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ENANTIOMER DIFFERENTIATION IN THE PHOTOINDUCED 1,5-PHENYL SHIFT OF 3-METHYL-3-PHENYL-2(3*H*)-OXEPINONE UTILIZING CHIRAL SENSITIZERS

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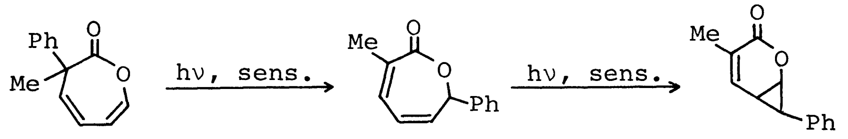
Enantiomer differentiation has been observed in the initial 1,5-phenyl shift of the sensitized photorearrangement of racemic 3-methyl-3-phenyl-2(3*H*)-oxepinone with chiral *N*-(1-phenylethyl)naphthalenecarboxamides leading to optically active 4-methyl-7-*exo*-phenyl-2-oxabicyclo[4.1.0]hept-4-en-3-one.

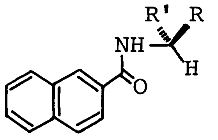
There have been several examples of asymmetric induction in photochemical experiments utilizing chiral sensitizers, all of which are reversible photoisomerizations.[1] Our recent studies[2] on the photorearrangement of 3-methyl-3-phenyl-2(3*H*)-oxepinone (**1**) have revealed that the rearranging pathway involves two sequential sensitized processes, the 1,5-phenyl shift leading to 3-methyl-7-phenyl-2(7*H*)-oxepinone (**2**) and the subsequent di-π-methane rearrangement leading to 4-methyl-7-*exo*-phenyl-2-oxabicyclo[4.1.0]hept-4-en-3-one (**3**) (Scheme 1). For such photoreactions, it might be also anticipated that enantiomer differentiation may take place by collisional energy transfer with chiral sensitizers. We report here the first example of asymmetric 1,5-phenyl shift of **1** sensitized by chiral sensitizers.

In view of the great effectiveness of 2-acetonaphthone for the photoreaction of **1**, the optically active naphthoyl amides, (*R*)-(-)-**4**, (*S*)-(+)-**4**, and (*R*)-(+)-**7**,[3] ester (*R*)-(-)-**5**,[5] and ketone (*S*)-(-)-**6**[6] were prepared and used as the sensitizers to effect stereochemical rearrangement of racemic **1**. A solution of racemic **1** (400 mg, 2 mmol, except run 6 in Table 1) and the sensitizer in methylene chloride (400 ml, except runs 5 and 6) was placed in a cylindrical reaction vessel having a neck for sampling, a neck for nitrogen flowing, and a neck to accomodate a Pyrex-jacketed, water-cooled immersion type, 500 W, high-pressure mercury arc lamp. From the previous finding

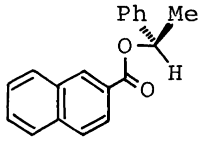
Scheme 1



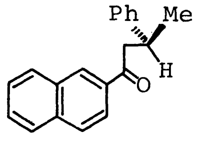
1 **2** **3**



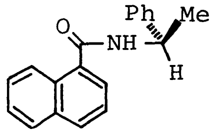
(*R*)-(-)-**4**: R=Me, R'=Ph
(*S*)-(+)-**4**: R=Ph, R'=Me



