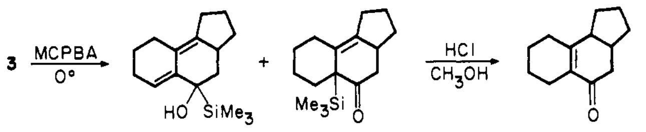

7 6 8

Since **3** may be thought of as the B,C,D portion of the steroid nucleus, oxidation to **8** is significant in light of the medicinal importance of the corticosteroids incorporating an 11-oxo function.

The synthetic *advantages of metal complexation* are demonstrated in Scheme II. Hydride abstraction from **2a** [$(C_6H_5)_3C^+PF_6^-$, CH_2Cl_2, -78 °C, room temperature, 70%) gave red, air-stable salt **9** (mp 219-224 °C dec).[3] Treatment with $NaBD_4$ (CH_3OH-petroleum ether, -78 °C, room temperature) yielded a 1:1 mixture of **10** (*m/e* 371) and **11**. The latter was obtained pure on reaction of **9** with base (K_2CO_3, CH_3OH-petroleum ether, 0 °C, 85%).[3,4] To our knowledge, this is the first reported neutral benzene complex of CpCo. ^{13}C NMR[4] data indicate that the metal is bound in the tetrahapto mode, as shown. The complex **11** is unstable and decomposes with liberation of the ligand. Reaction of **9** with KCN (CH_3OH-petroleum ether, room temperature, 87%) gave this ligand directly (mp 44-46 °C). Nucleophilic carbon-carbon bond formation is achieved with alkyllithium reagents. This is significant in light of the presence of angular alkyl substituents in many natural products. *tert*-Butyllithium (4 equiv, THF, -78 °C, 80%) resulted in the angular derivative **12**.[3,4] Surprisingly, methyllithium (5 equiv, THF, -78 °C, 60%) attacked the cyclopentadienyl ring, followed by what appears to be a cobalt-mediated hydrogen shift to the tricyclic ligand, resulting in **13**,[3,4] in addition to some **11** (15%). The presence of a methylated cyclopentadienyl ring in **13** is evident from mass spectroscopy and NMR measurements, although the assignment of the stereochemistry in the other ligand is tentative. It relies on the unusually high-field proton chemical shifts of the trimethylsilyl group (relative to **2a-c**, **11**, and **12**) and a single hydrogen, which we believe to be its neighbor. Moreover, the carbon spectrum reveals the absence of a terminal silyl diene carbon. Attack of methyllithium on **9** in this manner, if occurring by a simple nucleophilic mechanism, violates the Davis-Green-Mingos rules.[11]

It is evident that the described methodology should provide a powerful simplification of synthetic approaches to molecules containing the hydrophenanthrene, hydrobenzindan, and hydrodicyclopentabenzene frameworks.[2] Advantages are the simultaneous formation of three new carbon-carbon bonds to furnish three annelated rings in one step,[12] facile ligand liberation, use of silicon to mask extensive functionality, and the exploitation of the metal as an electronically activating and sterically directing group. The generation of a chiral center from achiral material in the cobalt-mediated step suggests the possibility of effecting asymmetric inductions by chiral and optically active cobalt. The latter possibility and the application of this reaction to the synthesis of natural products are under intensive investigation.

Acknowledgments. We thank Rudi Nunlist for valuable help in the measurement of high-field NMR spectra, Dr. K. M. Straub for field desorption mass spectra, Dr. M. P. Klein for allowing us generous access to instrumentation, and C. Chang, T. R. Gadek, and J. A. King for useful discussions and additional experimental results. This work was supported by NIH Grant GM 22479 and (in part) by NSF Grant CHE 79-03954.

Supplementary Material Available: Physical data of isolated compounds, including selected proton decoupling experiments and chemical shift assignments; copy of 180-MHz ^1H NMR spectrum of **2b**; ORTEP plot of the structure of **2c** (H_{exo} isomer); experimental procedures leading to **2a**, **9**, and **12** (8 pages). Ordering information is given on any current masthead page.

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(11) S. G. Davies, M. L. H. Green, and D. M. P. Mingos, *Tetrahedron*, **34**, 3047 (1978).

(12) The intermolecular variant of this reaction will be reported in due course.

(13) Fellow of the Alfred P. Sloan Foundation (1976-1980) and Camille and Henry Dreyfus Teacher Scholar (1978-1983).

