ORGANIC
LETTERS

2001
Vol. 3, No. 10
1567−1569

Enantioselective Photoreaction of 4-Isopropyltropolone Methyl Ether in Inclusion Crystals with Optically Active Host Compounds

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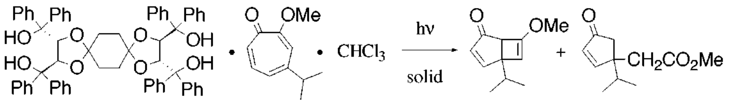
Received March 16, 2001

ABSTRACT

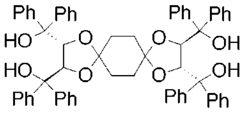


(-)-1 **3b** **(-)-6a** **(-)-7a**

Upon photoirradiation of a 2:1:1 inclusion complex of (–)-1, 4-isopropyltropolone methyl ether (3b) and chroloform, optically active photocyclization products (–)-6a and (–)-7a were obtained in 96% and 90% ee, respectively.

Achiral tropolone ethers are known to undergo intramolecular photocyclization to give racemic bicyclic cyclopentenone derivatives.[1] Recently, the enantiocontrol of this reaction has been studied by using chirally modified zeolite[2] and a chiral ionic auxiliary[3]. We have also reported the enantioselective photocyclization of tropolone alkyl ether in the inclusion crystals with optically active (−)-1,6-di(*o*-chlorophenyl)-1,6-diphenyl-hexa-2,4-diyne-1,6-diol, in which photocyclization products with high ee were obtained in relatively low chemical yields.[4] We have now found that enantioselective photoreaction of 4-isopropyltropolone methyl ether (**3b**) proceeds efficiently in the inclusion crystals with an optically active host compound (**1**)[5] derived from tartaric acid.

Treatment of hinokitiol (tautomeric mixture of **3a** and **4a**) with Me$_2$SO$_4$−K$_2$CO$_3$ in acetone gave a 1:1 mixture of 4-isopropyltropolone methyl ether (**3b**) and 6-isopropyltropolone methyl ether (**4b**) in 61% yield.



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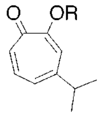

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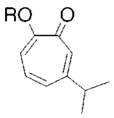
b: R = Me



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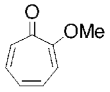
b: R = Me



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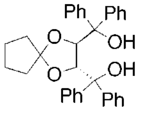

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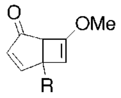
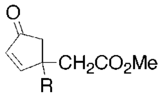


6 a: R = *i*-Pr
b: R = H



7 a: R = *i*-Pr
b: R = H

When a mixture of (−)-**1** and a 1:1 mixture of **3b** and **4b** in CHCl$_3$−acetonitrile (3:1) was kept at room temperature for 12 h, a 2:1:1 inclusion complex of (−)-**1**, **3b**, and CHCl$_3$ was obtained as colorless prisms.[6]

Upon photoirradiation of the inclusion complex with a 400-W high-pressure Hg-lamp (Pyrex filter) in the solid state

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10.1021/ol015857v CCC: $20.00

for 70 h at room temperature under atmosphere, a mixture of (−)-5-isopropyl-7-methoxy-bicyclo[3.2.0]hepta-3,6-dien-2-one (**6a**) of 96% ee and (−)-(1-isopropyl-4-oxo-cyclopent-2-enyl)-acetic acid methyl ester (**7a**) of 90% ee was obtained in 51% and 22% yields, respectively.[7] When the (+)-host (**1**) was used instead of (−)-**1**, a mixture of (+)-**6a** of 96% ee and (+)-(**7a**) of 89% ee was obtained in 27% and 62% yields, respectively (Table 1).

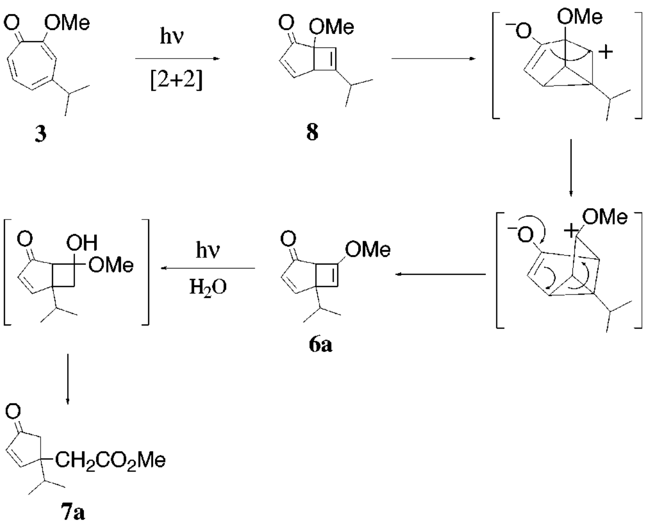
Table 1. Enantioselective Photoreaction of Tropolone Derivatives (**3** and **5**) in the Inclusion Crystals with Optically Active Hosts (**1** and **2**)