(*R*)-(-)-**5**

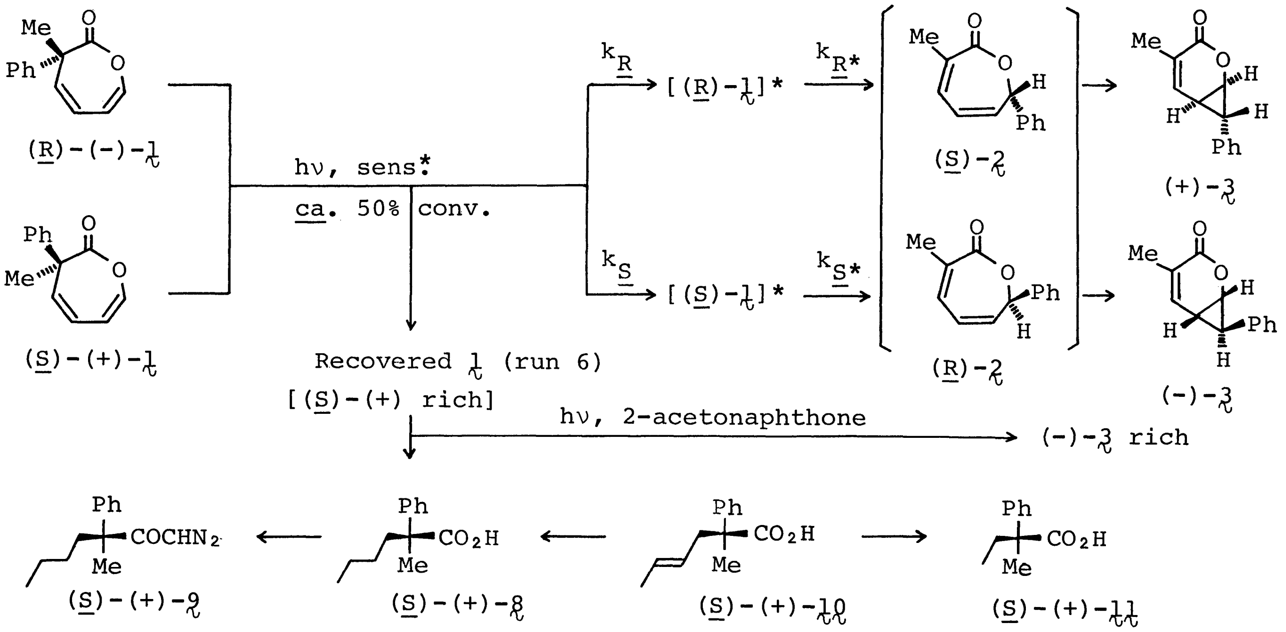


(*S*)-(-)-**6**



(*R*)-(+)-**7**

Scheme 2



that the initial product **2** is thermally very unstable,[2d] the photolysis was carried out at running water-bath temperature to complete the second photoprocess leading to **3**. Progress of the reaction was monitored by tlc (silica gel, 4:1 hexane–ethyl acetate), and irradiation was stopped at the stage of about 50% conversion. Unchanged **1** and the major rearrangement product **3** were isolated by preparative tlc on silica gel, and their optical rotations were measured. In several runs, recovered **1** was again irradiated in methylene chloride using 2-acetonaphthone (1 equiv) as the sensitizer.[2] The optical rotation of **3** thus obtained was also measured.

All compounds **4**∿**7** were found to effect the rearrangement of **1** to **3**, and the experiments with the amide sensitizer (*R*)-(−)-**4** were carried out in some detail. The results are summarized in Table 1. It is apparent that, especially in the cases of the amide sensitizers, both of recovered **1** and the major product **3** were certainly optically active; in both the (+)-enantiomer excess mixtures were obtained from the experiments with both 2- and 1-naphthoyl amides, (*R*)-(−)-**4** (runs 1∿6) and (*R*)-(+)-**7** (run 8), while the (−)-enantiomer excess mixtures with the comparable optical activities were produced from the reaction with the antipodal amide (*S*)-(+)-**4** (run 7). Furthermore, the sign of rotation of the secondary **3** derived from recovered **1** was clearly opposite to that of the primary **3** in both cases of (−)-**4** and (+)-**4** [runs 2 (or 6) and 7]. The effects of the amount of the sensitizer (runs 1,3, and 4) and of the solvent (run 5) to both efficiencies of the reaction rate and of the optical activities of **3** and recovered **1** were not large.

