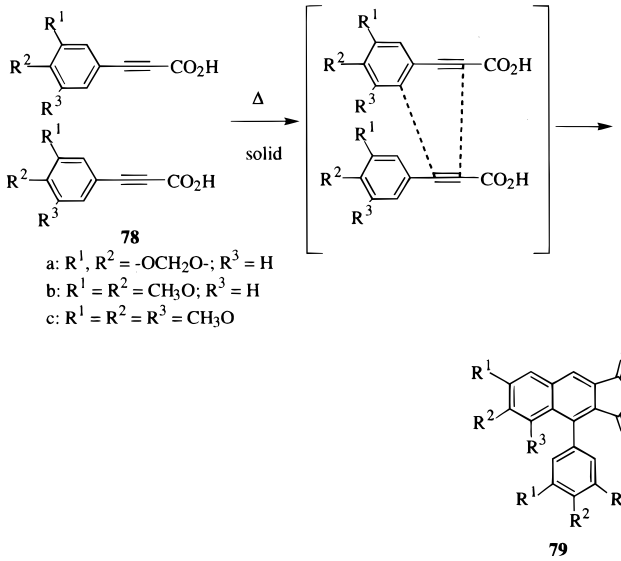
The thermal reactions of the binary salts of but-3-enoic acid and methacrylic acid (3-BA−MA) were also studied.[38] For example, heating of the binary salts obtained from a solution of an equimolar mixture of alkali metal or alkaline earth metal salts of but-3-enoic acid and methacrylic acid (3-BA−MA), after conversion to the methyl ester, gave mainly dimethyl (*E*)-hex-1-ene-1,5-dicarboxylate (**74**) as a cross-coupled dimer.



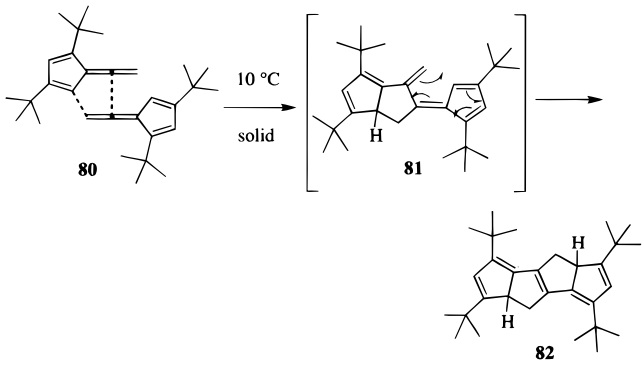
The butatrienecarboxylic acid ester **75** undergoes [2+2] cycloaddition reaction in the solid state to give a radialene **76** in 75% yield.[39] The corresponding reaction in boiling toluene does not proceed efficiently, and the dimer **76** was obtained in only 32% yield together with complex mixtures containing isomeric radialenes such as **77**.



It was found that solid-state Diels−Alder reactions of phenylpropiolic acid derivatives **78a**−**c** occur when heated at temperatures as low as 80 °C to give anhydrides **79a**−**c** in 20−50% yields.[40] X-ray crystallographic studies on the acids **78a**−**c** shows that the intermolecular distances between the two acetylenic bonds are 3.8−4.2 Å.



1,3-Di-*tert*-butyl-5-vinylidenecyclopentadiene (**80**) (mp 43−44 °C) dimerizes in the solid state at 10 °C within 14 days to give 1,3,5,7-tetra-*tert*-butyl-4,4a,8,-8a-tetrahydrodicyclopenta[*a*,*e*]pentalene (**82**) in 35% yield.[41] The formation of **82** involves a [6+2] cycloaddition reaction between two molecules of **80** via biradical intermediate to give the tetrahydropentalene derivative **81**, which cyclizes to **82** by a 8π-electrocyclization.



The thermal crystal-to-crystal conversion of *s-trans*-1,1,6,6-tetraaryl-3,4-dibromo-1,2,4,5-hexatetraenes (**83a**,**b** and **86b**) into the corresponding 3,4-bis-(diarylmethylene)-1,2-dibromocyclobutenes (**85a**,**b**, **88b**, and **89b**) via the *s-cis*-diallenes (**84a**,**b** and **87b**) was found to proceed stereoselectively.[42] These thermal conversions involve two crystal-to-crystal reactions. First the s-trans conformation of **83a** is rearranged to the s-cis conformer in the crystal to give **84a**. In the second step [2+2] conrotatory cyclization of **84a** occurs in the crystal to give **85a**. This cyclization proceeds stereoselectively; compound **83b** gave **85b**, and **86b** gave a 1:1 mixture of **88b** and **89b**, through a [2+2] conrotatory cyclization. For example, heating crystals of **83b** at 135 °C gave the in, out isomer **85b**, while heating **86b** at 145 °C gave a 1:1 mixture of the in, in isomer **88b** and the out, out isomer **89b** in quantitative yields. The DSC diagram of **86b** revealed a peak for an exothermic reaction at around 150 °C, which is attributable to the formation of a mixture of **88b** and **89b**, and a peak for an

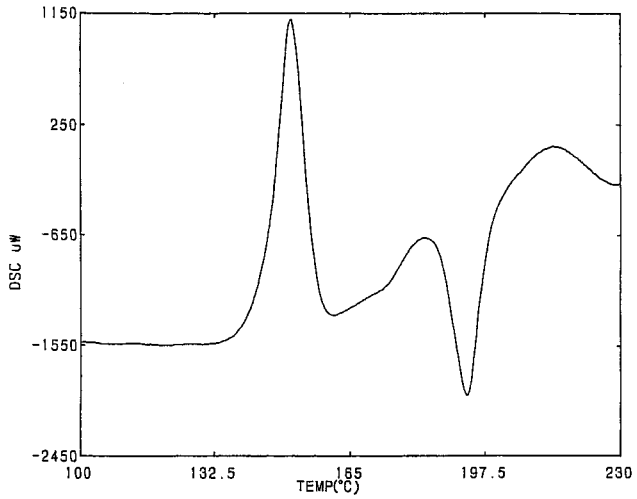


Figure 5. DSC diagram of **86b**.

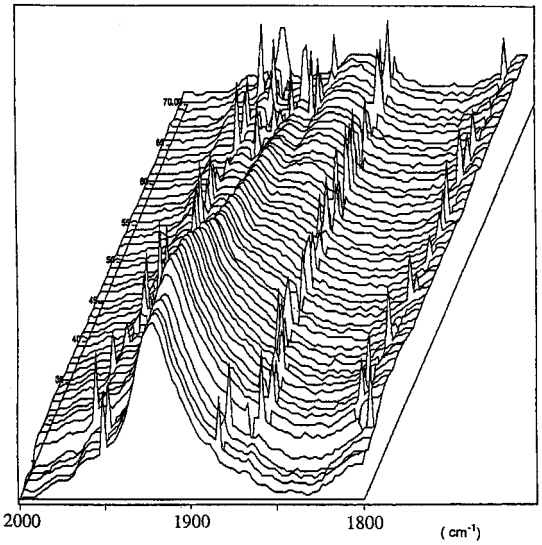


Figure 6. IR spectra showing the thermal reaction of **86b** in the crystalline state at 125 °C. The spectrum was measured every 1 min for 50 min.

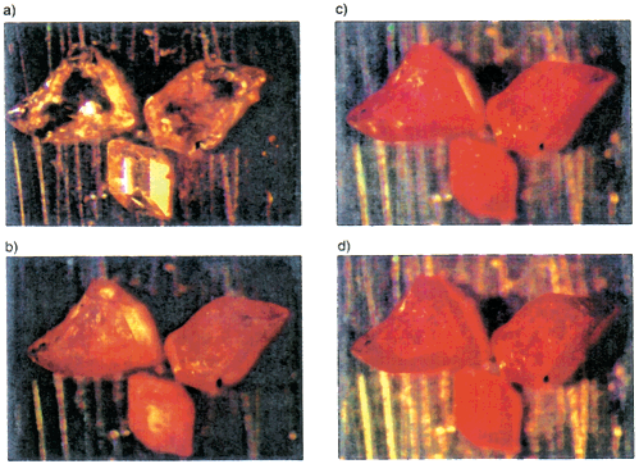
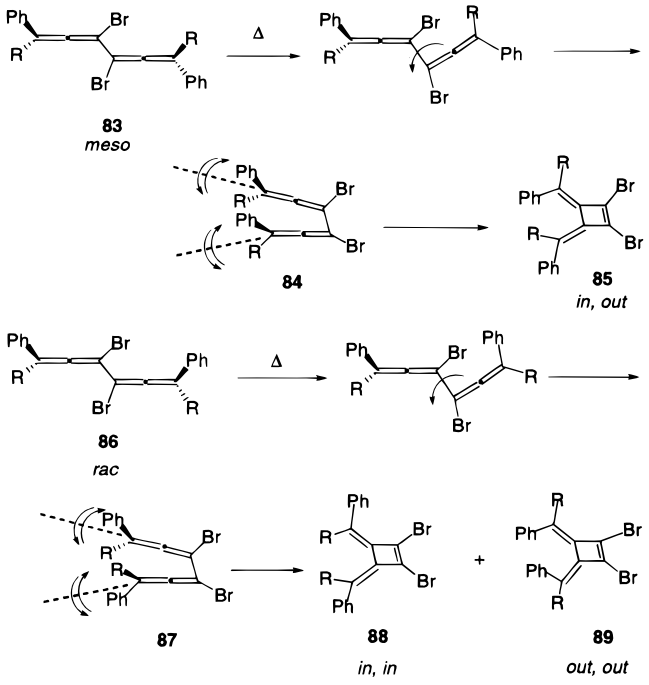


Figure 7. Thermal reaction of a crystal of **86b** to a crystal of a mixture of **88b** and **89b** as observed through a microscope. The photos show the crystal before heating (a), as well as after 15 (b), 40 (c), and 80 min (d) at 135 °C.

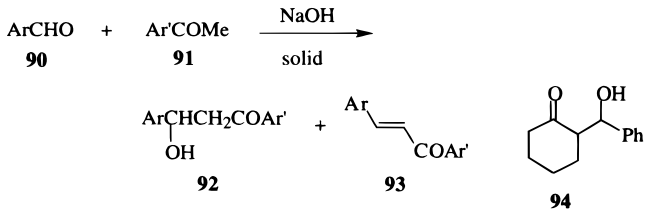
endothermic conversion at around 193 °C, which is attributable to the melting point of the cyclization

product (Figure 5). When the IR spectrum of a single crystal of **86b** was measured continuously every minute for 50 min at 125 °C, the signal at $\nu = 1927$ cm^{-1} (C═C═C) gradually decreased and finally disappeared (Figure 6). This conversion from crystal-to-crystal was monitored through a microscope, and a molten state was not observed throughout the reaction, although the reaction product was no longer a single crystal (Figure 7). It is surprising that the thermal rearrangement and stereoselective cyclization occur so readily despite the required movement of a sterically bulky group in the crystal.



2. Aldol Condensation Reaction

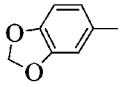
Some aldol condensation reactions proceed more efficiently and stereoselectively in the absence of solvent than in solution.[43] When a slurry mixture of *p*-methylbenzaldehyde, acetophenone, and NaOH was ground by pestle and mortar at room temperature for 5 min, the mixture turned to a pale yellow solid. The solid was combined with water and filtered to give *p*-methylchalcone (**93b**) in 97% yield. When the condensation was carried out in 50% aqueous EtOH according to the reported procedure for the same reaction time as above (5 min), the product was obtained only in 11% yield. The results of some other aldol reactions in the absence of solvent are shown in Table 10. In most cases, the condensation reactions proceed more efficiently in the absence of solvent than in 50% aqueous EtOH. Dehydration of the initially produced aldol **92** to chalcone **93** occurs more easily in the absence of solvent.



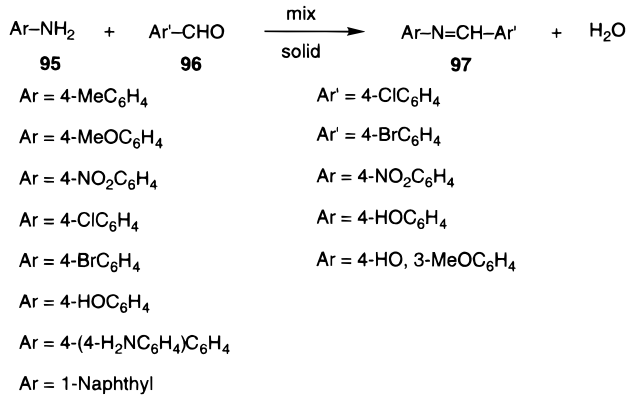
When host molecules are used, highly selective reactions were accomplished. For example, treatment of a 1:1 inclusion complex of cyclohexanone and (−)-**6a** with benzaldehyde (**90a**) and NaOH at room temperature gave a 20:80 mixture of the erythro and threo isomers of **94**.

Condensation reactions of anilines **95** and aromatic aldehydes **96** to azomethines **97** were also found to proceed very efficiently in the absence of solvent.

Table 10. Aldol Condensation Reaction of 90 and 91 in the Absence of Solvent and in 50% Aqueous EtOH

	90 Ar	**91** Ar'	reaction time (min)	solvent	yield(%) **92**	yield(%) **93**
a	Ph	Ph	30	–	10	0
				50%EtOH	0	36
b	*p*-MeC_6H_4	Ph	5	–	0	97
				50%EtOH	0	11
c	*p*-MeC_6H_4	*p*-MeC_6H_4	5	–	0	99
				50%EtOH	0	3
d	*p*-ClC_6H_4	Ph	5	–	0	98
				50%EtOH	18	59
e	*p*-ClC_6H_4	*p*-$MeOC_6H_4$	10	–	2	79
				50%EtOH	25	52
f	*p*-ClC_6H_4	*p*-BrC_6H_4	10	–	0	81
				50%EtOH	0	92
g		*p*-BrC_6H_4	10	–	0	91
				50%EtOH	0	0

Various kinds of azomethines **97** were obtained quantitatively (100% yield at 100% conversion) as hydrates by grinding together the solid anilines and solid benzaldehydes.[44] The reaction was determined to proceed without passing through liquid phases by measurements using atomic force microscopy (AFM).

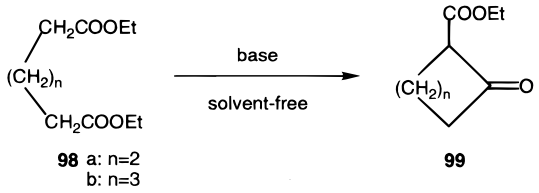


3. Dieckmann Condensation Reaction

Dieckmann condensation reactions of diesters have been carried out in dried solvent under high-dilution conditions in order to avoid intermolecular reaction. Recently, Dieckmann condensation reactions of diethyl adipate and pimelate were found to proceed efficiently in the absence of solvent, and the reaction products were collected by a direct distillation of the reaction mixture.[45] For example, when diethyl adipate (**98a**) and Bu^{t}OK powder were mixed using a mortar and pestle for 10 min, the reaction mixture solidified. The solidified mixture was neutralized by addition of *p*-TsOH·H_2O and was distilled under 20 mmHg to give **99a** in 82% yield. The solvent-free Dieckmann condensation of **98a**,**b** also proceeds efficiently in the presence of powdered Bu^{t}ONa, EtOK, and EtONa as summarized in Table 11.

Table 11. Yields of Solvent-Free Dieckmann Condensation Reaction Products 99a,b

base	yield of **99a** (%)	yield of **99b** (%)
Bu^{t}OK	82	69
Bu^{t}ONa	74	68
EtOK	63	56
EtONa	61	60



98 a: n=2
b: n=3

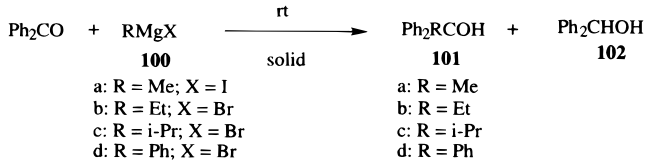
99

4. Grignard, Reformatsky, and Luche Reactions

Grignard reactions also occur in the solid state, and some give results different from those in solution. For example, the reaction of ketones in the solid state gives more reduction products rather than addition products.[46] Dried Grignard reagents are obtained as a white powder by evaporation of the solvent in vacuo from the Grignard reagent prepared by the usual method in solution. A 1 mol amount of powdered benzophenone and 3 mol of the powdered dried Grignard reagent **100** were well mixed using an agate mortar and pestle, and the mixture was then kept at room temperature for 0.5 h to give the products in the yields shown in Table 12.

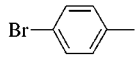
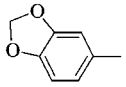
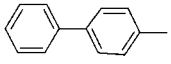
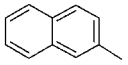
Table 12. Products and Yields of Grignard Reactions in the Solid State and in Solution

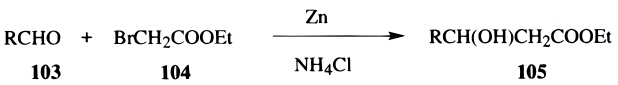
Grignard reagent	product and yield (%)			
	solid state		solution	
100a			**101a** (99)	
100b	**101b** (30)	**102** (31)	**101b** (80)	**102** (20)
100c	**101c** (2)	**102** (20)	**101c** (59)	**102** (22)
100d	**101d** (59)		**101d** (94)	



Treatment of the aromatic aldehydes **103a**−**e** with ethyl bromoacetate (**104**) and Zn−NH_4Cl gave the corresponding Reformatsky reaction products **105a**−**e** in the yields shown in Table 13.[47] The yields of **105** obtained in the solvent-free reaction are much better than that obtained by the reaction in dry benzene−ether solution. The solid-state Reformatsky reaction, which does not require the use of an anhydrous solvent, is thus advantageous.

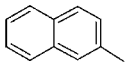
Table 13. Reaction Time and Yield of the Product 105 in the Reformatsky Reactions of 103 and 104 in the Absence of Solvent

103	R	reaction time (h)	yield (%) of **105**
a	Ph	2	91
b		3	94
c		3	94
d		3	83
e		3	80

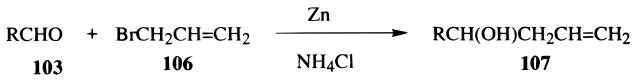


Synthesis of homoallylic alcohols by the Luche reaction can also be carried out efficiently in the

Table 14. Reaction Time and Yield of the Product 107 in the Luche Reactions of 103 and 106 in the Absence of Solvent

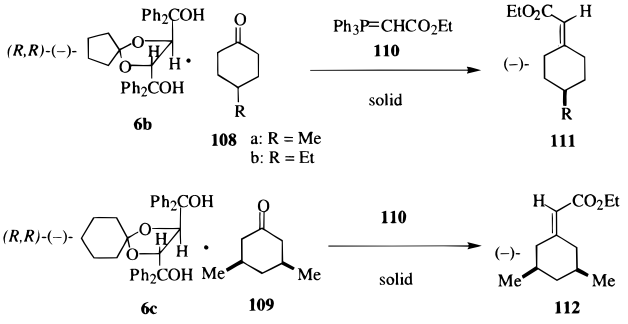
103	R	reaction time (h)	yield (%) of 107
a	Ph	4	99
e		4	87
f	*n*-Pent	1	83
g	*trans*-CH_3CH=CH-	1	98

absence of solvent. Treatment of aldehydes **103** with 3-bromopropene (**106**) and Zn−NH_4Cl in the absence of solvent gave the corresponding Luche reaction products **105** in the yields shown in Table 14.[47]



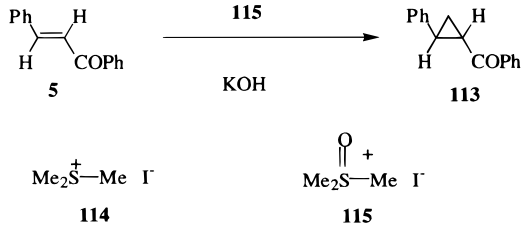
5. Wittig Reaction

Wittig reactions in the solid state of the inclusion compound of 4-methyl- and 3,5-dimethylcyclohexanone (**108** and **109**) and an optically active host compound with (carbethoxymethlene)triphenylphosphorane (**110**) gave optically active 4-methyl-**111** and 3,5-dimethyl-1-(carbethoxymethylene)cyclohexane (**112**), respectively.[48] For example, when a mixture of the finely powdered 1:1 inclusion compound of (−)-**6b** and 4-methylcyclohexanone (**108a**) and phosphorane **110** was kept at 70 °C, the Wittig reaction was completed within 4 h. To the reaction mixture was added ether−petroleum ether (1:1), and then the precipitated triphenylphosphine oxide was removed by filtration. The crude product left after evaporation of the solvent from the filtrate was distilled in vacuo to give (−)-4-methyl-1-(carbethoxymethylene)cyclohexane (**111a**) of 42% ee in 73% yield. (−)-4-Ethyl-1-(carbethoxymethylene)cyclohexane (**111b**) of 45% ee and (−)-3,5-dimethyl-1-(carbethoxymethylene)cyclohexane (**112**) of 57% ee were also obtained in 73% and 58% yield, respectively.



6. Ylid Reaction

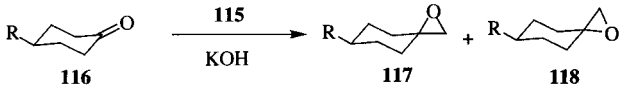
Treatment of chalcones **5**, cyclohexanones **116**, and imines **121** with trimethylsulfonium iodide (**114** or **115**) and KOH in the solid state gives cyclopropanones **113**, oxiranes **117** and **118**, and aziridines **122**, respectively, in good yields.[49] For example, when a mixture of powdered chalcone **5**, trimethylsulfonium iodide (**115**), and KOH was kept at room temperature for 3 h, *trans*-1-benzoyl-2-phenylcyclopropane (**113**) was obtained in 79% yield.



Application of the same methylene transfer reaction in the solid state to the cyclohexanone derivatives **116** gave the corresponding *trans*-oxiranes **117** selectively. For example, when a mixture of 4-*tert*-butylcyclohexanone (**116a**), **115**, and KOH was kept at room temperature for 3 h, the trans isomer **117a** was obtained as the major product in 83% yield. In all solid-state methylene insertions using the reagent **115** the trans isomer was the major product (Table 15).

Table 15. Yields of Oxiranes 117 and 118 from the Reaction of 116 and 115 and KOH at Room Temperature for 3 h in the Solid State

cyclohexanone **116**	yield (%) **117** + **118**	ratio **117** : **118**
116a	83	97 : 3
116b	33	91 : 9
116c	75	92 : 8
116d	82	97 : 3



a : R = Bu^t c : R = Et

b : R = Me d : R = Ph

This reaction was improved to avoid any solvent throughout the reaction, and the oxirane was isolated by a simple distillation technique.[50] For example, a mixture of propiophenone **119a**, **114**, and powdered *t*-BuOK was heated at 60 °C for 1 h in a flask, and then the reaction mixture was distilled using a Kugelrohr at 150 °C under 18 mmHg, to give **120a** in 75% yield. By a similar procedure, **120b**−**f** were prepared from the corresponding ketones **119b**−**f** and the products isolated by distillation in the yields indicated in Table 16.

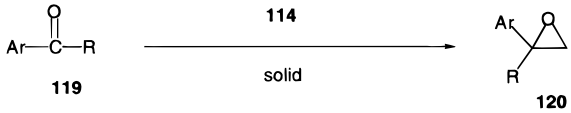
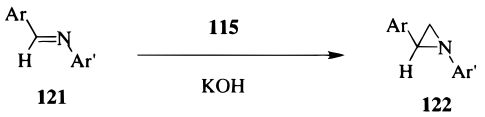


Table 16. Preparation of 120 by the Combination of Methylene Transfer Reaction to 119 in the Absence of Solvent and by Kugelrohr Distillation

	ketone **119**		reaction conditions			
	Ar	R	temp (°C)	time (h)	product	yield (%)
119a	Ph	Et	60	1	**120a**	75
119b	Ph	*i*-Pr	70	1	**120b**	89
119c	Ph		70	10	**120c**	91
119d	*p*-MeC_6H_4	Et	70	2	**120d**	86
119e	*p*-BrC_6H_4	Me	70	5	**120e**	64
119f	2-naphthyl	Me	70	3	**120f**	86

Methylene addition to the imines **121** in the solid state occurred at a relatively high temperature. For example, aziridines **122a**−**d** were obtained by the reaction of **121a**−**d** with **115** and KOH at 50 °C for 3 h in the solid state in 56, 34, 38, and 36% yields, respectively.[49]



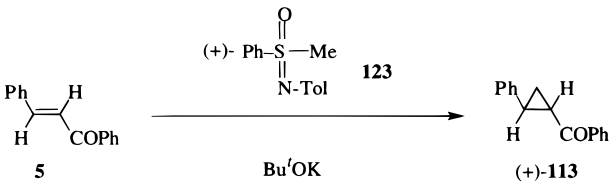
a Ar = Ar' = Ph

b Ar = Ph, Ar' = *p*-$MeOC_6H_4$

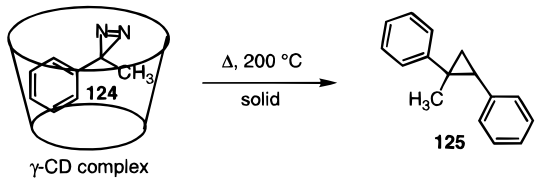
c Ar = *p*-ClC_6H_4, Ar' = *p*-MeC_6H_4

d Ar = *p*-MeC_6H_4, Ar' = *p*-$MeOC_6H_4$

Enantioselective methylene transfer also occurs in the solid state. By treatment of chalcone (**5**) with (+)-*S*-methyl-*S*-phenyl-*N*-(*p*-tolyl)sulfoximide (**123**) and Bu^{t}OK at room temperature, (+)-**113** of 24% ee was obtained in 94% yield.[49]



Treatment of an aqueous γ-CD solution with an equimolar amount of phenylmethyldiazirine **124** forms a stable 1:1 complex. Thermal decomposition of the γ-CD complex of diazirine **124** at 200 °C under Ar gives mainly *trans*-1,2-diphenyl-1-methylcyclopropane (**125**), whereas decomposition of neat diazirine produces mainly styrene.[51]

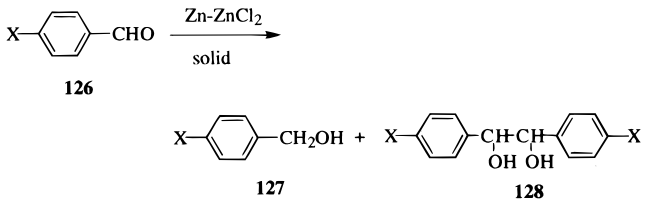


7. Pinacol Coupling Reaction

The Zn−$ZnCl_2$ reagent is effective for the coupling of aromatic aldehydes and ketones to produce α-glycols in the solid state.[52] For example, when a mixture of **126a**, Zn, and $ZnCl_2$ was kept at room temperature for 3 h, the α-glycol **128a** was obtained in 46% yield. Similar treatment of benzaldehyde derivatives **126b**−**e** with the reagent gave mainly α-glycols **128b**−**e** in the yields shown in Table 17.

Table 17. Yield of 127 and 128 Produced by Treatment of 126 with Zn−$ZnCl_2$ at Room Temperature for 3 h in 50% Aqueous THF and in the Solid State

126	solvent	yield (%)		
		127	128	meso:dl ratio in 128
a, X = H	aq THF	39	11	50:50
	−	trace	46	60:40
b, X = Me	aq THF	81	7	50:50
	−	trace	87	70:30
c, X = Cl	aq THF	82	16	50:50
	−	25	65	80:20
d, X = Br	aq THF	72	27	50:50
	−	19	55	70:30
e, X = Ph	aq THF	49	38	80:20
	−	2	64	70:30



The coupling reaction of aromatic ketones **129** with Zn−$ZnCl_2$ is more selective, and only the α-glycols **130** were produced (Table 18).[52]

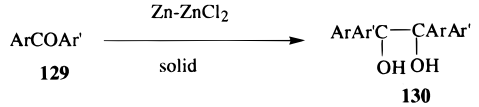
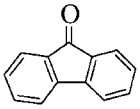


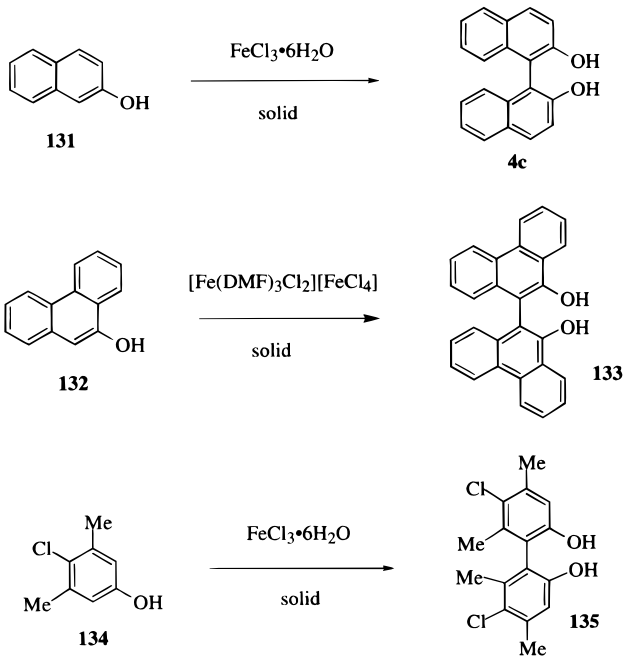
Table 18. Yield of 130 Produced by Treatment of 129 with Zn−$ZnCl_2$ in 50% Aqueous THF and in the Solid State

129 Ar	129 Ar′	solvent	reaction time (h)	temp[a] (°C)	yield of **130** (%)
Ph	Ph	aq THF	1	rt	84
		–	6	rt	86
p-MeC_6H_4	p-MeC_6H_4	aq THF	3	rt	84
		–	84	70	30
p-ClC_6H_4	p-ClC_6H_4	aq THF	1	rt	92
		–	6	70	39
Ph	p-ClC_6H_4	aq THF	2	rt	90
		–	6	70	26
		aq THF	0.5	rt	94
		–	3	rt	92

[a] rt = room temperature.

8. Phenol Coupling Reaction

Some oxidative coupling reactions of phenols in the presence of $FeCl_3 \cdot 6H_2O$ proceed faster and more efficiently in the solid state than in solution. For example, when a mixture of β-naphthol **131** and $FeCl_3 \cdot 6H_2O$ was finely powdered using an agate mortar and pestle, and then the mixture was kept at 50 °C for 2 h, bis(β-naphthol) (**4c**) was obtained in 95% yield after decomposition of the reaction mixture with dilute HCl.[53] In contrast, heating a solution of **131** and $FeCl_3 \cdot 6H_2O$ in 50% aqueous MeOH under reflux for 2 h gave **4c** in 60% yield. Some reactions are accelerated by an irradiation with ultrasound. For example, when a mixture of finely powdered **132** and 2 molar equiv of $[Fe(DMF)_3Cl_2][FeCl_4]$ was irradiated with ultrasound at 50 °C for 9 h in the solid state, 9,9′-bis(phenanthrol) (**133**) was obtained in 68% yield. Conversely, keeping of a solution of **132** and 2 molar equiv of $[Fe(DMF)_3Cl_2][FeCl_4]$ in CH_2Cl_2 at room temperature for 48 h gave **133** in only 33% yield in addition to byproducts such as 9-phenanthrone and 9,10-phenanthrenequinone. By a similar procedure, the bisphenol derivative **135** was obtained in 30% yield by oxidative coupling of **134** in the solid state.[54]

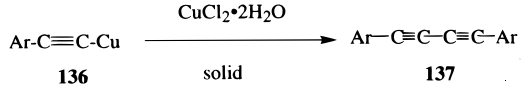


9. Oxidative Coupling Reaction of Acetylenic Compound

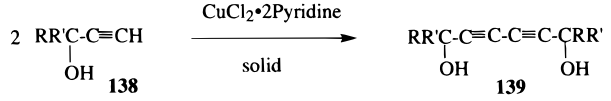
Glaser coupling of acetylenic compounds proceeds more efficiently in the solid state than in water.[55] When a mixture of powdered cuprous phenylacetylide (**136a**) and $CuCl_2 \cdot 2H_2O$ was kept at room temperature for 3 h, diphenyldiacetylene (**137a**) was obtained in 60% yield. By the same method, **136b**−**e** gave **137b**−**e** (Table 19).

