Diastereo- and Enantioselective δ-H Abstraction in the Solid State of 1-Benzoyl-8-benzylnaphthalene − Absolute Asymmetric Synthesis Due to a Chiral Crystal Environment

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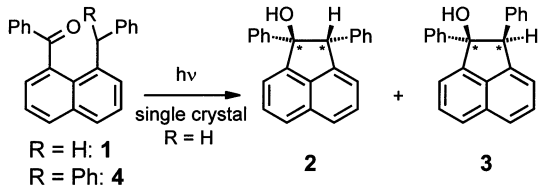
Due to the matrix effect of the crystal lattice, irradiation of ketone **1** yields **2** diastereoselectively as the main product (97% *de*). Furthermore, the chiral crystal environment in single crystals of **1** (space group $P2_12_12_1$) also renders the reaction enantioselective (86% *ee*). Both enantiomers of alcohol **2** could be produced, depending on which enantiomorphic form of the chiral crystal was irradiated. As the ketone **1** is achiral and the chiral induction is caused exclusively by physical influences, this reaction represents a further example of an absolute asymmetric synthesis.

Introduction

Absolute asymmetric syntheses (AAS)[1a][1b][1c] are enantioselective syntheses, in which the asymmetric induction is caused exclusively by physical influences, e.g. by chiral crystal structures. Achiral compounds crystallizing in a chiral space group are of special interest. In a single crystal of such a compound, a chemical reaction leading to a chiral product can, under optimal conditions, yield one of the enantiomers almost quantitatively, as a result of the chiral environment. Apart from additions of halogens, cycloadditions, electrocyclic reactions and rearrangements, only a few H abstractions have been carried out in an absolute asymmetric manner. To the best of our knowledge, four γ-H abstractions by oxygen[2a][2b][2c][2d], one γ-H abstraction by sulfur[2e], and one δ-H abstraction by a C=C double bond[2f] have been described as AAS to date. In extension of this work, we present here the first example of an absolute asymmetric, photochemically induced δ-H abstraction by oxygen in chiral single crystals of 1-benzoyl-8-benzylnaphthalene (**1**). In the first step, this reaction is analogous to a Norrish type-II photoreaction, but proceeds via a seven-membered ring transition state. The photoreaction in solution yields the diastereomeric alcohols **2** and **3**, with comparable amounts of these isomers having the two phenyl groups in *cis* and *trans* arrangements (42:58)[3]. However, in the solid state, because of the matrix effect of the crystal, the two phenyl groups can be pre-orientated, and so one of the two products **2** or **3** should be strongly favoured (Scheme 1).

Furthermore, if ketone **1** crystallizes in a chiral space group, irradiation of a single crystal should yield an excess of one enantiomer of the main product, either **2** or **3**, respectively. If this is the case, the structure of the crystal brings about a coupling of simple diastereoselective[4] and enantioselective control of the products. In this reaction, two new centres of chirality are generated. As a result of the conditions of the AAS, of the four possible stereoisomers, only one should be obtained as the main product.

Scheme 1. δ-H abstraction from 1-benzoyl-8-benzylnaphthalene (**1**)



Results and Discussion

Ketone **1** crystallizes in the chiral space group $P2_12_12_1$. As is apparent from an X-ray structure analysis[5], the phenyl groups in **1** are fixed in a *syn* conformation (Figure 1).

Semiempirical AM1 calculations[6] show that the *syn* conformation should also be preferred in the free molecule. The slight stabilization relative to the *anti* conformation is 12.6 kJ mol^{-1}. As shown in Figure 2, four parameters serve to define the geometry of hydrogen atom abstraction[7].

The first of these parameters is the length *d* of the distance vector between the abstracting oxygen atom and the H_δ atom being abstracted. The second parameter is the angle ω, the dihedral angle between the O−H_δ distance vector and the mean plane of the carbonyl group. The third is the angle Δ, defined as the C=O···H_δ angle, and the fourth is θ, the C−H_δ···O angle. The abstraction distance *d* should be close to the sum of the van der Waals radii of the abstracting atoms, 1.52 Å + 1.20 Å = 2.72 Å in the case of oxygen and hydrogen[8]. The model value of the angle ω is

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Figure 1. Molecular structures of **1** and **2** from X-ray structure analyses; the enantiomeric conformation **1** and configuration **2** are arbitrary