The recovery of optically active **1** clearly indicates that enantiomer differentiation took place at the stage of the initial photosensitization of **1**. From a separate experiment using racemic **2**[2d] and (*R*)-(−)-**4** (methylene chloride, 0 °C), it was found that the second stage of the reaction, **2** → **3**, also involves enantiomer differentiation in very small extent. The optical yield of recovered (+)-rich **1**, as well as the absolute configuration, was determined by the following experiments. Catalytic hydrogenation (PtO_2, EtOH) of a portion of recovered **1** from run 6 gave

Table 1. Photolysis of (±)-**1** with Chiral Sensitizers

run	sensitizer[a] (amount)	irradn time, min	recovd **1** yield, %[b]	recovd **1** $[\alpha]_D$[c]	product **3** initial yield, %[b]	product **3** initial $[\alpha]_D$[c]	product **3** from recovd **1**[d] $[\alpha]_D$[c]
	amide						
1	(-)-**4** (1 equiv)	60	59	+0.36° (*c* 1.96)	25	+3.63° (*c* 0.55)	
2	" (")	96	32	+0.56° (*c* 1.07)	47	+2.13° (*c* 1.41)	-4.08° (*c* 0.56)
3	" (2 equiv)	60	59	+0.38° (*c* 2.09)	31	+2.94° (*c* 1.12)	
4	" (0.5 equiv)	96	42	+0.39° (*c* 1.54)	33	+2.64° (*c* 1.17)	
5	" (") in MeOH	90	52	+0.41° (*c* 1.72)	29	+3.15° (*c* 1.02)	
6[e]	" (")	120	63	+0.50° (*c* 2.00)	24	+3.41° (*c* 2.02)	-2.13°[f] (*c* 1.03)
7	(+)-**4** (1 equiv)	120	49	-0.42° (*c* 1.66)	29	-3.18° (*c* 1.10)	+3.36° (*c* 0.77)
8	(+)-**7** (")	240	52	+0.56° (*c* 1.95)	24	+2.54° (*c* 0.87)	-1.85° (*c* 0.92)
	ester						
9	(-)-**5** (")	120	33	+0.16° (*c* 1.24)	44	+0.77° (*c* 1.69)	-1.43° (*c* 0.49)
	ketone						
10	(-)-**6** (0.5 equiv)	30	50	+0.05° (*c* 1.92)	32	+0.69° (*c* 1.15)	-0.41° (*c* 0.97)

a) Sensitizers were recovered quantitatively without loss of the optical purities. b) Isolated yield. c) Optical rotations of solutions in ethanol were measured at 20°C with Jasco Model DIP-4S Digital Polarimeter. d) Obtained by the sensitization with 2-acetonaphthone. e) A scale-up experiment. A solution of 1 g of **1** in 600 ml of methylene chloride was employed. f) A portion of recovered **1** was used.

quantitatively 2-methyl-2-phenylhexanoic acid (**8**), $[\alpha]_D^{20}$ +0.51° (*c* 1.18, benzene), which was then converted into the diazoketone **9**. The specific rotation of pure **9** thus obtained is +0.68° (*c* 1.47, benzene), which corresponds to about 1.0% optical yield with reference to the literature value +65.0° (benzene).[8]

Optical resolution of racemic 2-methyl-2-phenyl-4-hexenoic acid (**10**)[9] *via* the (+)-1-phenylethylamine salt gave (+)-**10**, α_D^{20} +0.897° (neat, 2 mm). The absolute configuration of (+)-**10** was determined to be *S* by the transformation into known (*S*)-(+)-2-methyl-2-phenylbutyric acid (**11**),[10] $[\alpha]_D^{20}$ +28.3° (*c* 2.62, benzene, optical purity 93.8%), through sequential reactions.[11] Catalytic hydrogenation of (*S*)-(+)-**10** afforded (*S*)-(+)-**8**, $[\alpha]_D^{20}$ +21.6° (*c* 2.83, benzene). These results establish the absolute configurations of enantiomers of **1**, as well as compounds **2** and **3** as shown in Scheme 2.