Table 19. Glaser Coupling Reaction in the Solid State and in Water

	Ar	yield (%) solid state	yield (%) water
a	Ph	60	40
b	p-MeC_6H_4	35	21
c	p-PhC_6H_4	67	
d	2,3,5,6-$(Me)_4C_6H$	42	25
e	$PhOCH_2$	74	

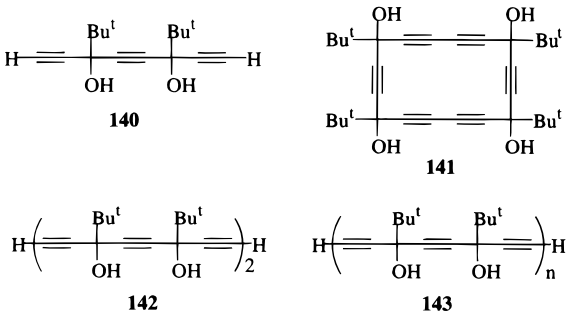


Eglinton coupling reaction could also be applied to the reaction of propargyl alcohols in the solid state. When a mixture of the powdered propargyl alcohols **138** and $CuCl_2$(pyridine)$_2$ complex was reacted under heating, the coupling products **139** were obtained in 50−70% yields.[55]



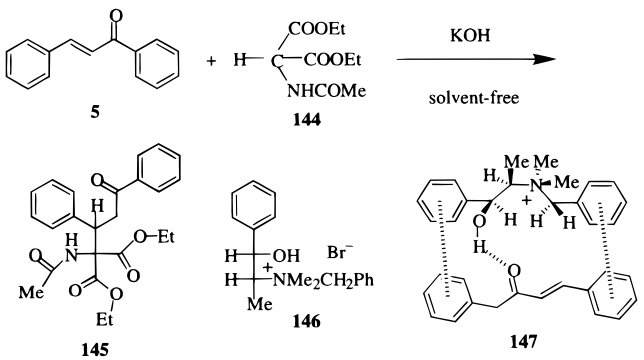
a: R=Ph; R'=Ph
b: R=Ph; R'=*o*-ClC_6H_4
c: R=*p*-MeC_6H_4; R'=*p*-MeC_6H_4
d: R=Ph; R'=2,4-$(Me)_2$-C_6H_3
e: R=2,4-$(Me)_2$-C_6H_3; R'=*o*-ClC_6H_4
f: R=Ph; R'=Me

Oxidative coupling reaction of (±)-**140** in pyridine gave the corresponding cyclic dimer (±)-**141**. When the reaction, however, was carried out in the solid state using $Cu(OAc)_2$·2Py complex, the linear coupling product **143** was obtained. On the other hand, (−)-**140** gave the optically active polymer **143** in solution and the optically active dimer (−)-**142** in the solid state as a major product, respectively.[55]



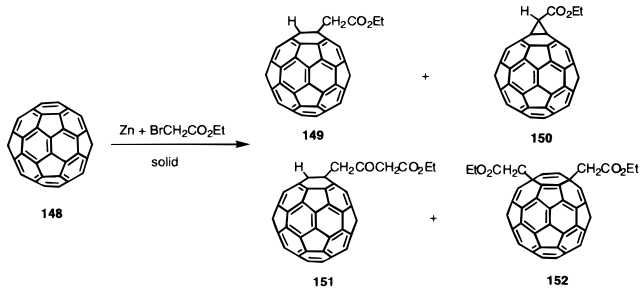
10. Phase Transfer Reaction

Michael addition of diethyl (acetylamido)malonate (**144**) to chalcone (**5**) using an asymmetric phase transfer catalyst without solvent has been successfully carried out in the presence of ephedrinium salts.[56] For example, reaction of chalcone **5** with diethyl acetamidomalonate (**144**) in the presence of potassium hydroxide and (−)-*N*-methyl-*N*-benzylephedrinium bromide (**146**) gives the Michael addition product (−)-**145** of 60% ee in 56% yield. When the reaction was carried out in CCl_4, (−)-**145** of 16% ee was obtained in 55% yield. The formation of the $\pi-\pi$ complex **147** between **146** and **5** can be enhanced when reactions are carried out in the absence of solvent.

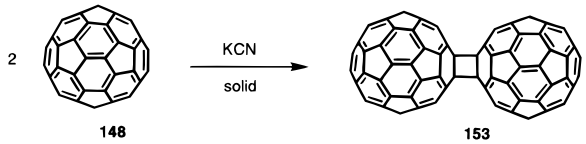


11. Addition and Coupling Reaction of [60]Fullerene

Chemical transformation of [60]fullerene in solution is limited due to its extremely low solubility in organic solvents. Recently, however, it was found that reactions of [60]fullerene proceed efficiently in the solid state. For example, a mixture of [60]fullerene (**148**), ethyl bromoacetate, zinc dust, and a stainless steel ball was vigorously agitated for 20 min at room temperature to give the adduct **149** (17.2%) together with **150**−**152**.[57]

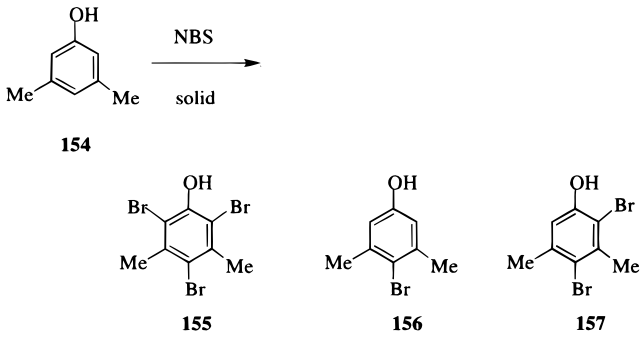


The dimerization reaction of [60]fullerene (**148**) in the presence of KCN was also found to proceed in the solid state. A mixture of **148** and 20 molar equiv of KCN powder was vigorously vibrated for 30 min under nitrogen to give the [2+2] adduct **153** in 18% yield.[58]



F. Substitution Reaction

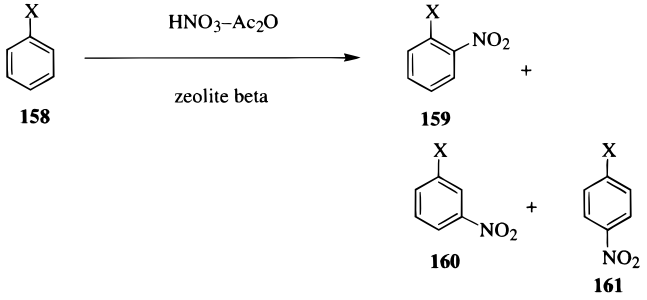
The nuclear bromination of phenols by *N*-bromosuccinimide (NBS) can be accomplished very easily in the solid state.[59] For example, when the phenol **154** was treated with 3 mol equiv of NBS in the solid state for 1 min, the tribromophenol **155** was obtained in 45% yield. In contrast to this, a mixture of the mono- and dibromo derivatives **156** and **157** was obtained from the reaction in solution.



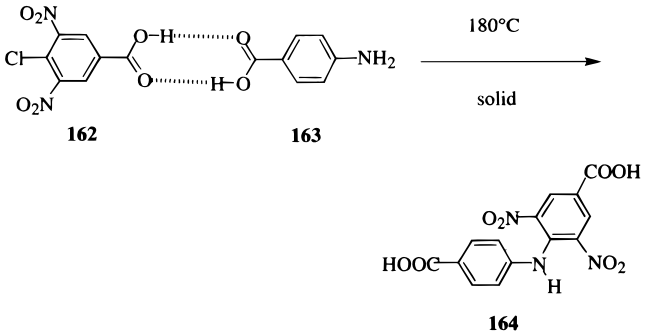
The nitration of aromatic compounds was found to proceed with high *para*-selectivity in the absence of solvent by use of a stoichiometric quantity of nitric acid and acetic anhydride at 0−20 °C in the presence of zeolite beta as catalyst (Table 20).[60]

Table 20. Yield and Proportions of the Nitration Products

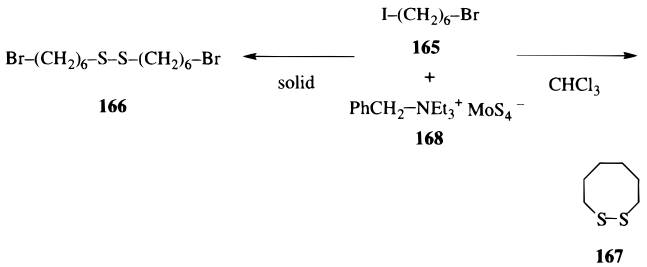
	X	yield (%)	product proportions (%)		
			159	**160**	**161**
a	Me	>99	18	3	79
b	*t*-Bu	92	8	trace	92
c	Cl	>99	7	0	93
d	NO_2	13	1	92	7



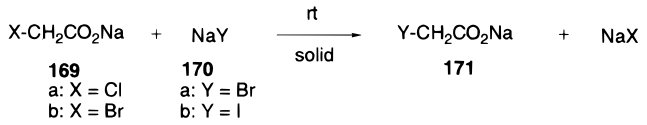
Nucleophilic aromatic substitution reactions also proceed efficiently in the solid state. For example, when cocrystals of 4-chloro-3,5-dinitrobenzoic acid (**162**) and 4-aminobenzoic acid (**163**), which can be made in the solid state by grinding the two components at room temperature, were heated in the solid state the aromatic nucleophilic substitution product **164** was produced.[61]



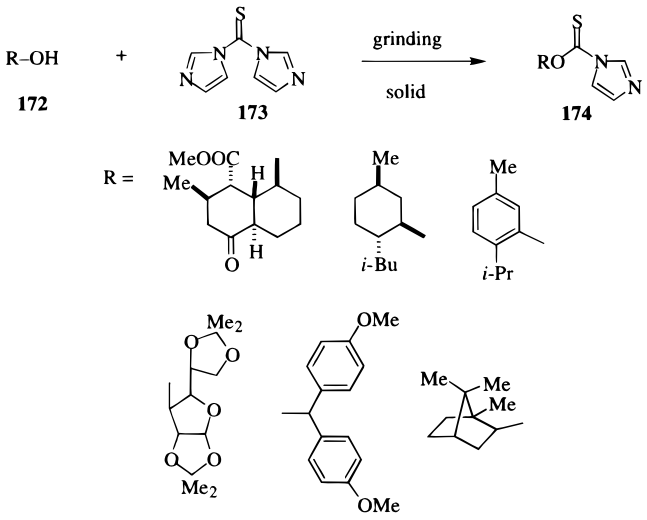
Benzyltriethylammonium tetrathiomolybdate (**168**) reacts with benzyl halides, alkyl halides, and acyl halides at room temperature in the solid state to give the corresponding disulfides selectively.[62] For example, butyl iodide, benzyl bromide and benzoyl chloride afforded the corresponding disulfides in 74, 72, and 70% yield, respectively. 1-Bromo-6-iodohexane (**165**) reacts with **168** to give exclusively the dibromo disulfide **166** in the solid state, while in solution it gives the eight-membered cyclic disulfide **167**.



The solid-state substitution reaction between halogenoacetates and metal halides has also been studied.[63] Keeping a powdered 1:2 mixture of **169** and **170** for 7−14 days at room temperature gives **171** in up to 15% yield.



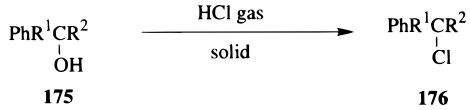
Thiocarbonylimidazolide derivatives **174** can be prepared from thiocarbonyldiimidazole (**173**) and alcohols **172** by grinding them in a mortar at room temperature.[64] Interestingly, grinding both substrates with a pestle and mortar is essential in this solid-state reaction, because simply stirring the powder or using ultrasound did not accelerate the reaction.



Conversion of secondary and tertiary alcohols **175** into the corresponding chlorides **176** also proceeds efficiently when powdered **175** is exposed to HCl gas in a desiccator (Table 21).[36]

Table 21. S_N Reaction of 175 in the Solid State

	R^1	R^2	reacn time (h)	yield (%)
a	Ph	H	5	92
b	Ph	Ph	1.5	97
c	*o*-ClC_6H_4	H	10	94

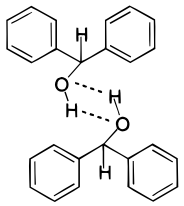


Formation of the ether **178** by treatment of alcohol **177** with TsOH in the solid state proceeds efficiently. For example, when a mixture of powdered 4-methylbenzhydrol (**177e**) and an equimolar amount of TsOH was kept at room temperature for 10 min, the corresponding ether **178d** was obtained in 96% yield. By the same procedure, other ethers were also synthesized in good yields (Table 22).[36] To know why the etherification of **177** proceeds more efficiently in

Table 22. TsOH-Catalyzed Etherification of 177 to 178 in the Solid State and in Solution

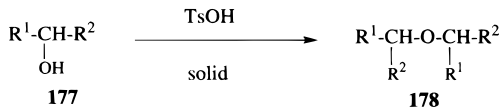
	177		yield (%) of 178		
	R^1	R^2	solid	benzene	MeOH
a	Ph	Ph	95	45	34
b	Ph	o-ClC_6H_4	94	73	37
c	Ph	*p*-BrC_6H_4	98	53	50
d	Ph	*p*-$NO_2C_6H_4$	74	58	1
e	Ph	*p*-MeC_6H_4	96	52	10

Chart 3



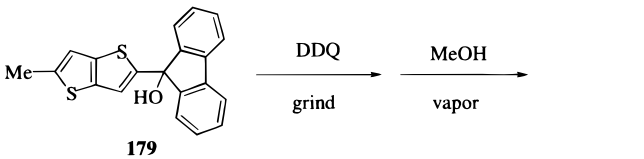
177a

the solid state, the X-ray crystal structure of **177a** was analyzed. The data showed that two molecules of **177a** form a hydrogen-bonded dimer as shown in Chart 3. The structure shows that the pair of **177a** molecules are located in close proximity and so the etherification reaction occurs readily by treatment with TsOH in the solid state.

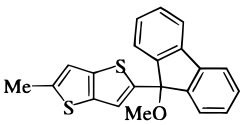


177 **178**

Solid-state solvolysis of 9-(thienothienyl)fluoren-9-ol (**179**) induced by charge-transfer complexation was also reported.[65] An equimolar mixture of **179** and DDQ was ground using a mortar and pestle, and the resulting dark green solid was exposed to MeOH vapor below 5 °C for 6 h to produce the methoxy-substituted compound **180** in 42% yield. Tetracyanoethylene also promoted the solvolysis to give **180** in 70% yield.

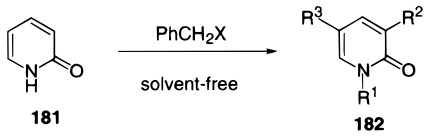


179



180

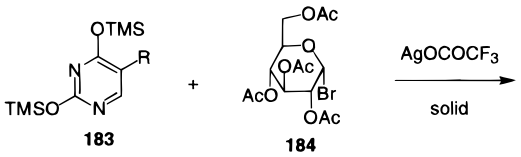
Regiospecific N- or C-benzylation of 2-pyridone (**181**) occurs under solvent-free conditions in the absence of base.[66] The regioselectivity is controlled by the conventional heating or irradiation with microwaves. For example, with benzyl chloride, N-alkylation occurred selectively. With benzyl bromide, the N-alkylation product **182a** is obtained by classical heating, while the C-alkylation products **182b**−**d** are obtained under microwave irradiation.



181 **182**

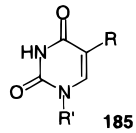
a: $R^1 = CH_2Ph$, $R^2 = R^3 = H$
b: $R^1 = R^3 = H$, $R^2 = CH_2Ph$
c: $R^1 = R^2 = H$, $R^3 = CH_2Ph$
d: $R^1 = H$, $R^2 = R^3 = CH_2Ph$

The solid to solid reactions of glucopyranosyl bromide and silylated uracil or thymine in the presence of silver trifluoroacetate provided glucopyranosyl uracil or thymine with an excellent stereoselectivity.[67] For example, a mixture of α-glucopyranosyl bromide (**184**), silylated uracil **183a**, and silver trifluoroacetate was ground at room temperature in a ball mill for 2 days to give **185** of *β*-configuration in 42% yield. On the other hand, the conventional fusion method affords an anomeric mixture.



183 **184**

a: R = H
b: R = Me

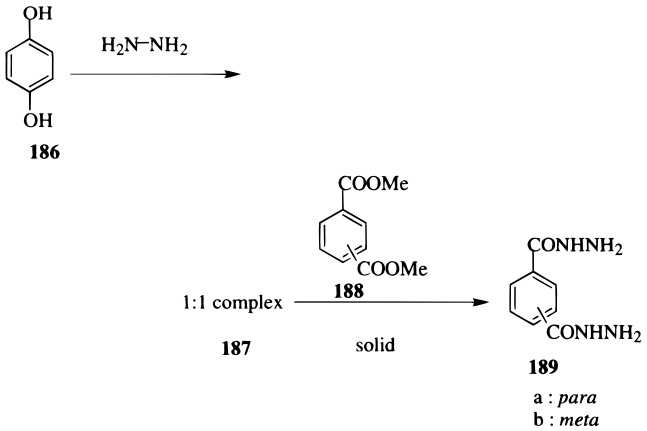


185

R' = 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranosyl

G. Aminolysis, Hydrolysis, and Transesterification

The solid-state reaction of a hydrazine inclusion complex with an ester gives a pure hydrazide.[68] Recrystallization of hydroquinone **186** from aqueous hydrazine gives a 1:1 inclusion complex **187** of anhydrous hydrazine with **186** as colorless crystals. A mixture of powdered dimethyl terephthalate **188a** and **187** was kept under a nitrogen atmosphere at 100−125 °C for 25 h. To the reaction mixture was added MeOH, and almost pure dihydrazide **189a** was obtained simply by filtration in 88% yield.

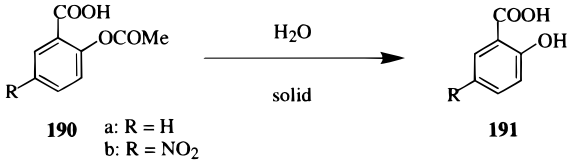


186 **188** **187** **189**

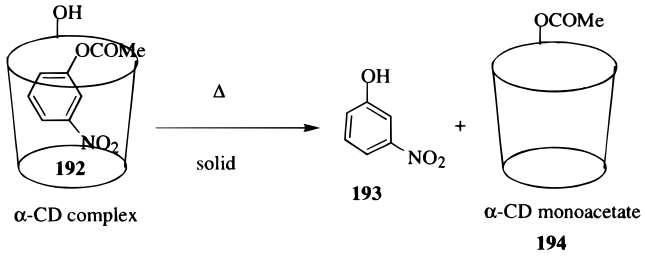
a : *para*
b : *meta*

The kinetics of aspirin hydrolysis **190a** to **191** has been studied in the solid state.[69] The relationship

between the morphological character of 5-nitroacetylsalicyclic acid (**190b**) crystals and the hydrolysis reaction efficiency was also studied.[70]

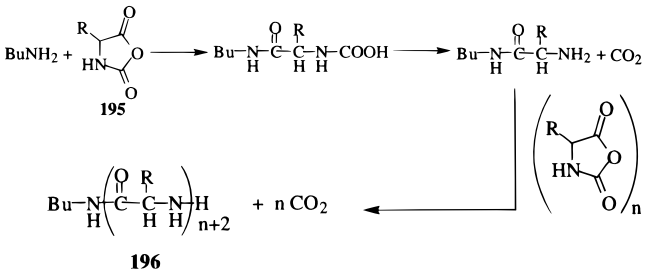


The solid α-cyclodextrin complex of *m*-nitrophenyl acetate (**192**) was heated at 117 °C under dry nitrogen to give *m*-nitrophenol (**193**) together with α-cyclodextrin monoacetate (**194**), whereas transesterification of *p*-nitrophenyl acetate is very slow under the same conditions.[71]

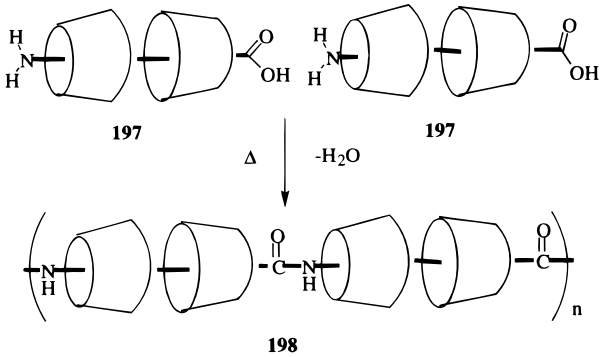


H. Polymerization

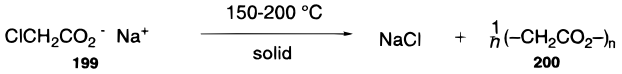
Solid-state polymerizations of *N*-carboxy anhydrides **195** of α-amino acids (L-leucine, L-alanine, γ-benzyl-L-glutamate, and glycine) have been found to proceed efficiently by using butylamine as initiator in a hexane suspension at 20−50 °C.[72] L-leucine was the most reactive and formed the high molecular weight polypeptide **196** in the solid state.



Solid-state polycondensation of 11-aminoundecanoic acid in its cyclodextrin complex **197** occurs at temperatures above 200 °C and affords the polyamide **198** of 16 repeating units as a CD complex.[73]



Thermal elimination of sodium chloride from sodium chloroacetate (**199**) leads to a polyester **200** in high yield.[74] The exothermic reaction occurs upon simply heating sodium chloroacetate above 140 °C without proceeding through any amorphous or liquid intermediate.



I. Rearrangement and Isomerization

1. Pinacol Rearrangement

The pinacol rearrangement in the solid state was found to proceed faster and more selectively than that in solution.[75] When a 1:3 molar ratio of powdered **201** and *p*-TsOH was kept at 60 °C, the rearrangement products **202** and **203** were obtained in the yields shown in Table 23. The hydride migrates more easily

Table 23. Pinacol Rearrangement Catalyzed by *p*-TsOH at 60 °C

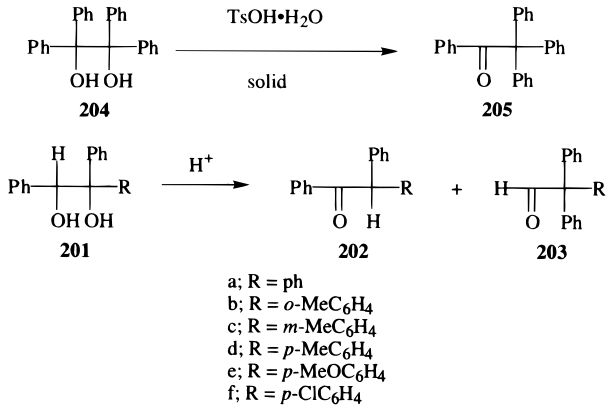
pinacol	reacn time (h)	yield (%)	
		202	**203**
201a	2.5	89	8
201b	0.5	45	29
201c	0.3	70	30
201d	0.7	39	19
201e	0.7	89	0
201f	1.0	54	41

than phenyl anion in **201**, and the yield of **202** is higher than that of **203** in all reactions shown above. In contrast, when a mixture of powdered **201** and CCl_3CO_2H was kept at 20 °C for the period shown in Table 24, **203** was obtained as the major product. The

Table 24. Pinacol Rearrangement Catalyzed by CCl_3CO_2H at 20 °C

pinacol	reacn time (h)	yield (%)	
		202	**203**
201a	2.0	21	68
201b	3.0	38	62
201c	3.0	18	43
201d	2.5	38	62
201e	1.0	59	30
201f	2.0	30	64

reaction efficiency is dramatically enhanced when the water formed during the reaction is continuously removed under reduced pressure.



The mechanism of solid-state pinacol rearrangement of **204** to **205** has been studied by atomic force microscopy (Figure 8)[76] and crystal structure analysis[77] of **204**. AFM reveals that no reaction occurs on (001) of **204** whereas (100) exhibits craters and volcano-like mounds. On (001) of **204**, the hydroxyl groups occur with their hydrogens up (lone pair down) and no protonation occurs. However, on (100) the hydroxyl hydrogens point down, the protonation occurs, and the reaction can start. The proton regenerates on the other side of the molecule **204** and attacks the next molecule of **204**, and so the reaction proceeds further and further along the channels in the crystals, leaving behind the water formed.

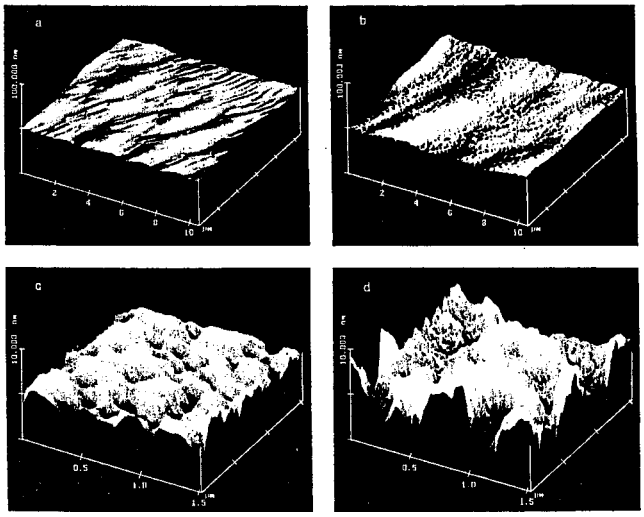
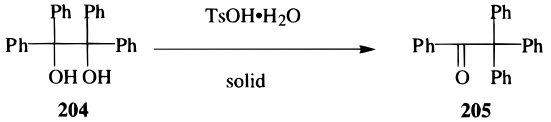


Figure 8. AFM surfaces of **204** on (100) showing distance-dependent phase rebuilding in its solid−solid pinacol rearrangement: (a) ca. 0.5 mm beside a tiny crystal of TsOH shortly after placing it; (b,c) at 0.5 mm distance; (d) at 0.1 mm distance after 12 h of reaction at 50 °C.

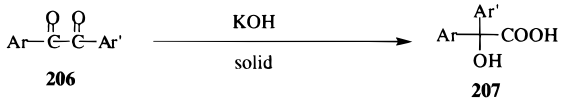


2. Benzilic Acid Rearrangement

Benzilic acid rearrangement has long been carried out by heating benzil derivatives and alkali metal hydroxide in aqueous organic solvent. However, the benzilic acid rearrangements proceed more efficiently and faster in the solid state than in solution. For example, a mixture of finely powdered benzil **206a** and KOH was heated at 80 °C for 0.2 h, and the reaction product was mixed with 3 N HCl to give benzilic acid **207a** as colorless needles. Similar treatment of benzil derivatives **206b**−**f** in the solid state also gave the corresponding benzilic acid **207b**−**f** (Table 25).[78]

Table 25. Yield of Benzilic Acid 207 Produced by Treatment of Benzil 206 with KOH at 80 °C in the Solid State

206	Ar	Ar′	reacn time (h)	yield (%) of 207
a	Ph	Ph	0.2	90
b	Ph	*p*-ClC$_6$H$_4$	0.5	92
c	*p*-ClC$_6$H$_4$	*p*-ClC$_6$H$_4$	6	68
d	Ph	*p*-NO$_2$C$_6$H$_4$	0.1	93
e	*m*-NO$_2$C$_6$H$_4$	*m*-NO$_2$C$_6$H$_4$	0.1	72
f	Ph	*p*-MeOC$_6$H$_4$	6	91



The effect of the alkali metal hydroxide on the reaction efficiency of the benzilic acid rearrangement in the solid state was different from that in solution. The effect on the reaction efficiency of the rearrangement of **206a** in the solid state increased in the following order: KOH > Ba(OH)$_2$ > NaOH > CsOH (Table 26). On the other hand, the reaction efficiency of rearrangement of **206a** in boiling 50% aqueous EtOH increases in the following order: KOH > NaOH > LiOH > Ba(OH)$_2$ > CsOH. The rearrangement using Ba(OH)$_2$ proceeds faster in the solid state than in solution. However, LiOH is inert to the solid state rearrangement, although it is effective in solution. The benzilic acid rearrangement has also been found to proceed via radical intermediate as in solution. For example, freshly prepared mixture of finely powdered **206e** and KOH showed a strong ESR signal (g = 2.0049) and the signal declined as the reaction proceeded.

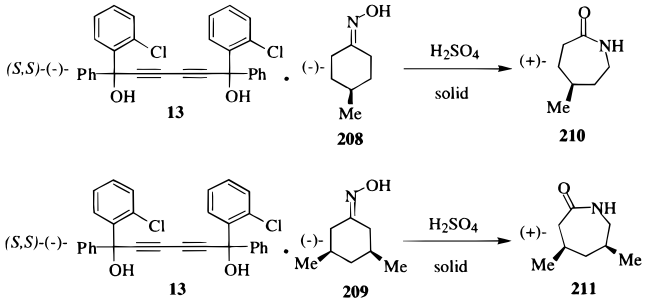
Table 26. Effect of Alkali Metal Hydroxide on the Benzilic Acid Rearrangement of 206a

alkali metal hydroxide	reaction time (h)	yield (%) of 207a	
		solid state	50% aq. EtOH
LiOH	6	0	70
NaOH	1	83	91
KOH	0.2	90	95
CsOH	5	89	43
Ca(OH)$_2$	6	0	trace
Ba(OH)$_2$	0.5	89	70
Al(OH)$_3$	6	0	trace

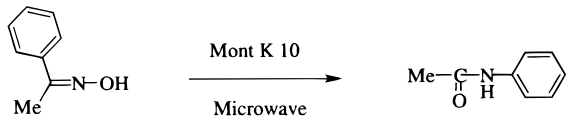
3. Beckmann Rearrangement

When a solution of racemic 4-methyl-1-(hydroxyimino)cyclohexane (**208**) and (−)-1,6-bis(*o*-chlorophe-

nyl)-1,6-diphenylhexa-2,4-diyne-1,6-diol (**13**) in ether−petroleum was kept at room temperature, a 1:1 inclusion compound of (−)-**13** and (+)-**208** of 79% ee was obtained as colorless needles. The same treatment of (±)-**209** and (−)-**13** gave a 1:2 inclusion compound of (−)-**13** and (+)-**209** of 59% ee. Heating of the 1:1 inclusion compound of (−)-**13** and (+)-**208** of 79% ee or the 1:2 inclusion compound of (−)-**13** and (+)-**209** of 59% ee with concentrated H_2SO_4 gave (−)-5-methyl-ϵ-caprolactam (**210**) of 80% ee or (+)-*cis*-3,5-dimethyl-ϵ-caprolactam (**211**) of 59% ee, respectively.[79]



Recently, the solid-state Beckmann rearrangement reaction employing microwave irradiation was found to proceed in much higher yield than the same reaction conducted by heating. For example, when acetophenone oxime (**212**) was simply mixed with montmorillonite and irradiated for 7 min in a microwave oven, acetanilide (**213**) was obtained in 91% yield.[80] The lower yield of 17% was obtained by conventional heating.

