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Communications

Highly Enantioselective Photocyclization of *N*-(Aryloylmethyl)- δ -valerolactams

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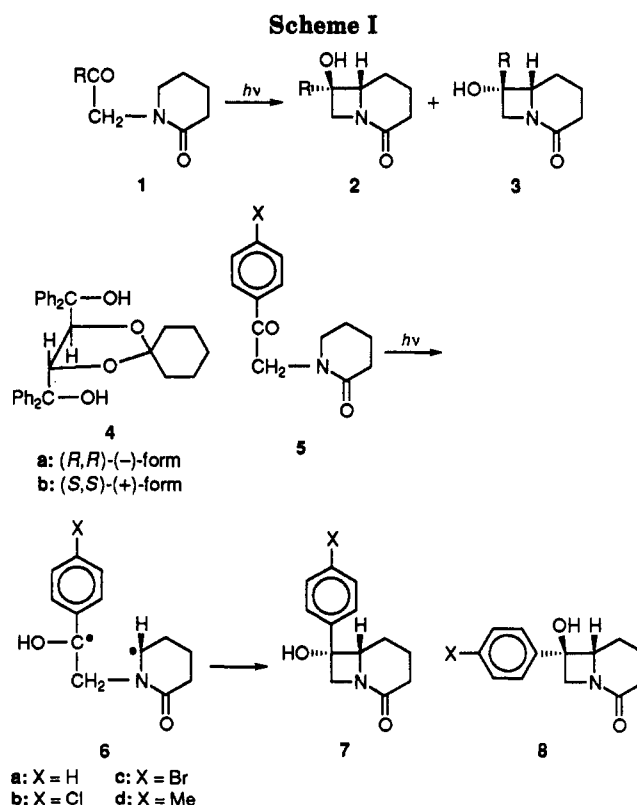
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Summary: Photoirradiation of powdered inclusion compounds of *N*-(aryloylmethyl)- δ -valerolactams with optically active host compound in a water suspension gave 7-aryl-7-hydroxy-1-azabicyclo[4.2.0]octan-2-one derivatives of high optical purities.

Selective synthesis of *trans*-(2) and *cis*-7-hydroxy-1-azabicyclo[4.2.0]octan-2-one (3) by classical chemistry is difficult.^{1,2} Although they can easily be obtained by photocyclization reaction of *N*-(acylmethyl)- δ -valerolactam 1, this reaction proceeds nonstereoselectively to give a mixture of *rac*-2 and *rac*-3 (Scheme I).³ We now report the stereoselective synthesis of optically active 2. Stereoselective synthesis was achieved by photocyclization of *N*-(aryloylmethyl)- δ -valerolactams (5a-d) as their 1:1 inclusion compounds with optically active hosts (*R,R*)-(-)-(4a) and (*S,S*)-(+)-*trans*-2,3-bis(hydroxydiphenylmethyl)-1,4-dioxaspiro[5.4]decane (4b).^{4,5}

The 1:1 inclusion compound of 5^{3,6} and 4 was prepared by recrystallization of equimolar amounts of them from benzene. When a solution of 5a (1.23 g, 5.66 mmol) and 4a (2.87 g, 5.66 mmol) in benzene (40 mL) was kept at room temperature for 1 week, crystals of a 1:1 inclusion compound (3.91 g, 95% yield) were obtained. Inclusion compounds showed sharp melting points as in Table I, except the case of 5d. When equimolar amounts of 5d and 4a were recrystallized from benzene and toluene, 1:1:1



(1) Gaertner, V. R. *J. Org. Chem.* 1967, 32, 2972-2976.
(2) Gat, B. J.; Moore, D. R. *Tetrahedron Lett.* 1967, 1155-1158.
(3) Ouazzani-Chadi, L.; Quirion, J.-C.; Troin, Y.; Gramain, J.-C. *Tetrahedron* 1990, 46, 7751-7762.
(4) Toda, F.; Tanaka, K. *Tetrahedron Lett.* 1988, 29, 551-554.
(5) Seebach, D.; Beck, A. K.; Imwinkelried, R.; Roggo, S.; Wonnacott, A. *Helv. Chim. Acta* 1987, 70, 954-974.
(6) Fujii, T.; Yoshifuji, S.; Yamada, K. *Chem. Pharm. Bull.* 1978, 26, 2071-2080.

complexes of 5d, 4a, and benzene and of 5d, 4a, and toluene were obtained, respectively. These inclusion compounds did not show a clear melting point (Table I).

A suspension of the powdered 1:1 inclusion compound of 5a and 4a (3.21 g) in water (120 mL) containing sodium alkylsulfate (2 drops of commercially available detergent) as a surfactant was irradiated for 12 h while being stirred

Table I. Photoreaction of Inclusion Crystal of 5 and 4 in a Water Suspension

5	host	mp of complex (°C)	irradiatn ^a time (h)	recovered 5 (%)	product (7) from	
					organic layer yield ^b (%) (% ee)	aqueous solution yield ^b (%) (% ee)
5a	4a	138–139.5	12	25	(+)-7a, 59 (98) ^c	(+)-7a, 28 (85) ^c
5a	4b	138–139.5	12	19	(-)-7a, 54 (99) ^c	(-)-7a, 28 (81) ^c
5b	4a	131–132	12	25	(-)-7b, 45 (84) ^c	(-)-7b, 25 (95) ^c
5c	4a	133–135	15	13	(-)-7c, 42 (98) ^d	
5d	4a	74–91 ^e	12	98		
5d	4a	82–104 ^f	12	93		

^a Irradiation was carried out through Pyrex filter at room temperature by using a 100-W high-pressure Hg lamp under stirring. ^b Yields were calculated based on the amount of reacted 5. ^c Optical purities were determined by HPLC on the chiral solid-phase Chiralcel OC.⁷ ^d Optical purity was determined by HPLC on the chiral solid phase Chiralcel OJ.⁷ ^e A 1:1:1 complex of 5d, 4a, and benzene. ^f A 1:1:1 complex of 5d, 4a, and toluene.

