Formation by Mixing of Chiral Host–Achiral Guest Inclusion Complexes in which the Guest Molecules are Arranged in a Chiral Form. Production of Optically Active Photocyclisation Compounds by Irradiation of the Inclusion Complexes

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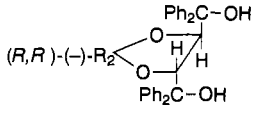
Mixing of powdered chiral hosts and achiral *N,N*-dialkylphenylglyoxylamide guest compounds gives inclusion complexes in which the latter molecules are arranged in a chiral form, although such complexes are not obtained by recrystallisation: the chirality of the guest compounds are frozen by photoreaction which gives optically active β-lactams and oxazolidinones.

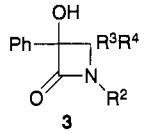
Host–guest inclusion complexes can be prepared by recrystallisation of the host and guest compounds from a solvent.[1,2] In some cases, however, the inclusion complex is not formed by this method. We have found that, in such cases, mixing of powdered host and guest compounds in the absence of solvent can give inclusion complexes. We also found that in the inclusion crystal of the chiral host and achiral *N,N*-dialkylphenylglyoxylamide guests prepared by the mixing procedure that the latter molecules are arranged and their chirality is frozen by photoreaction to give optically active β-lactams and oxazolidinones.

When powdered (*R,R*)-(−)-*trans*-4,5-bis(hydroxydiphenylmethyl)-2,2-dimethyl-1,3-dioxacyclopentane **1a**[3,4] (2.8 g, 6 mmol) and oily *N,N*-dimethylphenylglyoxylamide **2a** (0.53 g, 3 mmol) were mixed for 1 h using an agate mortar and pestle, the mixture solidified to give a 2 : 1 inclusion complex crystal of **1a** and **2a** (3.33 g). Upon formation of the complex, ν(OH) of **1a** (3600 and 3400 cm^{-1}) shifted to lower wavenumbers (3310 and 3230 cm^{-1}). The shift is probably due to the formation of hydrogen bonds between the OH group of **1a** and CO group of **2a** in the complex. A chiral arrangement of the achiral **2a** molecules in the inclusion complex was established by photoreaction which gives an optically active β-lactam. A suspension of the powdered 2 : 1 complex of **1a** and **2a** (3.2 g) in water (50 ml) containing hexadecyltrimethylammonium bromide (0.03 g) as surfactant was irradiated using a 100 W high-pressure Hg lamp for 10 h under stirring. The reaction mixture was filtered and crude **1a** was recovered which could be recrystallised from toluene to give pure **1a** (2.4 g, 87% yield). The filtrate was evaporated and the residue taken up in ethyl acetate. The solution was chromatographed on silica gel to give unchanged **2a** (0.09 g, 17% yield) and (+)-2-hydroxy-1-methyl-2-phenylazetidin-2-one **3a** with 61% e.e. (0.3 g, 70% yield). The enantiomeric excess was determined by HPLC using Chiralcel OC† as the chiral solid phase. The inclusion complex of **1a** and **2a** could not be obtained by recrystallisation, although more than 15 organic solvents were tested. In all cases **1a** crystallised out separately.



1a R = Me
b $R_2 = -(CH_2)_4-$
c $R_2 = -(CH_2)_5-$

2a $R^1 = R^2 = Me$
b $R^1 = R^2 = Et$
c $R^1 = R^2 = Pr^n$
d $R^1 = Pr^i$, $R^2 = Pr^n$



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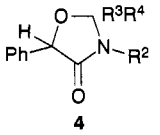
a $R^2 = Me$, $R^3 = R^4 = H$
b $R^2 = Et$, $R^3 = H$, $R^4 = Me$



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c $R^2 = Pr^n$, $R^3 = H$, $R^4 = Et$
d $R^2 = Pr^n$, $R^3 = R^4 = Me$

On the other hand, (*R,R*)-(−)-*trans*-2,3-bis(hydroxydiphenylmethyl)-1,4-dioxaspiro[4.4]nonane **1b**[3,4] formed a 1 : 1 inclusion complex with **2a** either by mixing in the solid state *or* by recrystallisation from diethyl ether. Photoirradiation of these inclusion complexes in a water suspension gave (−)-**3a** and (−)-3-methyl-5-phenyloxazolidin-4-one **4a** in the optical and chemical yields reported in Table 1. Optical and chemical yields are comparable by either preparative method.