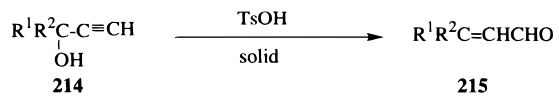


4. Meyer-Schuster Rearrangement

Toluene-*p*-sulfonic acid- (TsOH-)-catalyzed Meyer−Schuster rearrangement of propargyl alcohols **214** also occurs in the solid state.[36] Keeping a mixture of **214** and TsOH at 50 °C for 2−3 h gives the aldehydes **215** in the yields shown in Table 27.

Table 27. TsOH-Catalyzed Meyer−Schuster Rearrangement of 214 at 50 °C in the Solid State

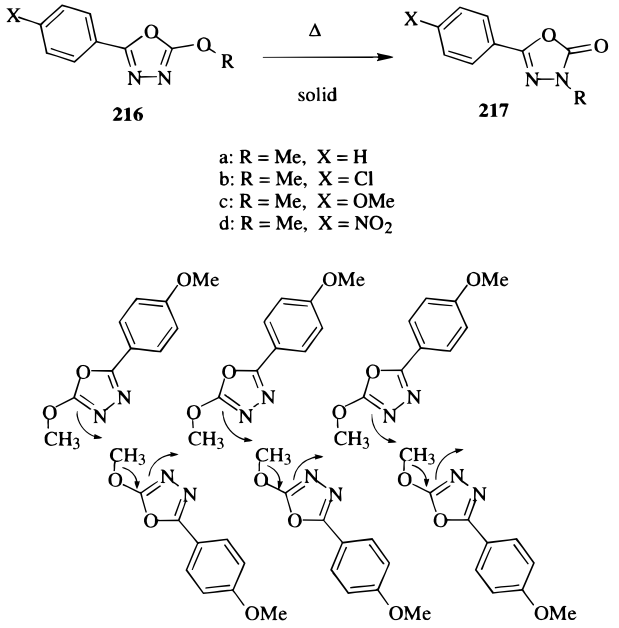
	R^1	R^2	reaction time (h)	yield (%)
a	Ph	Ph	2	58
b	Ph	o-ClC_6H_4	3	60
c	2,4-$Me_2C_6H_3$	2,4-$Me_2C_6H_3$	3	94



5. Chapman Rearrangement

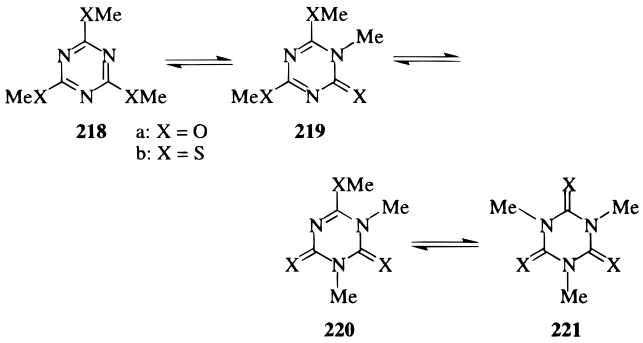
Some 5-methoxy-2-aryl-1,3,4-oxadiazoles **216** easily undergo a Chapman-like rearrangement in the solid state.[81] For example, **216a** rearranges to **217a** at

Scheme 1

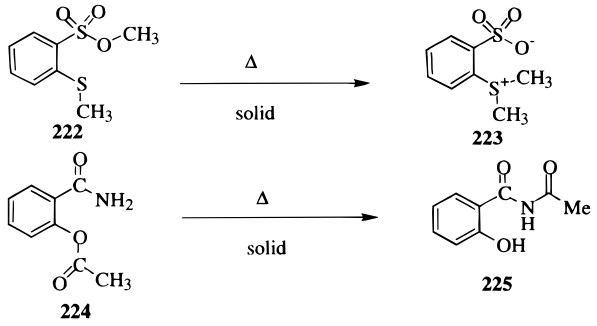


120−140 °C both in the molten and in the solid state. Also, on storage for about 2 years in the dark at room temperature, **216b**−**d** are rearranged into **217b**−**d** in 85, 90, and 9.5% yield, respectively in the crystalline state. The X-ray structure of **216b** shows a regular arrangement of the molecules with a distance of 2.9 Å between the methyl group and the nitrogen atom and the rearrangement occurs domino-like in the crystal (Scheme 1).

The same kind of rearrangement also occurs with some methyl cyanurates **218a** and thiocyanurates **218b** in the solid state.[82]

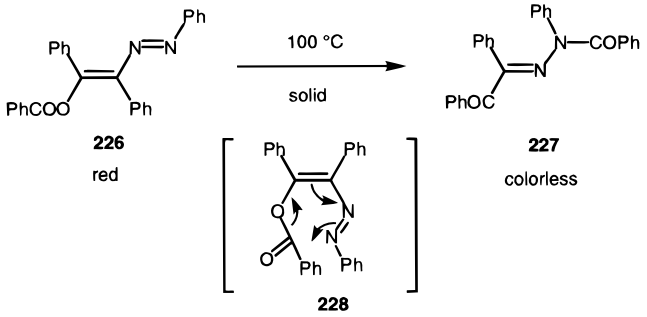


The rearrangement of methyl 2-(methylthio)benzenesulfonate (**222**) to 2-(dimethylsulfonium)benzenesulfonate (**223**) has been observed to occur in the



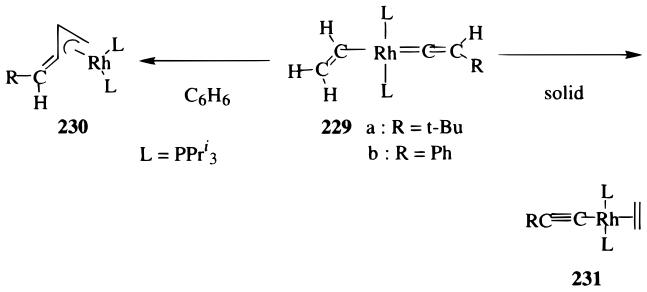
solid state.[83] Thermally induced O to N acyl migration reaction in crystalline salicylamides **224** to **225** has also been studied in detail.[84]

α-Phenylazo-β-(benzoyloxy)stilbene (**226**) rearranges in quantitative yield to benzil benzoylhydrazone (**227**) via a six-membered transition state **228** in the solid state.[85] The solid-state rearrangement takes place at 100 °C over a period of days. A red crystal of **226** retains its shape but becomes opaque and yellow. The rearrangement also occurs in the molten state over 140 °C within several minutes. The intramolecular nature of the rearrangement was confirmed by a crossover experiment of **226** labeled with deuterium in the benzoyl group and ^{15}N in the phenylazo group, respectively.

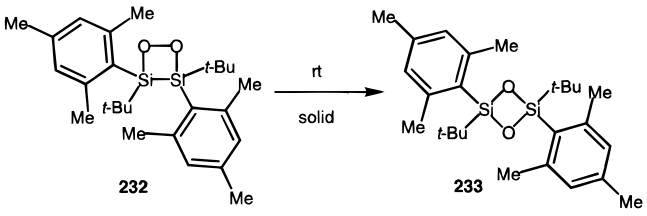


6. Isomerization

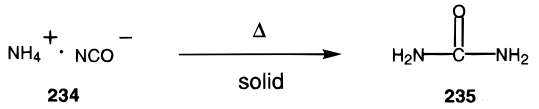
The vinyl(vinylidene)rhodium complexes **229** undergo isomerization, and different products are formed in the solid state and in solution. For example, the reaction of **229a**,**b** in benzene for 3 h at 45−50 °C afforded the η^3-2,3,4-*trans*-butadienyl complexes **230a**,**b**, respectively, whereas on keeping the crystals for 10−14 days at 25 °C the compounds **231a**,**b** are obtained, respectively.[86]



(*E*)-1,2-Dimesityl-1,2-di-*tert*-butyldisiladioxetane (**232**) rearranges at room temperature to 1,3-cyclodisiloxane **233** in the solid state.[87]



In 1828, Friedrich Wohler heated ammonium cyanate **234** to obtain urea **235**, and thus, organic chemistry started as is well-known. This reaction has recently been reexamined by the modern techniques, X-ray analysis, and synchrotron X-ray powder diffraction.[88]

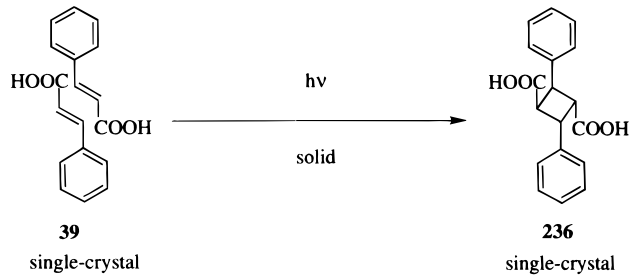


X-ray analysis of **234** showed that NH_4 cation is surrounded by eight NCO anions and each H atom forms a N−H···O hydrogen bond. Upon heating in the solid state, microcrystalline ammonium cyanate **234** transforms completely into microcrystalline urea **235** within 6 h. The solid-state transformation was monitored by synchrotoron X-ray powder diffraction at 50 °C. Using DSC measurement, an exothermic absorption peak appeared between 80 and 90 °C. This peak corresponds to the transformation from **234** to **235**.

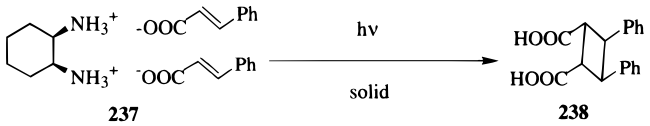
IV. Photoreaction

A. Photodimerization and Photopolymerization

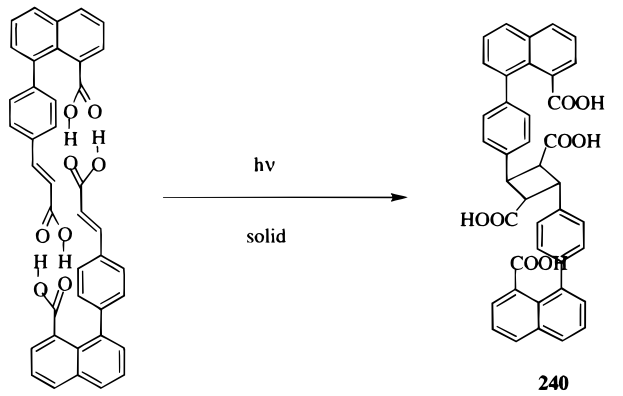
[2+2] photodimerizations of cinnamic acid and its derivatives have been extensively studied.[1] The crystalline−state photodimerizations of cinnamic acid (**39**) to truxillic acid (**236**) have been studied in detail by atomic force microscopy (AFM) and scanning near field optical microscopy (SNOM),[89] X-ray analysis,[90] X-ray powder diffraction,[91] and FT-IR spectroscopy.[92]



The photodimerization of cinnamic acid **39** can be controlled by irradiation of the double salts of **39** with certain diamines in the solid state. For example, the double salt crystals **237** of *cis*-1,2-cyclohexanediamine and *trans*-cinnamic acid gave, upon irradiation in the solid state, β-truxinic acid (**238**) predominantly.[93]

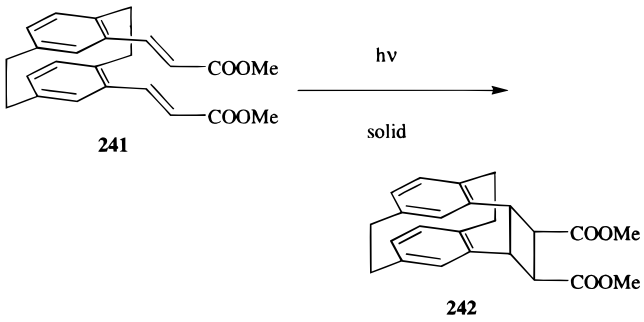


Irradiation of the naphthoic acid-derived cinnamic acid **239** in the solid state for 20−50 h afforded a single cyclobutane product **240** in 100% yield, while the corresponding methyl ester was inert under the same irradiation conditions.[94]



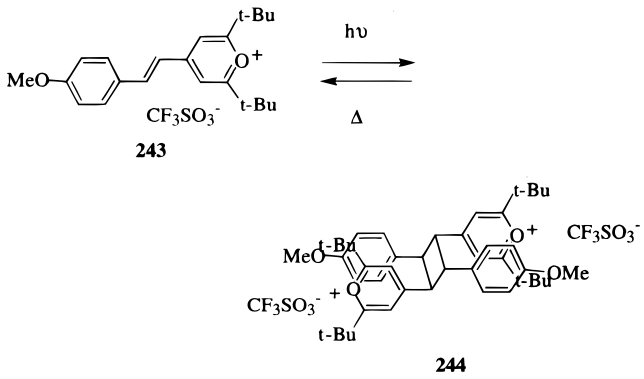
239 240

[2,2]Cinnamophane **241** is transformed into **242** upon photoirradiation both in the solid state and in solution.[95]



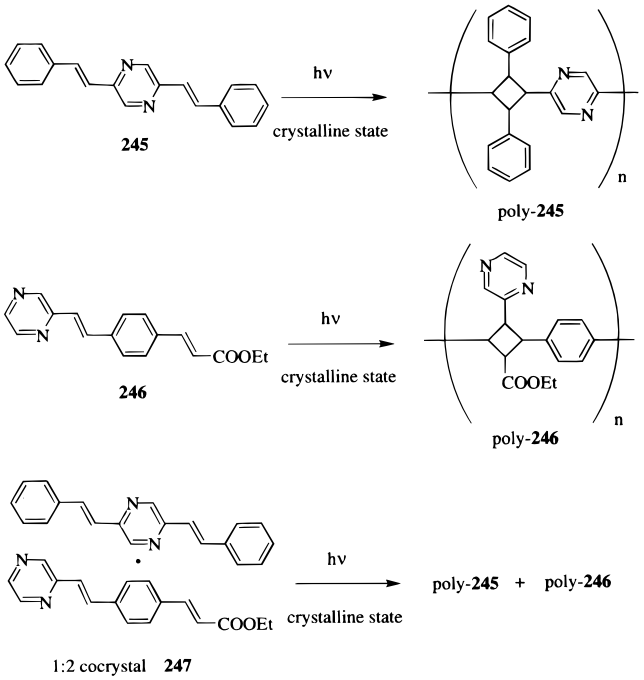
241 242

Reversible [2+2] photodimerization in the solid state has been reported.[96] Irradiation of the styrylpyrilium salt **243** at the wavelength of its absorption maximum (λ_{max} = 420 nm) leads to a heterogeneous reaction, and the original crystal of **243** breaks up completely. However, single-crystal to single-crystal transformation of **243** into **244** occurs by monochromatic irradiation with wavelengths up to 540 nm. Heating the dimer **244** at 100 °C in the solid state regenerates the monomer **243** smoothly.



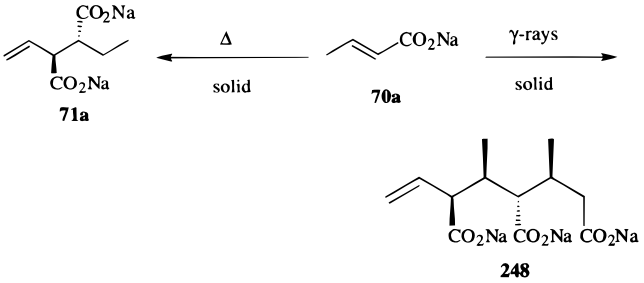
243 244

Upon photoirradiation in the solid state, each of 2,5-distyrylpyrazine (**245**) and ethyl 4-[2-(2-pyrazinyl)ethenyl]cinnamate (**246**) gave a crystalline polymer, poly-**245** and poly-**246**, respectively.[97] Interestingly, however, when a 1:2 cocrystal of **245** and **246** was irradiated with a 500 W super-high-pressure mercury lamp, a 1:2 mixture of poly-**245** and poly-**246** was obtained, but the corresponding cross dimer was not detected at all. The X-ray crystallographic analysis of the cocrystal showed that both of **245** and **246** form columns separately along the *c*-axis with sheets.



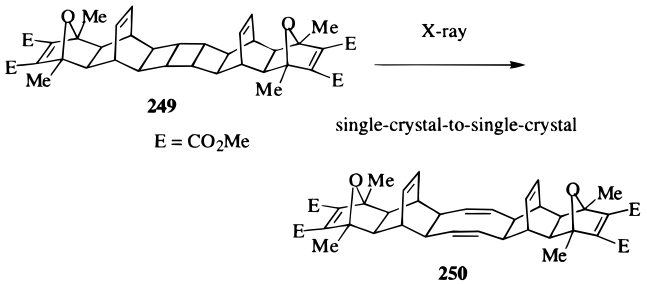
245 poly-245 246 poly-246 1:2 cocrystal 247

Irradiation of crystalline sodium *trans*-2-butanoate (**70a**) with ^{60}Co γ-rays leads to a mixture of trimer **248**, a head-to-tail dimer, and two other trimers in a 12:2:1:1 ratio,[98] while heating **70a** for 4 h at 320 °C converts it to a dimer **71a** in 84% yield.[37]



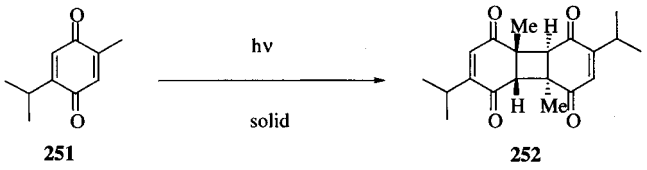
71a 70a 248

The X-ray-induced retro[2+2]cycloaddition reaction of the *syn*-tricyclo[4.2.2.0^{2,5}]octane derivative **249** to the *cis*,*cis*-cycloocta-1,5-diene derivative **250** occurs in the crystalline state without disrupting the crystal structure.[99] However, no reverse reaction from **250** to **249** occurs in the crystal.



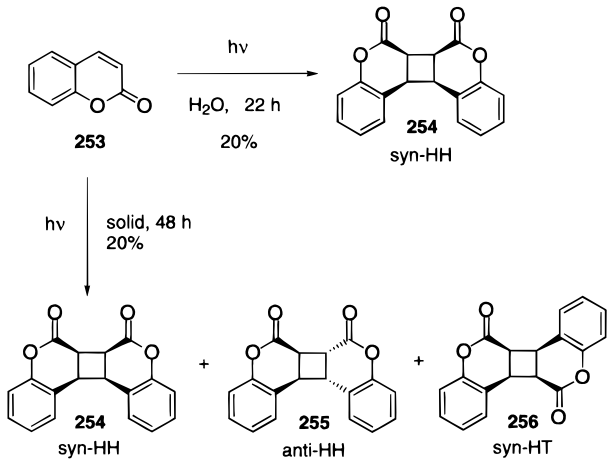
249 E = CO_2Me 250

Thymoquinone **251** undergoes a stereospecific solid-state photochemical [2+2]cyclodimerization to give the anti-head-to-tail cyclobutane derivative **252**.[100]



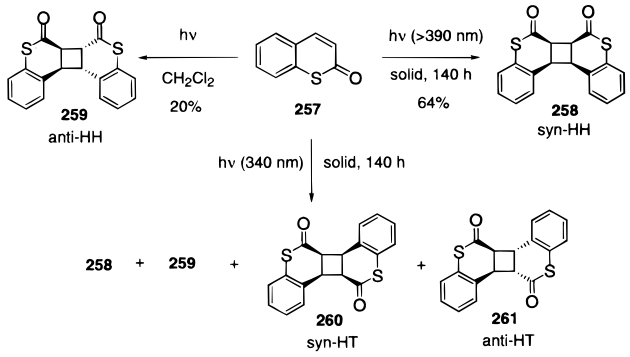
251 **252**

Solid-state photocyclizations of coumarin **253** and its derivatives have been studied extensively.[101] Irradiation of coumarin **253** for 48 h in the solid state gives a mixture of dimers (**254**−**256**) in 20% yield, while irradiation of an aqueous solution of **253** for 22 h affords only the syn-head-to-head dimer **254** in 20% yield.



253 **254** syn-HH **254** syn-HH + **255** anti-HH + **256** syn-HT

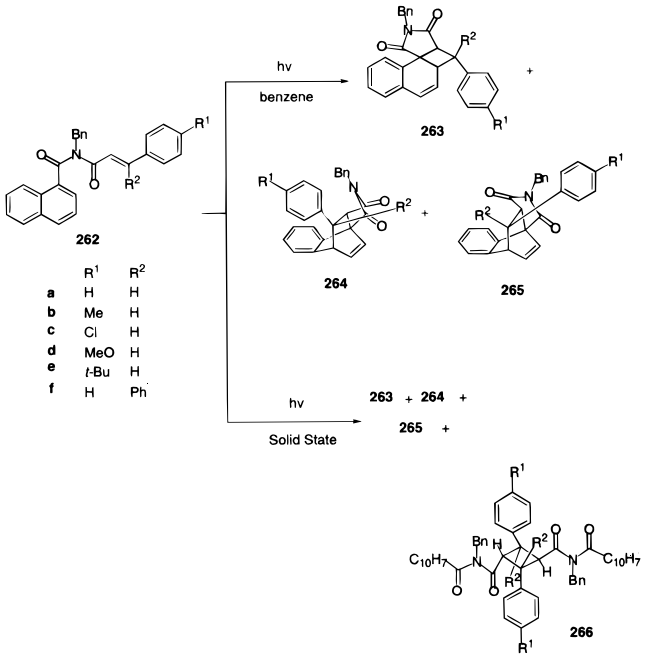
Wavelength dependence effects in the solid-state photodimerization of thiocoumarin **257** have been discovered recently.[102] For example, photoirradiation of **257** at wavelengths longer than 390 nm leads to exclusive formation of the syn-head-to-head dimer **258** in 30% yield, while photoirradiation of **257** in CH_2Cl_2 gives the anti-head-to-head dimer **259** in 20% yield. In contrast, a mixture of the dimers **258**−**261** was formed in a 10:11:1:3 ratio by using light of shorter wavelength (340 nm) in the solid-state irradiation of **257**.



259 anti-HH **257** **258** syn-HH

258 + **259** + **260** syn-HT + **261** anti-HT

Photoirradiation of *N*-cinnamoyl-1-naphthamides **262a**−**f** in solution gives only the intramolecular [2π+2π] product **263** and 4π+2π products (**264** and **265**). In contrast to this, the intermolecular [2π+2π] cyclization product **266**, along with intramolecular dimerization products (**263**−**265**), was obtained upon photoirradiation in the solid state.[103]



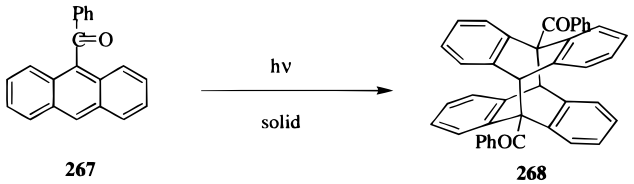
262

	R^1	R^2
a	H	H
b	Me	H
c	Cl	H
d	MeO	H
e	*t*-Bu	H
f	H	Ph

263 **264** **265**

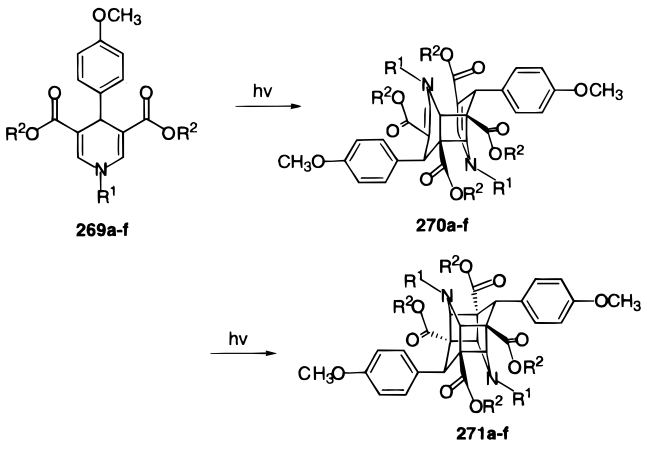
266

Photoreaction of 9-benzoylanthracene (**267**) in toluene under argon gives the [4+4]cycloadduct **268** in 60% yield, together with anthracene and 9,10-dibenzoylanthracene as byproducts. The 50% yield of **268** obtained by photoirradiation of crystalline **267** has its explanation in the crystal packing pattern.[104]



267 **268**

The crystalline 1,4-dihydropyridines **269a**−**f** yield [2+2]cycloadducts **270a**−**f** upon photoirradiation and on further irradiation give the cage dimers **271a**−**f** quantitatively.[105]



269a-f **270a-f** **271a-f**

a: R^1=H; R^2=Me
b: R^1=H; R^2=Et
c: R^1=Bz; R^2=Et
d: R^1=Me; R^2=Me
e: R^1=Me; R^2=Et

It is well-known that benzopinacol (**274**) can be obtained quantitatively upon photoirradiation of 4,4′-

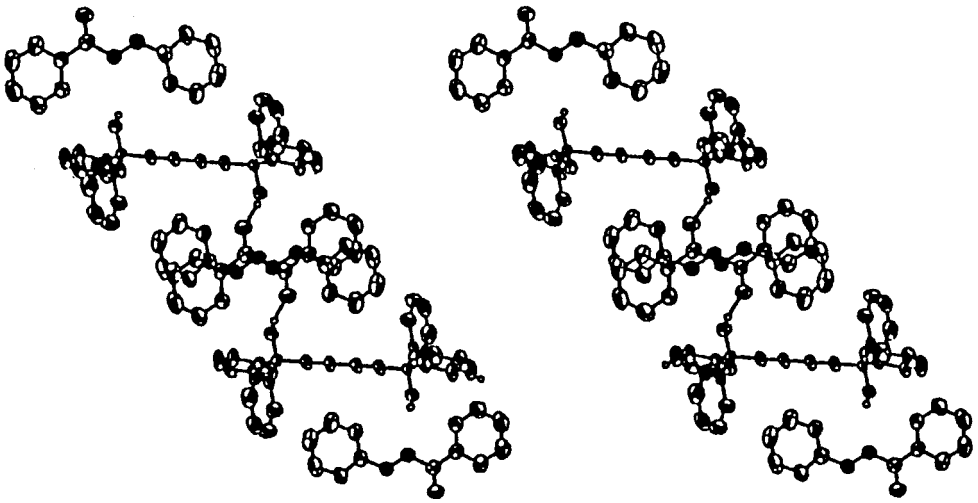
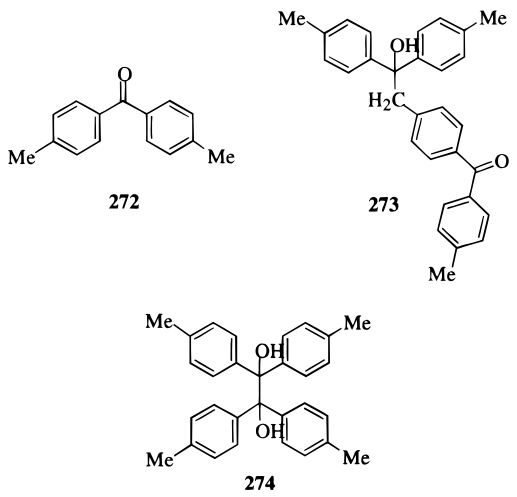


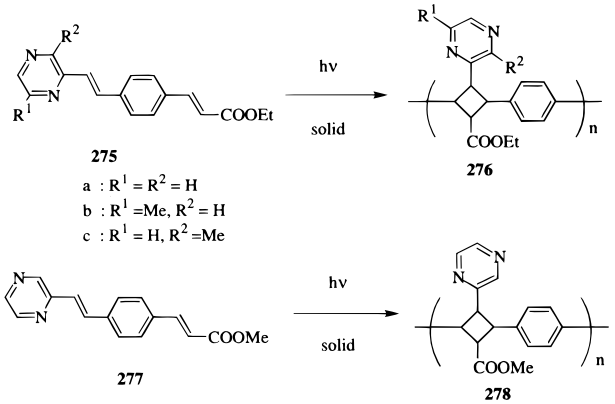
Figure 9. Stereoview of the 1:2 inclusion complex of **1** with **5**.

dimethylbenzophenone (**272**) in *i*-PrOH. On the other hand, upon UV irradiation in the solid state, **272** undergoes intermolecular hydrogen abstraction to give the dimeric compound **273** under topochemical control.[106]



272 **273** **274**

Upon photoirradiation, ethyl 4-[2-(unsubstituted and methyl-substituted pyrazinyl)ethenyl]cinnamates **275** give crystalline linear polymers **276**, whereas methyl 4-[2-(methyl-substituted pyrazinyl)ethenyl]cinnamate (**277**) affords mixtures of oligomers **278**.[107]



275
a : $R^1 = R^2 = H$
b : R^1 =Me, R^2 = H
c : R^1 = H, R^2 =Me

276 **277** **278**

Although photodimerizations of chalcone **5** and its derivatives have long been studied, most gave unsatisfactory results. For example, neither form I (mp 59 °C)[108] nor form II (mp 56 °C)[109] of chalcone (**5**) gives any dimer by photoirradiation in the solid state, although irradiation of **5** in EtOH for 147 h gives **281a** in only 9% yield.[110] Photodimerization of chalcone (**5**) was found, however, to undergo stereoselective control in inclusion crystals with host compounds **1**.[111] For example, irradiation of a 1:2 inclusion complex of benzylideneacetophenone (**5**) with 1,1,6,6-tetraphenylhexa-2,4-diyne-1,6-diol (**1**), in the solid state for 6 h, gave only the syn-head-to-tail dimer **279a** (of the four possible dimers **279**−**282**) in 82% yield. X-ray crystal structure analysis of the complex disclosed that two benzylideneacetophenone molecules **5** are packed close together through hydrogen bonds between the hydroxyl group of **1** and carbonyl oxygen of **5** in the complex (Figure 9). The double bonds are parallel, and the distance between the two is 3.862 Å (Figure 10). It was also found that photodimerization of chalcone proceeds stereoselectively in the molten state and gives the corresponding rac-anti-head-to-head dimers **281a** in relatively good yields.[112] Irradiation of one polymorphic crystal of chalcone (**5**) (form II, mp 56 °C) at 60 °C for 24 h by a 400W high-pressure Hg lamp gave the anti-head-to-head dimer **281a** in 31% yield. Similar irradiation of another polymorphic crystal form of chalcone (**5**) (form I, mp 59 °C) at 60 °C also gave **281a** in 28% yield. The molecular structures of **279a** and **281a**

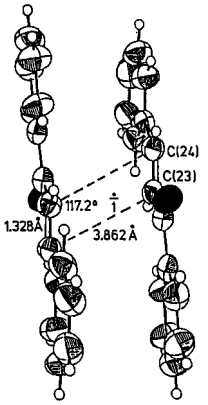


Figure 10. Mutual relation and geometrical parameters of the reacting centers of the guest molecules **5**.