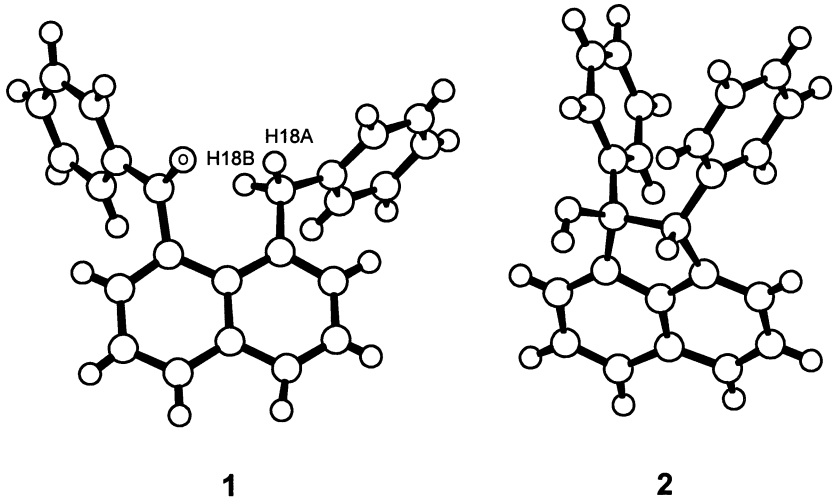


Figure 2. Definition of geometric quantities in Table 1

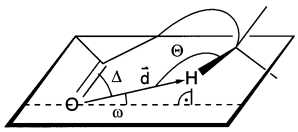


Table 1. Geometric values for the intramolecular H abstraction of H18A and H18B in **1** compared with model values

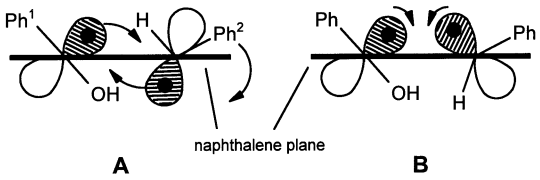
	H18A	H18B	Model values
ω [°]	78	87	90
Δ [°]	91	60	90
θ [°]	121	86	180

0°, if the hydrogen atom is abstracted by the oxygen atom of the CO group in the n,π* state. In solid-state H-abstraction reactions this mechanism was adopted in the discussions. For the photochemistry of **1** in solution the main character of the excited state was shown to be of π,π* type, which follows from the stabilizing property of the naphthyl substituent[3]. H abstractions by π,π*-excited CO groups were not described before for solid-state reactions. According to the π,π* state the model value of the angle ω is 90°. The observed angles ω = 78° and 87° for H18A and H18B respectively (Table 1) in crystals of **1** are not far from the model value. According to the assumed reaction mechanism, we define the model value of the angle Δ to be 90°. Finally, there seems to be general agreement that the optimum value of the angle θ is 180°[10]. For the Norrish type-II process, it has been observed, that the values for this angle can deviate significantly from the value regarded as ideal[7][11]. For the lowest triplet π,π* state in the solution reaction a mixing of only 8% with the lowest n,π* state was estimated. This contribution may be higher in the crystalline state since the stabilization of the π,π* state by the naphthalene substituent is weakened by the large degree of torsion (58°) between the naphthalene against the carbonyl group. Since the irradiations of the crystals were conducted at 40−50°C, competing thermal excitation to the lowest n,π* state can not be excluded.

Considering the distance *d*, the vector to H atom H18A is shorter (2.36 Å) than the sum of the van der Waals radii (2.72 Å), while that to H18B is slightly longer (2.88 Å). Both distances fall within the usual range (2.30−3.10 Å) for hydrogen abstractions[11]. While atom H18A attains a near ideal value for Δ of 91°, for H18B this angle (60°) deviates somewhat from the standard angle. Finally, considering the angle θ, both hydrogen atoms are within the observed limits (85−120°[11]), but that for H18A is closer to the ideal value of 180°. According to the geometric data of H18A and H18B, both hydrogens fulfil the conditions for abstraction, but H18A is the better candidate. If this H atom is abstracted, a biradical of approximate structure **A** (Figure 3) should be generated. The recombination of the biradical would lead to the *trans* product **3**. The abstraction of H18B should result in the *cis* product **2** from the biradical **B** (Figure 3). The formation of the main product **2** can easily be explained by abstraction of H18A and inversion of the formed benzylic C radical generating a biradical which looks like **B**. The following bond formation results in the *cis* product **2**. Another route to the main product **2** could be the abstraction of H atom H18B and recombination of the biradical **B** without steric hindrance. The formation of the *trans* product **3** requires a sterically hindered rotation of the phenyl ring Ph^2 across the edge of the naphthalene plane (Figure 3). Therefore only small amounts of *trans* product **3** are formed by this unfavourable route.

