Memory of Chirality in Photochemistry**

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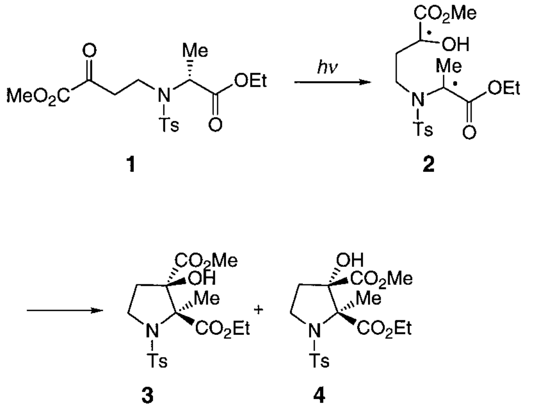
The concept of "spinisomers" was introduced in the chemical literature by Turro[1] and Quinkert[2] in order to differentiate excited molecules in the singlet and the triplet state (S_1 and T_1, respectively) from each other. Reactions of spinisomers often lead to different products;[3] molecules in the T_1 state react mostly less stereoselectively than the corresponding S_1 state molecules.[4] Herein, we compare the steric course of chemical reactions of T_1 and S_1 spinisomers using the Norrish–Yang photocyclization of alanine derivative **1**[5] which leads to proline derivatives **3** and **4** (Scheme 1).



Scheme 1. Photoinduced cyclization of alanine derivative **1** leading to proline derivatives **3** and **4**. Ts = Tosyl = $H_3CC_6H_4SO_2$.

Table 1. Selectivities of the photocyclizations of alanine derivative **1** leading to *cis* product **3** and *trans* product **4** in benzene at 20 °C.

Conditions	**3**:*ent*-**3**	**4**:*ent*-**4**	*cis*:*trans*	Overall yield [%][a]
hν/naphthalene (1 M)	24	16	5.7	47[b]
hν/naphthalene (0.5 M)	18	13	5.3	50[b]
hν/isoprene (0.5 M)	9.4	3.0	2.9	47[b]
hν/O_2	9.6	3.6	2.6	48[c]
hν/Ar	2.4	1.6	0.9	35[c]
hν/benzophenone (1 M)/Ar	1.4	1.4	0.8	10[d]

[a] Based on the conversion (80–90%). [b] Irradiation time 10 h. [c] Irradiation time 2 h. [d] Irradiation time 20 min.

The photoreaction[6] of **1** in the presence of the triplet sensitizer benzophenone led almost unselectively to four cyclization products (**3** + *ent*-**3** and **4** + *ent*-**4**). In contrast, in the presence of the triplet quencher naphthalene,[7] proline derivative **3** was obtained with high enantioselectivity (Table 1, lines 1 and 6). Under these singlet conditions, the configuration of the attacked sp^3-hybridized chiral center in **1** was transferred into product **3** with retention, although it was converted into a prochiral, sp^2-hybridized radical center in the intermediate diradical **2**. This enantioselective reaction path demonstrates the existence of a memory of chirality[8] whose magnitude is given by the retention:inversion ratio at the chiral center.

In the presence of naphthalene (1 M) as quencher of the T_1-excited carbonyl group, the memory effect was 24 (e.r. = 96:4) for the *cis* isomer **3** (Table 1, line 1). Decreasing either the amount or the efficiency of the triplet quencher led to a smaller memory effect of 18 (0.5 M naphthalene, Table 1, line 2), 9.4 (0.5 M isoprene, Table 1, line 3), and 9.6 (O_2, Table 1, line 3).[9] In the absence of a triplet quencher[10] the memory effect dropped to 2.4 (Table 1, line 5), and disappeared almost completely when the reaction was performed in the presence of the triplet sensitizer benzophenone (Table 1, line 6). The success of the photocyclization in the presence of large amounts of naphthalene showed that H-abstraction can occur not only from the triplet state but also from the excited singlet state of oxoester **1**.[11] The high yields of 47–50%, obtained in the presence of naphthalene, are surprising, even though the irradiation time was increased by a factor of five. Presumably, naphthalene not only acts as a triplet quencher but also as a singlet sensitizer for oxoester **1**.[12] The subsequent cyclization of the singlet diradical is obviously so fast that the C–C bond is formed almost completely under retention. In contrast, the T_1-spinisomer forms a long-lived triplet diradical which leads to racemic products.