Infrared spectra in Nujol mulls of these inclusion complexes prepared either by mixing or recrystallisation are identical. Furthermore, irradiation of a concentrated solution of **1b** (3.33 mmol) and **2a** (3.33 mmol) in diethyl ether (50 ml) for 10 h under stirring gave *rac*-**3a** in 10% yield and *rac*-**4a** in 66% yield. These data clearly show that the same inclusion complex is obtained by either mixing or recrystallisation.

A similar chiral host, (*R,R*)-(−)-*trans*-2,3-bis(hydroxydiphenylmethyl)-1,4-dioxaspiro[5.4]decane **1c**[3,4] also formed a 2 : 1 inclusion complex with **2a** by either the mixing or recrystallisation procedure, however, photoirradiation of these two complexes in an aqueous suspension gave (+)- and (−)-**3a**, respectively (Table 1), although the optical yield of (−)-**3a** was higher than that of (+)-**3a**. It is very interesting that the direction of the chiral arrangement of **3a** in the complex with **1c** changes depending on the preparation method used.

This result is very interesting not only from the viewpoint of synthetic potential but also in terms of fundamental molecular behaviour. Thus, one can obtain *both* enantiomeric photoreaction products by using a single optically active host

Table 1 Formation of optically active **3a** and **4a** by irradiation for 10 h of the inclusion complexes of chiral host compounds and **2a** prepared by mixing in the solid state or recrystallisation from toluene

Host	Host : guest	Product *via* mixing (% yield, % ee)		Product *via* recrystallisation (% yield, % ee)	
1a	2 : 1	(+)-**3a** (70, 61)	—	—	—
1b	1 : 1[a]	(−)-**3a** (29, 82)	(−)-**4a** (35, 45)	(−)-**3a** (47, 79)	(−)-**4a** (23, 42)
1c	2 : 1	(+)-**3a** (48, 41)	—	(−)-**3a** (39, 85)	—
5	2 : 1[b]	(+)-**3a** (22, 4)	(−)-**4a** (19, 49)	—	—
6	2 : 1	(−)-**3a** (44, 14)	—	—	—
7	2 : 1[c]	(−)-**3a** (27, 36)	—	—	—

[a] Diethyl ether was used for complexation by recrystallisation. [b] Irradiation for 10 days. [c] Irradiation for 5 days.

Table 2 Formation of optically active **3b** and **4b** by irradiation for 10 h of the inclusion complexes of chiral host compounds and **2b** prepared by mixing in the solid state and recrystallisation from toluene

Host	Host : guest	Product *via* mixing (% yield, % ee)		Product *via* recrystallisation (% yield, % ee)	
1a	1 : 1	(+)-**3b** (37, 57)	(+)-**4b** (20, 24)	—	—
1b	1 : 1[a]	(+)-**3b** (14, 64)	(−)-**4b** (33, 48)	(+)-**3b** (18, 73)	(−)-**4b** (57, 58)
1c	1 : 1	(+)-**3b** (11, 72)	(−)-**4b** (53, 64)	(+)-**3b** (10, 85)	(−)-**4b** (41, 64)
5	2 : 1[b]	(−)-**3b** (6, 14)	(+)-**4b** (38, 32)	—	—
7	2 : 1[b]	(−)-**3b** (28, 10)	(−)-**4b** (10, 10)	—	—

[a] Diethyl ether was used for complexation by recrystallisation. [b] Irradiation for 5 days.