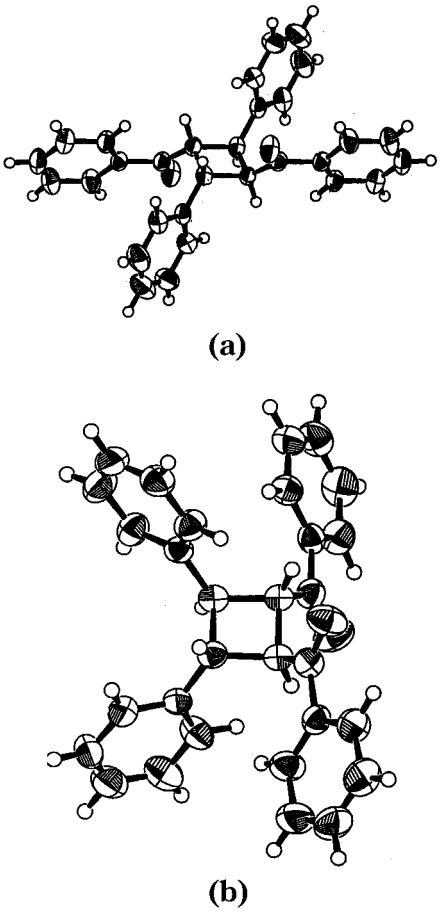


Figure 11. Molecular structures of (a) **279a** and (b) **281a**.

were determined by X-ray analysis (Figure 11).

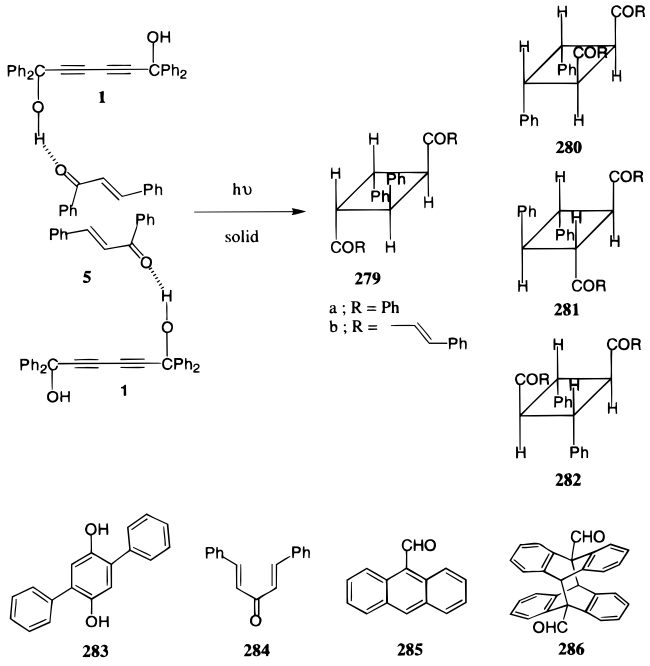
The hydroquinone host compound **283** is also effective in assisting photodimerization of **5** or benzylideneacetone (**284**). For example, irradiation of the 1:2 inclusion complex of **284** with **283** in the solid state for 6 h gave only the syn-head-to-tail dimer **279b** in 70% yield (Table 28). X-ray crystal analysis

Table 28. Yields of the Photocycloaddition Reaction Products

host	guest	reaction time (h)	product	yield (%)
1	**5**	6	**279a**	90
283	**5**	6	**279a**	85
283	**284**	6	**279b**	70
1	**285**	8	**286**	86

shows that hydrogen bonding plays an important role in packing the guest molecules **284** with the crystal, and the resulting distance between the double bonds of **284** is short enough (3.787 Å) to allow easy reaction. [111]

Irradiation of the 1:2 inclusion complex of 9-formylanthracene **285** with **1** for 8 h in the solid state afforded the anti dimer **286** in 86% yield. Two molecules of **285** are arranged between two host molecules through hydrogen bonding in an orientation which leads to the anti dimer **286** on photodimerization and where the distance between the two reaction centers is short enough (4.042 Å) to permit this.[111]



Since 2-pyridone (**287a**) exists as an equilibrium mixture with 2-hydroxypyridine (**288a**), it is difficult to isolate **287a** in pure state. However, inclusion complexation can be applied to the isolation of the keto-form in a pure form. For example, the host compound **1** selectively includes the keto form **287a** to form a 1:2 inclusion crystal. This selective inclusion of **287a** can be used for its efficient dimerization. Irradiation of the 1:2 inclusion complex composed of **1** and **287a** in the solid state for 6 h gave the trans-anti dimer **290a** in 76% yield.[113] In contrast to this, solution photodimerization of **287a** in EtOH gave **290a** only in 18% yield after longer (100 h) irradiation. X-ray crystal structural study of the complex shows that two molecules of **287a** are arranged between host molecules in positions which allow

Table 29. Yields of Photoreaction Products of 2-Pyridones 287 and 1-Methyl-2-pyridones 289 in the Crystalline Complex and in EtOH Solution

substituent	yield (%)[a]			
	290		**291**	
	complex	EtOH soln	complex	EtOH soln
a	76	18	32	30
b	22[b]	18	19	30
c	1	7	85	21
d	0	45	0	41
e	0	9	74	9
f	0	69	1	40
g	0	10	74	3
h	0	40	91	37
i	0	32	9	19
j	0	0	84	0

[a] The irradiation times were 6 h for complexes and 100 h for ethanol solution. [b] The intermolecular dimer **292** was obtained.

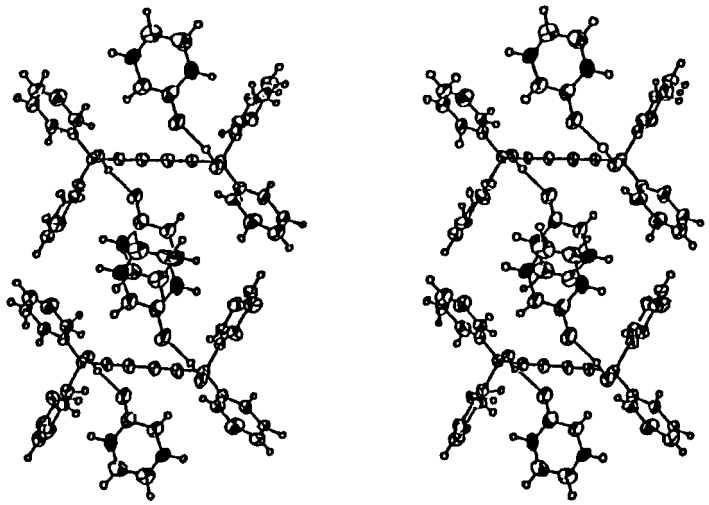


Figure 12. Stereoview of the 1:2 inclusion complex of **1** with **287a**.

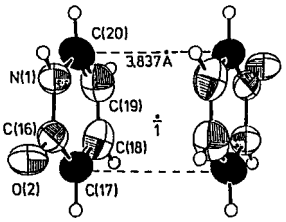
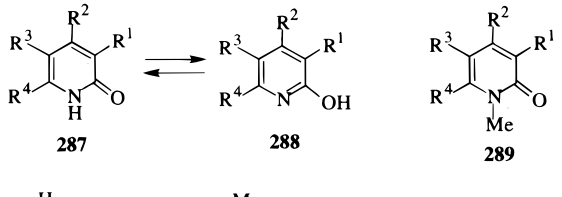
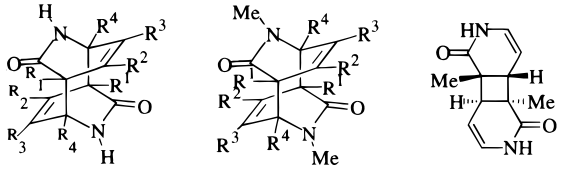


Figure 13. Mutual relation and geometrical parameters of the reactivity centers of the guest molecules **287a**.

formation of the trans-anti dimer **290a** by dimerization (Figure 12) since the distance between the reaction centers is very close (3.837 Å) (Figure 13). Similar photodimerizations of *N*-methylpyridones **289b**,**c**,**e**,**g**,**h**,**j** also proceed efficiently in inclusion crystals rather than in solution, although the inclusion complexes **287c**−**j** are photostable (Table 29).



287 **288** **289**

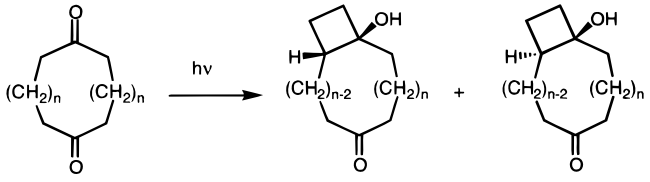


290 **291** **292**

a: R^1 = R2 = R3 = R4= H
b: R2 = R3 = R4 = H, R1 = Me
c: R1 = R3 = R4 = H, R2 = Me
d: R1 = R2 = R4 = H, R3 = Me
e: R1 = R2 = R3 = H, R4 = Me
f: R2 = R4 = H, R1 = R3 = Me
g: R1 = R3 = H, R2 = R4 = Me
h: R1 = R2 = H, R3 = R4 = Me
i: R1 = H, R2 = R3 = R4 = Me
j: R1 =R2 = R3 = H, R4 = OMe

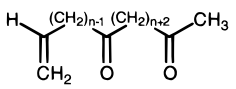
B. Photocyclization

The Norrish type II photochemistry of cyclic diketones ranging in size from 10-membered to 26-membered has been found to occur much more selectively in the solid state than in solution.[114] For example, irradiation of **293h** in the solid sate gave only the intramolecular photocyclization product *cis*-**294h** in 98% yield, while irradiation of **293h** in hexane affords a mixture of **294h** (15%), **295h** (27%) and **296h** (58%). Similar photoirradiation of **293b**, **293c**−**g**, **293i** (needles), and **293i** (prisms) yields **294b** (99%), **294c** (58%), **294d** (89%), **295e** (84%), **294f** (90%), **295g** (91%), **295i** (91%), and **295i** (97%), respectively, as the major photoreaction products.



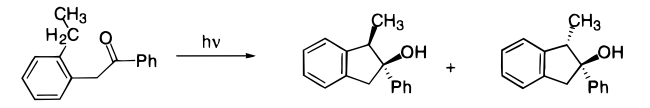
293 **294** **295**

a: n = 2 f: n = 7
b: n = 3 g: n = 8
c: n = 4 h: n = 9
d: n = 5 i: n = 10
e: n = 6

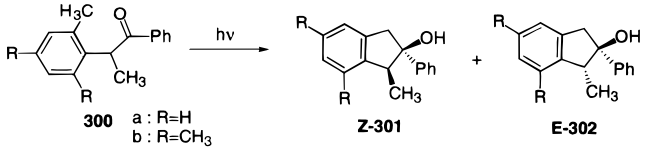


296

Photocyclization of the acetophenone derivatives (**297**, **300a**,**b**) via δ-hydrogen abstraction occurs more diastereoselectively in the solid state than in solution.[115] For example, irradiation of the MeOH solution of **297** gives a mixture of *cis*-**298** and *trans*-**299** in 67 and 33% yields, while irradiation of 2**97** in the solid state affords *cis*-**298** exclusively.



297 **Z-298** **E-299**



300 a : R=H
b : R=CH_3

Z-301 **E-302**

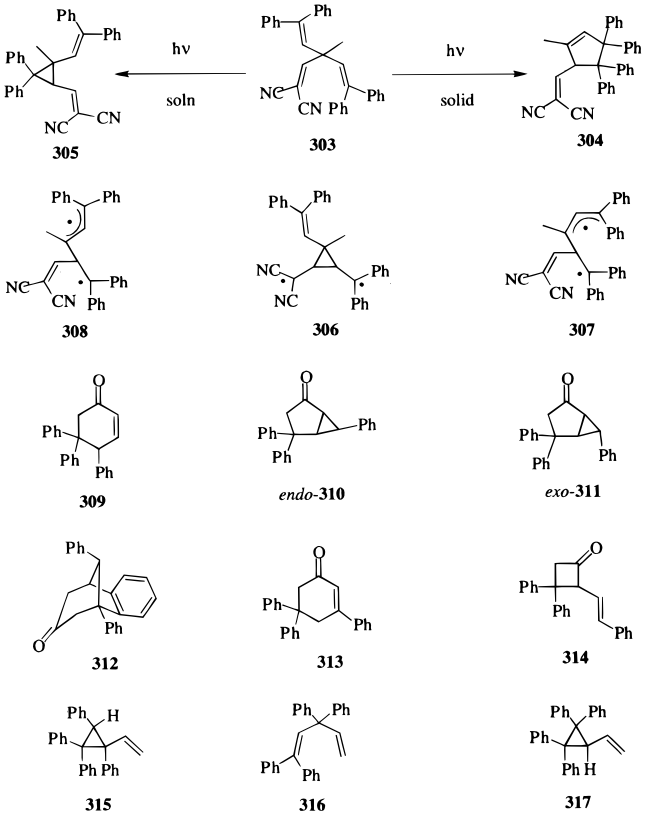
C. Photorearrangement and Photoisomerization

Photochemical rearrangement can also be successfully controlled in the crystalline state.[116] For ex-

ample, tetraphenyldicyanotriene (**303**) affords only the di-π-methane photoproduct **305** upon photoirradiation in benzene. In contrast, irradiation of **303** in the solid state gives only cyclopentene **304**. These results can be explained by the preferred formation of transoid (**308**) and cisoid (**307**) diradicals in solution and in the solid state, respectively, through the common diradical intermediate **306**.

Upon irradiation of 4,5,5-triphenyl-2-cyclohexenone (**309**) in solution, exo-bicyclic ketone **311**, cyclohexenone (**313**), and vinylcyclobutanone (**314**) are formed. Photolysis of crystalline **309**, however, leads to the *endo*-**310** and benzobicyclic ketone **312** in a 4:1 ratio.

1,1,3,3-Tetraphenyl-1,4-pentadiene (**316**) affords vinylcyclopropanes **315** and **317** in solution in a 1:1.3 ratio. However, irradiation of crystalline **316** gives selectively **317**.



Irradiation of 1,2-diphenyldiazoalkane (**318**) in EtOH produces a mixture of compounds (**320**, **321**, **322**, and **323**) in 36% yield, along with products of carbene insertion into the OH bond of EtOH in 64% yield. On the other hand, irradiation of powdered samples of **318** at 0 °C with $\lambda > 380$ nm gives only compound **320** in 96% yield.[117] It was also found that this reaction proceeds selectively at ambient temperatures entirely in the solid phase up to 95% conversion. The solid-state reaction mechanism was studied by ^{13}C CPMAS NMR, X-ray analysis, FT-IR, and DSC measurement. For example, the progress of the reaction can clearly be monitored by ^{13}C CPMAS NMR at intermediate stages (Figure 14). These spectroscopic and thermal analyses suggest that solid-state reaction of **318** proceeds by a continuous-phase mechanism maintaining a structural similarity between the reactant, the intermediate, the transition state, and the final product.[118]

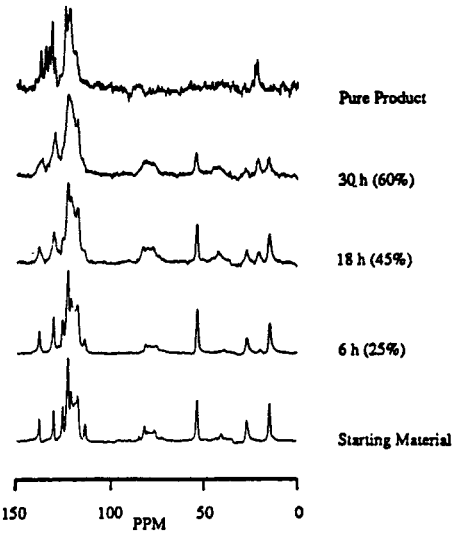
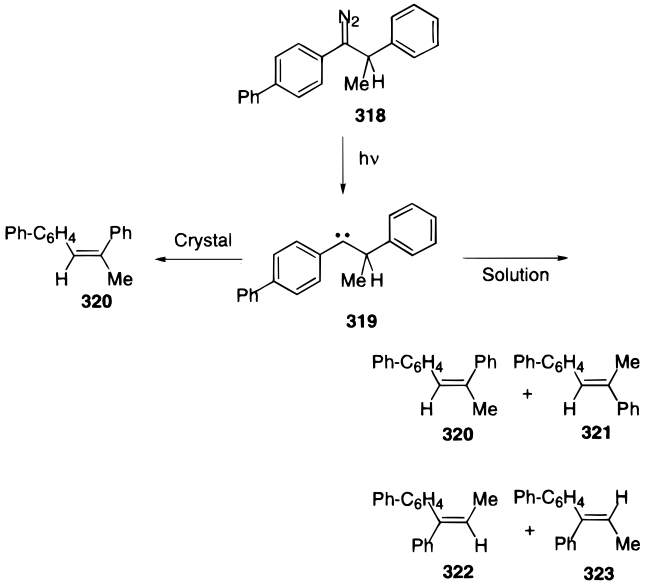
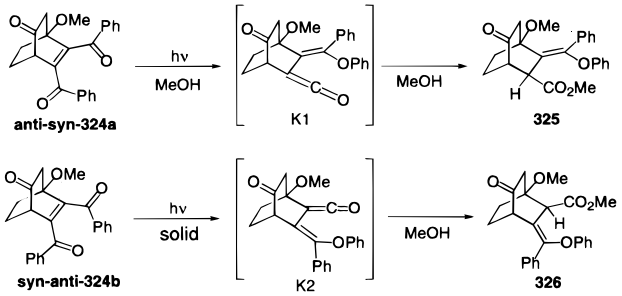


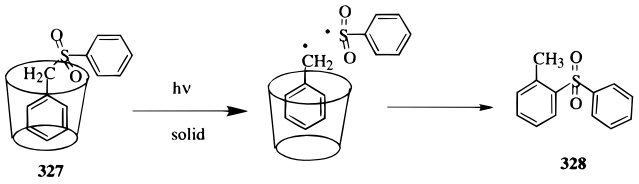
Figure 14. ^{13}CPMAS spectra of **318** (bottom) and **320** (top) along with partially reacted samples to 25, 45, and 60% conversions.



Photorearrangement of the *cis*-1,2-dibenzoylalkane derivative **324** in the solid state and in MeOH solution gave **326** and **325**, respectively, via ketene intermediates (**K1** and **K2**).[119] This indicates that the anti-syn form **324b** and syn-anti form **324a** exist predominantly in the solid state and in MeOH, respectively.



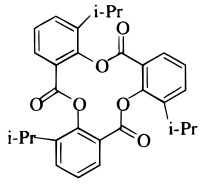
Upon solid-state photoirradiation, the β-cyclodextrin complex of benzyl phenyl sulfone (**327**) undergoes a intramolecular rearrangement yielding *o*-methyldiphenyl sulfone (**328**) selectively, while, in solution, dibenzyl is obtained as the major product.[120]



327 **328**

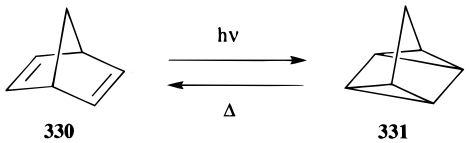
Photoisomerization reactions of stilbene and methyl cinnamate in their inclusion crystals with tri-orthothymotide (**329**) have been reported to proceed differently from those observed in solution or in the pure guest crystal.[121]

compound	inclusion crystal	guest crystal
stilbenes	cis → trans	cis ↛ trans
	cis ↚ trans	cis ↚ trans
methyl cinnamates	cis ⇌ trans	cis ← trans
		cis ↛ trans

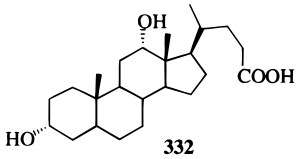


329

When the isomerization reaction of norbornadiene **330** to quadricyclene **331** is carried out in solution, a large quantity of byproducts (e.g. cyclohepta-1,3,5-triene, 6-methylfulvene, and polymers) is formed. However, if the isomerization reaction is carried out in the channels of deoxycholic acid (**332**) by exposing the inclusion crystals to solar light, a significant decrease has been found in the amount of such byproducts.[122]

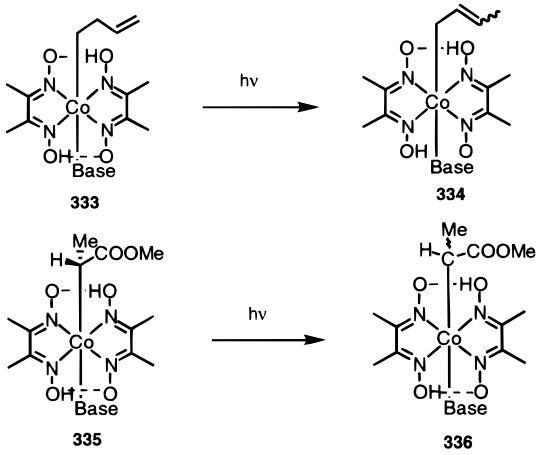


330 **331**



332

The photoisomerization in the solid state of the alkyl group bonded to the cobalt atom in cobaloximes has been extensively studied. For example, the but-3-en-1-yl group in crystalline **333** is isomerized to the but-2-en-1-yl group of **334** in the solid state on exposure to a xenon lamp.[123] It was also found that the chiral 1-cyanoethyl group bonded to the cobalt atom in the crystals of **335** is racemized by X-ray exposure without degradation of the crystallinity.[124]

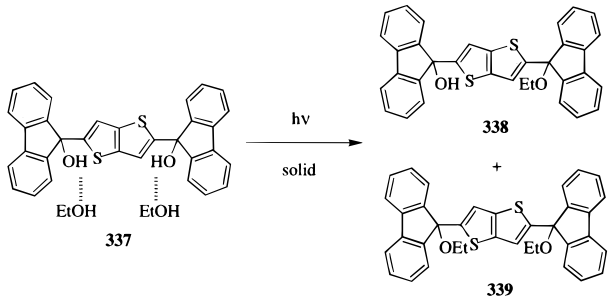


333 **334**

335 **336**

D. Photosolvolysis

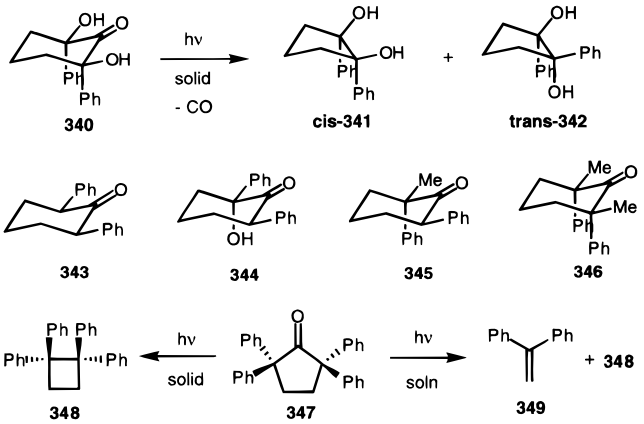
Solid-state photosolvolysis was found to proceed in host−guest clathrate crystals. When a 1:2 inclusion complex of the diol host compound **337** with EtOH was irradiated using a high-pressure mercury lamp at room temperature for 6 h, the monoether **338** (43%) and diether **339** (21%) were obtained along with recovered **337** (36%).[125]



337 **338** **339**

E. Photodecarbonylation

Irradiation of the cyclohexanone derivative **340** in solution gives the cyclopentanediols *cis*-**341** and



340 **cis-341** **trans-342**

343 **344** **345** **346**

348 **347** **349**

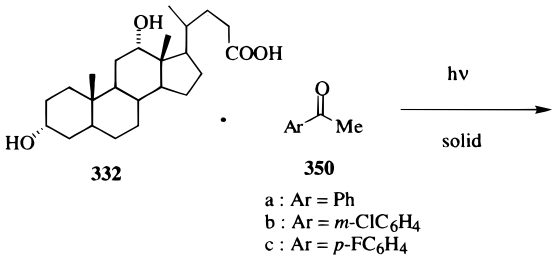
trans-**342** in a 51:49 ratio by decarbonylation. However, irradiation of **340** in the solid state gave a 19:1

ratio of *cis*-**341**/*trans*-**342** with retention of the stereochemistry of the starting material.[126] The similar photodecarbonylation reactions of **343**−**346** also showed high selectivity in the solid state.[127] Irradiation of crystalline cyclopentanone derivative **347** gives cyclobutane **348** as the only solid-state product, whereas its solution photochemistry gives a 3:1 mixture of 1,1-diphenylethylene (**349**) and **348**.[128]

F. Photoaddition Reaction between Different Molecules

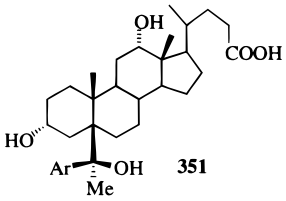
The crystalline 5:2 host−guest complex of deoxycholic acid and acetophenone gives a single topochemical addition product **351a** with a new chiral carbon center of *S* configuration in 25% yield upon photoirradiation for 30 days in the solid state.[129]

Similar treatment of both the 3:1 inclusion complexes of **332**:*m*-chloroacetophenone **350b** and **332**:p-fluoroacetophenone **350c** gave similar photoadducts **351b** and **351c**, respectively.



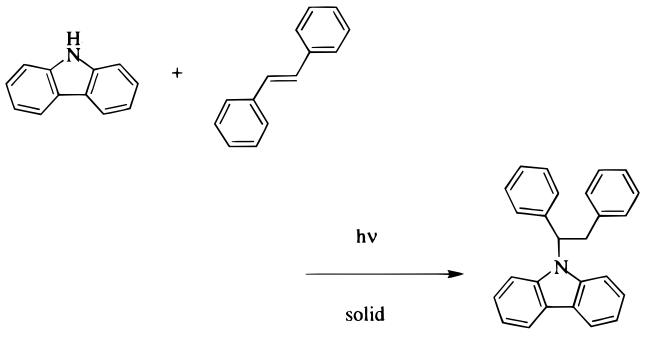
332 **350**

a : Ar = Ph
b : Ar = *m*-ClC$_6$H$_4$
c : Ar = *p*-FC$_6$H$_4$



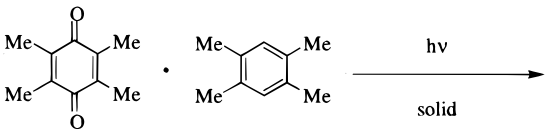
351

Photoreaction between carbazole and trans-stilbene, occurring at the interface of their crystallite, has been reported. The mixed crystal was prepared by melting a 1:1 molar mixture of carbazole and trans-stilbene followed by resolidification at room temperature. The powdered sample was irradiated at room temperature for 20 h to give the photoadduct **352** in 25% yield.[130]

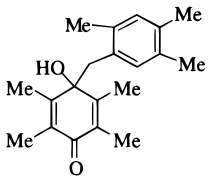


352

Upon irradiation, the 2:1 mixed crystal of duroquinone and durene gave the photoaddition product **353** in 20% yield.[131]

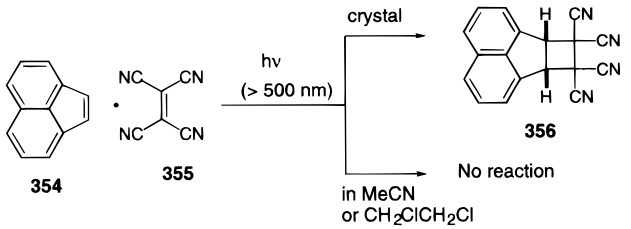


2:1 mixed crystal



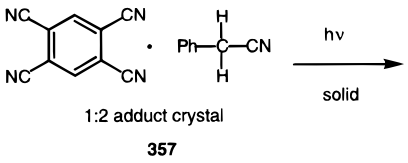
353

On irradiation of the crystalline 1:1 complex of **354** and **355** with light of wavelength longer than 500 nm, the [2+2]cycloadduct **356** was isolated in 80% yield. In contrast, irradiation of an equimolar mixture of **354** and **355** in MeCN or dichloromethane did not result in any reaction.[132] X-ray analysis of the 1:1 complex showed that molecules of **354** and **355** are stacked alternatively with a distance of 4.0 Å between their planes and with a dihedral angle of 0.8°.



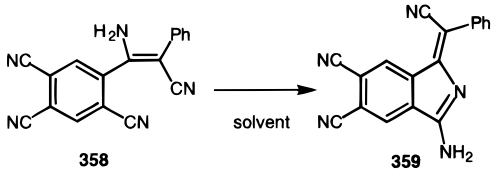
354 **355** **356**

The photocoupling reaction in the two-component crystal **357** formed from tetracyanobenzene and benzyl cyanide produces the product **358**, which rearranges to the isoindole derivative **359** in solution. Conversely, irradiation of tetracyanobenzene in benzyl cyanide solution gives a complex mixture of the compounds **360**−**362**.[133]

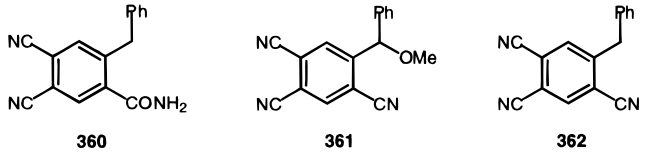


1:2 adduct crystal

357



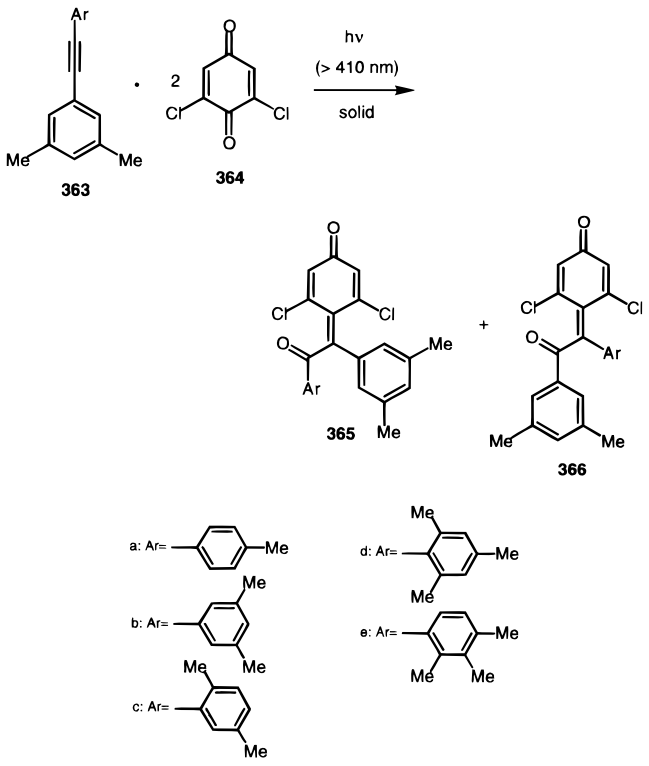
358 **359**



360 **361** **362**

Photoirradiation of crystalline electron donor−acceptor complexes of the diarylacetylenes **363** and dichlorobenzoquinone **364** gives the [2+2]photocycloaddition products **365** and **366**. For example, when a 1:2 complex of **363a** and **364** was irradiated using a medium-pressure Hg lamp (410 nm, −60 °C, 5 h),

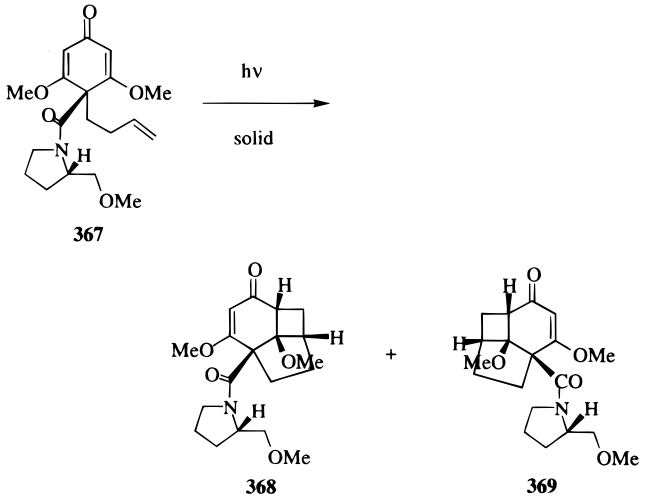
a 4:1 mixture of **365a** and **366a** was obtained in 90% yield after 17% conversion.[134]



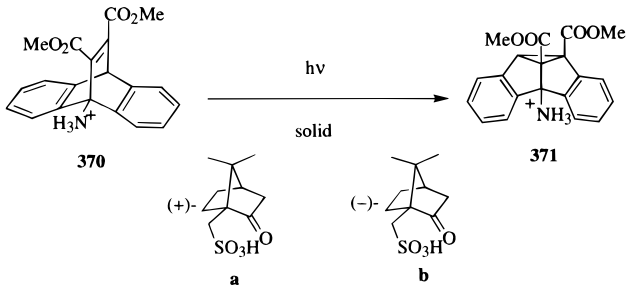
G. Enantioselective Photoreaction

1. Enantioselective Photoreactions of Chiral Molecules

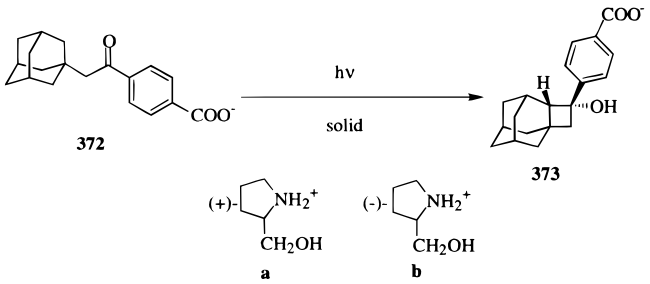
The enantioselective intramolecular [2+2] photocycloaddition of cyclohexadienone derivative **367**, which has an attached chiral auxiliary, was found to proceed efficiently in the solid state.[135] Two crystal modifications, the α-form (mp 102−104 °C) and *β*-form (mp 127−128 °C), gave **368** and **369**, respectively, upon photoirradiation in the solid state.



