Stereoselectivity of Triplet Photocycloadditions:[1] Diene−Carbonyl Reactions and Solvent Effects

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The diastereoselectivity of the photocycloaddition of benzaldehyde to furan was determined (exo/endo = 212:1) and compared with the reaction of other carbonyl compounds and carbonyl analogues. These results were compared with Paternò−Büchi reactions of cycloalkenes and cyclic enol ethers. An increase in steric demand of the α-substituent in benzoyl compounds led to a change in exo/endo-selectivity for furan cycloadditions that was not observed for cycloalkenes or cyclic enol ethers. Different ISC-reactive conformers with enhanced spin−orbit coupling are postulated as a reasonable explanation for the stereoselectivities observed. Additionally, solvent effects were studied, demonstrating the influence of photoinduced electron-transfer steps on the regio- and diastereoselectivity of Paternò−Büchi reactions with 2,3-dihydrofuran in polar solvents. Two bicyclic oxetanes (**8** and **10**) were characterized by X-ray structure analysis.

Introduction

Intermolecular photocycloaddition reactions with one triplet excited component are mostly conducted via triplet biradical intermediates.[1] These species are separated from their closed-shell successors by an activation barrier due to the spin-forbidden intersystem crossing (ISC) process. Thus, the triplet 1,4-biradicals that are formed in [2 + 2] cycloaddition reactions have relatively long lifetimes (1 ns to 1 μs).[2] Spin−orbit coupling (SOC) controls the rate of ISC for these type of intermediates, i.e., strong SOC enhances the ISC rate and lowers the lifetime of the triplet biradicals. In recent publications by Michl[3] and Adam and co-workers,[4] the long-known and successfully applied Salem−Rowland rules[5] for estimating the magnitude of SOC were modified due to new experimental and theoretical results. The spatial orientation of the two singly occupied orbitals has been determined to be highly important for the biradical lifetimes, whereas the through-space distance between the radical centers[3] plays a subordinate role and the degree of ionic contribution in the corresponding singlet state[4] often seems to be overestimated. This clearly indicates that for flexible 1,4-triplet biradicals not only one conformational arrangement is responsible for facilitating ISC, but many. After transition from the triplet to the singlet potential energy surface, immediate product formation is expected. Thus, the ISC is expected to be concerted with the formation of a new bond *or* the cleavage of the primarily formed single bond. This picture resembles the concept by Turro of "tight" and "loose" geometries of biradicals (originally used for singlets and triplets), which are precursors to cycloaddition and cleavage products, respectively.[6]

In recent publications, we have tried to combine these theoretical models with experimental results using the following concept: if the second bond-forming step in triplet [2 + 2] cycloaddition reactions is coupled with a stereochemical probe, the biradical geometry most favorable for rapid ISC should be reflected in the product configuration.[7] We have used intermolecular Paternò−Büchi reactions[8] and investigated a series of cycloalkenes reacting with prochiral triplet excited carbonyls. In these cases, triplet 2-oxatetramethylenes are formed during the course of the reaction—species that are known to have lifetimes of 1−5 ns,[9] i.e., relatively short-lived in comparison with the 1,4-biradicals without oxygen contribution.[10] For these systems, the degree of stereoselectivity was dependent on the size of the α-substituent of the carbonyl component, on the substituent pattern, as well as on the flexibility of the alkene addend. In most cases, selectivities not higher than 90:10 resulted. A remarkable exception was found for furan[11] (and also for other heteroaromatic substrates such as thiophenes, pyrroles, imidazoles, and pyrazoles)[12] and furan derivatives.[13] The photocycloaddition of these cyclo-1,3-dienes with aromatic