As a consequence of the fixed *syn* conformation of **1** in the solid state, irradiation of single crystals of **1** yields the *cis*-1,2-diphenylacenaphthen-1-ol **2** as the main product, with up to 97% *de*, as demonstrated in a series of experiments. Only a small amount of *trans*-acenaphthenol **3** is also generated in the solid state, presumably due to an increased thermal motion of the molecules in the crystal dur-

Figure 3. Approximate structure of the formed biradicals after abstraction of H18A (**A**) and H18B (**B**)



ing the irradiation (40−55°C). The photoreaction is frozen when the probe is cooled below 0°C. As the ketone **1** crystallizes as a conglomerate, an excess of one enantiomer of the *cis*-acenaphthenol **2** is found in selected single crystals after the irradiation. In optimal cases, we found 86% *ee* of the first enantiomer **2** and 49% *ee* of the other enantiomer *ent*-**2**. The absolute configuration of **2** was not determined. In fifteen experiments, we obtained the first enantiomer twelve times and the other enantiomer three times. This deviation from the expected equal distribution of the enantiomorphic forms of the crystals of **1** is possibly due to a self-seeding effect during the growth of the crystals. The enantiomeric excess was determined using the enantiomerically pure shift reagent tris-[3-(trifluoromethyl-hydroxymethylene)-*d*-camphorato]-europium(III), Eu(facam)$_3$, in ^{1}H-NMR experiments on the solutions of the irradiated single crystals in $CDCl_3$. The integral of the CH proton in **2** was measured for both enantiomers. Because of the generation of minor quantities of **3** as a by-product, there are four signals in the region of aryl substituted methine groups. It is possible to assign the four signals in pairs to **2** and **3**, respectively, on the basis of their integrals, the form of the signals, and the constant distance between two of them. The signals at δ = 5.14 and δ = 5.30 can be assigned to the *cis* product **2**, and those at δ = 4.95 and δ = 5.15 to the *trans* product **3**.

The *cis* and *trans* products **2** and **3** respectively were obtained in sufficient amounts by photoreaction in solution. The isomers were separated and characterized by chromatography, spectroscopy and for compound **2** also by X-ray diffraction. The solid-state products were identified by comparison with these data. The acenaphthenol **2** crystallizes in the racemic centrosymmetric space group $P\bar{1}$ (Figure 1)[5].

During the irradiation of **1**, the elimination product 1,2-diphenylacenaphthylene is also generated. In order to make the dehydration impossible, we synthesized the analogous ketone **4**. However, **4** crystallizes in the achiral space group $P2_1/n$[5] and is therefore unsuitable for an asymmetric synthesis.

Conclusion

Due to the matrix effect of the crystal lattice, irradiation of ketone **1** yields **2** diastereoselectively as the main product, along with minor quantities of **3**. The geometric conditions for the δ-H abstraction are nearly ideal for a π,π* mechanism, which was discussed for the photochemistry in solution[3] and was applied the first time to an H-abstraction reaction in the solid state. Furthermore, the chiral crystal environment in single crystals of **1** renders the reaction enantioselective. Both enantiomers of alcohol **2** could be produced, depending on which enantiomorphic form of the chiral crystal was irradiated. Because the ketone **1** is achiral and the chiral induction is caused exclusively by physical influences, this reaction represents a further example of an absolute asymmetric synthesis.