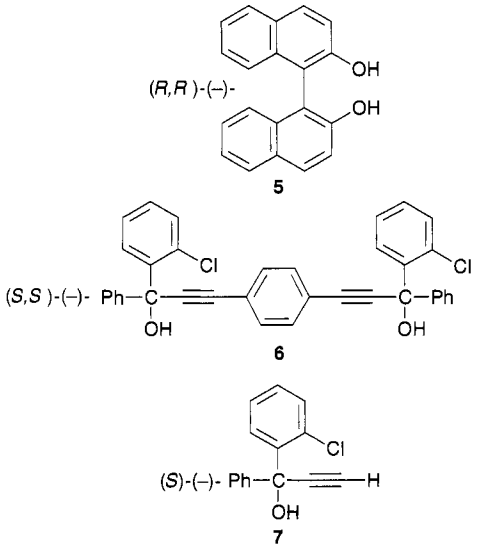

Table 3 Formation of optically active **3c** and **3d** by irradiation for 10 h of the inclusion complexes of chiral host compounds and **2c** and **2d** prepared by mixing in the solid state and recrystallisation from toluene

Host	Guest[a]	Product *via* mixing (% yield, % ee)	Product *via* recrystallisation (% yield, % ee)
1a	**2c**	(−)-**3c** (21, 52)	—
1b	**2c**[b]	(+)-**3c** (41, 50)	—
1c	**2c**	(+)-**3c** (54, 29)	(+)-**3c** (43, 16)
1a	**2d**	—	—
1b	**2d**	(+)-**3d** (26, 81)	(+)-**3d** (28, 89)
1c	**2d**	(+)-**3d** (25, 85)	(+)-**3d** (35, 90)
5	**2d**[c]	(−)-**3d** (16, 30)	—
7	**2d**[c]	(−)-**3d** (35, 1)	—

[a] All host : guest ratios are 2 : 1 except in the case of **1c** and **2d** (1 : 1). [b] Diethyl ether was used for complexation by recrystallisation. [c] Irradiation for 5 days.

compound; and it is clearly of interest that the molecular assembly of host and guest compounds occurs in a different manner in the solid state and in solution.

The chiral host compounds (*R,R*)-(+)-2,2′-dihydroxy-1,1′-binaphthyl **5**,[1,2] (*S,S*)-(−)-1,4-bis[3-(*o*-chlorophenyl)-3-hydroxy-3-phenyl-1-propynyl]benzene **6**[5] and (*S*)-(−)-1-(*o*-chlorophenyl)-1-phenyl-2-propyn-1-ol **7**[6] formed 2 : 1 inclusion complexes with **2a** only by mixing. Photoirradiation of an aqueous suspension of these inclusion complexes gave optically active **3a** and **4a** (Table 1) although enantiomeric excesses were not so as for **1a**.

For some other phenylglyoxylamide derivatives, *N,N*-diethyl- **2b**, *N,N*-dipropyl- **2c** and *N*-propyl-*N*-isopropyl-phenylglyoxylamide **2d**, similar results were observed (Tables 2 and 3). For **2b**, formation of inclusion complexes by recrystallisation was accomplished only with the hosts **1b** and **1c**. In the case of **2c** and **2d**, inclusion complexes were obtained by recrystallisation only with **1c** and **1b**, **1c**, respectively. Although photoirradiation of the inclusion complex of **2b** gave optically active β-lactam **3b** and oxazolidinone **4b**, the complexes of **2c** and **2d** gave only β-lactams **3c** and **3d**, respectively.

Previously we have reported formation of a host–guest complex by mixing both components in the solid state.[7] However, this is the first example of the formation of host–guest complexes by mixing which can not be obtained by recrystallisation and of the chiral arrangement of achiral molecules in the complex formed on mixing.

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Footnote

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References

1 F. Toda, *Top. Curr. Chem.*, 1987, **140**, 43.
2 F. Toda, *Top. Curr. Chem.*, 1998, **149**, 211.
3 D. Seebach, A. K. Beck, R. Imwinkelried, S. Roggo and A. Wonnacott, *Helv. Chim. Acta*, 1987, **70**, 954.
4 F. Toda and K. Tanaka, *Tetrahedron Lett.*, 1988, **29**, 551.
5 K. Tanaka, O. Kakinoki and F. Toda, *J. Chem. Soc., Perkin Trans. 1*, 1992, 307.
6 F. Toda, *Bioorg. Chem.*, 1991, **19**, 157.
7 F. Toda, K. Tanaka and A. Sekikawa, *J. Chem. Soc., Chem. Commun.*, 1987, 279.