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ENANTIOSELECTIVE PHOTOCONVERSION OF PYRIDONES INTO β-LACTAM DERIVATIVES IN INCLUSION COMPLEXES WITH OPTICALLY ACTIVE HOST COMPOUNDS

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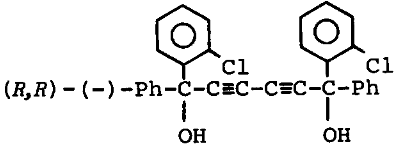
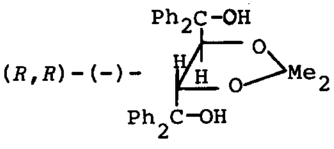
Summary - Irradiation of inclusion complexes of pyridones and optically active host compounds, (R,R)-(-)-1,6-di(o-chlorophenyl)-1,6-diphenylhexa-2,4-diyne-1,6-diol and (R,R)-(-)-trans-4,5-bis(hydroxydiphenylmethyl)-2,2-dimethyl-1,3-dioxacyclopentane, in the solid state gave optically active β-lactam derivatives.

Enantioselective synthesis of optically active β-lactam derivatives is one of the most interesting subjects in synthetic organic chemistry. One idea of enantioselective synthesis is photoconversion of achiral β-lactam precursor into optically active β-lactam under chiral conditions. We have reported some successful examples of such reaction: for example, irradiation of inclusion complex of oxoamides and optically active 1,6-di(*o*-chlorophenyl)-1,6-diphenylhexa-2,4-diyne-1,6-diol (1) in the solid state gave optically active β-lactam derivatives.1,2) Irradiation of chiral crystals of achiral N,N,-diisopropylglyoxylamide in the solid state also gave optically active β-lactam, 3-hydroxy-1-isopropyl-4,4-dimethyl-3-phenylazetidin-2-one.3) We now report enantioselective photoconversion of pyridones (4) into optically active β-lactam derivatives, 2-azabicyclo[2.2.0]hex-5-en-3-ones (5) by irradiation of inclusion complex of 4 and optically active 1 or *trans*-4,5-bis(hydroxydiphenylmethyl)-2,2-dimethyl-1,3-dioxacyclopentane (2) in the solid state.

Previously we reported that irradiation of 2:1 complexes of 4a-c and 4e with 1,1,6,6-tetraphenylhexa-2,4-diyne-1,6-diol (3) in the solid state gives the photodimers, 6a-c and 6e, respectively.4) However, it was disclosed that 4f forms a 1:1 complex with 3 (mp 128-129 °C) and its irradiation for 12 h in the solid state gives intramolecular photocyclization product 5f in 50% yield. This result suggests that irradiation of a 1:1 complex of 4 with optically active host compound gives optically active 5. Firstly, we prepared complexes of 4 with 1 and 2 (Table 1). Fortunately, most of the pyridones formed a 1:1 complex with 1 and 2, but 4a and 4e formed a 1:2 complex with 1.



1



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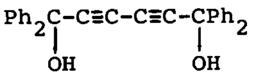
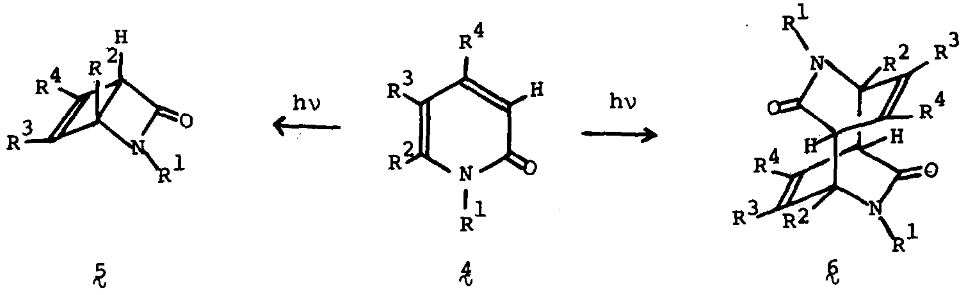


$Ph_2\underset{OH}{C}-C\equiv C-C\equiv C-\underset{OH}{C}Ph_2$

3



	a	**b**	**c**	**d**	**e**	**f**	**g**
R^1	H	Me	Me	Me	Me	Me	Me
R^2	H	H	Me	H	H	H	H
R^3	H	H	H	Me	H	H	H
R^4	H	H	H	H	Me	OMe	OEt

Table 1. Molar Ratios of Host:Guest and No. and Melting Points of Host-Guest Complexes

Guest	Host **1**			Host **2**		
	No.	Host:Guest	Mp (°C)	No.	Host:Guest	Mp (°C)
4a	**7a**	1:2	not clear	--	---	---
4b	**7b**	1:1	98-102	**8b**	1:1	125-131
4c	**7c**	1:1	121-122	**8c**	1:1	not clear
4d	**7d**	1:1	137-139	**8d**	1:1	114-118
4e	**7e**	1:2	90-91	**8e**	1:1	157-159
4f	**7f**	1:1	161-162	**8f**	1:1	136-137
4g	**7g**	1:1	129-131	**8g**	1:1	107-109

However, **4a** did not form a complex with **2**. All complexes were obtained as stable colorless crystals.