Since it is assumed that both enantiomeric triplet states [(*R*)-**1**]* and [(*S*)-**1**]* decay with identical rate constant, $k_{R*}=k_{S*}$, the development of optical activity in recovered **1** is due to a kinetic photoresolution of **1**. From the value of the optical yield of recovered **1** at the stage of 63% recovery (37% conversion) in run 6, we can calculate roughly the ratio of the apparent rate constants, k_R/k_S, = about 1.04.

The ester 5 and the ketone 6 also sensitized the transformation of 1 into 3, in the latter case the reaction proceeded most rapidly. However, the optical activities of 3 and recovered 1 were considerably smaller than the case of the amide sensitizers. Thus, from the structural points of view, the amide functionality in the sensitizers, in comparison with the ester and ketone ones having the same chiral structure, might favor formation of the intimately interacting collisional states between the systems constituted by one enantiomer of 1 or the other and the triplet excited state of the sensitizer. Furthermore, the generation of the same (+)-enantiomeric excess mixtures in both 3 and recovered 1 from the reactions by (-)-4, (-)-5, (-)-6, and (+)-7 suggests that the same chiral moiety, 1-phenylethyl group, would contribute to the collisional states with the same orientational preference.

Experiments with other substrates and chiral sensitizers are in progress.

References and Notes

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2) (a) K. Sato, H. Hagiwara, H. Uda, M. Sato, and N. Harada, J. Am. Chem. Soc., 98, 8281 (1976); (b) K. Sato, H. Hagiwara, and H. Uda, Chem. Lett., 175 (1977); (c) N. Hoshi, H. Hagiwara, and H. Uda, ibid., 1291 (1979); (d) Idem. ibid., 1295 (1979).

3) (*R*)-(-)-4: mp 167–168.5°C, $[\alpha]_D^{20}$ -94.9° (*c* 0.20, EtOH). (*S*)-(+)-4: mp 168.5–169.5 °C, $[\alpha]_D^{20}$ +94.0° (*c* 0.20, EtOH). (*R*)-(+)-7: mp 133–135°C, $[\alpha]_D^{20}$ +85.8° (*c* 0.20, EtOH). Prepared by the reaction of 2- or 1-naphthoyl chloride with (*R*)-(+)- or (*S*)-(-)-1-phenylethylamine.[4]

4) A. Ault, "Org. Synth.," Coll. Vol. V, 932 (1973).

5) Mp 42–42.5°C, $[\alpha]_D^{20}$ -112.0° (*c* 1.01, EtOH). Prepared by the reaction of 2-naphthoyl chloride with commercially available (*R*)-(+)-1-phenylethyl alcohol.

6) Mp 75–76.5°C, $[\alpha]_D^{20}$ -57.4° (*c* 1.00, EtOH). Prepared from (*S*)-(+)-3-phenylbutyric acid[7] through sequential reactions (esterification, lithiation, condensation with 2-naphthoyl chloride, and deethoxycarbonylation).

7) C. S. Marvel, J. Dec, and H. G. Cook, Jr., J. Am. Chem. Soc., 62, 3499 (1940); D. J. Cram, ibid., 74, 2137 (1952); J. Barry, H. -B. Kagan, and G. Snatzke, Tetrahedron, 27, 4737 (1971).

8) J. F. Lane and E. S. Wallis, J. Am. Chem. Soc., 63, 1674 (1941); J. Org. Chem., 6, 443 (1941).

9) Prepared by the reaction of the dianion of α-phenylpropionic acid with 1-chloro-2-butene.

10) W. Klyne and J. Buckingham, "Atlas of Stereochemistry," 2nd ed, Vol. 1, Chapman and Hall, London (1978), p. 60, and references therein.

11) Esterification, ozonolysis to the aldehydic ester, reduction of the tosylhydrazone with sodium cyanoborohydride, and hydrolysis.

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