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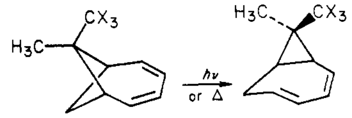
Stereochemistry of the Thermal and Photochemical Rearrangement of 7,7-Dimethylbicyclo[4.1.1]octa-2,4-diene to 8,8-Dimethylbicyclo[5.1.0]octa-2,4-diene

Sir:

In 1974, Klarner[1] reported that the norcaradiene ring-walk, first discovered by Berson and Willcott,[2] proceeds with inversion of configuration at the migrating carbon atom. This finding, which is the opposite of that anticipated on the basis of the Woodward-Hoffmann rules for [1,5] sigmatropic shifts,[3] has been questioned by Baldwin and Broline.[4] Nevertheless, subsequent studies by Klarner and co-workers[5] have confirmed that, at least in the systems investigated by them, the norcaradiene ring-walk does proceed with a large preference for inversion over retention at the migrating carbon.[6]

We have found[7] that 7,7-dimethylbicyclo[4.1.1]octa-2,4-diene (**1a**)[8] undergoes rearrangement on direct photolysis or on pyrolysis to 8,8-dimethylbicyclo[5.1.0]octa-2,4-diene (**2a**). Both **1a** and **2a** are homologues of 7,7-dimethylnorcaradiene, but the stereochemistry of the [1,5] sigmatropic shift that transforms **1a** to **2a** is much easier to study than the corresponding norcaradiene ring-walk. Unlike the ring-walk, the rearrangement of **1a** to **2a** is not degenerate, and in contrast to norcaradiene, neither hydrocarbon is in reversible equilibrium with a valence isomer. Thus, the determination of whether the transformation of **1** to **2** proceeds with retention or inversion requires only a suitably labeled migrating carbon in **1** and a method for establishing the stereochemistry at this center in **2**.



1a, X = H
b, X = D

2a, X = H
b, X = D

In order to minimize possible perturbations of the stereochemical outcome by differences in bulk between the two substituents at the migrating carbon, we utilized **1b**, in which CD_3 replaces the endo CH_3 group in **1a**. Since **1a** is synthesized from α-pinene,[8] the fact that α-pinene-9,9,9-d_3 had been prepared[9] made **1b** especially attractive for study. However, instead of using the route of Gibson and Erman,[10] which leads to a mixture of α- and β-pinenes, we instead elected to cleave[11] the cyclic ether **3**[10,12] before oxidizing. The remaining steps required to transform **3**

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(1) Klarner, F.-G. *Angew. Chem., Int. Ed. Engl.* **1974**, *13*, 268.

(2) Berson, J. A.; Willcott, M. R., III *J. Am. Chem. Soc.* **1965**, *87*, 2751-52; **1966**, *88*, 2494.

(3) Woodward, R. B.; Hoffmann, R. *Angew. Chem., Int. Ed. Engl.* **1969**, *8*, 781.

(4) Baldwin, J. E.; Broline, B. M. *J. Am. Chem. Soc.* **1978**, *100*, 4599.

(5) Klarner, F.-G.; Yaslak, S.; Wette, M. *Chem. Ber.* **1979**, *112*, 1168. Klarner, F.-G.; Brassel, B. *J. Am. Chem. Soc.* **1980**, *102*, 2469.

(6) See also: Hansen, R. T. Ph.D. Thesis, Yale University, **1976**; *Diss. Abstr. Int. B* **1977**, *37*, 6130.

(7) Young, S. D.; Borden, W. T. *J. Org. Chem.* **1980**, *45*, 724.

(8) Young, S. D.; Borden, W. T. *Tetrahedron Lett.* **1976**, 4019.

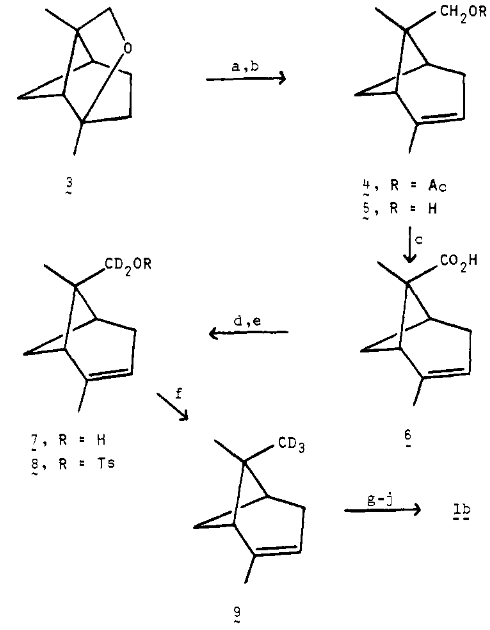
(9) Shaffer, G. W.; Pesaro, M. *J. Org. Chem.* **1974**, *39*, 2489.