Finely powdered complexes (**7** and **8**) were irradiated by 100W high-pressure Hg-lamp at room temperature in the solid state. Although **7a**-**d**, **7g**, and **8c** were photoinactive, **7e**-**f**, **8b**, and **8e**-**g** gave photoreaction products. In the case of **7e** and **8d**, crude reaction product was mixed with MeOH to give **6e** and **6d**, respectively, as MeOH-insoluble crystals. In the other cases, the crude reaction product was chromatographed on silica gel using $CHCl_3$ as a solvent to give a mixture of host compound and **5**, from which **5** was isolated by distillation. From the residue left after the distillation, the host compound was recovered unchanged. Irradiation time, products, conversions, yields, melting points, $[\alpha]_D$ values, and optical purities of products are summarized in Table 2.

Table 2. Irradiation Time, Conversions, Products, and Yields, Melting Points, $[\alpha]_D$ Values, and Optical Purities of Products

			Product				
Complex	Irradiation Time (h)	Conversion (%)	No.	Yield (%)[a]	Mp (°C)	$[\alpha]_D$ Value (°) (c, $CHCl_3$)	Optical Purity (% ee)[b]
7e	40	100	**6e**	93	230-233	---	---
7f	47	50	**5f**	97	oil	-123 (0.026)	100
8b	45	15	**5b**	93	oil	+359 (0.032)	100
8d	60	100	**6d**	95	203-205	---	---
8e	57	60	**5e**	99	oil	-21.3 (0.094)	17
8f	96	15	**5f**	99	oil	+88.6 (0.035)	72
8g	144	10	**5g**	76	oil	+80.0 (0.01)	---[c]

[a] Calculated based on reacted **4**. [b] Determined by HPLC on an optically active solid phase, Chiralcel OC (Daicel Chemical Industries, Ltd.). [c] Could not be determined.

Structures of **5b**,[6)] **5e**,[6)] and **5f**[7)] were elucidated by comparison of their IR spectra with those reported. Structure of **5g** was determined by the IR spectrum which shows characteristic β-lactam νC=O absorption at 1730 cm^{-1}. Photoreactions of **7f**, **8b**, and **8e**-**g** which give optically active **5f**, **5b**, and **5e**-**g**, respectively, are valuable, although the purity of **5e** is not high. The optical purity of **5g** was not determined, but it seems quite high because the $[\alpha]_D$ value is comparable to that of **5f** of 72% ee. Optically active **5** is useful as a precursor of synthesis of various antibiotic β-lactam derivatives. As far we are aware, no enantioselective synthesis of optically active **5** has been reported so far, although preparation of optically active 5-(*l*-menthoxy)-2-azabicyclo[2.2.0]hex-5-en-3-one by optical resolution has been reported.[8)]

Yields of photoconversion of **4** into **5** in solution are low. For example, irradiation of **4b** and **4e** in MeOH for 60 and 72 h, respectively, gave **5b** and **5e** in 15 and 16% yields, respectively.[6)] Furthermore, efficiency of the photoreaction in solution is very low, because the reaction should be carried out at a low concentration in order to avoid dimerization of **4**. Contrarily, photoreaction of **4** in the complex is very effective, although the reaction takes a little longer. Yields are much higher than those in solution, and preparation of **5** on a large scale is possible since the reaction is independent of concentration. In 1:1 complexes of **4** with **1** and **2**, molecules of **4** are arranged apart from one another so as not to produce dimeric product **6**. This will be clarified in the near future by X-ray structural analysis of the complex.

It is reasonable that irradiation of a 1:2 complex of host compound and **4** in the solid state gives the dimeric product **6**. It is, however, curious that irradiation of a 1:1 complex (**8d**) of **4d** and **2** gives **6d** instead of **5d** (Table 2). Since one unit of **8d** contains only one molecule of **4d**, this result shows that at least two of these units should take part the photoreaction. This will also be clarified in the near future by X-ray structural analysis. Meanwhile, however, a similar result has been reported. Irradiation of a 2:1 complex of **1** and cycloocta-2,4-dien-1-one in the solid state gives its optically active (-)-dimer of 78% ee, *anti*-tricyclo[8.6.0.0^{2,9}]hexadeca-7,11-diene-3,16-dione, in 55% yield.9)

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