# Asymmetric Transformation in Photoequilibrium Systems: Diastereoselective Isomerization of *N*-(*R*)-(+)-α-Arylethylfluorene-9-spiro-1′-cyclopropane-2′-carboxamide Derivatives

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Photochemically induced asymmetric transformation in the isomerizations of *N*-(*R*)-(+)-α-arylethylfluorene-9-spiro-1′-cyclopropane-2′-carboxamide derivatives showed moderate to high diastereoselectivity.

Although asymmetric induction in photochemical processes has received considerable attention,[1] photochemically induced asymmetric transformation[2] between diastereoisomers in equilibrium has not been reported. We report moderately to highly diastereoselective photoisomerization of *N*-(*R*)-(+)-α-arylethylfluorene-9-spiro-1′-cyclopropane-2′-carboxamide derivatives.

The first system investigated is shown in Scheme 1. Occurrence of this isomerization of (**1a**) was directly confirmed by the photosensitized racemization (Φ 0.44†) of optically pure (+)-(**1a**).‡ Irradiation of a benzene solution of an equimolar mixture of the diastereoisomers (**1b**) derived from (*R*)-(+)-α-phenylethylamine in the presence of acetophenone at room temperature§ showed essentially no diastereoselectivity. However, when an equimolar mixture of (**1c**) derived from (*R*)-(+)-α-(1-naphthyl)ethylamine was irradiated under similar conditions, the diastereoisomer ratio changed and reached a constant value [(+)-(**1c**) to (−)-(**1c**)

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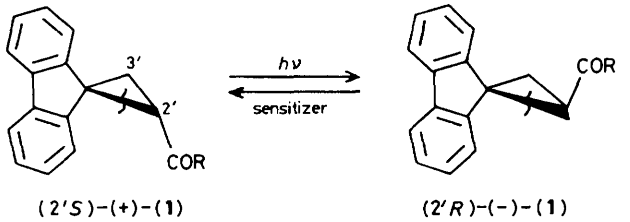
† Quantum yields were determined for concentrations: [substrate], $1.2 \times 10^{-3}$ M and [acetophenone], $2.5 \times 10^{-2}$ M in benzene, by use of the acetophenone-sensitized *cis*- to *trans*-isomerization of (**3a**)[6] as a secondary chemical actinometer with a 500 W Xenon light source (>310 nm).

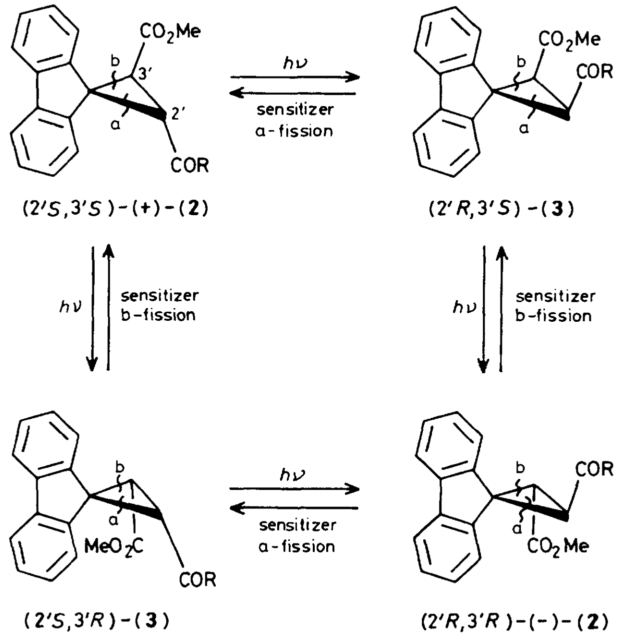
‡ Optically pure (+)-(**1a**) {$[\alpha]_D^{25}$ +265° (*c* 0.4, EtOH)} and (+)-(**2a**) {$[\alpha]_D^{25}$ +340° (*c* 0.5, EtOH)} were obtained either by acidic hydrolysis of (+)-(**1c**) and (+)-(**2c**), respectively, or by direct h.p.l.c. resolution using a poly(triphenylmethylmethacrylate) column ['Chiralpak' OT(+)], available from Daicel Chemical Industries, Japan.

§ The temperature of the benzene solution during irradiation is about 42 °C.

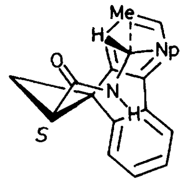


**a**; R = MeO
**b**; R = (*R*)-(+)-MeCHPhNH
**c**; R = (*R*)-(+)-MeCHNpNH

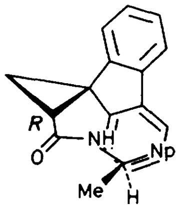
**Scheme 1.** Np = 1-naphthyl.