(10) Gibson, T. W.; Erman, W. F. *J. Am. Chem. Soc.* **1969**, *91*, 4771.

(11) Bessiere-Chretien, Y.; Grison, C. *Bull. Soc. Chim. Fr.* **1975**, 2499.

(12) Hortmann, A. G.; Youngstrom, R. E. *J. Org. Chem.* **1969**, *34*, 3392.

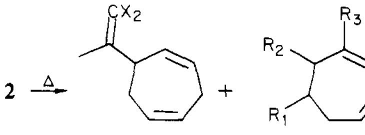
Scheme I



[a] (a) Ac_2O, Py·HCl, 100 °C, 60%; (b) $LiAlH_4$, ether, 95%; (c) PDC, DMF, 50%; (d) *n*-BuLi (1 equiv), $LiAlD_4$, THF, reflux, 95%; (e) TsCl, Py, 0 °C, 100%; (f) $LiB(C_2H_5)D$, THF, reflux, 85%; (g) O_3, THF, then Zn, H_2SO_4, 90%; (h) piperidine, AcOH, xylene, reflux, 25%; (i) $TsNHNH_2$, 100%; (j) LDA, HMPA, THF, reflux, 20% isolated by GLC.

into α-pinene-9,9,9-d_3 (**9**) are outlined in Scheme I. Mass spectroscopy indicated the presence of 95% d_3 and 5% d_2 in **9** and in **1b**, to which **9** was transformed in four additional steps.[8] The very small quintet expected for the 5% of molecules with *endo*-methyl-d_2 was not visible in the ^1H NMR spectrum of either **9** or **1b**.

On photolysis of **1b**, the ^1H NMR spectrum of the rearrangement product displayed a singlet at δ 1.00 with slightly less than 10% of the integrated area of the methyl singlet at δ 1.06. Essentially the same ratio of peak areas was observed when **1b** was pyrolyzed in a flow system at 250 °C and **2** separated from the other pyrolysis products (**10**–**14**)[7] by preparative GLC. In both the photolysis and pyrolysis, recovered starting material showed negligible epimerization.



10a, X = H
b, X = D

11, $R_1 = CH_3C{=}CX_2$
12, $R_2 = CH_3C{=}CX_2$
13, $R_3 = CH_3C{=}CX_2$
14, $R_4 = CH_3C{=}CX_2$
a, X = H
b, X = D

The structure of the major stereoisomer formed in these reactions was assigned by utilizing the previously discovered[7] sigmatropic rearrangements of **2a** to the isopropenylcycloheptadienes **10a**–**14a**.[13] The photoproduct formed from **1b** was pyrolyzed at 275 °C, and the three major products (**10b**, **13b**, and **14b**) were isolated by preparative GLC. In each compound, the resonance for the vinyl methylene protons had only about 13% of the integrated area of that in the all-protio hydrocarbon. The slightly larger protium content at this carbon in **10**, **13**, and **14** than in **2** is apparently due to primary isotope effects in the hydrogen-transfer reactions; the ^1H NMR spectrum of the 20% of the photoproduct recovered from the pyrolysis reaction showed the small methyl resonance at δ 1.00 to have almost disappeared.

The results obtained from pyrolyzing the photoproduct indicate that the sigmatropic reactions leading to **10** and to **13** and **14** (via the intermediacy of **12**)[7] are concerted. This fact suggests that **2** is indeed the immediate precursor of **12**, since **12** can be formed by a symmetry-allowed hydrogen shift from the *endo*-methyl group in **2** but not in **1**. Furthermore, were the pathway **2** → **1** → **12** to be followed, some loss of stereochemistry would be expected to occur in the first step of the rearrangement, as is observed in the transformation of **1** to **2**. The high stereospecificity of the hydrogen transfer observed in the formation of **13** and **14** from **2** provides additional evidence, therefore, that **2** is the immediate precursor of **12**. Simiarly, the fact that **10** is formed with the same high stereospecificity as **13** and **14** implicates **2** as the immediate precursor of **10** as well. With this evidence that the *endo*-methyl of **2** is transformed into the vinyl methylene of **10**–**14**,[14] the results obtained from the pyrolysis of the photoproduct also establish that **2b** represents the structure of the major stereoisomer formed from photolysis of **1b**.