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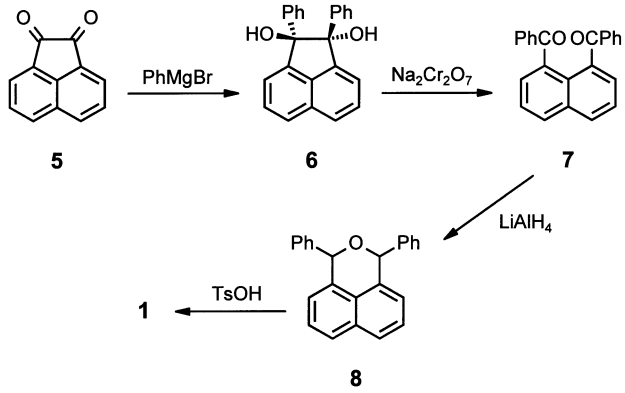
Experimental Section

General Remarks: The title compound **1** was synthesized from acenaphthenequinone **5** via the diol **6**, the diketone **7**, and the benzoisochromene **8**, according to a literature procedure[3] (Scheme 2).

Scheme 2. Synthesis of 1-benzoyl-8-benzylnaphthalene (**1**)



We present a detailed characterization of the compounds for the first time. − IR: Bruker IFS 66. − UV/Vis: Hewlett-Packard 8452A. − NMR: Bruker AC 300, Bruker AC 200 (sweep frequencies as indicated). $CDCl_3$ as solvent δ_H = 7.24, δ_C = 77.0. − MS: VG MICROMASS ZAB-2F sector field MS (70 eV).

Irradiation Experiments: Hg high-pressure lamp Q1200 (Heraeus, Hanau, Germany); 21−51 h irradiation at a distance of 4−9 cm; single crystals (EtOH) of typical dimensions 2.5 × 0.8 × 0.8 mm, 0.5−4 mg; temp. 40−50°C in the surroundings of the crystals. Cooling from 20 to 0°C decreased the yield, and experiments between 0 and −40°C froze the reaction. Variation of the experimental conditions, such as carrying out the irradiation in ampoules, under nitrogen, in suspension, or using a filter (WG 360, Schott, Mainz, Germany, cut-off: 360 nm) had no influence on the course of the reaction. The crystals turned yellow during the irradiation owing to the formation of 1,2-diphenylacenaphthylene as an elimination product. Earlier experiments with polycrystalline material yielded 5.8% of the alcohols **2** and **3**, and 2.1% of the elimination product generated from them. The conversion in the crystal is therefore likely to be typically 8%.

trans-1,2-Diphenylacenaphthene-1,2-diol (**6**): M.p. 157°C (EtOH). − IR (KBr): $\tilde{\nu}$ = 3540 cm^{-1}, 3390, 3050, 1600, 1490, 1440, 1340, 1170, 1150, 1120, 1060, 1025, 1000, 810, 780, 740, 690. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.16 (s, 2 H, OH), 7.23−7.27 (m, 4 H, aromatic H), 7.34−7.39 (m, 8 H, aromatic H), 7.65 (dd, ^3J = 8.3

Hz, ^4J = 7.0 Hz, 2 H, aromatic H), 7.91 (d, ^3J = 8.3 Hz, 2 H, aromatic H). − MS (70 eV); *m/z* (%): 339 (1) [M^+ + H], 338 (5) [M^+], 233 (19), 232 (12), 231 (36), 215 (14), 202 (11), 155 (12), 127 (16), 105 (100), 91 (26), 78 (10), 77 (94), 51 (18). − $C_{24}H_{18}O_2$ (338.4): calcd. C 85.18, H 5.36; found C 85.13, H 5.38.

(8-Benzoylnaphthalen-1-yl)phenylmethanone (**7**): M.p. 185°C (EtOH). − IR (KBr): $\tilde{\nu}$ = 3057 cm^{-1}, 1656, 1596, 1578, 1449, 1315, 1272, 1210, 1179, 1018, 830, 773, 718, 707, 690. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.38 (t, ^3J = 7.6 Hz, 4 H, naphthalene), 7.50−7.59 (m, 6 H, Ph), 7.81−7.84 (m, 4 H, Ph), 8.07 (dd, ^3J = 7.6 Hz, ^4J = 1.9 Hz, 2 H, naphthalene). − MS (70 eV); *m/z* (%): 336 (1) [M^+], 232 (38), 231 (100), 203 (11), 202 (55), 201 (14), 200 (14), 105 (61), 77 (95), 51 (25). − $C_{24}H_{16}O_2$ (336.4): calcd. C 85.69, H 4.80; found C 85.47, H 4.91.