host	guest	H:G	mp (°C)	conv[a] (%)	product	yield (%)	ee[b] (%)
(−)-**1**	**3**	2:1:$CHCl_3$	118−123	100	(−)-**6a**	51	96
					(−)-**7a**	22	90
(+)-**1**	**3**	2:1:$CHCl_3$	118−123	100	(+)-**6a**	27	96
					(+)-**7a**	62	89
(−)-**1**	**5**	1:2	105−110	34	(+)-**7b**	10	91
(+)-**1**	**5**	1:2	105−110	34	(−)-**7b**	10	91
(−)-**2**	**5**	1:1	115−117	38	(−)-**6b**	10	91
					(+)-**7b**	28	53
(+)-**2**	**5**	1:1	115−117	38	(+)-**6b**	10	90
					(−)-**7b**	22	48

[a] Conversion was estimated by ^1H NMR after photoirradiation for 70 h at room temperature. [b] Optical purity was determined by HPLC (Chiralcel OD, Daicel).

This reaction involved the following steps according to Chapman's mechanism.[1] First, disrotatory photocyclization of **3b** occurred enantioselectively to form 6-isopropyl-1-methoxy-bicyclo[3.2.0]hepta-3,6-dien-2-one (**8**), which was converted to optically active 5-isopropyl-7-methoxy-bicyclo-[3.2.0]hepta-3,6-dien-2-one (**6a**) (Scheme 1). Optically active (1-isopropyl-4-oxo-cyclopent-2-enyl)-acetic acid methyl ester (**7a**) might be obtained by photochemical addition of water in the atmosphere to the double bond of **6a** followed by ring opening during the photoirradiation, since photoirradiation of (−)-**6a** in the presence of water gave (−)-**7a** quantitatively.

Scheme 1



Compound (−)-**1** formed a 1:2 inclusion complex with tropolone methyl ether (**5**), which upon photoirradiation in the solid state for 70 h gave only (*R*)-(−)-(4-oxo-cyclopent-2-enyl)-acetic acid methyl ester (**7b**) of 91% ee in 10% yield after 34% conversion. (*S*)-(+)-**7b** of 91% ee was also obtained in 10% yield when the (+)-host compound (**1**) was used instead of (−)-**1**.

The enantioselective photocyclization of tropolone methyl ether (**5**) was also found to proceed when the host compound (**2**) was used. For example, when a solution of a 1:1 mixture of (−)-**2** and **5** in ether was kept at room temperature for 12 h, a 1:1 inclusion complex of (−)-**2** with **5** was obtained as colorless prisms. Upon photoirradiation of the inclusion complex with a 400-W high-pressure Hg-lamp (Pyrex filter) in the solid state for 70 h at room temperature, a mixture of (*1R,5S*)-(−)-7-methoxy-bicyclo[3.2.0]hepta-3,6-dien-2-one (**6b**) of 91% ee and (*S*)-(+)-**7b** of 53% ee was obtained in 10% and 28% yields, respectively. When the (+)-host (**2**) was used instead of (−)-**2**, a mixture of (*1S,5R*)-(+)-**6b** of 90% ee and (*R*)-(−)-**7b** of 48% ee was obtained in 10% and 22% yields, respectively.

The lower optical purities of **7b** might be due to a photochemical racemization of **6b** via its reversible enolization.[4]

To elucidate the mechanism of the enantioselective photoreaction of tropolone methyl ether in the inclusion crystals, X-ray crystal structure analysis of the inclusion complex was studied at 180 K. A suitable crystal for X-ray analysis was obtained in the 1:2 inclusion complex of (−)-**1** and **5**. Figure 1 shows two molecules of **5** bound via strong C═O···HO [O1b···O5c = 2.724(3) Å, H1b···O5c = 1.85(4) Å, angle 168(4)°] and weak C═O···HC [C36b···O5c = 3.340(4) Å, H36b···O5c = 2.45(3) Å, angle 153(3)°] hydrogen bonds to the nearest [i.e., translated by *x*, *y*, *z* − 1 symmetry] host