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(3) Michl, J. *J. Am. Chem. Soc.* **1996**, *118*, 3568.
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(7) (a) Buhr, S.; Griesbeck, A. G.; Lex, J.; Mattay, J.; Schröer, J. *Tetrahedron Lett.* **1996**, *37*, 1195. (b) Griesbeck, A. G.; Mauder, H.; Stadtmüller, S. *Acc. Chem. Res.* **1994**, *27*, 70. (c) Griesbeck, A. G.; Stadtmüller, S.; Bringmann, G.; Busse, H.; Buddrus, J. *Chem. Ber.* **1992**, *125*, 933. (d) Griesbeck, A. G.; Stadtmüller, S. *J. Am. Chem. Soc.* **1991**, *113*, 6923. (e) Griesbeck, A. G.; Stadtmüller, S. *J. Am. Chem. Soc.* **1990**, *112*, 1281. (f) Griesbeck, A. G.; Mauder, H.; Peters, K.; Peters, E.-M.; von Schnering, H. G. *Chem. Ber.* **1991**, *124*, 407. (g) Griesbeck, A. G.; Stadtmüller, S. *Chem. Ber.* **1990**, *123*, 357.
(8) For reviews: (a) Griesbeck, A. G. In *Handbook of Organic Photochemistry and Photobiology*; Horspool, W. M., Song, P.-S., Eds.; CRC Press: Boca Raton, 1995; p 550; (b) p 755. (c) Porco, J. A.; Schreiber, S. L. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Paquette, L. A., Eds.; Plenum Press: New York, 1991; Vol. 5, p 151. (d) Carless, H. A. J. In *Synthetic Organic Photochemistry*; Horspool, W. M., Ed.; Plenum Press: New York, 1984; p 425. (e) Jones, G., II. In Padwa, A., Ed. *Org. Photochem.* **1981**, *5*, 1.
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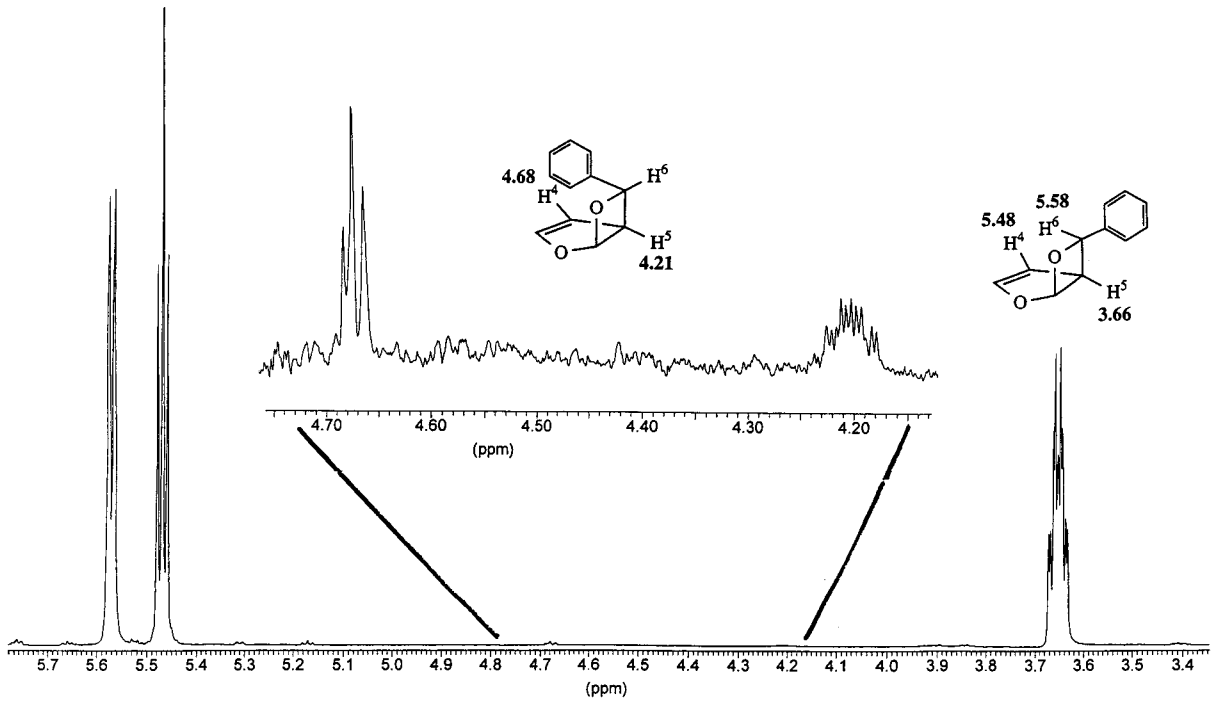


Figure 1. 500 MHz ^{1}H NMR spectrum of *exo*- and *endo*-**2**.

and aliphatic aldehydes proceeds with unusually high stereoselectivity. Exact values, however, cannot be found in the literature. To understand this effect, we have investigated solvent and substituent effects as well as diene modifications.

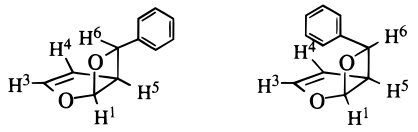
Results and Discussion

Solvent Effects and Regio- and Stereoselectivity for the Parent Systems: Furan/Benzaldehyde and 2,3-Dihydrofuran/Benzaldehyde. For comparison with the cycloadditions of monoalkenes, we tried to determine the exact degree of stereo- and regioselectivity of the benzaldehyde cycloaddition with furan (**1**): in the 500 MHz ^{1}H NMR spectrum of the crude reaction mixture, 0.47% of the minor (endo) diastereoisomer **2** was detected (relative to the exo diastereoisomer), thus resulting in a 212:1 diastereoisomeric ratio. The relevant signals for determination of this ratio are shown in Figure 1.