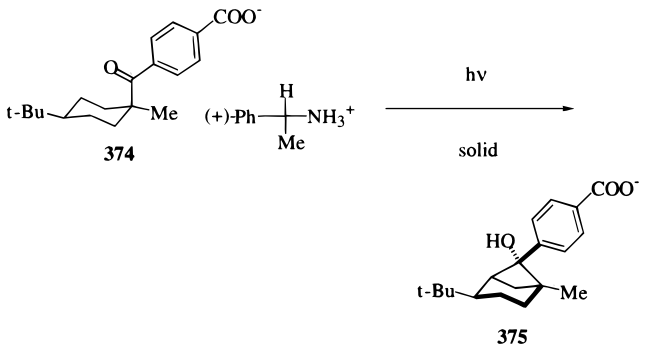
A new method for asymmetric induction in the solid-state photochemistry of salts of prochiral amines with optically active acids as "ionic chiral auxiliaries" has been developed. For example, (+)- and (−)-**371** were obtained by irradiation of the salts **370a**,**b** at −40 °C in the solid state.[136]



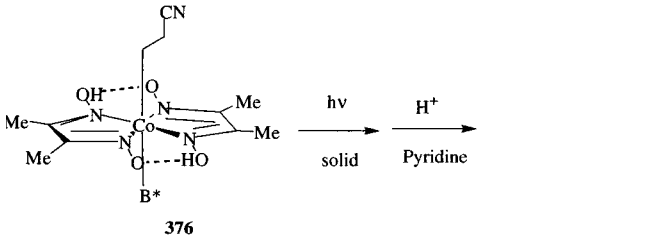
(+)- or (−)-prolinol salts of keto acid **372** afforded the (+)- or (−)-cyclobutanol **373** in 97% ee upon irradiation in the solid state, while racemic **373** was obtained on irradiation in solution.[137]

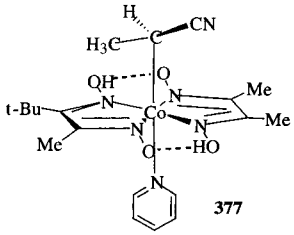


High enantioselectivity of 97% ee was also obtained in the solid-state photocyclization of keto acid **374** to cyclobutanol **375**.[138]



Photoisomerization of 2-cyanoethylcobaloximes coordinated with chiral axial ligands has been reported to proceed enantioselectively in the solid state.[139] For example, finely powdered (2-cyanoethyl)cobaloxime (**376**), suspended in liquid paraffin and spread onto a





a: B* = *(R)*-1-Methylpropylamine

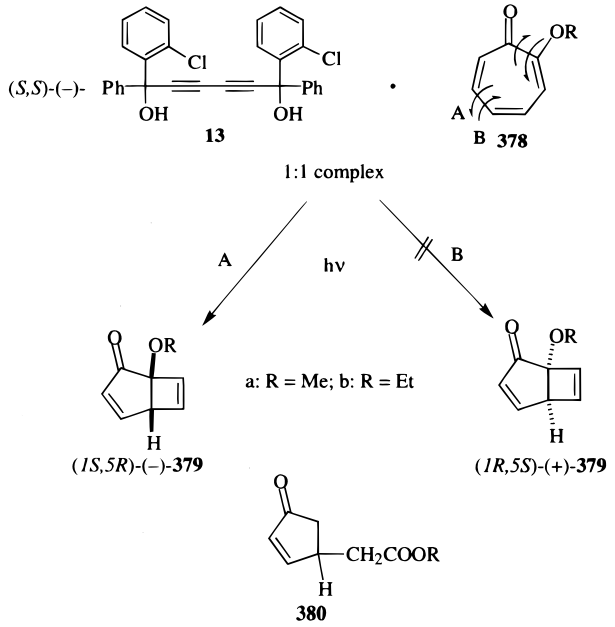
b: B* = *(R)*-1-(1-Naphthyl)ethylamine

c: B* = *(R)*-2-Phenylglycinol

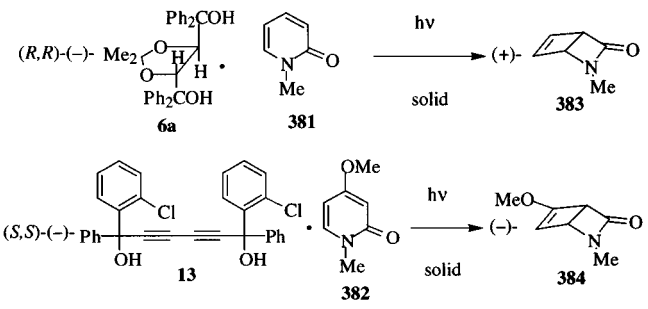
Petri dish, was irradiated to give (*S*)-(−)-**377** of 81.6% ee after displacement from the complex by pyridine.

2. Enantioselective Photoreaction of Achiral Molecules in Chiral Inclusion Crystals

It has been found that enantioselective photoreactions can be successfully controlled in crystalline inclusion complexes by using optically active host compounds. For example, disrotatory [2+2] photocyclization of tropolone alkyl ethers can be controlled perfectly by using optically active hosts. Irradiation of a 1:1 complex of α-tropolone methyl ether (**378a**) and (*S*,*S*)-(−)-**13** in the solid state gave (1*S*,5*R*)-(−)-**379a** of 100% ee and (+)-**380a** of 91% ee in 11 and 26% yields, respectively.[140] Similar irradiation of a 1:1 complex of **378b** with (−)-**13** gave (1*S*,5*R*)-(−)-**379b** of 100% ee and (+)-**380b** of 72% ee in 12 and 14% yields, respectively. The enantioselective photoreaction can be interpreted as follows: disrotatory [2+2] photoreaction of **378** in the inclusion crystals with (−)-**13** occurs only in the *A* direction due to the steric hindrance of (−)-**13**. This interpretation was seemed to be reasonable through an X-ray crystal structure study of the inclusion complex.[141]

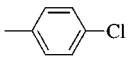
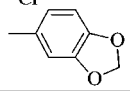


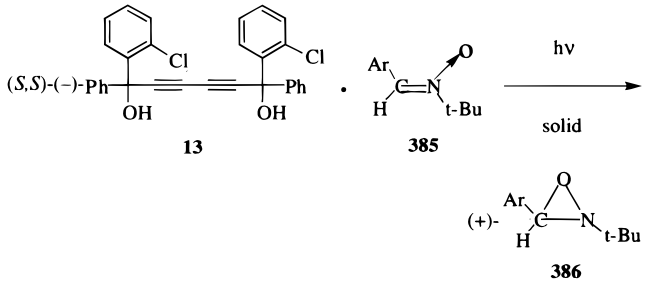
Similar disrotatory [2+2] photocyclization of pyridones into β-lactam derivatives also proceeds efficiently within inclusion crystals.[142] Irradiation of either powdered inclusion complexes of *N*-methylpyridone (**381**) with (−)-**6a** or *N*-methyl-4-methoxypyridone (**382**) with (−)-**13** gave enantiomerically pure (+)-**383** or (−)-**384** in 49 and 8% yields, respectively.



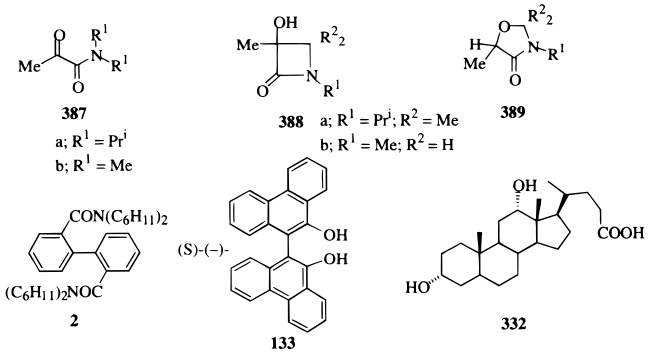
Optically active oxazolidinones **386a**−**d** of 9.5−100% ee were obtained by irradiating the 1:1 inclusion complexes of nitrones **385a**−**d** and optically active host compound (−)-**13** in the solid state (Table 30).[143]

Table 30. Yield and Optical Purity (% ee) of Oxaziridines 386a−d

	Ar	yield (%)	optically purity (% ee)
a	Ph	41	9.5
b		74	30
c		51	100
d		52	94



It has been reported that irradiation of *N*,*N*-diisopropylpyruvamide (**387a**) in benzene gives the oxaziridine **389a** exclusively and that irradiation in the solid state at −78 °C gives β-lactam **388a** and **389a** in 31 and 29% yields, respectively.[144] On the other hand, irradiation of the 1:1 inclusion compound of **387a** and **2** in the solid state for 40 h gave only **388a** in 60% yield. Similar irradiation of the 1:1 inclusion compound of **387b** and **2** gave **388b** selectively in 56% yield. Enantiomerically pure **388b** was easily obtained by complexation with optically active **133**.[145] (+)-**388b** of 16% ee was also obtained in 42% yield, together with oxaziridine **389b**, by irradiation of the inclusion crystals of **387b** with **332**.[146]



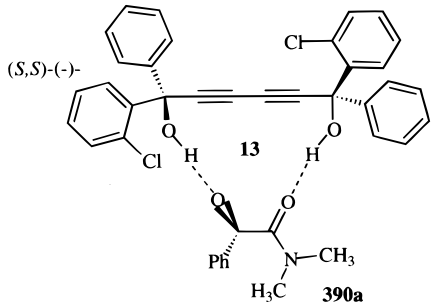
Stereo- and enantioselective photoreactions of the *N*,*N*-dialkylphenylglyoxylamides **390** were accomplished by irradiation of their respective inclusion complexes with optically active host compounds **13**

Table 31. Photoreaction of the Phenylglyoxylamides 390 as Inclusion Complexes with the Hosts 6b,c and 13

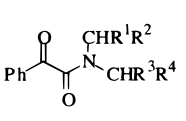
host	amide	391	yield (%)	% ee	392	yield (%)	% ee
(−)-**13**	**390a**	(−)-**391a**	90	100			
(−)-**13**	**390g**	(−)-*cis*-**391g**	29	63			
		(−)-*trans*-**391g**	21	95			
(−)-**13**	**390h**	(−)-*cis*-**391h**	31	56			
		(−)-*trans*-**391h**	9	a			
(−)-**6b**	**390a**	(−)-**391a**	40	67	(−)-**392a**	55	100
(−)-**6c**	**390a**	(−)-**391a**	40	100			
(−)-**6b**	**390d**	(−)-**391d**	11	100	(−)-**392d**	20	39
(−)-**6c**	**390d**	(+)-**391d**	17	61	(−)-**392d**	71	43
(−)-**6b**	**390g**	(+)-*cis*-**391g**	17	96	(−)-**392g**	28	95
		(+)-*trans*-**391g**	32	44			
(−)-**6c**	**390g**	(+)-*cis*-**391h**	15	100	(−)-**392g**	9	52
		(+)-*trans*-**391h**	34	95			
(−)-**6b**	**390h**				(−)-**392h**	100	100
(−)-**6c**	**390h**				(−)-**392h**	100	100

[a] % ee was not determined.

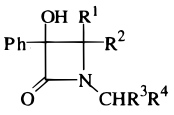
or **6b**,**c** (Table 31).[147] For example, when a 1:1 inclusion complex of (−)-**13** with **390a** was irradiated by a 400 W high-pressure Hg lamp at room temperature for 24 h, optically pure *β*-lactam (−)-**391a** was obtained in 90% yield. X-ray crystal structural studies showed that the conformation of **390a** is fixed in the solid state by the formation of two hydrogen bonds so as to give (−)-**391a** shown as follows:



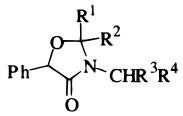
Enantiocontrol of the reaction was also achieved in inclusion crystals using the optically active host compounds **6b** or **6c**, although the efficiency was not very high.[148] For example, irradiation of the powdered 2:1 complex of **390a** with (−)-**6c** gave (−)-**391a** of 100% ee in 40% yield. Similar photoirradiation of the 2:1 inclusion complex of **390d** with (−)-**6c** gave (−)-**391d** of 100% ee in 11% yield and (−)-**392d** of 39% ee in 20% yield. However, photoreaction of **390h** as an inclusion complex with either (−)-**6b** or (−)-**6c** proceeded very selectively and gave only **392h** of 100% ee in quantitative yield (Table 31).



390



391



392

a; $R^1=R^2=R^3=R^4=H$
b; $R^1=R^3=H$; $R^2=R^4=Me$
c; $R^1=R^3=H$; $R^2=R^4=Et$
d; $R^1=R^2=H$; $R^3=R^4=Me$
e; $R^1=H$; $R^2=Me$; $R^3=R^4=Me$
f; $R^1=R^2=R^3=R^4=Me$
g; $R^1=R^3=H$; R^2, $R^4=-(CH_2)_3-$
h; $R^1=R^3=H$; R^2, $R^4=-CH_2OCH_2-$

Photocyclization reactions of the *N*-(aryloylmethyl)-*δ*-valerolactams **393** occur stereoselectively and enantioselectively in their inclusion crystals with optically active hosts.[149] For example, irradiation of the powdered inclusion complex of **393a** and the optically active host compound (−)-**6b**, as a suspension in water for 12 h, gave (+)-**394a** of 98% ee in 59% yield. By similar irradiations of the 1:1 inclusion compounds of **393b** and **393c** with (−)-**6c**, (−)-**394b** of 84% ee and (−)-**394c** of 98% ee were also obtained enantioselectively (Table 32). Conversely, photoreaction of **393a**−**c** in *t*-BuOH afforded a mixture of *rac*-**394a**−**c** and *rac*-**395a**−**c**. To elucidate the mechanism of the enantioselective photocyclization of **393**, the X-ray structure of the 1:1 complex of **393c** with **6c** was determined (Figure 15).[150] The molecules of **393c** are arranged in a chiral form within the crystal so as to give (6*S*,7*S*)-(−)-**394c** selectively. The distances for C1···C3 and O1···H3B are 3.24 and 2.82 Å, respectively, and hence, the H3b atom is abstracted by O1 to form a hydroxyl group. The C3 atom

Table 32. Photoreaction of 393 in the Inclusion Crystal and in Solution

393	host	irradiation time (h)	394			395		
				yield (%)	% ee		yield (%)	% ee
393a	**(-)-1c**	12	(+)-**394a**	59	98			
393a	**(+)-1c**	12	(-)-**394a**	54	99			
393a	*a*	27	(±)-**394a**	33	0	(±)-**395a**	50	0
393b	**(-)-1c**	12	(-)-**394b**	45	84			
393b	*a*	24	(±)-**394b**	34	0	(±)-**395b**	50	0
393c	**(-)-1c**	15	(-)-**394c**	42	98			
393c	*a*	27	(±)-**394c**	26	0	(±)-**395c**	45	0

[a] Irradiation was carried out in *t*-BuOH.

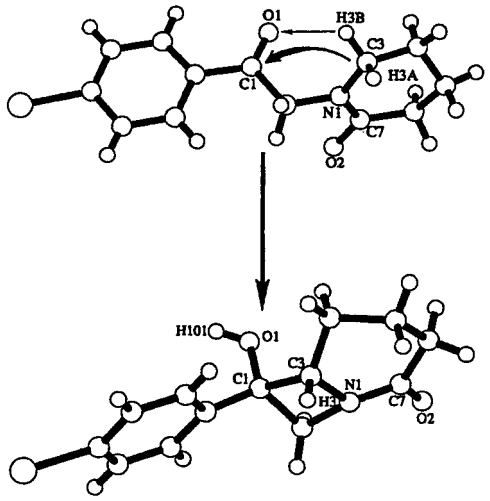
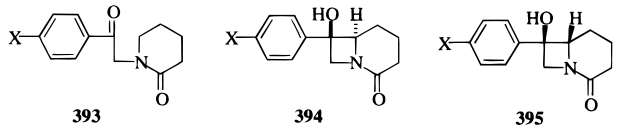


Figure 15. Photocyclization process of **393c** to **394c** in the inclusion crystals with (−)-**6c**. Reprinted with permission from ref 150. Copyright 1994 Chemical Society of Japan.

attacks C1 from the *re*-face of the carbonyl group to give (6*S*,7*S*)-(−)-**394c**.

The chiral arrangement of **393a** molecules in (−)-**6c** is also easily detected by measurement of CD spectra as Nujol mulls. For example, the inclusion crystal of **393a** with (−)-**6c** showed a (−)-Cotton effect, and that of **393a** with (−)-**6c** showed a (+)-Cotton effect at around 260 and 310 nm, respectively, although the host molecules itself does not show any CD absorption (Figure 16).



393 **394** **395**

a: X=H
b: X=Cl
c: X=Br

The photocyclization reaction of acrylanilide to 3,4-dihydroquinoline was first reported in 1971, and its application to alkaloid synthesis has long been studied.[151] Although stereo- and enantiocontrol are important in this reaction, no such attempt has been reported, except one enantioselective photocyclization

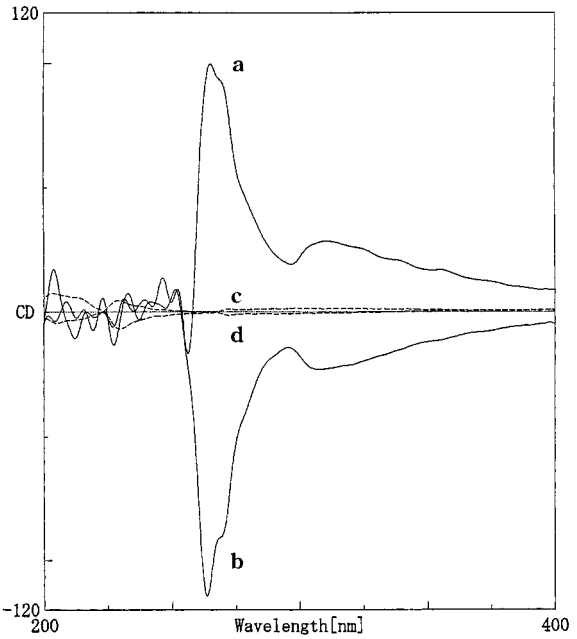
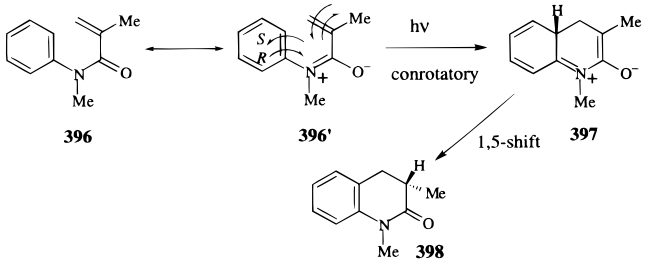


Figure 16. CD spectra of 1:1 inclusion complex of (a) **393a** with (+)-**6c** and (b) **393a** with (−)-**6c** and of host molecule (c) (+)-**6c** and (d) (−)-**6c** in Nujol mulls.

of 1-(methylacryl)-*N*-methylanilide (**396**) in benzene−ether containing (+)-bis(*p*-toluoyl)tartaric acid to give (−)-3-methyl-*N*-methyl-3,4-dihydroquinoline (**398**) of 12−16% ee.[152]



Recently, the host−guest inclusion method was found to be useful for a selective photocyclization of acrylanilides. For example, irradiation of the 1:1 inclusion compound of **396** with (−)-**6b** gave (−)-**398** of 98% ee in 46% yield. On the other hand, similar irradiation of the 1:1 inclusion compound of 396 with (−)-**6c** gave (+)-**398** of 95% ee in 29% yield (Table 33).[153] It is surprising that the two host compounds (−)-**6b**

Table 33. Photocyclization of Anilides in the Inclusion Crystals

anilides	host	yield (%)		% ee
396	**(-)-6b**	(-)-**398**	46	98
396	**(-)-6c**	(+)-**398**	29	95
399a	**(-)-6b**	(-)-**400a**	65	98
399a	**(-)-6c**	(+)-**400a**	44	98
399b	**(-)-6b**	(+)-**400b**	62	70
399b	**(-)-6c**	(-)-**400b**	29	99

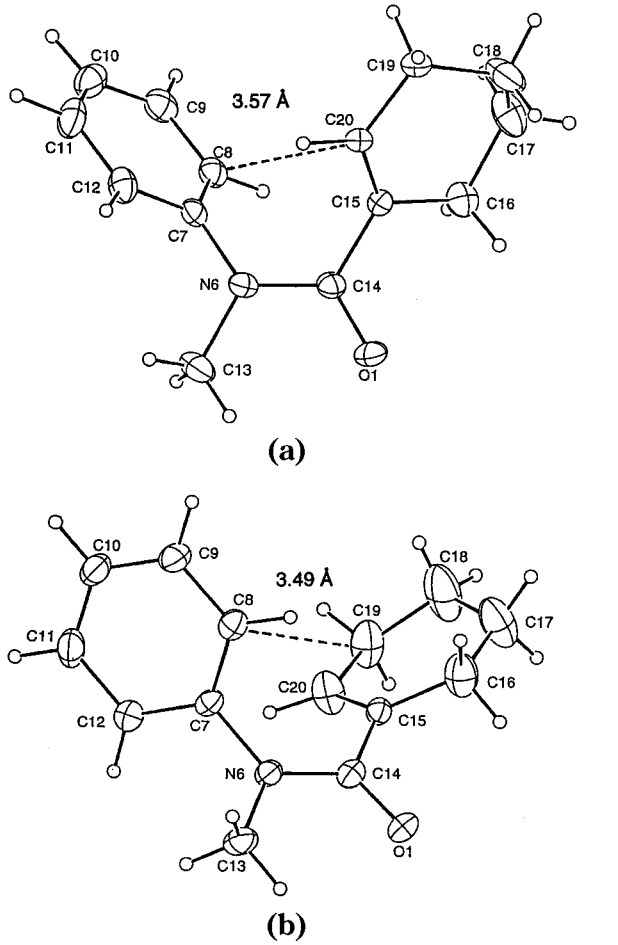
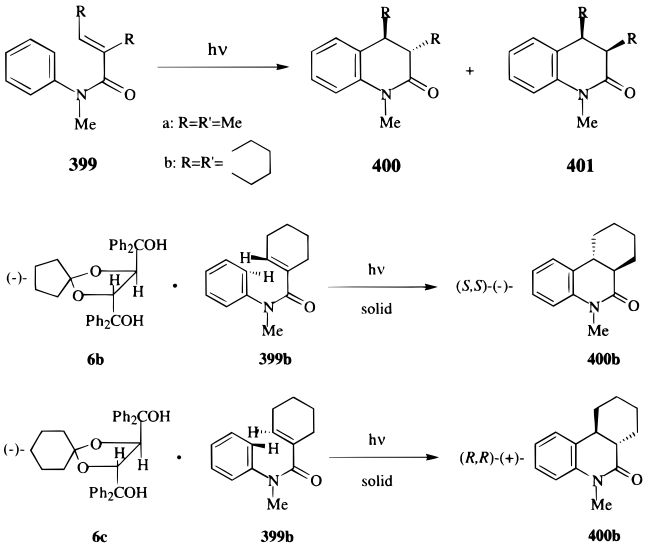


Figure 17. Molecular structures of **399b** in the inclusion crystals with (a) (−)-**6b** and (b) (−)-**6c** with thermal ellipsoids at the 20% probability level.

and (−)-**6c** of so little structural difference (i.e. five membered ring and six membered ring) caused such disparate enantioselectivity. The 1,5-hydrogen shift in the photocyclization of **399** in its inclusion crystals with (−)-**6b** or (−)-**6c** is also controlled precisely and finally gives the trans-isomer **400** of high optical purity (Table 33). When the irradiation of **399** was carried out in solution, a 1:1 mixture of *rac*-**400** and *rac*-**401** was obtained.



The selective conversion of **396** to **398** in the inclusion crystal can be interpreted as follows: of the two possible directions (*S* and *R*) of the conrotatory ring closure of the iminium form (**396′**) of **396**, only the rotation toward *S*, for example, occurs through control by the host **6b** (or **6c**) to give the intermediate **397**. 1,5-Hydrogen shift of the intermediate **397** occurs in a suprafacial manner to give the optically active photocyclization product **398**. The chiral conformation of **399** in the inclusion crystals with **6b** and **6c** were determined by X-ray analysis. For example, the molecular structure of **399b** in its inclusion crystals with (−)-**6b** is enantiomorphic to that in the inclusion crystals with (−)-**6c**, as shown in Figure 17. In the inclusion crystal of **399b** with (−)-**6b**, conrotatory photocyclization of **399b** with a positive torsion angle for C7−N6−C14−C15 will occur in a way that the hydrogens at C8 and C20 do not come into collision. Afterward a 1,5-hydrogen shift will occur in a suprafacial manner to give (*R*,*R*)-(+)-**400b**. (*S*,*S*)-(−)-**400b** will be obtained in a similar way upon photoirradiation of **399b** with a negative torsion angle for C7−N6−C14−C15 in its inclusion crystal with (−)-**6c**. These assignments are supported by the known absolute configuration of the photoproducts.[151]

Table 34. Photocyclization of 402 in a 2:1 Inclusion Compound with 6

host	guest	product		
			yield (%)	opt purity (%)
(–)-**6b**	**402a**	**403a**	*a*	
(–)-**6b**	**402b**	**403b**	18	>99.9
(–)-**6b**	**402c**	**403c**	41	>99.9
(–)-**6b**	**402d**	**403d**	51	>99.9
(–)-**6c**	**402e**	**403e**	53	>99.9

[a] No reaction occurred.

Photoirradiation of inclusion crystals of 3-oxo-2-cyclohexanecarboxamide (**402a**) with the optically active host compound **6b** as a water suspension for 4 h gave optically active 2-aza-3,3-dimethyl-1,5-dioxaspiro[3,5]nonane (**403a**). Optically pure **403b**,**c** can be prepared by the combination of photoirradiation of **402b**,**c**, respectively, in their inclusion crystals with **6b** and purification of the reaction product via the oxime derivatives **404b**,**c** (Table 34).[154]

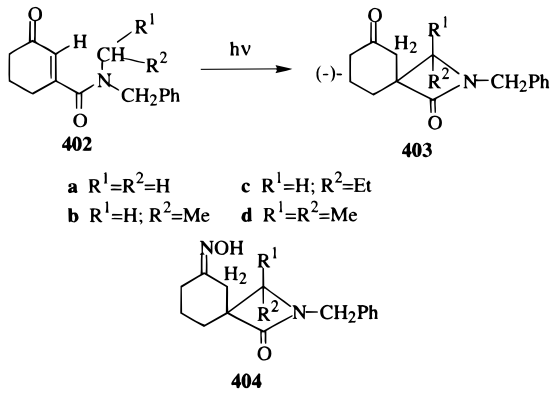
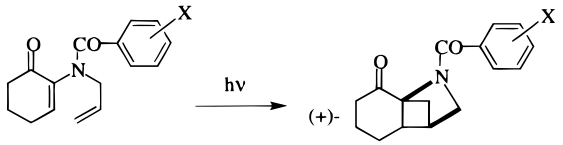


Table 35. Photocyclization of 405 in a 2:1 Inclusion Compound with 6

host	guest	product		
			yield (%)	$[\alpha]_D$ (deg) (*c* in CCl_4)
(−)-**6b**	**405a**	**406a**	64	+70 (0.10)
(−)-**6c**	**405a**	**406a**	81	+90 (1.32)
(−)-**6c**	**405b**	**406b**	71	+77 (0.85)
(−)-**6c**	**405c**	**406c**	65	+61 (0.53)

Intramolecular [2+2] photocyclization reactions are also controlled enantioselectively within inclusion crystals. Photoirradiation of inclusion crystals of the 2-[*N*-(2-propenyl)amino]cyclohex-2-enones **405** with the optically active host compound **6b** in the solid state gave the optically active 9-azatricyclo[5.2.1.$0^{1,6}$]-decan-2-ones **406** (Table 35).[154]

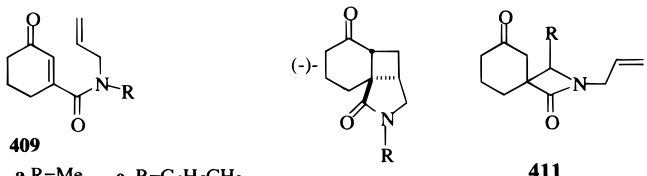


405 **a:** X=H **b:** m-Cl **c**: p-Me **406**

Photoirradiation of inclusion crystals of the 4-(3-butenyl)cyclohexa-2,5-dien-1-ones **407** with the optically active host compounds **6c** in the solid state gave optically active 1-carbomethoxytricyclo[4.3.1.$0^{7,10}$]dec-2-en-4-ones **408**.[154] For example, reaction of a powdered 2:1 inclusion crystal of **407a** with (−)-**6b** as a water suspension for 5 h gave (+)-**408a** of 73% ee in 50% yield. In the case of **407b**, enantioselective inclusion complexation occurred to give a 1:1 complex of optically pure (−)-**407b** with (−)-**6b**, and its irradiation in a water suspension gave optically pure (+)-**408b** in 57% yield.