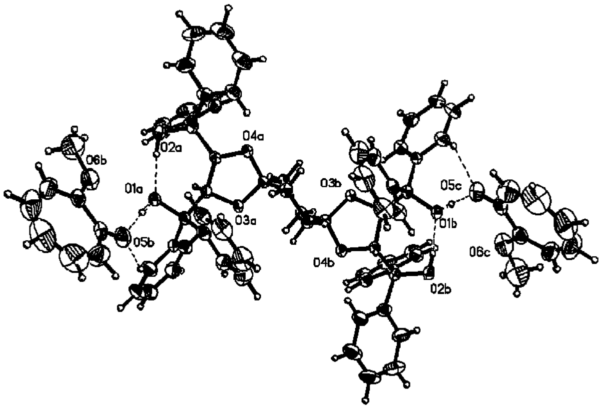


Figure 1. Solid-state structure of the complex containing host molecule (−)-**1** and two hydrogen bonded molecules of **5**.

molecule (−)-**1**.[8] The complex has crystallographic 2-fold symmetry with nearly planar conformation of the guest molecules. The product (*S*)-(+)-**7b** might be obtained via (*1R,5S*)-(−)-**6b** formed by enantioselective disrotatory photocyclization of **5** in the complex according to a steric hindrance of the phenyl group of the host (*R*,*R*,*R*,*R*)-(−)-**1**.

Acknowledgment. K.T. acknowledges financial support from The Sumitomo Foundation.

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[6] **Typical Procedure**. When a mixture of (−)-**1** (6.05 g, 6.51 mmol) and a 1:1 mixture of **3b** and **4b** (4.53 g, 25.4 mmol) in $CHCl_3-CH_3CN$ (3:1, 50 mL) was kept at room temperature for 12 h, a 2:1:1 complex of (−)-**1**, **3b**, and $CHCl_3$ was obtained as colorless prisms (4.5 g, mp 118−123 °C) in 64% yield.

[7] **Typical Procedure.** A crystalline powder of the 2:1:1 complex of (−)-**1**, **3b**, and $CHCl_3$ (4.44 g) was irradiated by a 400-W high-pressure Hg lamp (Pyrex filter) in the solid state for 70 h. Separation of the reaction mixture by silica gel column chromatography gave a mixture of (−)-5-isopropyl-7-methoxybicyclo[3.2.0]hepta-3,6-diene-2-one (**6a**) ($[\alpha]_D$ −207° (*c* 0.23, $CHCl_3$), 96% ee) and (−)-methyl-1-isopropyl-4-oxocyclopent-2-ene-1-acetate (**7a**) ($[\alpha]_D$ −94.6° (*c* 0.10, $CHCl_3$), 90% ee). The optical purities were determined by HPLC (Chiralcel OD, Daisel). Data for **6a**: colorless oil; IR (ν, cm^{-1}) 1701 (C═O), 1634 (C═C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65 (d, $J = 5.7$ Hz, 1 H), 5.89 (d, $J = 5.7$ Hz, 1 H), 5.08 (s, 1 H), 3.61 (s, 3 H), 3.30 (s, 1 H), 1.96−2.10 (m, 1 H), 1.03 (d, $J = 6.9$ Hz, 3 H), 0.94 (d, $J = 6.9$ Hz, 3 H). Data for **7a**: colorless oil; IR (ν, cm^{-1}) 1734, 1716 (C═O); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59 (d, $J = 5.7$ Hz, 1 H), 6.14 (d, $J = 5.7$ Hz, 1 H), 3.63 (s, 3 H), 2.59 (s, 1 H), 2.34 (s, 1 H), 1.86−2.00 (m, 1 H), 0.94 (d, $J = 7.2$ Hz, 3 H), 0.87 (d, $J = 7.2$ Hz, 3 H).

[8] **X-ray Studies of 1:2 Complex of (−)-1 and 5.** A suitable crystal of dimensions 0.5 × 0.27 × 0.21 mm^3, covered by epoxy glue has been used. Crystal data: $a = 10.9410(1)$, $b = 33.5620(2)$, $c = 8.7360(5)$ Å, $V = 3207.9(2)$ Å^3, $Z = 2$; orthorhombic space group $P2_12_12$, Mo Kα radiation, $\lambda = 0.7107$ Å, $d_{calc} = 1.281$ Mg m^{-3}. A total of 6772 reflections were collected on the Nonius BV Kappa CCD system (180 K); 4115 unique reflections were used in the structure solution using SHELXS86[9] and refinement using SHELXL97.[10] All non-hydroxyl H-atoms were place geometrically and refined with a riding mode with the U_{iso} constrained to be 1.2 times of that of U_{eq} of the carrier atom. Positions for hydroxy group hydrogens and proton attached to aromatic carbon C36, forming hydrogen bond with tropolone carbonyl O5,[11] were found from $\Delta\rho$ maps and refined with isotropic temperature factors. Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 160041. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, U.K. (fax +44 1223 336033 or e-mail deposit@ccdc.cam.ac.uk).

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