However, the pyrolysis of **2b** reveals isotopic discrimination in favor of transferring protium in the rearrangement of **2** to **10** and **12**. These rearrangements accompany the formation of **2** in the pyrolysis of **1**, even at low conversions. Consequently, the deuterium content of the *endo*-methyl group in the **2** that is isolated from pyrolysis of **1b** does not provide an accurate assay for the stereochemistry of this reaction.

In order to determine accurately the stereochemical course of thermal transformation of **1** to **2**, **1b** was pyrolyzed at 325 °C. At this temperature, all the **2** that was formed rearranged to **10**, **13**, and **14**. These three products were each isolated by GLC and found by NMR to contain 20% protium in the vinyl methylene. The results obtained from the pyrolysis of **2b** show that the protium content of this group should reflect accurately the protium content of the *endo*-methyl in the **2** that is formed as the initial product when **1b** is pyrolyzed at 325 °C. The thermal rearrangement of **1** to **2** is thus indicated to proceed with 80% inversion of configuration at the migrating carbon.

The predominant inversion of configuration observed in the photochemical transformation of **1** to **2** is in accord with the Woodward–Hoffmann prediction for a photoinduced [1,5] sigmatropic reaction.[15] However, the fact that the thermal reaction also exhibits a predilection for inversion raises the question of whether orbital symmetry considerations of the Woodward–Hoffmann type are relevant to either process. At least in the thermal reaction, factors other than interactions between the frontier orbitals must control the stereochemical course.

Conceivably, a diradical intermediate is formed by homolytic bond cleavage in **1**. Since the migrating carbon is tertiary, there is precedent[16] for rotation being slower than closure in the putative intermediate.[17] Closure via the least-motion pathway would

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[13] Unlike the case in substituted norcaradienes,[2] these hydrogen shifts are irreversible. Thus, a hydrogen-rebound mechanism is excluded for the transformation of **1** to **2**. This represents another feature that makes the stereochemistry of the rearrangement of **1** to **2** easier to study than that of the norcaradiene ring-walk.

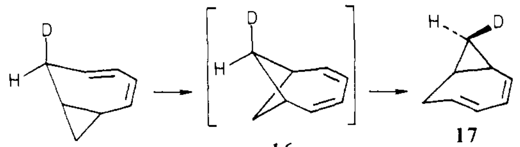
[14] Additional evidence for **2** as the immediate precursor of both **10** and **12** comes from the compositions of the product mixtures formed when **1** and **2** are pyrolyzed at 250 °C.[7] The compositions show that the rate constants for both hydrogen shifts in **2** are larger than those for formation of **2** from **1** and for reversion of **2** to **1**, a reaction so slow that it is not observed at all. Therefore, the pathway **2** → **1** → **10** + **12** is kinetically unimportant compared to the direct formation of **10** and **12** from **2**. Moreover, the fact that the ratio of **2** to the other pyrolysis products is similar whether **1** or **2** is pyrolyzed suggets that the source of **10** and **12** is the same in both reactions. Since the slow rate of reversion of **2** to **1** excludes **1** as the immediate precursor of **10** and **12** in the pyrolysis of **2**, it may be inferred that **10** and **12** are formed only via the intermediacy of **2** when **1** is pyrolyzed.

[15] The triplet-sensitized ring-walk in norcaradiene has also been shown to proceed with predominant inversion of configuration: Klarner, F.-G.; Yastak, S. *Chem. Ber.* **1979**, *112*, 2286.

[16] Rates of rotation vs. closure in diradicals have been reviewed. See: Borden, W. T. In "Reactive Intermediates", Jones, M., Jr.; Moss, R. A., Eds.; Wiley: New York, 1980; Vol. 2, in press. Berson, J. A. In "Rearrangements in Ground and Excited States", de Mayo, P., Ed.; Academic Press: New York, 1980; p 311. Leading references are: Dervan, P. B.; Santilli, D. S. *J. Am. Chem. Soc.* in press. Dervan, P. B.; Uyehara, T.; Santilli, D. S. *Ibid.* **1979**, *101*, 2069. Bartlett, P. D.; Porter, N. A. *Ibid.* **1968**, *90*, 5317.

produce inversion of configuration. Alternatively, the transformation of **1** to **2** might proceed by a concerted pathway with subjacent orbital interactions[18] contributing to the observed preference for inversion.