**Scheme 2.** **a**—**c** as for Scheme 1.



(A)



(B)

64 : 36 by h.p.l.c.]. Recovery of the diastereoisomers exceeded 90%. Regardless of whether one starts from pure (+)-(**1c**) (Φ 0.16†) or pure (−)-(**1c**) (Φ 0.28†), the same diastereoisomer ratio is obtained. After acidic hydrolysis and re-esterification, optically active (+)-(**1a**) was obtained in 28% enantiomeric excess (e.e.). Absolute stereochemistries of (+)-(**1a**—**c**) were determined as depicted in Scheme 1 by chemical correlation (details to be published elsewhere) with the known trimethyl (*S*)-(+)-cyclopropane-1,1,2-tricarboxylate.[3]

Interestingly, the diastereoisomer ratios are sensitizer-dependent. As shown in Table 1, the diastereoselectivity increases from 28 to 72% diastereoisomeric excess (d.e.), as the triplet energy of the sensitizers decreases. This result strongly suggests that energy transfer from the sensitizers to (**1c**) is the key step for the diastereoselective isomerization. In the energy transfer, the triplet energy will be distributed to the fluorenespirocyclopropane and naphthyl moieties. The excited naphthyl triplet at least in part sensitizes the ring opening of the cyclopropane by intramolecular energy transfer to the fluorenespirocyclopropane moiety.¶ Since triplet–triplet energy transfer is generally accepted to occur *via* an electron exchange mechanism,[4] overlap[4] of the naphthyl and fluorenyl groups will be critical. Such an overlap is easily achieved in the configuration (*R*)-(−)-(**1c**) rather than (*S*)-(+)-(**1c**), in which steric repulsion[5] between methyl and fluorenyl groups is experienced [see structures (A) and (B)].** Thus (*S*)-(+)-(**1c**) is photochemically more inert than (*R*)-(−)-(**1c**). This explanation is consistent with the observed absolute stereochemistry of the major diastereoisomer.

**Table 1.** Diastereoisomer ratios[a] at the photostationary state for the isomerization of (**1b**,**c**) and (**2b**,**c**) [(**3b**,**c**)].

| Starting substrate | Sensitizer ($E_T$[b]) | | Diastereoisomer ratio[a] |
|---|---|---|---|
| (**1b**)[c] | Acetophenone | (73.7) | 50 : 50 |
| (**1c**)[d] | Acetophenone | | 64 : 36 |
| (**1c**)[c] | *p*-Methoxy-acetophenone | (71.8) | 75 : 25 |
| (**1c**)[c] | Triphenylene | (66.5) | 83 : 17 |
| (**1c**)[c] | Phenanthrene | (61.9) | 85 : 15 |
| (**1c**)[c] | *p*-Phenyl-acetophenone | (61.1) | 86 : 14 |
| (**2b**)[c] or (**3b**)[c] | Acetophenone | | 55 : 45 |
| (**2c**)[c] or (**3c**)[c] | Acetophenone | | 87 : 13 |
| (**2c**)[d] | Acetophenone | | 87 : 13 |
| (**2c**)[c] | *p*-Methoxy-acetophenone | | 83 : 17 |
| (**2c**)[c] | Triphenylene | | 94 : 6 |
| (**2c**)[c] | Phenanthrene | | 95 : 5 |
| (**2c**)[c] | *p*-Phenyl-acetophenone | | 98 : 2 |

[a] (2′*S*/2′*R*) for (**1b**,**c**): (2′*S*,3′*S*)/(2′*R*,3′*R*) for (**2b**,**c**). [b] Triplet energy of sensitizer in kcal/mol (1 cal = 4.184 J). All values are taken from: S. L. Murov, 'Handbook of Photochemistry,' Marcel Dekker, New York, 1973, p. 3. [c] Starting from an equimolar mixture of diastereoisomers. [d] Starting from pure diastereoisomers.

The investigation was successfully extended to the more complicated Decker's *cis–trans*-isomerization[6] system (Scheme 2) using the 3′-methoxycarbonylfluorene-9-spiro-1′-cyclopropane-2′-carboxamide derivatives (**2b**,**c**) and (**3b**,**c**). The *trans*/*cis*-diastereoisomer ratios at the photostationary state are >99.6 : 0.4 and recovery of the *trans*-isomers exceeds 80% in both cases. The diastereoisomer ratio (2′*S*,3′*S*) to (2′*R*,3′*R*) of the *trans*-isomers is also shown in Table 1. As observed in the isomerization of (**1c**), the presence of the naphthyl group is again important. The diastereoselectivity is also sensitizer-dependent. However the correlation of the selectivity-sequence with the triplet energy is rather poor in

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¶ The triplet energy of (**1a**) is ~61 kcal/mol by analogy with (**2a**),[6] and this value is almost equal to that of the naphthalene triplet. In fact, 1-methylnaphthalene slowly sensitizes the isomerization by intermolecular energy transfer. Since the probability of encounter of these two chromophores within the triplet lifetime of the naphthyl group is much higher intramolecularly, the sensitization will be effectively performed.

** The fact that the $^1$H resonances of the methyl proton (δ in $CDCl_3$, 1.32 or 1.37) of (*S*)-(+)-(**1c**) or (2′*S*,3′*S*)-(+)-(**2c**) are at higher field than those (δ in $CDCl_3$, 1.59 or 1.65, respectively) of (*R*)-(−)-(**1c**) or (2′*R*,3′*R*)-(−)-(**2c**) supports the proposed conformational models.

this case. This is probably due to the multistep isomerization of (**2c**), in which energy transfers from the sensitizers to both the *trans*- and *cis*-diastereoisomers are involved.

For both (**1c**) and (**2c**), the highest selectivity was achieved with *p*-phenylacetophenone. Acidic hydrolysis and subsequent methylation gave optically active (+)-(**1a**) and (+)-(**2a**) in 74 and 94% e.e., respectively.

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