407 a: $R^1 = R^2$ = OMe b: R^1 = OMe; R^2 = H **408**

Photoirradiation of the 1:2 inclusion compounds of **409a**−**g** with (−)-**6c** gave the optically active photocycloaddition products **410a**−**g** in high optical purity.



409

a R=Me **b** R=Et **c** R=Pr^n **d** R=Bu^n **e** R=$C_6H_5CH_2$ **f** R=*p*-$MeC_6H_4CH_2$ **g** R=*p*-$ClC_6H_4CH_2$

410 **411**

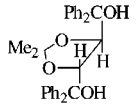
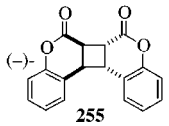
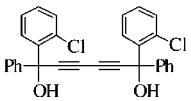
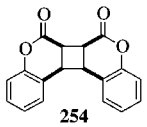
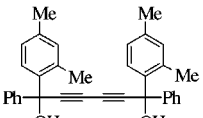
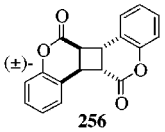
However, photoirradiation of the 1:2 inclusion compound of **409c** and (−)-**6c** gave the optically active spiro *β*-lactam **411c** of 97% ee in 69% yield (Table 36).[155]

Table 36. Photocyclization of 409 in a 1:2 Inclusion Compound with (−)-6c

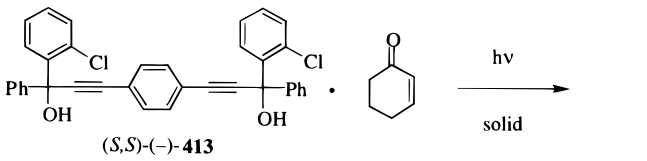
host	guest	product		
			yield (%)	opt purity (%)
(−)-**6c**	**409a**	**410a**	17	68
(−)-**6c**	**409b**	**410b**	30	67
(−)-**6c**	**409c**	**411c**	69	97
(−)-**6c**	**409d**	**410d**	25	53
(−)-**6c**	**409e**	**410e**	87	100
(−)-**6c**	**409f**	**410f**	56	100
(−)-**6c**	**409g**	**410g**	42	100

Regio- and enantioselective photodimerization of coumarin (**253**) was achieved in the inclusion complexes with (*R*,*R*)-(−)-**6a**, (*S*,*S*)-(−)-**13** and *meso*-**412**. (Table 37). For example, irradiation of the 1:1 inclu-

Table 37. Photodimerization of Coumarin

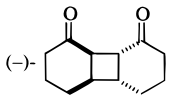
Host	H:G	Irradiation time (h)	Product	Yield (%)
 (*R*,*R*)-(−)-**6a**	1:1	1	 (−)- **255** *anti-head-to-head*	96
 (*S*,*S*)-(−)-**13**	1:2	5	 **254** *syn-head-to-head*	75
 *meso*-**412**	1:2	4	 (±)- **256** *anti-head-to-tail*	94

sion compound of coumarin with (*R*,*R*)-(−)-**6a** gave the anti-head-to-head dimer (−)-**253** of 96% ee in 96% yield.[156] On the other hand 1:2 inclusion crystal of (*S*,*S*)-(−)-**13** with **253** or the 1:2 inclusion crystal of *meso*-**412** with **253** afforded the syn-head-to-head-dimer **254** in 75% yield or anti-head-to-tail dimer (+)-**256** in 94% yield, respectively.[157] A suspension of the powdered 1:2 complex of (*S*,*S*)-(−)-**413** with cyclohexenone in a water containing a small amount of surfactant was irradiated for 24 h to give (−)-**414** of 48% ee. An optically pure sample of (−)-**414** was easily obtained by repeated complexation with (−)-**13**.[158]



(*S,S*)-(−)-**413**

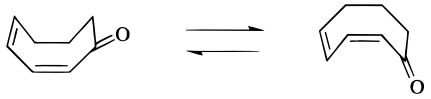
1:2 complex



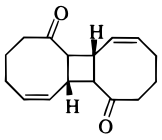
414

anti-head-to-head

Cycloocta-2,4-dien-1-one (**415**) exists as an equilibrium mixture of the conformers **415a**,**b** in solution, and conversion between these two enantiomeric forms is too fast to allow their isolation at room temperature. Photoreaction of **415** in pentane for 1 h gives racemic **416** in 10% yield along with polymers. When a solution of (−)-**13** and **415** was kept at room temperature for 12 h, a 3:2 inclusion complex of (−)-**13** with **415a** was obtained as colorless needles. Irradiation of the 3:2 complex of (−)-**13** with **415a** for 48 h gave (−)-**416** of 78% ee in 55% yield.[159] The chiral conformation of **415a** was determined by X-ray crystal structure analysis.[160]



415a **415b**



416

Enantioselective photocyclization of *N*-allylfuran-2-carboxanilide (**417**) in its inclusion crystals with the optically active host compound **6b** was accomplished successfully.[161] More interestingly, (−)-**418** and (+)-**418** were obtained selectively upon photoirradiations of the 1:1 and 2:1 complexes of **417** with (−)-**6b**, respectively. For example, photoirradiation of the powdered 1:1 complex of **417** with (−)-**6b** gave (−)-**418** of 96% ee in 50% yield. On the other hand, similar irradiation of the 2:1 complex of **417** with (−)-**6c** gave the other enantiomer (+)-**418** of 98% ee in 86% yield (Table 38). The chiral arrangement of **417**

Table 38. Photocyclization of 417 in the Inclusion Crystal with 6

host	H:G	product		
		compd	yield (%)	% ee
(−)-**6b**	1:1	(−)-**418**	50	96
(−)-**6b**	2:1	(+)-**418**	86	98
(−)-**6c**	2:1	(+)-**418**	77	98

molecules in the 1:1 and 2:1 complexes with (−)-**6b** were observed by measurement of their CD spectra

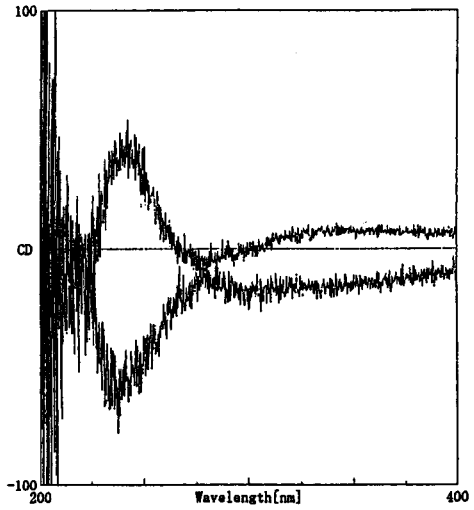


Figure 18. CD spectra of 1:1 complex of **417** with (a) (−)-**6b** and (b) (+)-**7b**.

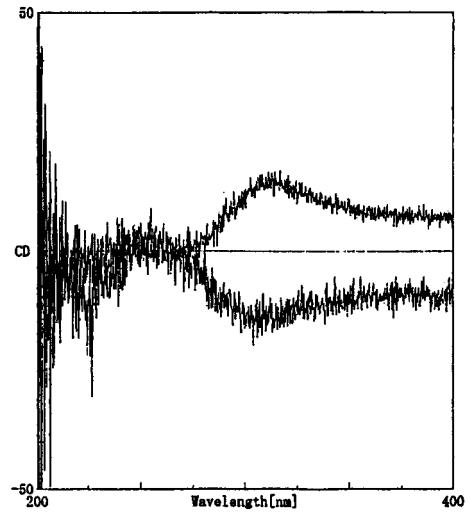
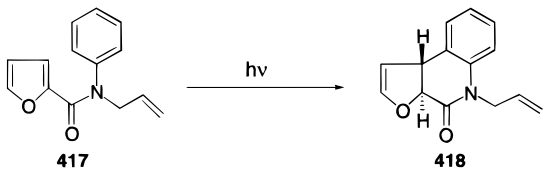


Figure 19. CD spectra of 1:2 complex of **417** with (a) (−)-**6b** and (b) (+)-**7b**.

as Nujol mulls (Figures 18 and 19). The CD absorptions of the 1:1 complex at 240 nm correspond to the UV absorption of **417** in MeOH at 256 nm. On the other hand, the CD absorptions of 2:1 complex at around 300 nm correspond to those of their UV absorptions in the solid state at 280 nm. These results indicate that **417** molecules in the 2:1 complex have more planar structure than do **417** molecules in MeOH solution and the 1:1 complex.

The 1:1 complexation was achieved by mixing the host and guest in the solid state, and the inclusion complexation was followed by measurement of CD spectra every 30 min in Nujol mull (Figure 20). For example, as the complexation between (−)-**6c** and **417** proceeds, the (+)- and (−)-Cotton effects ap-



417 **418**

peared at about 275 and 300 nm, respectively, and these absorptions increased until the complexation

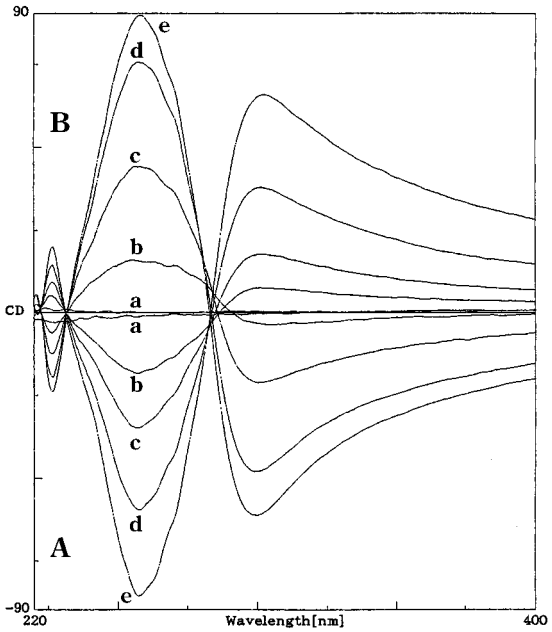


Figure 20. CD spectra of a 1:1 mixture of **417** with (−)-**6b** (A) or (+)-**7b** (B) after (a) 0 min, (b) 30 min, (c) 60 min, (d) 90 min, and (e) 120 min in Nujol mulls.

was completed after 2 h, although no absorption was present at the beginning of the mixing process.

Enantioselective photocyclization of 2-(arylthio)-3-methylcyclohexan-1-ones **419** to dihydrobenzothiophene derivatives **421** was also achieved in inclusion crystals using chiral host molecules.[162] Photoirradiation of the 1:1 inclusion crystals of **419g** with (−)-**6b** as a water suspension gave the corresponding photocyclization product (+)-*cis*-**421g** of 82% ee in 83% yield. Similar photoirradiation of the inclusion crystals of **419a**−**f** with (−)-**6b** afforded (+)-*cis*-**421b**−**f** of the optical purities listed in Table 39. X-ray crystal

Table 39. Photocyclization of 419 in the Inclusion Crystals with 6b

host	guest	product		
		compd	yield (%)	opt purity (% ee)
(−)-**6b**	**419a**	(+)-**421a**	90	32
(−)-**6b**	**419b**	(+)-**421b**	75	60
(−)-**6b**	**419c**	(+)-**421c**	92	62
(−)-**6b**	**419d**	(+)-**421d**	94	65
(−)-**6b**	**419e**	(+)-**421e**	85	77
(−)-**6b**	**419f**	(+)-**421f**	83	59
(−)-**6b**	**419g**	(+)-**421g**	83	82

structural analysis of the 1:1 inclusion complex of **419g** with (−)-**6b** showed the dihedral angle between the two average ring planes of the guest molecule to be about 74°. The photoreactive carbon C12 is 3.7 Å away from the target C3 on one side of the cyclohexenone ring plane, favoring the *R*-configuration at C3 (Figure 21). This assumption was ascertained by X-ray analysis of the photocyclization product (+)-**421g**. The chiral host molecule (−)-**6c** did not show strong absorption nor CD peaks in the 400−250 nm

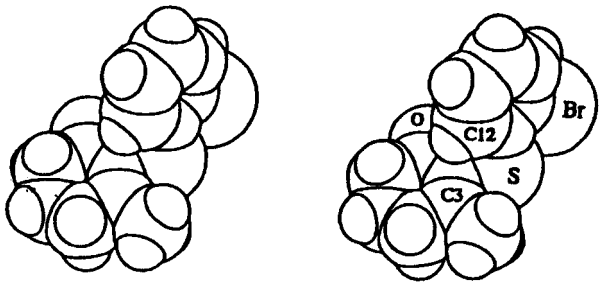


Figure 21. Molecular conformation of **419g** in the inclusion complex with (−)-**6b**.

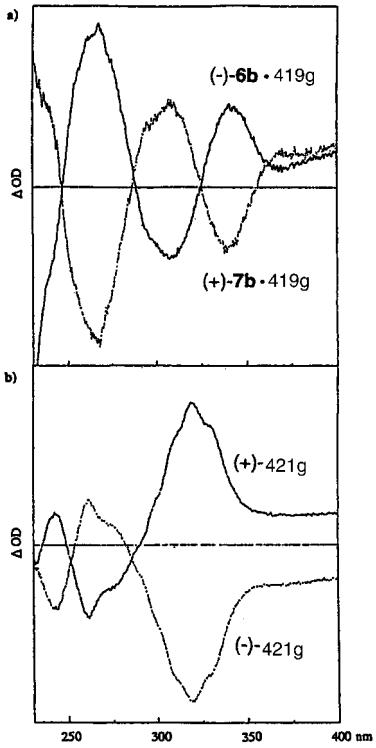
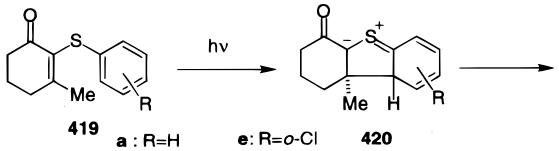


Figure 22. CD spectra of (a) inclusion complexes of **419g** with (−)-**6b** and (+)-**7b** and of (b) (+)-**421g** and (−)-**421g**.

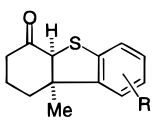
region. In contrast, the inclusion compound of prochiral molecules **419g** exhibited a rather strong CD spectrum (Figure 22). When cocrystallized with the opposite enantiomer, host (+)-**7b**, an almost mirror image solid-state CD spectrum was obtained. Solid-state CD spectra of the reaction product (+)-**421g** and its enantiomer also exhibited mirror image related CD spectra (Figure 22).



419

a: R=H **e**: R=*o*-Cl
b: R=*p*-Me **f**: R=*p*-Br
c: R=*o*-Me **g**: R=*o*-Br
d: R=*p*-Cl

420



(+)-cis-**421**

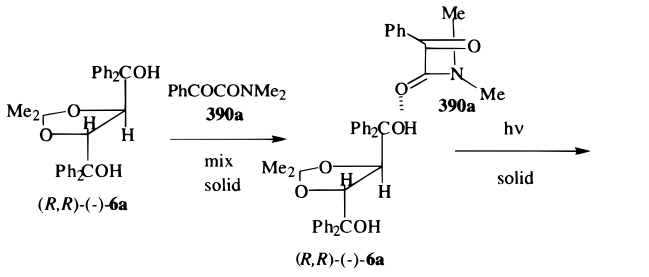
Host−guest inclusion complexes can be prepared by recrystallization of the host and guest compounds

from a solvent. In some cases, however, the inclusion complex is not formed by this method. In such cases, mixing of powdered host and guest compounds in the absence of solvent can give inclusion complexes.[163] For example, when the powdered 2:1 complex of (−)-**6a** with MeOH and *N*,*N*-dimethylphenylglyoxylamide (**390a**) were mixed for 1 h using an agate mortar and pestle, the mixture solidified to give the 2:1 inclusion complex crystal of (−)-**6a** and **390a**. Upon formation of this complex, the ν(OH) of **6a** (3550 and 3380 cm^{-1}) shifted to lower wavenumbers (3310 and 3250 cm^{-1}) due to hydrogen bond formation between the OH group of **6a** and the CO group of **390a** in the complex. Irradiation of the powdered 2:1 complex of (−)-**6a** and **390a** as a suspension in water for 10 h gave (+)-**391a** of 61% ee in 70% yield. On the other hand, (−)-**6b** formed a 1:1 inclusion complex with **390a** either by mixing in the solid state or by recrystallization from diethyl ether. Photoirradiation of these inclusion complexes in a water suspension gave (−)-**391a** and (−)-**392a** in the optical and chemical yields shown in Table 40. (−)-**6c** also formed a 2:1 inclusion

Table 40. Formation of Optically Active 391a and 392a by Irradiation for 10 h of the Inclusion Complexes of Chiral Host Compounds and 390a Prepared by Mixing in the Solid State or Recrystallization from Toluene

host	H:G	product via mixing			product via recrystallization		
		compd	yield (%)	% ee	compd	yield (%)	% ee
(−)-**6a**	2:1	(+)-**391a**	70	61			
(−)-**6b**	1:1	(−)-**391a**	29	82	(−)-**391a**	47	79
		(−)-**391a**	35	45	(−)-**392a**	23	42
(−)-**6c**	2:1	(+)-**391a**	48	41	(−)-**391a**	39	85

complex with **390a** by either the mixing or recrystallization methods; however, photoirradiation of these two complexes in an aqueous suspension gave (+)- or (−)-**391a**, respectively. It is very interesting that the direction of the chiral arrangement of **390a** in the complexes with (−)-**6c** changes depending on the preparation method used.



Most interestingly, interconversion between the molecular arrangement of **390e** in the (−)- and (+)-

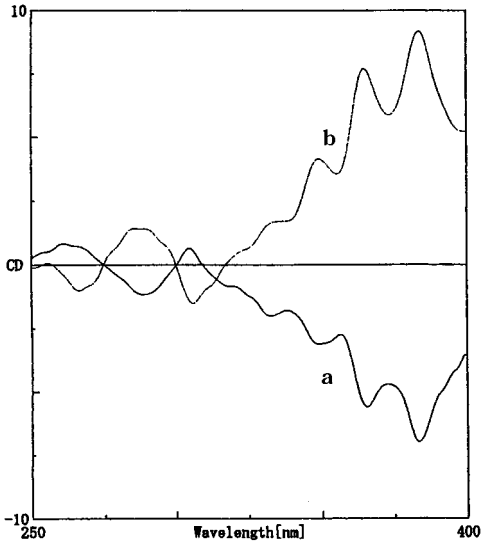


Figure 23. CD spectra of the (a) (*S*)-(−)- and (b) (*R*)-(+)-**390e** crystals.

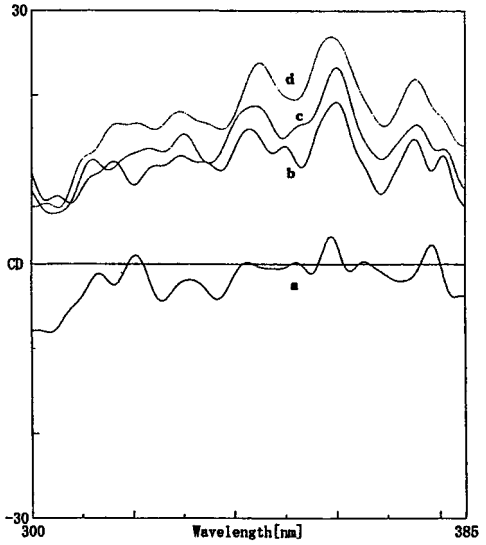


Figure 24. CD spectra of a mixture of (*S*)-(−)-**390e** and a 2:1 complex of (−)-**6b** with MeOH in Nujol mulls after (a) 0 min, (b) 30 min, (c) 60 min, and (d) 180 min.

forms easily occurs by complexation with the chiral host (−)-**6c** in the solid state.[164] By mixing of the powdered 1:1 MeOH complex of (−)-**6c** and powdered (−)-crystals of **390e**, 1:1 inclusion crystals of (−)-**6c** and (+)-**390e** were formed. The (+)-arrangement of **381e** in the above inclusion crystals can be proven by its photoirradiation in a water suspension for 5 h which gives (+)-**391e** of 76% ee in 72% yield, and its absolute configuration was determined by X-ray analysis. The chirality of **390e** was also easily detected by measurement of CD spectra in Nujol mulls as shown in Figure 23. The conversion of (*S*)-(−)-**390e** into (*R*)-(+)-**390e** during the complexation in the solid state was observed by continuous measurement of CD spectra as Nujol mulls. As the complexation proceeds, strong CD spectra showing a (−)-Cotton effect due to (*S*)-(−)-**390e** are gradually converted into spectra showing the (+)-Cotton effect of (*R*)-(+)-**390e** (Figure 24). This reaction was also

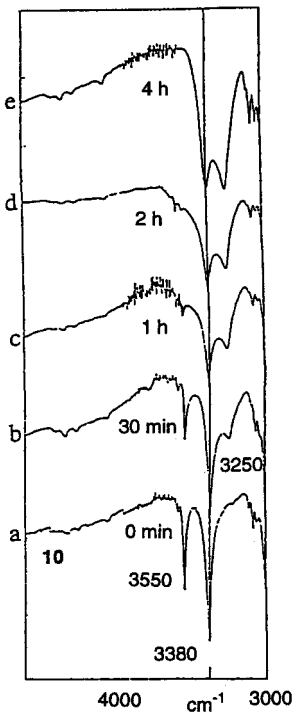
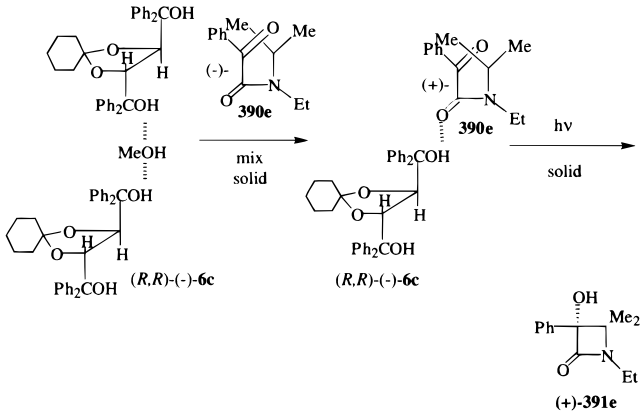


Figure 25. IR spectra of a mixture of (*S*)-(−)-**390e** and a 2:1 complex of (−)-**6b** with MeOH in Nujol mulls.

monitored by recording IR spectra as Nujol mulls (Figure 25).



Mixing of powdered thiocoumarin (**257**) and the optically active host compound (*R*,*R*)-(−)-**6b** in the solid state gave their 1:1 complex, in which the former molecules are arranged in a chiral form. Photoirradiation of these 1:1 inclusion crystals in the solid state gave the optically active anti-head-to-head dimer (+)-**259** of 100% ee in 73% yield. The inclusion complexation of **257** and (−)-**6b** was followed by continuous measurement of CD spectra as Nujol mulls.[165] Although a mixture of **257** and (−)-**6b** in Nujol did not show a clear CD absorption initially, induced CD absorption of **257** appeared and increased as the complexation proceeded (Figure 26). The enantioselective photodimerization reaction of **257** was also followed by CD spectral measurement. CD absorptions at 260, 320, and 370 nm due to **257** in the inclusion crystal disappeared and the new CD absorptions of 259 at 270 and 330 nm appeared after 5 min photoirradiation (Figure 27).

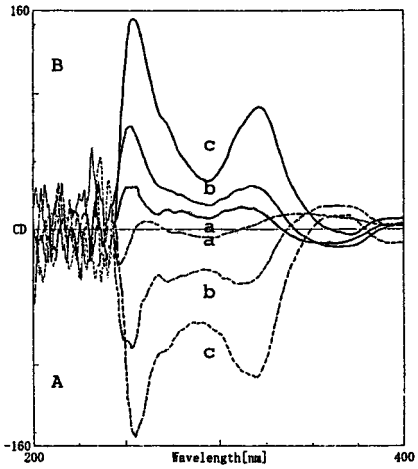


Figure 26. CD spectra of a mixture of (−)-**6b** (A) or (+)-**7b** (B), **257**, and liquid paraffin after (a) 0 min, (b) 30 min, and (c) 60 min.

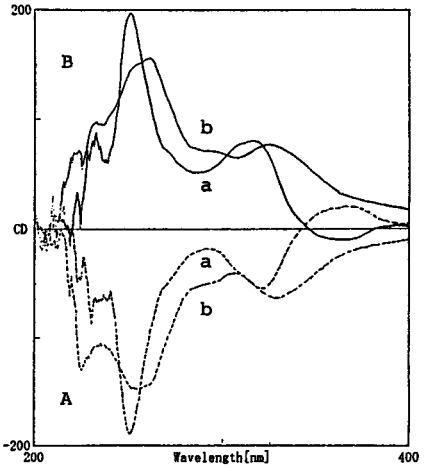
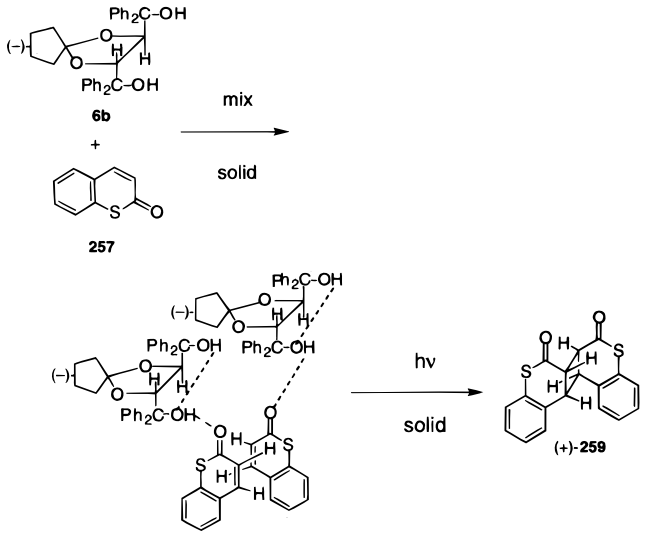
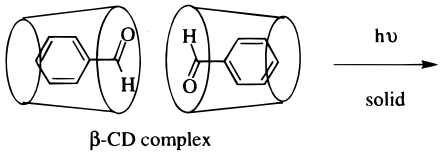


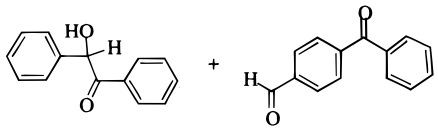
Figure 27. CD spectra of a 1:1 complex of **257** with (−)-**6b** (A) or (+)-**7b** (a) before and (b) after photoirradiation for 5 min.



Irradiation of solid β-cyclodextrin complexes of benzaldehyde produces optically active benzoin **422** of 15% ee in 56% yield along with the byproduct **423**.[166]

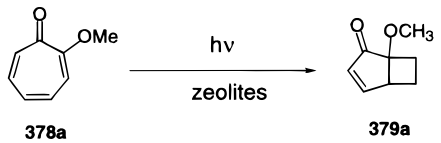


β-CD complex

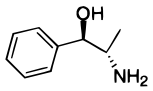


422 **423**

Chirally modified zeolites can also act as chiral host for asymmetric photoreaction. For example, a mixture of tropolone methyl ether **378a**, (−)-norephedrine, and zeolite (NaY) in dichloromethane−hexane was stirred for 12 h and filtered to give the zeolite containing both the reactant and a chiral inductor. Photoirradiation of the zeolite as a hexane slurry for 2 h gave the optically active photocyclization product **379a** of up to 50% ee.[167]



378a **379a**

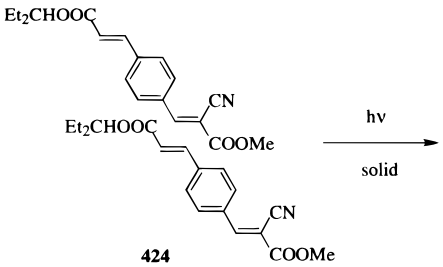


(−)-Norephedrine

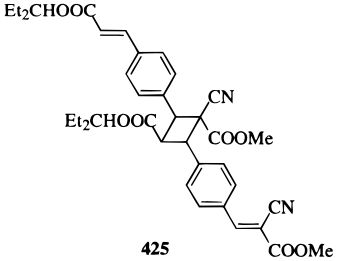
3. Enantioselective Photoreaction of Achiral Molecules in Their Chiral Crystals

Several successful examples of so-called "absolute" asymmetric synthesis by using chiral crystals of achiral molecules in the absence of any external chiral source have been found recently, and they provide an attractive and new method for asymmetric synthesis. It is also highly relevant in relation to the origin of optically active compounds on the earth.

The 1,4-disubstituted phenylenediacrylate derivative **424** crystallizes in the chiral space group $P2_1$ and gives the optically active dimer **425** of 100% ee upon irradiation in the solid state.[168]

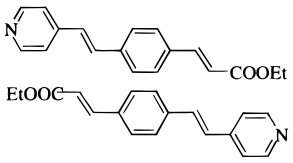


424

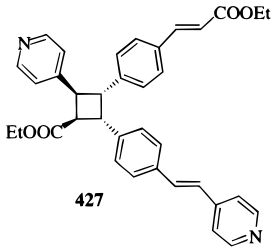


425

Chiral crystals of ethyl 4-[2-(4-pyridyl)ethenyl]-cinnamate (**426**) afford upon photoirradiation the optically active dimer **427** of 90% ee, while the corresponding methyl ester gave a highly crystalline linear polymer through a typical [2+2] topochemical photopolymerization.[169]

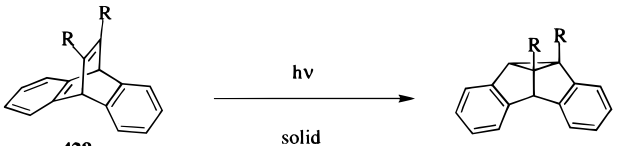


426



427

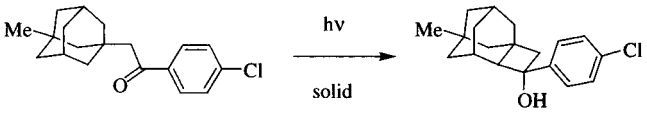
Recrystallization of the compound **428a** from cyclohexane affords chiral crystals of space group $P2_12_12_1$. Irradiation of these chiral crystals in the solid state gives rise to the enantiomerically pure di-π-methane photorearrangement product **429a**. The ethanol complex of **428b** also crystallizes in a chiral space group ($P2_12_12_1$) and afforded the optically active product **429b** of 89% ee on photolysis.[170]



428
a: R = COO*i*-Pr
b: R = $POPh_2$

429

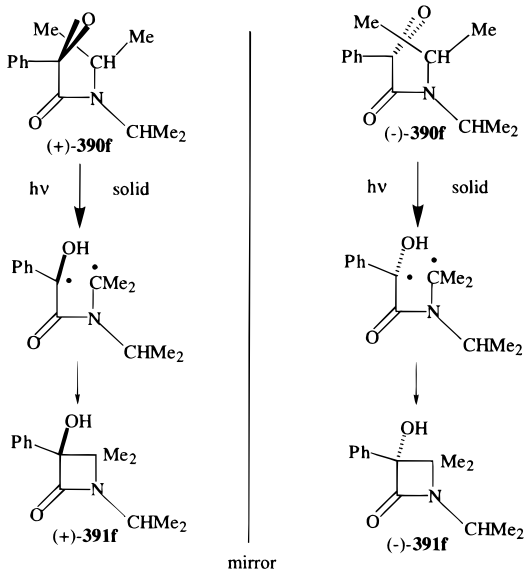
The chiral crystals of α-(3-methyladamantyl)-*p*-chloroacetophenone (**430**) give, upon irradiation, the optically active cyclobutanol **431** of about 80% ee.[170]



430 **431**

N,*N*-Diisopropylbenzoylformamide (**390f**) forms chiral crystals which give the optically active *β*-lactam derivative **391f** of high optical purity upon photoirradiation in the solid state.[171] Recrystallization of **390f** from benzene afforded colorless prisms. Crystals of **390f** which give (+)- and (−)-**391f** on photocyclization have been tentatively identified as the (+)- and (−)-crystal forms of **390f**, respectively. Large amounts of the (+)- and (−)-crystals of **390f** can easily be prepared by seeding with finely powdered (+)- and (−)-crystals, respectively, during recrystalization of **390f**. Irradiation of (+)-crystals of **390f** with a 400 W high-pressure Hg lamp for 40 h

Scheme 2



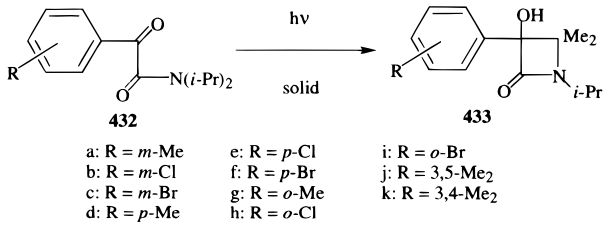
at room temperature gives (+)-**391f** of 93% ee in 74% yield. Irradiation of (−)-crystals of **390f** under the same conditions gives (−)-**391f** of 93% ee in 75% yield. X-ray crystal structural analysis of a (+)-crystal of **390f** shows that molecules of **390f** are twisted around the CO−CO bond in the chiral crystal and hence photocyclization gives optically active **391f** (Scheme 2).