Figure 1 shows how the asymmetric center based chirality of the starting material **1** is transferred through the helix-based chirality of the diradical intermediate **2** into the asymmetric center based chirality of the product **3.**

A memory effect of about 25 means that racemization of the helical chiral singlet diradical **2** occurs with an activation energy that is about 3 kcal mol^{-1} higher than that of the cyclization to give product **3**. Racemization requires rotations around the α-, β-, and γ-single bonds of diradical **2** (Figure 1, Scheme 2). For steric reasons, the first step is probably a rotation from the *gauche* conformation **I** into the *anti* conformation **II**. From quantum chemical estimations[13] a β-rotation of the singlet diradical (**I** → **II**) requires about 5 kcal mol^{-1} and the subsequent α- and γ-rotations of conformer **II** about 1.5 and 3.0 kcal mol^{-1}, respectively. From these estimated racemization barriers and a memory effect of 25 (ca. 3 kcal mol^{-1}), we conclude that the cyclization of singlet diradical **2** requires an activation energy of 2 kcal mol^{-1}. This low activation energy is expected for a recombination of two radical centers. In contrast, the loss of the memory of chirality under triplet conditions (Table 1,

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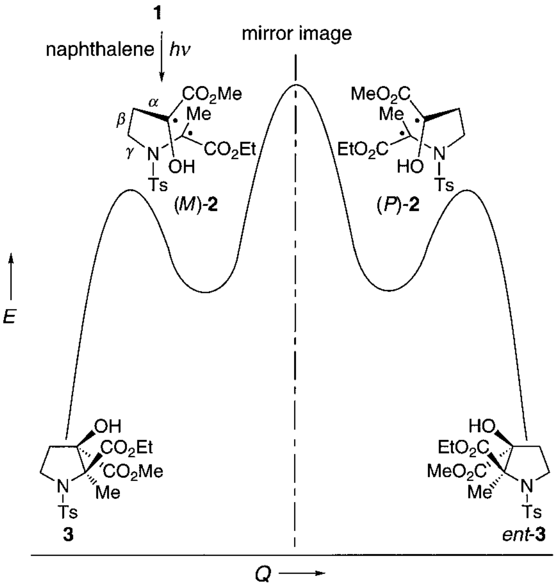
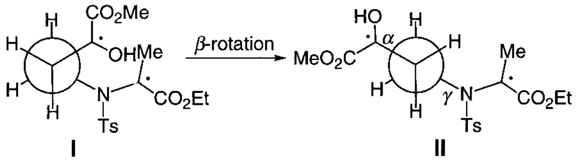


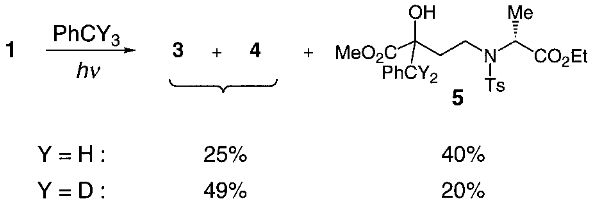
Figure 1. Energy profile diagram of the racemization and cyclization reactions of the singlet diradical (*M*)-**2**.



Scheme 2. Rotation around the β-single bond of the intermediate diradical.

line 6) shows that the lifetime of triplet diradical **2** is so high that its racemization can occur.

The solvent for this Norrish-Yang photocyclization is not limited to benzene. Similar trends were observed in acetonitrile and toluene. However, in toluene intermolecular H-abstraction led to adduct **5**.[14] As expected, the yield of acyclic 1:1 adduct **5** decreases (from 40% to 20%) when trideuterotoluene was used. At the same time, the yield of cyclization products **2** and **3** was doubled (Scheme 3).



Scheme 3. Photochemical reactions of alanine derivative **1** in toluene.

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[1] N. J. Turro, *Chem. Eng. News* **1967**, *45*(20), 84.

[2] G. Quinkert, *Angew. Chem.* **1975**, *87*, 851; *Angew. Chem. Int. Ed. Engl.* **1975**, *14*, 790.

[3] See for instance: a) D. A. Plattner, *Angew. Chem.* **1999**, *111*, 86; *Angew. Chem. Int. Ed.* **1999**, *38*, 82; b) W. Adam, G. Fragale, D. Klapstein, W. M. Nau, J. Wirz, *J. Am. Chem. Soc.* **1995**, *117*, 12578.