cis- and trans-1,3-Diphenyl-1H,3H-benzo[de]isochromene (**8**): M.p. 196−198°C (MeOH). − IR (KBr): $\tilde{\nu}$ = 3326 cm^{-1}, 1601, 1492, 1451, 1253, 1029, 1015, 1005, 814, 772, 724, 698. − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 6.67 (s, 2 H, OCH), 6.70 (s, 2 H, OCH), 7.24−7.35 (m, 20 H, Ph), 7.43 (t, ^3J = 7.7 Hz, 4 H, naphthalene), 7.58 (d, ^3J = 6.0 Hz, 4 H, naphthalene), 7.88 (dd, ^3J = 8.0 Hz, ^4J = 1.5 Hz, 4 H, naphthalene). − MS (70 eV); *m/z* (%): 323 (1) [M^+ + H], 322 (6) [M^+], 232 (21), 231 (100), 215 (21), 105 (29), 79 (10), 77 (37). − $C_{24}H_{18}O$ (322.4): calcd. C 89.41, H 5.63; found C 89.36, H 5.65.

(8-Benzylnaphthalen-1-yl)phenylmethanone (**1**): M.p. 130−131°C (EtOH). − IR (KBr): $\tilde{\nu}$ = 3020 cm^{-1}, 2890, 2830, 1655, 1590, 1575, 1490, 1450, 1430, 1310, 1270, 1240, 1200, 1170, 1000, 870, 820, 770, 740, 710, 695. − UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 250 nm (4.30). − ^{1}H NMR (200 MHz, $CDCl_3$): δ = 4.17 (s, 2 H, CH_2), 6.82−6.89 (2 t, 2 H, naphthalene), 7.05−7.16 (m, 4 H, Ph), 7.30−7.55 (m, 6 H, Ph), 7.73 (dd, ^3J = 8.8 Hz, ^4J = 1.3 Hz, 2 H, naphthalene), 7.83 (dd, ^3J = 8.8 Hz, ^4J = 1.3 Hz, 1 H, naphthalene), 8.00 (dd, ^3J = 8.8 Hz, ^4J = 1.3 Hz, 1 H, naphthalene). − ^{13}C NMR (50 MHz, $CDCl_3$): δ = 41.83 (CH_2), 123.74, 126.04, 126.17, 127.61, 127.87, 128.17, 128.31, 129.52, 129.87, 130.12, 130.44, 131.67, 132.79, 133.02, 134.99, 137.12, 137.49, 137.64, 140.13 (all aromatic C), 198.57 (CO). − MS (70 eV); *m/z* (%): 323 (1) [M^+ + H], 322 (4) [M^+], 232 (22), 231 (100), 215 (35), 213 (10), 202 (19), 167 (10), 139 (11), 122 (10), 107 (11), 105 (30), 91 (10), 78 (12), 77 (76), 51 (28). − $C_{24}H_{18}O$ (322.4): calcd. C 89.41, H 5.63; found C 89.20, H 5.65.

cis-1,2-Diphenylacenaphthen-1-ol (**2**): IR (KBr): $\tilde{\nu}$ = 3550 cm^{-1}, 3400, 3060, 3020, 1600, 1490, 1450, 1440, 1360, 1120, 1060, 1030, 975, 810, 780, 770, 750, 700, 690. − UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 290 nm (3.84). − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.74 (s, 1 H, OH), 5.13 (s, 1 H, CH), 6.74−6.78 (m, 2 H, Ph), 6.84−6.87 (m, 2 H, Ph), 6.93−6.97 (m, 6 H, Ph), 7.21 (d, ^3J = 6.9 Hz, 1 H, naphthalene), 7.34 (d, ^3J = 7.2 Hz, 1 H, naphthalene), 7.59 (dd, ^3J = 8.4 Hz, ^4J = 6.9 Hz, 1 H, naphthalene), 7.64 (dd, ^3J = 8.4 Hz, ^4J = 7.2 Hz, 1 H, naphthalene), 7.81 (d, ^3J = 8.4 Hz, 1 H, naphthalene), 7.89 (d, ^3J = 8.4 Hz, 1 H, naphthalene). − MS (70 eV); *m/z* (%): 323 (2) [M^+ + H], 322 (7) [M^+], 232 (22), 231 (100), 215 (22), 202 (12), 167 (11), 122 (22), 107 (15), 105 (17), 77 (26). − $C_{24}H_{18}O$ (322.4): calcd. C 89.41, H 5.63; found C 89.29, H 5.65.