Interestingly, the formation of such chiral crystals depends on the substituent on the benzene ring of the phenylglyoxylamide.[172] All the meta-substituted *N*,*N*-diisopropylphenylglyoxylamides **432a**−**c** tested formed chiral crystals, and their photoirradiation in the solid state gave the optically active *β*-lactams **433a**−**c**, respectively. The optical purity and yield for these products are shown in Table 33. However, all the para-substituted isomers tested, **432d**−**f**, did not form chiral crystals, and these gave rac-*β*-lactams upon photoirradiation (Table 41). On the other hand,

Table 41. Photocyclization of Substituted Phenylglyoxylamides in Their Crystals

phenylglyoxylamide	irradiation time (h)	yield (%)	opt purity (% ee)
432a	7	63	91
432b	10	75	100
432c	5	97	96
432d	5	60	0
432e	5	50	0
432f	12	65	0
432g	10	54	9
432h	24	42	0
432i	24	48	0
432j	5	74	0
432k	5	62	54

although *ortho*-methyl-substituted phenylglyoxylamide **432g** formed chiral crystals and gave optically active **433g** on irradiation, the *ortho*-chloro-**432h** and the *ortho*-bromo-substituted compound **432i** did not form chiral crystals and gave *rac*-**433h** and **433i**, respectively. However, meta-substituted phenylglyoxylamide **432j** did not form chiral crystals, and its photoreaction gave *rac*-**433j**, although the meta, para-disubstituted one **432k** formed chiral crystals and gave optically active **433k** (Table 41). When the isopropyl group of **432** is replaced with other alkyl groups such as benzyl or cyclohexyl, no chiral crystals are formed, and photoirradiation of these derivatives gave *rac*-*β*-lactams. Hence the isopropyl group may play an important role in formation of these chiral crystals.



To elucidate the process of asymmetric photocyclization, the crystal structures of **432b**,**e**,**h** were determined. (Table 42). When the crystal of **432e** is

Table 42. Crystal Data for 432b, 432e, and 432h

crystal data	432h	432b	432e
cryst system	monoclinic	orthorhombic	orthorhombic
space group	$P2_1/n$	$P2_12_12_1$	$Pbca$
Z	4	4	8
a (Å)	9.582	12.800	15.177
b (Å)	21.494	14.941	15.558
c (Å)	7.591	7.611	12.555
β (°)	111.40	–	–
V (Å^3)	1455.6	1455.6	2964.6

irradiated with UV light, a radical is probably produced at the oxygen, O1, of the carbonyl group. The oxygen radical produced should abstract the hydrogen atom H9 of the isopropyl group to form a hydroxy group. The radical produced at C9 due to this abstraction of H9 would then attack the C7 atom to form a C−C single bond. This forms a *β*-lactam ring as shown in Figure 28. The absolute structures

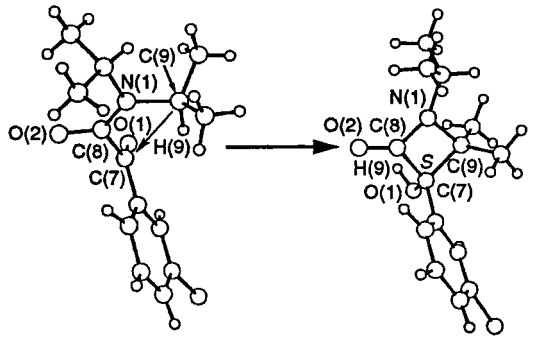


Figure 28. Process of enantioselective photocyclization of **432b** to **433b**.

of **432b** and **433b** in Figure 28 are in agreement with those determined with anomalous dispersion terms

for the chlorine atoms. If the radical C9 attacks the atom C7 from the *si*-face of the carbonyl group as shown in Figure 28, the β-lactam produced should have the *S* configuration, which is in agreement with the experimental result. This mechanism also explain why racemic β-lactams were produced from the crystals of **432e**,**h**. Since both crystals have a center of symmetry, both chiral enviroments for the starting material exist in the crystals. This brings about the racemic product after the photocyclization.

The photoconversion of the *m*-bromophenyl derivative **432c** (which shows relatively strong CD absorptions) to the corresponding β-lactam **433c** was followed by CD spectral measurement. As shown in Figure 29, CD spectra due to the chiral crystal of

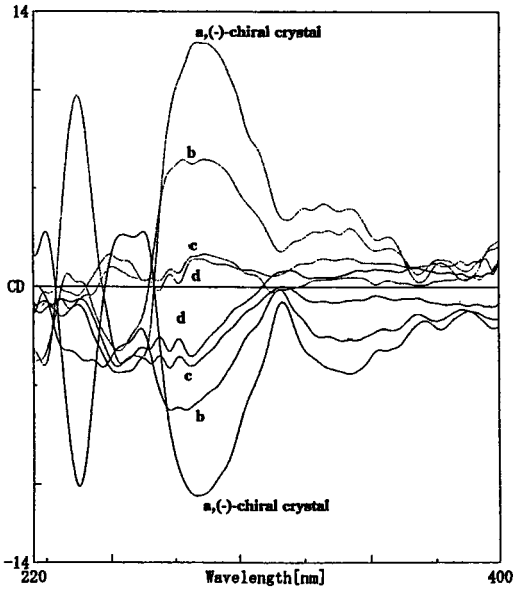
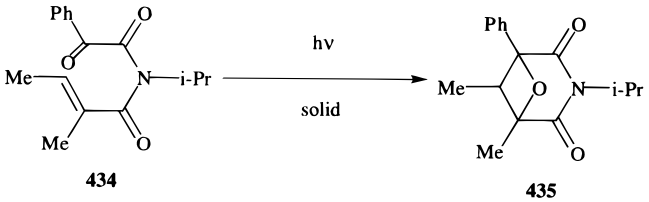


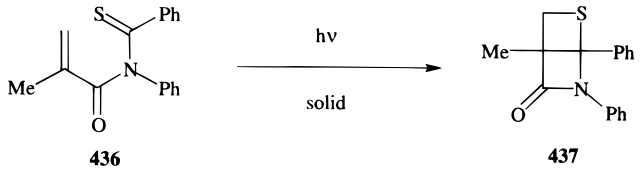
Figure 29. Photoconversion of (+)- and (−)-**432c** to (+)- and (−)-**433c**, respectively, by continuous measurements of CD spectra in Nujol mulls, after (a) 0 min, (b) 2 min, (c) 4 min, and (d) 6 min of irradiation.

432c in Nujol turn into the weak absorptions of **433c** as the photoreaction proceeds. Photolysis of chiral crystals of the achiral *N*-isopropyl-*N*-tiglylbenzoylformamide (**434**) in the solid state at 0 °C proceeded by [2+2]cycloaddition to give the chiral oxetane **435** of 35% ee in 84% yield. This solid-state photoreaction proceeds even at −78 °C to give **435** in higher optical purity of 95% ee.[173]



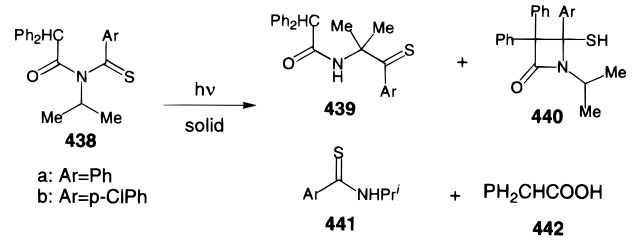
434 **435**

When powdered chiral crystals of the monothioimide **436** were irradiated under nitrogen at 0 °C for 12 h, the optically active β-lactam **437** of 10% ee was obtained in 75% yield. This solid-state photoreaction proceeds even at −45 °C, and optically active **437** of 40% ee was formed in 70% yield.[174]

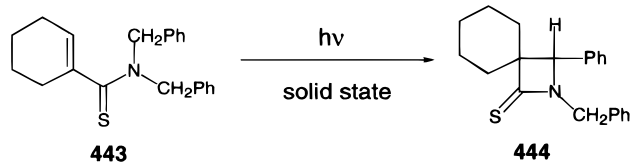


436 **437**

N-(Diphenylacetyl)-*N*-isopropylthiobenzamide (**438**) forms chiral crystals which give the optically active β-lactam **440** of 20% ee, along with byproducts (**439**, **441**, and **442**), upon photoirradiation at −45 °C in the solid state.[175]



Crystal-to-crystal absolute asymmetric photoreaction of α,β-unsaturated thioamide **443** to β-thiolactam **444** was also reported. Powdered crystals of **443** were irradiated (500 W Hg lamp, 0 °C, 2 h) to give the optically active β-thiolactam **444** of 94% ee in 96% yield at 58% conversion. The solid-state photoreaction was found to proceed crystal-to-crystal manner right up to 100% reaction conversion.[176]



443 **444**

The achiral molecule 3,4-bis(diphenylmethylene)-succinimide (**445**) was found to arrange itself in a chiral form in the crystalline state.[177] The chirality of **445** was frozen by photoirradiation in the solid state to give the optically active photocyclization product **447**. Recrystallization of **445** from acetone formed chiral crystals as orange hexagonal plates (A converts to C by heating at 260 °C) and two types of racemic crystals as orange rectangular plates (B, mp 302 °C) and yellow rectangular plates (C, mp 297 °C) (Figure 30). The chirality of the crystal **A** can be easily detected by measurement of its CD spectra in Nujol mulls. The crystal **A** exhibits strong CD absorptions at around 250 and 330 nm, while the crystal types **B** and **C** do not show any CD absorption in these regions (Figure 31).

Irradiation of powdered (+)-**A** crystals using a 100 W high-pressure Hg lamp for 50 h gave (+)-**447** of 64% ee in quantitative yield. Similar irradiation of (−)-**A** crystals gave (−)-**447**. However, photoirradiation of crystals **B** and **C** gave racemic **447**. This enantioselective photoconversion consists of two steps, the conrotatory ring closure of **445** to the intermediate **446** and then a 1,5-hydrogen shift to give the product **447**. X-ray crystal structure analysis disclosed that crystal **A** consists of **445** molecules in either a purely right-handed or a purely left-handed

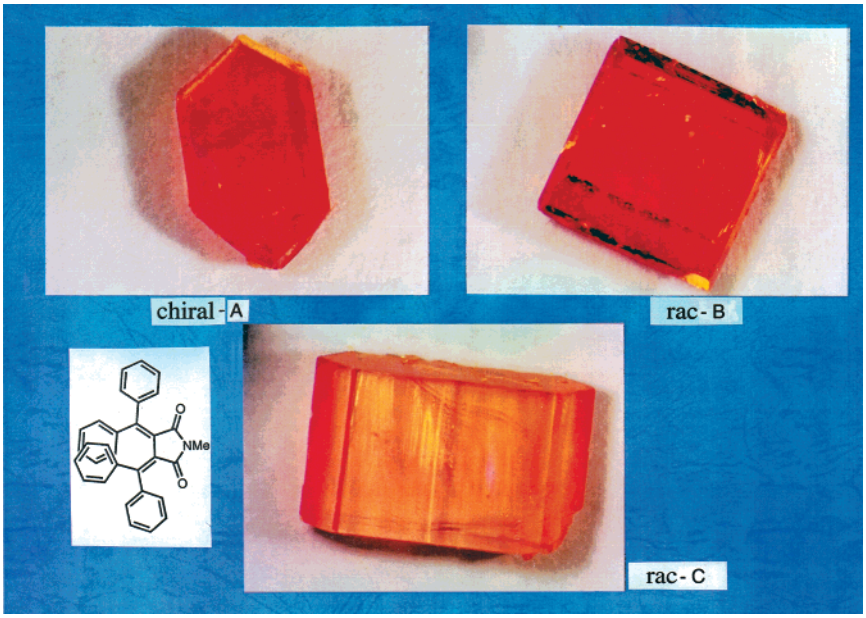


Figure 30. Photographs of three crystal modifications of **445**.

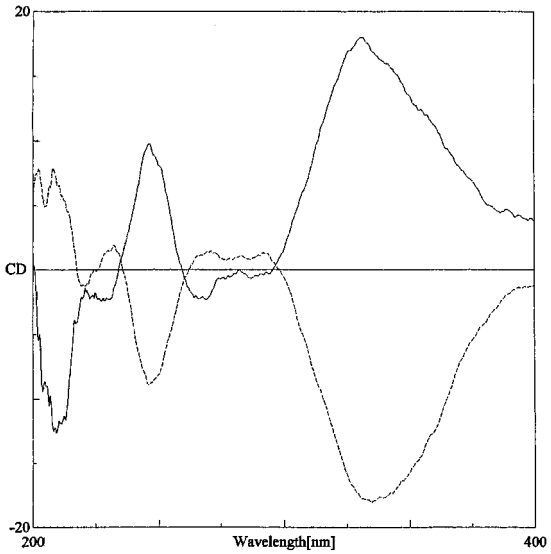
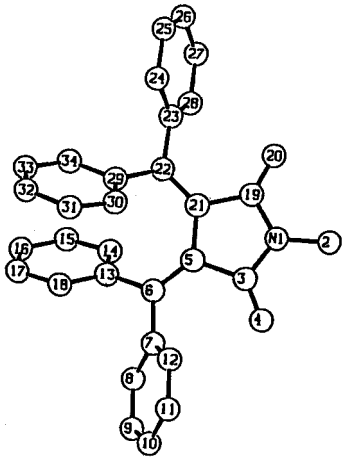


Figure 31. CD spectra of two enantiomeric crystal of **445A**.

helical configuration (Figure 32). Crystals **B** and **C** contain equal amounts of the two configurations and,



hence, are racemic (Figures 33 and 34). The phenyl rings a and a′ are almost parallel to one another and

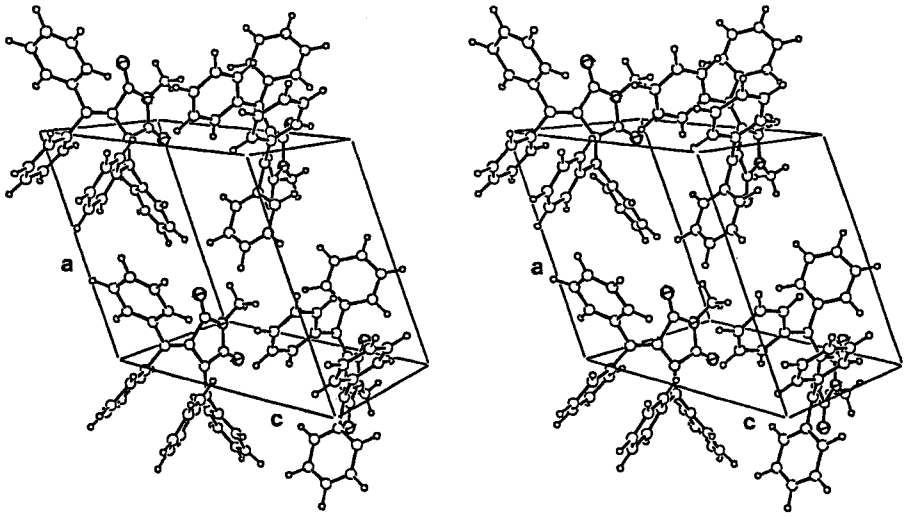


Figure 32. Stereoview of the molecular packing of **445A**.

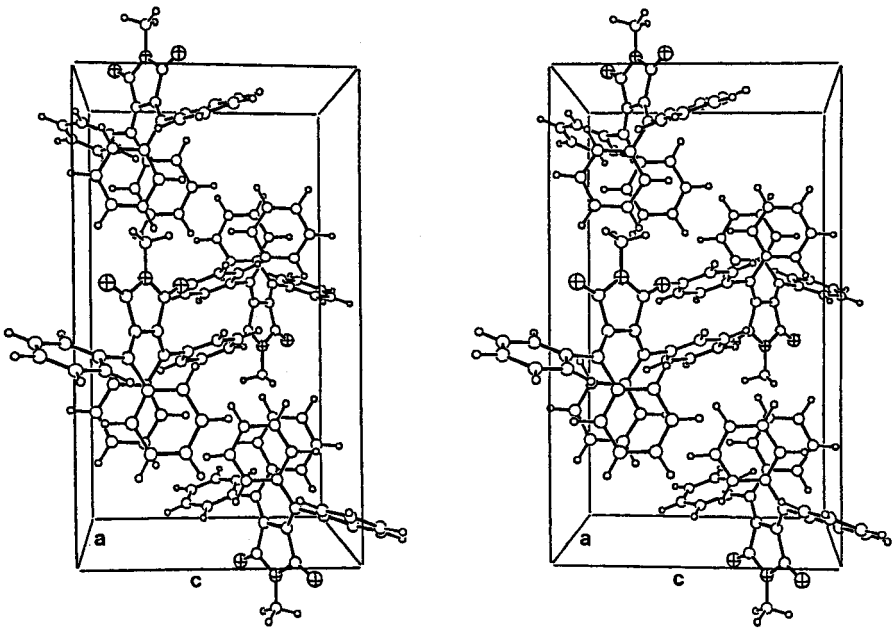


Figure 33. Stereoview of the molecular packing of **445B**.

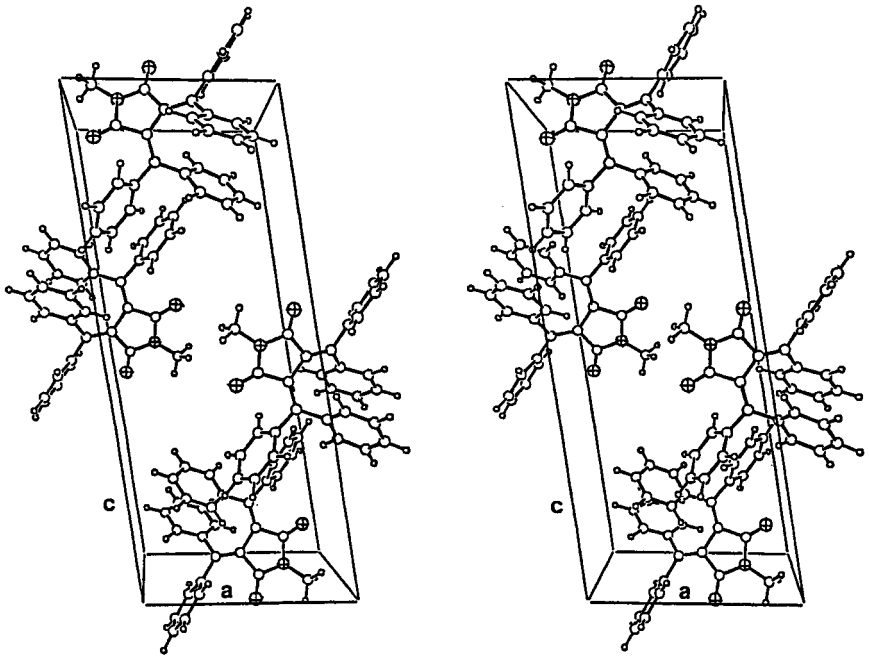


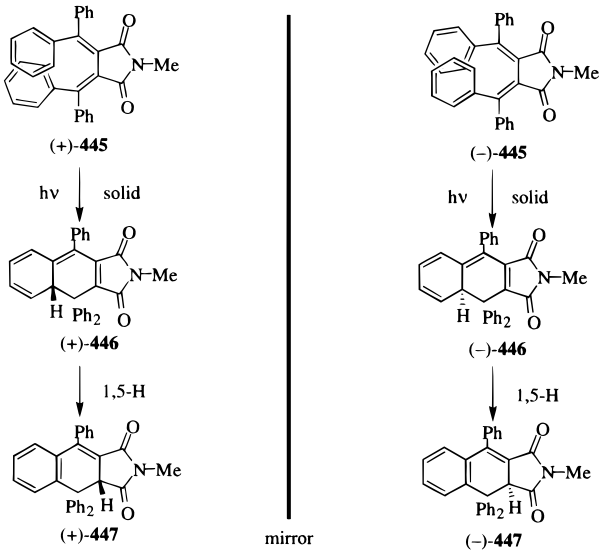
Figure 34. Stereoview of the molecular packing of **445C**.

Table 43. Crystal Data and Selected Structural Parameters of Three Polymorphic Crystals of 445

cryst data	A	B	C
cryst system	monoclinic	orthorhombic	monoclinic
space group	$P2_1$	*Pbcn*	$P2_1/n$
a (Å)	11.640	9.964	9.485
b (Å)	9.257	20.181	11.014
c (Å)	12.103	11.622	22.945
intramolecular nonbonding dists (Å)			
C(6)•••C(30)	3.381	3.353	3.348
C(14)•••C(22)	3.273	3.353	3.338
torsion angles (°)			
C(6)–C(5)–C(21)–C(22)	38.8	34.7	43.2
C(4)–C(3)–C(5)–C(6)	19.6	13.7	20.2
C(20)–C(19)–C(21)–C(22)	14.3	13.7	20.9

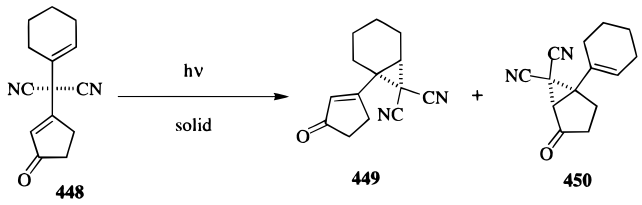
overlap significantly: the dihedral angles between these rings are within the range 9−12° (Table 42). The corresponding distances between the unsaturated carbon sites which join during the photoreaction, C6···C30 and C14···C22, are 3.38 and 3.27 Å in **A**, 3.35 Å in **B**, and 3.35 and 3.34 Å in **C** (Table 43). These values match perfectly well the topochemical requirements of the photoreaction in the solid state.

Transformations between the different polymorphs can easily be accomplished both in the solid state and in solution. Addition of one piece of (−)-**A** crystal during the recrystallization of (+)-**A** crystal (50 mg) from acetone gave (−)-**A** (23 mg), **B** (4 mg), and **C** crystals (8 mg). The thermal racemization of **A** to **C** occurs before melting, by heating to 260 °C on a hot plate. During this process the color change from orange to yellow spreads dramatically from one end

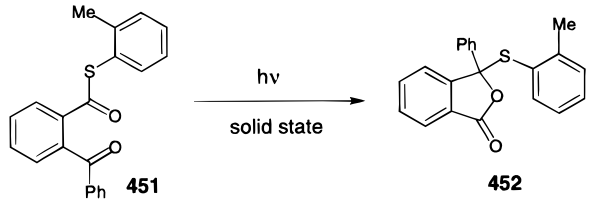


of the crystal to the other with retention of the crystal morphology.

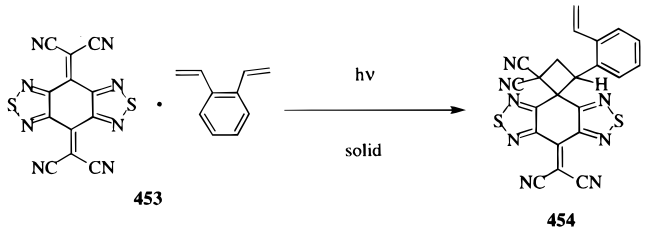
Solid-state photochemical di-π-methane-type rearrangement of chiral crystals of **448** have been found to give **449** and **450** in 44% ee and 96% ee, respectively.[178]



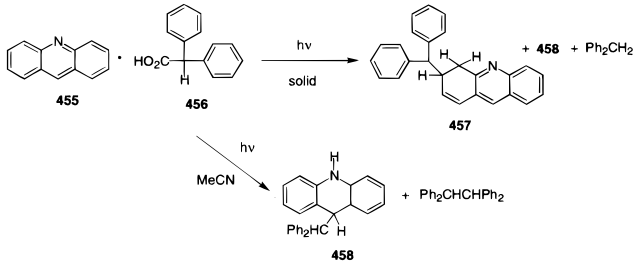
Absolute asymmetric photocyclization of an achiral *S*-aryl o-benzoylbenzothioate to an optically active phthalide via phenyl migration upon photoirrathiation in the solid phase has been reported. The thioester **451** was irradiated with UV light at 0 °C for 6 h to give the optically active phthalide **452** of 30% ee in 65% yield.[179]



Optically active [2+2] cycloadduct **454** was found to be formed in 95% ee upon irradiation of chiral crystals of the CT complex between bis([1,2,5]-thiadiazolo)tetracyanoquinodimethane (**453**) and *o*-divinylbenzene.[180]



Photoirradiation of a two-component chiral crystal of acridine **455** and diphenylacetic acid **456** in the solid state gives the optically active product **457** of about 35% ee via photodecarboxylative condensation.[181] In contrast to the solid-state photoreaction, irradiation of a solution of **455** and **456** in acetonitrile gives the achiral condensation product **458** along with 1,1,2,2-tetraphenylethane.



V. Conclusion

As described in the previous chapters, there is no doubt that molecules can move quite freely in the solid state and even enantioselectively. It is also clear that organic reactions can occur by mixing powdered reactant and reagent in the absence of solvent and that reaction products can be obtained efficiently. In some cases, organic synthesis can be accomplished without using any solvent throughout the processes of reaction and isolation of product. When a chiral host compound is used for the solid-state reaction of prochiral guest, enantioselective thermal and photochemical reactions can be carried out. The most interesting enantioselective photosynthesis is that involving irradiation of chiral crystals of achiral compounds in which the molecules are arranged in a chiral form, although examples of this phenomenon are still rare.

Solvent-free thermal organic synthesis seems to be a highly useful technique, especially for industry. However, not all organic synthesis can be carried out in the absence of solvent. Some organic reactions proceed explosively in the solid state. In such cases, solvent is useful in order to mediate the reaction rate. Finally, it is always important to choose the best conditions for organic synthesis. For reactions that proceed moderately in the absence of solvent or in a water suspension, then solid-state reaction would be the better choice. For reactions that proceed vigorously in the solid state, then solution reaction in a nontoxic solvent would be better.

Anyway, the typical organic synthetic procedure which has long been carried out in solvent throughout the 19th and 20th centuries, should be modified to more modern, elegant, and safe versions in the 21st century.

VI. References

(1) Thomas, J. M.; Mori, S. E.; Desvergne, J.−P. *Adv. Phys. Org. Chem.* **1977**, *15*, 63. Thomas, J. M. *Pure Appl. Chem.* **1979**, *51*, 1065. Curtin, D. Y.; Paul, I. C. *Chem. Rev.* **1981**, *81*, 525. Gavezzoti, A.; Simonetta, M. *Chem. Rev.* **1982**, *82*, 1. Ramamurthy, V. *Tetrahedron* **1986**, *42*, 5753. Ramamurthy, V.; Venkatesan, K. *Chem. Rev.* **1987**, *87*, 433. *Organic Solid State Chemistry*; G. R., Desiraju, Elsevier: 1987. *The Design of Organic Solids*; G. R., Desiraju, Ed.; Elsevier: New York, 1989. *Photochemistry in Organized and Constraint Media*; Ramamur-

thy, V., Ed.; VCH: Weinheimn, Germany, 1991. Toda, F. *Synlett* **1993**, 303. Singh, N. B.; Singh, R. J.; Singh, N. P. *Tetrahedron* **1994**, *50*, 6441. Toda, F. *Acc. Chem. Res.* **1995**, *28*, 480. Kaupp, G. Cyclobutane Synthesis in the Solid State. In *CRC Handbook of Organic Photochemistry and Photobiology*; Horspool, W. M., Ed.; CRC Press: Boca Raton, FL, 1995, pp 50−63. Kaupp, G. In Comprehensive Supramolecular Chemistry; Davies, J. E. D., Ed.; Elsevier: Oxford, U.K., 1996, Vol. 8, pp 381−423. Olovsson, G.; Scheffer, J. R.; Trotter, J. *Pure Appl. Chem.* **1997**, *69*, 815. *Supramolecular Photochemistry*; Ramamurthy, V., Schanze, K., Eds.; Marcel Decker: New York, 1998.