[4] a) P. S. Engel, *Chem. Rev.* **1980**, *80*, 137; b) C. P. Casey, R. A. Boggs, *J. Am. Chem. Soc.* **1972**, *94*, 6457; c) L. M. Stephenson, J. I. Braumann, *J. Am. Chem. Soc.* **1971**, *93*, 1988; d) N. C. Yang, S. P. Elliott, *J. Am. Chem. Soc.* **1969**, *91*, 7550; e) P. D. Bartlett, N. A. Porter, *J. Am. Chem. Soc.* **1968**, *90*, 5317.

[5] Compound **1** was prepared by S_N2 substitution of ethyl *O*-trifluoromethanesulfonyl-L-lactate with methyl 4-tosylamino-2-siloxybutyrate followed by Dess-Martin periodinane oxidation. Its structure was elucidated by elemental analysis, NMR spectroscopy, and CD spectroscopy.

[6] Photocyclizations of **1** (2mM in benzene) were carried out at 20°C with a 150-W Hg high-pressure lamp (Heraeus, TQ-150, 3 mm pyrex cuvette). The irradiation times depended on the reaction conditions (benzophenone: 20 min; Ar or O_2: about 2 h; naphthalene or isoprene: about 10 h). At 80-90% conversion the solutions were directly analyzed by analytical HPLC (column: Daicel Chiralcel OD, eluent: hexane/isopropyl alcohol, 3/1) to determine the yields (Table 1); yields refer to the conversions. Decreasing the irradiation times reduces the yields but has no effect on the product ratios. The four products were separated by preparative HPLC by using the same chiral column. The structural evidence is based on X-ray crystal structure analyses of derivatives of **3** and **4** in which the corresponding OH groups were esterified with (+)- and (−)-camphanic acid chloride, respectively. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC-116102 and CCDC-116103. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44)1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

[7] Norrish II photoeliminations of α-oxoesters that occur in the presence of a triplet quencher via a S_1-spinisomer are known: S. Davidson, D. Goodwin, P. Fornier de Violet, *Tetrahedron Lett.* **1981**, *22*, 2485.

[8] The term "memory of chirality" is used here with the meaning that was proposed by K. Fuji: K. Fuji, T. Kawabata, *Chem. Eur. J.* **1998**, *4*, 373. The chirality of a sp^3 center is lost because it is converted into a sp^2 center. Nevertheless, a new sp^3-hybridized chiral center is created from the sp^2 center in an enantioselective reaction. For a discussion on the memory effect in photochemical reactions, see: a) A. G. Griesbeck, H. Mauder, S. Stadtmüller, *Acc. Chem. Res.* **1994**, *27*, 70; b) J. C. Scaiano, *Tetrahedron* **1982**, *38*, 819.

[9] Oxygen probably accelerates the triplet-singlet crossing of diradical **2**. This diminishes the lifetime of the triplet state so strongly that the contribution coming from racemization of the helical triplet intermediate decreases: W. Adam, S. Grabowski, R. M. Wilson, *Chem. Ber.* **1989**, *122*, 561; R. D. Small, J. C. Scaiano, *J. Am. Chem. Soc.* **1978**, *100*, 4512.

[10] The decomposition quantum yields of **1** under triplet conditions (toluene, N_2) were determined following the actinometer method. It amounts to 0.07 ± 0.02 (*trans*-azobenzene as reference).

[11] For the differences between excited singlet and triplet states in intermolecular H-abstractions, see: W. M. Nau, F. L. Cozens, J. C. Scaiano, *J. Am. Chem. Soc.* **1996**, *118*, 2275.

[12] According to our measurements the triplet and singlet energies of an oxoester analogous to **1** (glycine instead of alanine) are 68 and 87 $kcal\,mol^{-1}$, respectively. The triplet and singlet energies of naphthalene are 60 and 92 $kcal\,mol^{-1}$, respectively. The lifetime (96 ns) of the S_1 state of naphthalene should be long enough for a diffusion-controlled energy transfer in a 1M naphthalene solution.

[13] The quantum chemical estimations were calculated following the "unrestricted Hartree-Fock" method with the 3-21G* basis set (Gaussian 94). The keyword "guess = mix" was used for the calculation of the singlet diradicals. Until now, DFT calculations of singlet diradical **2** did not lead to converging energies in our hands. For DFT calculations of singlet diradicals, see: E. R. Davidson, *Int. J. Quant. Chem.* **1998**, *69*, 241; J. Gräfenstein, E. Kraka, D. Cremer, *Chem. Phys. Lett.* **1998**, *288*, 593.

[14] The structure determination of **5** was performed by MS and 600 MHz NMR spectroscopy (two diastereomers in a ratio of about 1:1).