trans-1,2-Diphenylacenaphthen-1-ol (**3**): IR (KBr): $\tilde{\nu}$ = 3550 cm^{-1}, 3060, 3010, 2930, 2860, 1600, 1500, 1450, 1120, 910, 820, 690. − ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.10 (s, 1 H, OH), 5.13 (s, 1 H, CH), 7.08−7.11 (m, 2 H, naphthalene), 7.23−7.37 (m, 10 H, Ph), 7.58 (d, ^3J = 6.9 Hz, 1 H, naphthalene), 7.61 (d, ^3J = 6.9 Hz, 1 H, naphthalene), 7.82 (d, ^3J = 8.4 Hz, 1 H, naphthalene), 7.86 (d, ^3J = 7.8 Hz, 1 H, naphthalene). − MS (70 eV); *m/z* (%): 323 (2) [M^+ + H], 322 (8) [M^+], 232 (21), 231 (100), 215 (16), 105 (16), 84 (12), 77 (29), 57 (12), 55 (10).

[1] For reviews on AAS see: [1a] G. Kaupp, M. Haak, *Angew. Chem.* **1993**, *105*, 727−728; *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 694−695. − [1b] M. Sakamoto, *Chem. Eur. J.* **1997**, *3*, 684−689. − For a new example, see: [1c] L.-C. Wu, C. J. Cheer, G. Olovsson, J. R. Scheffer, J. Trotter, S.-L. Wang, F.-L. Liao, *Tetrahedron Lett.* **1997**, *38*, 3135−3138.

[2] [2a] S. V. Evans, M. Garcia-Garibay, N. Omkaram, J. R. Scheffer, J. Trotter, F. Wireko, *J. Am. Chem. Soc.* **1986**, *108*, 5648−5650. − [2b] F. Toda, M. Yagi, S. Soda, *J. Chem. Soc., Chem. Commun.* **1987**, 1413−1414. − [2c] M. Sakamoto, M. Takahashi, T. Fujita, T. Nishio, I. Iida, S. Watanabe, *J. Org. Chem.* **1995**, *60*, 4682−4683. − [2d] M. Leibovitch, G. Olovsson, J. R. Scheffer, J. Trotter, *J. Am. Chem. Soc.* **1997**, *119*, 1462−1463. − [2e] M. Sakamoto, M. Takahashi, M. Shimizu, T. Fujita, T. Nishio, I. Iida, K. Yamaguchi, S. Watanabe, *J. Org. Chem.* **1995**, *60*, 7088−7089. − [2f] M. Sakamoto, M. Takahashi, K. Kamiya, K. Yamaguchi, T. Fujita, S. Watanabe, *J. Am. Chem. Soc.* **1996, 118**, 10664−10665.

[3] C. D. DeBoer, W. G. Herkstroeter, A. P. Marchetti, A. G. Schultz, R. H. Schlessinger, *J. Am. Chem. Soc.* **1973**, *95*, 3963−3969.

[4] G. Helmchen, *Methoden Org. Chem. (Houben-Weyl)*, 4th ed., **1995**, vol. E21a, pp. 53−56.

[5] Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-100979. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, U.K. [Fax: (internat.) + 44-1223-336033; E-mail: deposit@ccdc.cam.ac.uk].

[6] *HyperChem 4.5*, Hypercube, Inc., Gainesville, Florida, USA, **1995**.

[7] P. Wagner, B.-S. Park, *Org. Photochem.* **1991**, *11*, 227−366.

[8] A. Bondi, *J. Phys. Chem.* **1964**, *68*, 441−451.

[9] N. J. Turro, *Modern Molecular Photochemistry*, Benjamin/Cummings, Menlo Park, CA, **1978**, pp. 362−413.

[10] A. E. Dorigo, K. N. Houk, *J. Am. Chem. Soc.* **1987**, *109*, 2195−2197, and references cited therein.

[11] J. R. Scheffer, M. Garcia-Garibay, O. Nalamasu, *Org. Photochem.* **1987**, *8*, 249−347.

[98161]