A result already in the literature may bear on this question. Grimme and Doering have observed the interconversion of bicyclo[5.1.0]octa-2,4-dienes **15** and **17**.[19] Although they proposed a concerted sigmatropic reaction to account for this transformation, we have noted[7] that the intermediacy of bicyclo[4.1.1]octa-2,4-diene **16** is at least a possibility.



If **16** is, in fact, an intermediate, Grimme and Doering's result would indicate that the [1,5] sigmatropic shift of **16** to **17**, like that of **1** to **2**, proceeds with inversion of configuration. However, unlike the case in **1** or in the norcaradienes that have been studied,[17] the migrating carbon in **16** is unsubstituted. Therefore, if the rearrangement of **15** to **17** is shown to involve **16**, slow rotation at a tertiary carbon in a putative diradical intermediate cannot be invoked to explain the stereochemical outcome of this reaction.[20]

Acknowledgments. We thank the National Science Foundation for support of this research and George Renzoni for FT-NMR and mass spectra.

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[17] The migrating carbon has been tertiary in each of the norcaradienes that has been used to study the stereochemistry of the ring-walk.[1,4-6]

[18] Berson, J. A.; Salem, L. *J. Am. Chem. Soc.* **1972**, *94*, 8917. Borden, W. T.; Salem, L. *Ibid.* **1973**, *95*, 932.

[19] Grimme, W.; Doering, W. von E. *Chem. Ber.* **1973**, *106*, 1965.

[20] **Note Added in Proof:** Evidence supporting the mechanism proposed by Grimme and Doering for the rearrangement of **15** to **17** has recently been published by Kirmse, W.; Kuhr, R.; Murawski, H.-R.; Scheidt, F.; Ullrich, V. *Chem. Ber.* **1980**, *113*, 1272.

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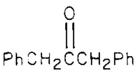
Magnetic Field and Magnetic Isotope Effects on Cage Reactions in Micellar Solutions

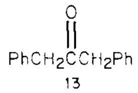
Sir:

A fundamental premise of the theory of CIDNP is the postulate that the chemical reactivity of radical pairs in solution may be influenced by nuclear spins, because intersystem crossing in radical pairs may occur predominately by electron–nuclear hyperfine interactions.[1] Several chemically significant corollaries follow[2] from the radical-pair model of CIDNP: (1) observed kinetic isotope effects may arise from differences in nuclear magnetic moments rather than from differences in nuclear masses, e.g., isotope effects on the competition between cage reactions and cage escape (the cage effect) may be due to nuclear spin isotope effects;[3] (2) products of reactions of radical pairs may be enriched in (or impoverished in) magnetic isotopes, e.g., ^{13}C may be enriched in cage products of triplet radical pairs;[4] (3) the cage effect and isotope enrichment will be magnetic field dependent.[5] It has been proposed that the following is an important criterion for distinguishing between nuclear spin isotope effects and mass isotope effects:[6] *the yields of products from a radical pair containing a magnetic nucleus should be magnetic field dependent with an extremum near the field corresponding to the hyperfine coupling between the nucleus and the unpaired electron in the radical.* We report here an investigation of the cage effect and ^{13}C isotope enrichment in the photolysis of dibenzyl ketone (DBK) and of isotopically labeled ketones in aqueous solutions containing hexadecyltrimethylammonium chloride (HDTCl) which meets this criterion and clearly establishes the operation of kinetic nuclear spin isotope effects.



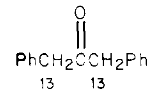
$$PhCH_2\overset{\overset{O}{\|}}{C}CH_2Ph$$

DBK
(natural abundance)



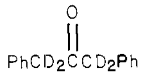
$$PhCH_2\overset{\overset{O}{\|}}{\underset{13}{C}}CH_2Ph$$

DBK-1-^{13}C
(90% ^{13}C, carbonyl)



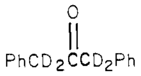
$$Ph\underset{13}{C}H_2\overset{\overset{O}{\|}}{C}\underset{13}{C}H_2Ph$$