(2) Toda, F.; Tanaka, K.; Sekikawa, A. *J. Chem. Soc., Chem. Commun.* **1987**, 279.
(3) Toda, F. J. *Synth. Org. Chem. Jpn.* **1990**, *48*, 494.
(4) Toda, F.; Tanaka, K.; Miyamoto, H.; Koshima, H.; Miyahara, I.; Hirotsu, K. *J. Chem. Soc., Perkin Trans. 2* **1997**, 1877.
(5) Kaftory, M.; Tanaka, K.; Toda, F. *J. Org. Chem.* **1985**, *50*, 2154.
(6) Toda, F.; Mori, K.; Matsuura, Y.; Akai, H. *J. Chem. Soc., Chem. Commun.* **1990**, 1591.
(7) Toda, F.; Takumi, H. *Enantiomer* **1996**, *1*, 29.
(8) Toda, F.; Sato, A.; Tanaka, K.; Mak, T. C. W. *Chem. Lett.* **1989**, 873. Kaupp, G.; Schmeyers, J.; Toda, F.; Takumi, H.; Koshima, H. *J. Phy. Org. Chem.* **1996**, *9*, 795.
(9) Toda, F.; Yagi, M.; Kiyoshige, K. *J. Chem. Soc., Chem. Commun.* **1988**, 958.
(10) Toda, F.; Takumi, H.; Nagami, M.; Tanaka, K. *Hetrocycles* **1998**, *47*, 469.
(11) Wei, Y.; Bakthavatchalam, R. *Tetrahedron Lett.* **1991**, *32*, 1535.
(12) Seebach, D.; Amstutz, R.; Laube, T.; Schweizer, W. B.; Dunitz, J. D. *J. Am. Chem. Soc.* **1985**, *107*, 5403.
(13) Tokitoh, N.; Arai, Y.; Sasamori, T.; Okazaki, R.; Nagase, S.; Uekusa, H.; Ohashi, Y. *J. Am. Chem. Soc.* **1998**, *120*, 433.
(14) Toda, F.; Kiyoshige, K.; Yagi, M. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 320.
(15) Epple, M.; Ebbinghaus, S.; Reller, A.; Gloistein, U.; Cammenga, K.; *Thermochim. Acta* **1995**, *269/270*, 433. Epple, M.; Ebbinghaus, S. *J. Thermal Anal.* **1998**, *52*, 165.
(16) Toda, F.; Mori, K. *J. Chem. Soc., Chem. Commun.* **1989**, 1245.
(17) Toda, F.; Tanaka, K. *Tetrahedron Lett.* **1988**, *29*, 551.
(18) Nassimbeni, L. R.; Niven, M. L.; Tanaka, K.; Toda, F. *J. Cryst. Spectrosc. Res.* **1991**, *21*, 451.
(19) Toda, F.; and Shigemasa, T. *Carbohydr. Res.* **1989**, *192*, 363.
(20) Mehta, G.; Khan, F. A.; Lakshmi, K. A. *Tetrahedron Lett.* **1992**, *33*, 7977.
(21) Marhand, A. P.; Reddy, G. M. *Tetrahedron* **1991**, *47*, 6571.
(22) Sabra, F.; Bassus, J.; Lamartine, R. *Mol. Cryst. Liq. Cryst.* **1990**, *186*, 69.
(23) Schmitt, A. *Liebigs Ann. Chem.* **1863**, *127*, 319.
(24) Kaupp, G. *Mol. Cryst. Liq. Cryst.* **1994**, *242*, 153. Kaupp, G.; Matthies, D. *Chem. Ber.* **1987**, *120*, 1897.
(25) Hamazaki, H.; Ohba, S.; Toda, F.; Takumi, H. *Acta Crystallogr.* **1997**, *C53*, 620.
(26) Tanaka, Y.; Sakuraba, H.; Oka, Y.; Nakanishi, H. *J. Incl. Phenom.* **1984**, *2*, 841.
(27) Penzien, K.; Schmidt, M. J. *Angew. Chem., Int. Ed. Engl.* **1968**, *8*, 608. Rabinovich, D.; Shakked, Z. *Acta Crystallogr.* **1974**, *B30*, 2829. Green, B. S.; Rabinovich, D.; Shakked, Z. *Acta Crystallogr.* **1981**, *B37*, 1376.
(28) Satish, B.; Panneerselvam, K.; Zacharias, D.; Desiraju, G. R. *J. Chem. Soc., Perkin Trans. 2* **1995**, 325.
(29) Diez-Barra, E.; de la Hoz, A.; Merino, S.; Sanchez-Verdu, P. *Tetrahedron Lett.* **1997**, *38*, 2359.
(30) Boruah, A.; Baruah, M.; Prajapati, D.; Sandhu, J. S. *Chem. Lett.* **1996**, 965.
(31) Kloetzel, M. C. *J. Am. Chem. Soc.* **1947**, *69*, 2271.
(32) Sakuraba, H.; Tanaka, Y.; Toda, F. *J. Incl. Phenom.* **1991**, *11*, 195.
(33) Toda, F.; Tanaka, K.; Sato, J. *Tetrahedron: Asymmetry* **1993**, *4*, 1771.
(34) Wei, Y.; Bakthavatchalam, R. *Tetrahedron Lett.* **1991**, *32*, 1535.
(35) Khruscheva, N. S.; Loim, N. M.; Sokolov, V. I.; Makhaev, V. D. *J. Chem. Soc., Perkin Trans. 1* **1997**, 2425.
(36) Toda, F.; Takumi, H.; Akehi, M. *J. Chem. Soc., Chem. Commun.* **1990**, 1270. Toda, F.; Okuda, K. *J. Chem. Soc., Chem. Commun.* **1991**, 1212.
(37) Naruchi, K.; Miura, M. *J. Chem. Soc., Perkin Trans. 2* **1987**, 113.
(38) Akutsu, F.; Aoyagi, K.; Nishimura, N.; Kudoh, M.; Kasashima, Y.; Inoki, M.; Naruchi, K. *J. Chem. Soc., Perkin Trans. 2* **1996**, 889.
(39) Nader, F. W.; Wacker, C.-D.; Irngartinger, H.; Huber-Patz, U.; Jahn, R.; Rodewald, H. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 852.
(40) Kishan, K. V. R.; Desiraju, G. R. *J. Org. Chem.* **1987**, *52*, 4641; Desiraju, G. R.; Kishan, K. V. R. *J. Am. Chem. Soc.* **1989**, *111*, 4838.
(41) Stowasser, B.; Hafner, K. *Angew. Chem. Int. Ed. Engl.* **1986**, *25*, 466.
(42) Toda, F.; Tanaka, K.; Tamashima, T.; Kato, M. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 2724.
(43) Toda, F.; Tanaka, K.; Hamai, K. *J. Chem. Soc., Perkin Trans. 1* **1990**, 3207.
(44) Schmeyers, J.; Toda, F.; Boy, J.; Kaupp, G. *J. Chem. Soc., Perkin Trans. 2* **1998**, 989.
(45) Toda, F.; Suzuki, T.; Higa, S. *J. Chem. Soc., Perkin Trans. 1* **1998**, 3521.
(46) Toda, F.; Takumi, H.; Yamaguchi, H. *Chem. Exp.* **1989**, *4*, 507.
(47) Tanaka, H.; Kishigami, S.; Toda, F. *J. Org. Chem.* **1991**, *56*, 4333.
(48) Toda, F.; Akai, H. *J. Org. Chem.* **1990**, *55*, 3446.
(49) Toda, F.; Imai, N. *J. Chem. Soc., Perkin Trans. 1* **1994**, 2673.
(50) Toda, F.; Kanemoto, K. *Hetrocycles* **1997**, *46*, 185.
(51) Albelt, C. J.; Pleier, J. M. *J. Org. Chem.* **1988**, *53*, 2159.
(52) Tanaka, H.; Kishigami, S.; Toda, F. *J. Org. Chem.* **1990**, *55*, 2982.
(53) Toda, F.; Tanaka, K.; Iwata, S. *J. Org. Chem.* **1989**, *54*, 3007.
(54) Higashizima, T.; Sakai, N.; Nozaki, K.; Takaya, H. *Tetrahedron Lett.* **1994**, *35*, 2023.
(55) Toda, F.; Tokumaru, Y. *Chem. Lett.* **1990**, 987.
(56) Loupy, A.; Sansoulet, J.; Zaparucha, A.; Merinne, C. *Tetrahedron Lett.* **1989**, *30*, 333.
(57) Wang, G.-W.; Murata, Y.; Komatsu, K.; Wan, T. S. M. *J. Chem. Soc., Perkin Trans. 1* **1996**, 2059.
(58) Wang, G.-W.; Komatsu, K.; Murata, Y.; Shiro, M. *Nature* **1997**, *387*, 583.
(59) Goud, B. S.; Desiraju, G. R. *J. Chem. Res., Synop.* **1995**, 244.
(60) Smith, K.; Musson, A.; DeBoos, G. A. *J. Chem. Soc., Chem. Commun.* **1996**, 469.
(61) Etter, M. C.; Frankenbach, G. M.; Bernstein, J. *Tetrahedron Lett.* **1989**, *30*, 3617.
(62) Ramesha, A. R.; Chandresekaran, S. *J. Chem. Soc., Perkin Trans. 1* **1994**, 767.
(63) Epple, M.; Seifert, R. *J. Solid State Chem.* **1996**, *121*, 129.
(64) Hagiwara, H.; Ohtsubo, S.; Kato, M. *Mol. Cryst. Liq. Cryst.* **1996**, *279*, 291.
(65) Tanaka, M.; Kobayashi, K. *J. Chem. Soc., Chem. Commun.* **1998**, 1965.
(66) Almena, I.; Díaz-Ortiz, A.; Díez-Barra, E.; Hoz, A.; Merino, S.; Loupy, A. *Chem. Lett.* **1996**, 333.
(67) Im, J.; Kim, J.; Kim, S.; Hahn, B. *Tetrahedron Lett.* **1997**, *38*, 451.
(68) Toda, F.; Hyoda, S.; Okada, K.; Hirotsu, K. *J. Chem. Soc., Chem. Commun.* **1995**, 1531.
(69) Ball, M. C. *J. Chem. Soc., Faraday Trans.* **1994**, *90*, 997.
(70) Okamura, M.; Hanano, M.; Awazu, S. *Chem. Pharm. Bull.* **1980**, *28*, 578.
(71) Wernick, D. L.; Savion, Z.; Levy, J. *J. Incl. Phenom.* **1988**, *6*, 483.
(72) Kanazawa, H. *Polymer* **1992**, *32*, 2557.
(73) Steinbrunn, M. B.; Wenz, G. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 2139.
(74) Epple, M.; Tröger, L. *J. Chem. Soc., Dalton Trans.* **1996**, 11.
(75) Toda, F.; Shigemasa, T. *J. Chem. Soc., Perkin Trans. 1* **1989**, 209.
(76) Kaupp, G.; Haak, M.; Toda, F. *J. Phys. Chem.* **1995**, *8*, 545.
(77) Bond, D. R.; Bourne, S. A.; Nassimbeni, L. R.; Toda, F. *J. Cryst. Spectrosc. Res.* **1989**, *19*, 809.
(78) Toda, F.; Tanaka, K.; Kagawa, Y.; Sakaino, Y. *Chem. Lett.* **1990**, 373.
(79) Toda, F.; Akai, H. *J. Org. Chem.* **1990**, *55*, 4973.
(80) Almena, I.; Diaz-Ortiz, A.; Diez-Barra, E.; Hoz, A.; Loupy, A. *Chem. Lett.* **1996**, 333. Caddick, S. *Tetrahedron* **1995**, *38*, 10403.
(81) Dessolin, M.; Golfier, M. *J. Chem. Soc., Chem. Commun.* **1986**, 38. Dessolin, M.; Eisenstein, O.; Golfier, M.; Prange, T.; Sautet, P. *J. Chem. Soc., Chem. Commun.* **1992**, 132.
(82) Tosato, M. L.; Soccorsi, L. *J. Chem. Soc., Perkin Trans. 2* **1982**, 1321.
(83) Venugoplan, P.; Venkatesan, K.; Klausen, J.; Novotny-Breggar, E.; Leumann, C.; Eschenmoser, A.; Dunitz, J. D. *Helv. Chim. Acta* **1991**, *74*, 662.
(84) Vyas, K.; Manohar, H.; Venkatesan, K. *J. Phys. Chem.* **1990**, *94*, 6069.
(85) Russell, C. S. *J. Solid State Chem.* **1987**, *69*, 43.
(86) Wiedemann, R.; Wolf, J.; Werner, H. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1244.
(87) McKillop, K.; Gillette, G. R.; Powell, D. R.; West, R. *J. Am. Chem. Soc.* **1992**, *114*, 5203.
(88) Dunitz, J. D.; Harris, K. D.; Johnston, R. L.; Kariuki, B. M., MacLean, E. J.; Psallidas, K.; Schweizer, W. B.; Tykwinski, R. R. *J. Am. Chem. Soc.* **1998**, *120*, 13274.
(89) Kaupp, G. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 592. Kaupp, G.; Haak, M. *Mol. Cryst. Liq. Cryst.* **1998**, *313*, 193. Kaupp, G.; Herrmann, A.; Haak, M. *Internet Photochem. Photobiol.* [Online] **1998**; http://www.photobiology.com/IUPAC98/page2.htm.
(90) Enkelmann, V.; Wegner, B. *J. Am. Chem. Soc.* **1993**, *115*, 10390.
(91) Harris, K. D.; Patterson, L. J. *J. Chem. Soc., Perkin Trans. 2* **1994**, 1201.
(92) Savion, Z.; Wernick, D. L. *J. Org. Chem.* **1993**, *58*, 2424.

(93) Ito, Y.; Borecka, B.; Trotter, J.; Scheffer, J. R. *Tetrahedron Lett.* **1995**, *36*, 6083. Ito, Y.; Borecka, B.; Olovsson, G.; Trotter, J.; Scheffer, J. R. *Tetrahedron Lett.* **1995**, *36*, 6087. Ito, Y.; B.; Olovsson. *J. Chem. Soc., Perkin Trans. 1* **1997**, 127.
(94) Feldman, K. S.; Campbell, R. F. *J. Org. Chem.* **1995**, *60*, 1924.
(95) Greiving, H.; Hopf, H.; Jones, P. G.; Bubenitschek, P.; Desvergne, J. P.; Bouas-Laurent, H. *J. Chem. Soc., Chem. Commun.* **1994**, 1075.
(96) Novak, K.; Enkelmann, V.; Wegner, G.; Wagener, K. B. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1614.
(97) Hasegawa, M.; Kinbara, K.; Adegawa, Y.; Saigo, K. *J. Am. Chem. Soc.* **1993**, *115*, 3820. Takeuchi, A.; Komiya, H.; Tsutsumi, Y.; Hashimoto, Y.; Hasegawa, M.; IItaka, Y.; Saigo, K. *Bull. Chem. Soc. Jpn.* **1993**, *66*, 2987.
(98) Diaz de Delgado, G. C.; Wheeler, K. A.; Snider, B. B.; Foxman, B. M. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 420.
(99) Mori, A.; Kato, N.; Takeshita, H.; Kurahashi, Y.; Ito, M. *J. Chem. Soc., Chem. Commun.* **1994**, 869.
(100) Robbins, R. J.; Falvey, D. E. *Tetrahedron Lett.* **1993**, *34*, 3509.
(101) Gnanaguru, K.; Ramasubbu, N.; Venkatesan, K.; Ramamurthy, V. *J. Org. Chem.* **1985**, *50*, 2337. Moorthy, J. N.; Venkatesan, K.; Weiss, R. G. *J. Org. Chem.* **1992**, *57*, 3292. Vishnumurthy, K.; Guru Row: T. N.; Venkatesan, K. *J. Chem. Soc., Perkin Trans. 2* **1996**, 1475. Vishnumurthy, K.; Guru Row, T. N.; Venkatesan, K. *J. Chem. Soc., Perkin Trans. 2* **1997**, 615.
(102) Klaus, C. P.; Thiemann, C.; Kopf, J.; Margaretha, P. *Helv. Chim. Acta* **1995**, *78*, 1079.
(103) Kohmoto, S.; Kobayashi, T.; Nishio, T.; Iida, I.; Kishikawa, K.; Yamamoto, M.; Yamada, K. *J. Chem. Soc., Perkin Trans. 1* **1996**, 529.
(104) Becker, H. D.; Langer, V.; Becker, H.-C. *J. Org. Chem.* **1993**, *58*, 6394.
(105) Hilgeroth, A. *Chem. Lett.* **1997**, 1269.
(106) Ito, Y.; Matsuura, T.; Tabata, K.; Ji-Ben, M. *Tetrahedron Lett.* **1987**, *43*, 1307.
(107) Saigo, K.; Sukegawa, M.; Maekawa, Y.; Hasegawa, M. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 2355.
(108) Rabinovich, D. *J. Chem. Soc. B* **1970**, 11.
(109) Ohkuma, K.; Kashino, S.; Haida, M. *Bull. Chem. Soc. Jpn.* **1972**, *46*, 627.
(110) Stobbe, H.; Brener, K. *J. Prakt. Chem.* **1929**, *123*, 241.
(111) Tanaka, K.; Toda, F. *J. Chem. Soc., Chem. Commun.* **1983**, 593. Kaftory, M.; Tanaka, K.; Toda, F. *J. Org. Chem.* **1985**, *50*, 2154.
(112) Toda, F.; Tanaka, K.; Kato, M. *J. Chem. Soc., Perkin Trans. 1*, **1998**, 1315.
(113) Tanaka, K.; Toda, F. *Nippon Kagakukaishi* **1984**, 141. Kuzuya, M.; Noguchi, A.; Yokota, N.; Okuda, T.; Toda, F.; Tanaka, K. *Nippon Kagakukaishi* **1986**, 1746. Fujiwara, T.; Tanaka, N.; Tanaka, K.; Toda, F. *J. Chem. Soc., Perkin Trans. 1* **1989**, 663.
(114) Gudmundsdottir, A. D.; Lewis, T. J.; Randall, L. H.; Scheffer, J. R.; Rettig, S. J.; Trotter, J.; Wu, C.-H. *J. Am. Chem. Soc.* **1996**, *118*, 6167.
(115) Zand, A.; Park, B.-S.; Wagner, P. J. *J. Org. Chem.* **1997**, *62*, 2326.
(116) Zimmerman, H.; Zuraw, M. J. *J. Am. Chem. Soc.* **1989**, *111*, 2358.
(117) Shin, S. H.; Keating, A. E.; Garcia-Garibay, M. A. *J. Am. Chem. Soc.* **1996**, *118*, 7626.
(118) Shin, S. H.; Cizmeciyan, D.; Keating, A. E.; Khan, S. I.; Garcia-Garibay, M. A. *J. Am. Chem. Soc.* **1997**, *119*, 1859.
(119) Maji, D.; Singh, R.; Mostafa, G.; Ray, S.; Lahiri, S. *J. Org. Chem.* **1996**, *61*, 5165.
(120) Pitchumani, K.; Velusamy, P.; Banu, H. S.; Srinivasan, C. *Tetrahedron Lett.* **1995**, *36*, 1149.
(121) Yelline, R. A.; Green, B. S.; Knossow, M.; Rysanek, N.; Tsoucaris, G. *J. Incl. Phenom.* **1985**, *3*, 317.
(122) Guarino, A.; Possagno, E.; Bassanelli, R. *J. Incl. Phenom.* **1987**, *5*, 563.
(123) Yamada, T.; Ohashi, Y. *Bull. Chem. Soc. Jpn.* **1998**, *71*, 2527.
(124) Kurihara, T.; Uchida, A.; Ohashi, Y.; Sasada, Y.; Ohgo, Y. *J. Am. Chem. Soc.* **1984**, *106*, 5718. Ohgo, Y.; Ohashi, Y. *Bull. Chem. Soc. Jpn.* **1996**, *69*, 2425. Ohhara, T.; Uekusa, H.; Ohashi, Y.; Tanaka, I.; Kumazawa, S.; Niimura, N. *Chem. Lett.* **1998**, 365.
(125) Hayashi, N.; Mazaki, Y.; Kobayashi, K. *Tetrahedron Lett.* **1994**, *35*, 5883.
(126) Choi, T.; Cizmeciyan, D.; Khan, S. I.; Garcia-Garibay, N. A. *J. Am. Chem. Soc.* **1995**, *117*, 12893.
(127) Choi, T.; Peterfy, K.; Khan, S. I.; Garcia-Garibay, N. A. *J. Am. Chem. Soc.* **1996**, *118*, 12477.
(128) Peterfy, K.; Garcia-Garibay, N. A. *J. Am. Chem. Soc.* **1998**, *120*, 4540.
(129) Tang, C. P.; Chang, H. C.; Popovitz-Biro, R.; Frolow, F.; Lahav, M.; Leiserowitz, L.; McMullan, R. K. *J. Am. Chem. Soc.* **1985**, *107*, 4058. Weisinger-Lewin, Y.; Vaida, R.; Popovitz-Biro, H. C.; Chang, F.; Manning, F.; Frolow, M.; Lahav, M.; Leizerowitz, L. *Tetrahedron* **1987**, *43*, 1452.
(130) Koshima, H.; Ichimura, H.; Matsuura, T. *Chem. Lett.* **1994**, 847.
(131) Koshima, H.; Chisaka, Y.; Wang, Y.; Yao, X.; Wang, H.; Wang, R.; Maeda, A.; Matsuura, T. *Tetrahedron* **1994**, *50*, 13617. Ito, Y.; Asaoka, S.; Saito, I.; Ohba, S. *Tetrahedron Lett.* **1994**, *35*, 8193. Koshima, H.; Ding, K.; Matsuura, T. *J. Chem. Soc., Chem. Commun.* **1994**, 2053.
(132) Haga, N.; Nakajima, H.; Takayanagi, H.; Tokumaru, K. *J. Chem. Soc., Chem. Commun.* **1997**, 1171. Haga, K.; Nakajima, H.; Takayanagi, H.; Tokumaru, K. *J. Org. Chem.* **1998**, *63*, 5372.
(133) Ito, Y.; Endo, S.; Ohba, S. *J. Am. Chem. Soc.* **1997**, *119*, 5974.
(134) Bosch, E.; Hubig, S. M.; Lindeman, S. V.; Kochi, J. K. *J. Org. Chem.* **1998**, *63*, 592.
(135) Schultz, A. G.; Taveras, A. G.; Taylor, R. E.; Tham, F. S.; Kulling, R. K. *J. Am. Chem. Soc.* **1992**, *114*, 8725.
(136) Gudmundsdottir, A. D.; Scheffer, J. R. *Photochem. Photobiol.* **1991**, *54*, 535.
(137) Jones, R.; Scheffer, J. R.; Trotter, J.; Yang, J. *Tetrahedron Lett.* **1992**, *33*, 5481.
(138) Leibovitch, M.; Olovsson, G.; Sundarababu, G.; Ramamurthy, V.; Scheffer, J. R.; Trotter, J. *J. Am. Chem. Soc.* **1996**, *118*, 1219. Leibovitch, M.; Olovsson, G.; Scheffer, J. R.; Trotter, J. *J. Am. Chem. Soc.* **1998**, *120*, 12755.
(139) Koura, T.; Ohashi, Y. *Bull. Chem. Soc. Jpn.* **1997**, *70*, 2417; Sekine, A.; Arai, Y.; Ohgo, Y.; Kamiya, N.; Iwasaki, H. *Bull Chem. Soc. Jpn.* **1995**, *68*, 2517. Ohgo, Y.; Arai, Y.; Hagiwara, M.; Takeuchi, S.; Kogo, H.; Sekine, A.; Uekusa, H.; Ohashi, Y. *Chem. Lett.* **1994**, 715.
(140) Toda, F.; Tanaka, K. *J. Chem. Soc., Chem. Commun.* **1986**, 1429. Toda, F.; Tanaka, K.; Yagi, M. *Tetrahedron* **1987**, *43*, 1493.
(141) Kaftory, M.; Yagi, M.; Tanaka, K.; Toda, F. *J. Org. Chem.* **1988**, *53*, 4391.
(142) Toda, F.; Tanaka, K. *Tetrahedron Lett.* **1988**, *29*, 4299. Fujiwara, T.; Tanaka, N.; Tanaka, K.; Toda, F. *J. Chem. Soc., Perkin Trans. 1* **1989**, 663.
(143) Toda, F.; Tanaka, K. *Chem Lett.* **1987**, 2283. Toda, F.; Tanaka, K.; Mak, T. C. W. *Chem. Lett.* **1989**, 1329.
(144) Aoyama, H.; Hasegawa, T.; Omote, Y. *J. Am. Chem. Soc.* **1979**, *101*, 5343.
(145) Toda, F.; Tanaka, K.; Yagi, M.; Stein, Z.; Goldberg, I. *J. Chem. Soc., Perkin Trans. 1* **1990**, 1215.
(146) Aoyama, H.; Miyazaki, K.; Sakamoto, M.; Omote, Y. *J. Chem. Soc., Chem. Commun.* **1983**, 333. Aoyama, H.; Miyazaki, K.; Sakamoto, M.; Omote, Y. *Tetrahedron* **1987**, *43*, 1513.
(147) Toda, F.; Tanaka, K.; Yagi, M. *Tetrahedron* **1987**, *43*, 1493. Kaftory, M.; Yagi, M.; Tanaka, K.; Toda, F. *J. Org. Chem.* **1988**, *53*, 4391.
(148) Toda, F.; Miyamoto, H.; Matsukawa, R. *J. Chem. Soc., Perkin Trans 1* **1992**, 1461. Hashizume, D.; Uekusa, H.; Ohashi, Y.; Matsugawa, R.; Miyamoto, H.; Toda, F. *Bull. Chem. Soc. Jpn.* **1994**, *67*, 985.
(149) Toda, F.; Tanaka, K.; Kakinoki, O.; Kawakami, T. *J. Org. Chem.* **1993**, *58*, 3783.
(150) Hashizume, D.; Ohashi, Y.; Tanaka, K.; Toda, F. *Bull. Chem. Soc. Jpn.* **1994**, *67*, 2383.
(151) Chapman, O. L.; Adams, W. R. *J. Am. Chem. Soc.* **1968**, *90*, 2333. Ninomiya, I.; Naito, T. *The Alkaloids*; Academic Press: San Diego, CA, 1983, Vol. 22, pp 189−279.
(152) Ninomiya, I.; Yamauchi, S.; Kiguchi, T.; Shinohara, A.; Naito, T. *J. Chem. Soc., Perkin Trans 1* **1974**, 1747.
(153) Tanaka, K.; Kakinoki, O.; Toda, F. *J. Chem. Soc., Chem. Commun.* **1992**, 1053.
(154) Toda, F.; Miyamoto, H.; Takeda, K.; Matsugawa, R.; Maruyama, N. *J. Org. Chem. Soc.* **1993**, *58*, 6208. Akutsu, S.; Miyahara, I.; Hirotsu, K.; Miyamoto, H.; Maruyama, N.; Kikuchi, S.; Toda, F. *Mol. Cryst. Liq. Cryst.* **1996**, *277*, 87.
(155) Toda, F.; Miyamoto, H.; Kikuchi, S. *J. Chem. Soc., Chem. Commun.* **1995**, 621.
(156) Tanaka, K.; Toda, F. *J. Chem. Soc., Perkin Trans. 1* **1992**, 943.
(157) Moorthy, J. N.; Venkatesan, K. *J. Org. Chem.* **1991**, *56*, 6957.
(158) Tanaka, K.; Kakinoki, O,; Toda, F. *J. Chem. Soc., Perkin Trans. 1* **1992**, 307.
(159) Toda, F.; Tanaka, K.; Oda, M. *Tetrahedron Lett.* **1988**, *29*, 653.
(160) Fujiwara, T.; Nanba, N.; Hamada, K.; Toda, F.; Tanaka, K. *J. Org. Chem.* **1990**, *55*, 4532.
(161) Toda, F.; Miyamoto, H.; Kanemoto, K. *J. Org. Chem.* **1996**, *61*, 6490.
(162) Toda, F.; Miyamoto, H.; Kikuchi, S.; Kuroda, R.; Nagami, F. *J. Am. Chem. Soc.* **1996**, *118*, 11315.
(163) Toda, F.; Miyamoto, H.; Kanemoto, K. *J. Chem. Soc., Chem. Commun.* **1995**, 1719. Toda, F.; Miyamoto, H. *Chem. Lett.* **1995**, 809.
(164) Toda, F.; Miyamoto, H.; Koshima, H.; Urbanczyk-Lipkowska, Z. *J. Org. Chem.* **1997**, *62*, 9261.
(165) Tanaka, K.; Toda, F. *Mol. Cryst. Liq. Cryst.* **1998**, *313*, 179.
(166) Rao, V. P.; Turro, N. *J. Tetrahedron Lett.* **1989**, *30*, 4641.
(167) Joy, A.; Scheffer, J. R.; Corbin, D. R.; Ramamurthy, V. *J. Chem. Soc., Chem. Commun.* **1998**, 1379.
(168) Addadi, L.; Mil, J.; Lahav, M. *J. Am. Chem. Soc.* **1982**, *104*, 3422.
(169) Chung, C. M.; Hasegawa, M. *J. Am. Chem. Soc.* **1991**, *113*, 7311.

(170) Evans, S. V.; Garcia-Garibay, M.; Omkaram, N.; Scheffer, J. R.; Trotter, J.; Wireko, F. *J. Am. Chem. Soc.* **1986**, *108*, 5648. Fu, T. Y.; Liu, Z.; Scheffer, J. R.; Trotter, J. *J. Am. Chem. Soc.* **1993**, *115*, 12202.

(171) Toda, F.; Yagi, M.; Soda, S. *J. Chem. Soc., Chem. Commun.* **1987**, 1413. Sekine, A.; Hori, K.; Ohashi, Y.; Yagi, M.; Toda, F. *J. Am. Chem. Soc.* **1989**, *111*, 697.

(172) Toda, F.; Miyamoto, H. *J. Chem. Soc, Perkin Trans. 1* **1993**, 1129. Hashizume, D.; Kogo, H.; Sekine, A.; Ohashi, Y.; Miyamoto, H.; Toda, F. *J. Chem. Soc., Perkin Trans. 2* **1996**, 61. Hashizume, D.; Kogo, H.; Sekine, A.; Ohashi, Y.; Miyamoto, H.; Toda, F. *Acta Crystallogr.* **1995**, *C51*, 929. Asahi, T.; Nakamura, M.; Kobayashi, J.; Toda, F.; Miyamoto, H. *J. Am. Chem. Soc.* **1997**, *119*, 3665. Hashizume, D.; Kogo, H.; Ohashi, Y.; Miyamoto, H.; Toda, F. *Anal. Sci.* **1998**, *14*, 1187.

(173) Sakamoto, M.; Takahashi, M.; Fujita, T.; Watanabe, S.; Iida, I.; Nishio, T.; Aoyama, H. *J. Org. Chem.* **1993**, *58*, 3476.

(174) Sakamoto, M.; Hokari, N.; Takahashi, M.; Fujita, T.; Watanabe, S.; Iida, I.; Nishio, T. *J. Am. Chem. Soc.* **1993**, *115*, 818.

(175) Sakamoto, M.; Takahashi, M.; Shimizu, T.; Fujita, T.; Nishio, S.; Watanabe, S. *J. Org. Chem.* **1995**, *60*, 7088.

(176) Sakamoto, M.; Takahashi, M.; Kamiya, K.; Yamaguchi, K.; Fujita, T.; Watanabe, S. *J. Am. Chem. Soc.* **1996**, *118*, 10664.

(177) Toda, F.; Tanaka, K. *Supramol. Chem.* **1994**, *3*, 87. Toda, F.; Tanaka, K.; Stein, Z.; Goldberg, I. *Acta Crystallogr.* **1995**, *B51*, 856. Toda, F.; Tanaka, K.; Stein, Z.; Goldberg, I.; *Acta Crystallogr.* **1995**, *C51*, 2722.

(178) Roughton, A. L.; Muneer, M.: Demuth, M. *J. Am. Chem. Soc.* **1993**, *115*, 2085.

(179) Sakamoto, M.; Takahashi, M.; Moriizumi, S.; Yamaguchi, K.; Fujita, T.; Watanabe, S. *J. Am. Chem. Soc.* **1996**, *118*, 8138. Takahashi, M.; Sekine, N.; Fujita, T.; Watanabe, S.; Yamaguchi, K. *J. Am. Chem. Soc.* **1998**, *120*, 12770.

(180) Suzuki, T.; Fukushima, T.; Yamashita, Y.; Miyashi, T. *J. Am. Chem. Soc.* **1994**, *116*, 2793.

(181) Koshima, H.; Ding, K.; Chisaka, Y.; Matsuura, T. *J. Am. Chem. Soc.* **1996**, *118*, 12059.

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