Table II. Photoreaction of 5 in *t*BuOH^a

5	mp of 5 (°C)	irradiatn time (h)	7 ^b		8 ^b	
			yield (%)	mp (°C)	yield (%)	mp (°C)
5a ^c	61–63	27	33	171–172	50	135–137
5b	65–67	24	34	180–182	50	148–151
5c	85–87	27	26	182–184	45	164–166
5d	93–95	24	28	153–154	51	134–135

^a Photoirradiation was carried out in *t*BuOH through a Pyrex filter at room temperature by using a 100-W high-pressure Hg lamp. ^b 7 and 8 were isolated in pure state by fractional recrystallization of their mixture from AcOEt. ^c Data reported in the literature.³

at room temperature. The reaction mixture was filtered to give crude crystals and an aqueous solution. The crude crystals were purified by column chromatography on silica gel followed by recrystallization from AcOEt to give (+)-7a of 98% ee (0.42 g, 59% yield) and recovered 5a (0.24 g, 25% yield). The host compound 4a was recovered unchanged in almost quantitative yield and reused. The aqueous solution was evaporated to dryness, and the residue was extracted with acetone (250 mL) and dried over MgSO₄. The crude product obtained by evaporation of the solvent was purified by column chromatography on silica gel and by recrystallization from AcOEt to give (+)-7a of 85% ee (0.2 g, 28% yield). When the (+)-host compound 4b was used instead of the (-)-enantiomer 4a for the photocyclization of 5a, (-)-7a was obtained. Irradiation of the powdered 1:1 inclusion compound of 4b and 5a in a water suspension for 12 h yielded (-)-7a (99% ee, 54% yield) and (-)-7a (81% ee, 28% yield) from the water-insoluble organic layer and the water solution, respectively (Table I). By similar irradiations of 1:1 inclusion compounds of 5b and 5c with 4a, (-)-7b and (-)-7c were obtained, respectively; the optical and chemical yields are shown in Table I. In most cases, photocyclization products of higher optical purities were obtained from the organic layer but not from aqueous solution. Since 7 did not racemize by photoirradiation in water and by evaporation of its water solution, the relatively lower optical purity of the 7 obtained from the water solution is probably due to photocyclization reaction of the isolated 5 from the inclusion compound with 4 by its partial decomposition during the photoreaction in water. It is clear, however, that efficiency of the enantioselective photocyclization of 5 in the inclusion complex with 4 is very high. All optical purities were determined by HPLC on the chiral solid-phase Chiralcel OC or OJ.⁷

Nevertheless, 5d was inert to the photoreaction in the

inclusion compound with 4a. Irradiation of both the 1:1:1 complex of 4a, 5d and benzene or toluene in water suspension did not give any photoreaction product, and 5d was recovered unchanged (Table I). The packing pattern of 5d molecules in its inclusion complexes with 4a may not lead to 7 via the diradical intermediate 6. For an effective hydrogen abstraction from the α -position of the nitrogen in the δ -valerolactam moiety by the carbonyl of the benzoyl group, both groups should be close to each other. In these inclusion compounds of 4a and 5d containing benzene or toluene, these two groups might not be arranged at a close position. This will be clarified by X-ray crystal structure study in the future.

For comparison with the solid-state reaction of 5 in the inclusion crystal, photoreaction of 5b–d in *t*BuOH solution was carried out according to the reported method for the reaction of 5a.³ In all cases, a mixture of *rac-trans*-7 and *rac-cis*-product 8 was obtained (Table II). Furthermore, it takes longer to complete the reaction in solution (Table II). It is very clear that the photoreaction of 5 in the inclusion compound with 4 proceeds not only stereo- and enantioselectively but also very efficiently.

In the inclusion complex with 4, 5 may give initially by irradiation the biradical 6 in which Ar and Ha moieties are arranged in *trans* positions and a radical coupling reaction gives *trans*-product 7 with high selectivity. It is not clear why the biradical intermediate 6 leads exclusively to 7. Enantiocontrol of the photoreaction of 5 by the host 4 is also good. The mechanism for stereocontrol may be clarified by an X-ray crystal structure analysis of the inclusion compounds when suitable crystals for analysis are obtained.

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Supplementary Material Available: Detailed data for the preparation of 5a–d and their inclusion complexes with 4, detailed photoreaction procedures of the inclusion crystal in the solid state and of 5a–d in *t*BuOH, and IR, ¹H NMR, and ¹³C NMR spectra data and elemental analytical data of all new materials obtained (2 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(7) Chiralcel OC and OJ are available from Daicel Chemical Industries, Ltd., Himeji, Japan.