DBK-α,α′-$^{13}C_2$
(90% ^{13}C, methylene)



$$PhCD_2\overset{\overset{O}{\|}}{C}CD_2Ph$$

DBK-α,α,α′,α′-d_4
(>90% D, methylene)



$$PhCD_2\overset{\overset{O}{\|}}{C}CD_2Ph$$

DBK-^{13}C,α,α,α′,α′-d_4
(90% ^{13}C, carbonyl, >90% D methylene)

The salient features of our results are the following: (1) the efficiency of ^{13}C enrichment (Figure 1) and the magnitude of the cage effect (Figure 2) are strongly magnetic field dependent in the range 0–500 G; (2) the behavior of enrichment efficiency as a function of magnetic field strength is qualitatively different for $PhCH_2COCH_2Ph$ and for $PhCD_2COCD_2Ph$; (3) the extent of cage reaction for $Ph^{13}CH_2CO^{13}CH_2Ph$ is dramatically higher than that for $PhCH_2COCH_2Ph$.

The photolysis of DBK in micellar (HDTCl) solution has been shown[7] to result in the ^{13}C enrichment of recovered DBK. The mechanism of the enrichment (Scheme I) was proposed to be a nuclear spin isotope effect on the competition between decarbonylation and intersystem crossing of the triplet radical pair $^3D(PhCH_2\dot{C}O\ \dot{C}H_2Ph)$.

We have measured the efficiency of ^{13}C enrichment of recovered DBK in terms of Bernstein's parameter,[8] α. This parameter was evaluated by mass spectrometric analysis of the ^{13}C content of DBK recovered from partially photolyzed solutions (α^{MS})[7] and by determination of the ratio of quantum yield of reaction of DBK-1-^{13}C to that of DBK (α^{Φ}).[9a,10] For quantum yield measurements, the photolysis lamp was situated approximately 1 m away from the sample which in turn was centered between the pole faces of an electromagnet. The magnetic field strength in the vicinity of the lamp housing was measured to be about 10 G when the magnet was operated at 0 G. The additional magnetic field strength near the lamp housing was less than 0.5 G when the magnet was operated in the range 0–500 G, and less than 1 G when the magnet was operated at 5 KG.

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[1] Kaptein, R. *Adv. Free-Radical Chem.* **1975**, *5*, 381. Closs, G. L. *Proc. Int. Congr., Pure Appl. Chem. 23rd ed.* **1971**, *4*, 19. Ward, H. R. *Acc. Chem. Res.* **1972**, *5*, 18. Lawler, R. G. *Ibid.* **1972**, *5*, 25. Buchachenko, A. L.; Zhiromirov, F. M. *Russ. Chem. Rev.* **1971**, *40*, 801.

[2] Lawler, R. G.; Evans, G. T. *Ind. Chim. Belge* **1971**, *36*, 1087.

[3] Buchachenko, A. L. *Russ. Chem. Rev.* **1976**, *45*, 761.

[4] Buchachenko, A. L. *Russ. J. Phys. Chem.* **1977**, *51*, 2461.

[5] Sagdeev, R. Z.; Salikhov, K. M.; Molin, Y. M. *Russ. Chem. Rev.* **1977**, *46*, 297.

[6] Lawler, R. G. *J. Am. Chem. Soc.* **1980**, *102*, 430.

[7] Turro, N. J.; Kraeutler, B. *J. Am. Chem. Soc.* **1978**, *100*, 7432.

[8] Bernstein, R. B. *J. Phys. Chem.* **1952**, *56*, 893; *Science* **1957**, *126*, 119.

[9] (a) Turro, N. J.; Kraeutler, B.; Anderson, D. R. *J. Am. Chem. Soc.* **1979**, *101*, 7435. (b) For a derivation of the relationship of α to photochemical quantum yields, see: Kraeutler, B. J.; Turro, N. J. *Chem. Phys. Lett.* **1980**, *70* 266.

[10] Typically, the measurement of α^{Φ} was made as follows: an aqueous solution containing 0.005 M ketone and 0.05 M HDTCl was photolyzed to 10% conversion (1000-W high-pressure Hg lamp, Pyrex filter). Analyses were performed on a Varian 3700 gas chromatograph (6 ft 3% OV-17 column, column temperature = 185 °C) employing a Varian CDS 111 minigrator. Typically, α^{MS} was determined by photolysis of solutions as described for determination of α^{Φ}. Conversions were generally between 40 and 90% and analyses were made by GC-MS (Finnigan 3200, 10%, SE-30 column).

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