Well-separated signals were obtained for 5-H and 4-H of the major diastereoisomer at 3.65 and 5.47 ppm. The corresponding signals of the minor (*endo*-phenyl) diastereoisomer were detected at 4.21 and 4.68 ppm with the corresponding multiplicities and similar coupling constants. The other proton signals were detected by TOCSY, and the coupling pattern was successfully simulated (see Table 1).

No signals could be detected for the two possible regioisomeric diastereoisomers, indicating a regioselectivity of >600:1. The latter result is in agreement with the assumption of regiocontrol exhibited by the radical-stabilizing effects of the ring substituents, i.e., α-alkoxy radical vs allylic radical (ΔE_{RS} = ca. 10−12 kJ/mol).[14] The pronounced stereoselectivity of 212:1, however, cannot

Table 1. ^{1}H NMR Shifts and Calculated Coupling Constants for *exo*- and *endo*-2



exo-**2** endo-**2**

	δ^a (ppm)				
	1-H	3-H	4-H	5-H	6-H
exo-**2**	6.54	6.71	5.47	3.65	5.57
endo-**2**	6.36	6.52	4.68	4.21	6.07

	J^b (Hz)							
	1−3	3−4	3−5	1−6	1−5	4−6	5−6	4−5
exo-**2**	0.78	2.92	1.22	0.74	4.37	0.00	3.12	2.99
endo-**2**	0.72	2.88	1.33	0.00	4.20	0.25	5.69	2.92

[a] 500 MHz NMR ($CDCl_3$). [b] Calculated using PANIC.

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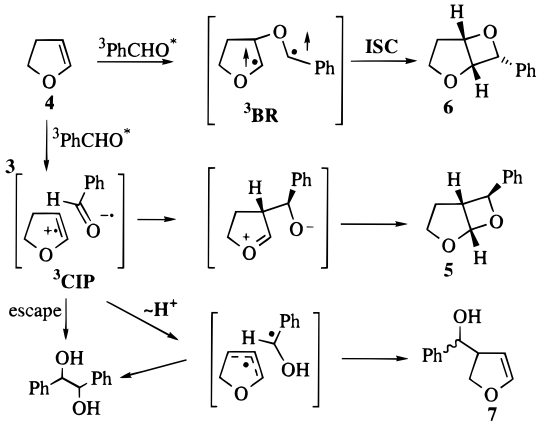
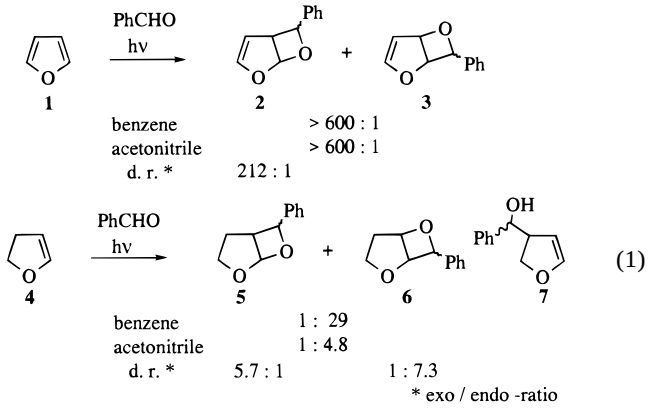
Scheme 1



be explained by any model published in the literature. The SOC-geometry model, which we have postulated for similar cycloaddition reactions with cyclic enol ethers,[7e] predicts only moderate diastereoselectivity (ca. 1:10) and the *reverse* direction of stereocontrol. For comparison, the selectivity values for the benzaldehyde addition with furan (**1**) and 2,3-dihydrofuran (**4**) are listed in eq 1. Both reactions have been conducted in benzene and acetonitrile, respectively, as solvents. The furan cycloaddition proceeded with identical regio- and diastereoselectivity in both solvents. The high oxidation potential of furan ($E_{ox.}$ ca. 2.0 V)[15] excludes electron transfer pathways even in highly polar solvents.



(1)

When 2,3-dihydrofuran (**4**) was irradiated in benzene in the presence of benzaldehyde, a 12:88 mixture of exo/endo diastereoisomers **6** resulted (Scheme 1).[6g] The regioselectivity of this reaction is high, but only in benzene: only 3% of the acetal-type regioisomer **5** was formed. Like for furan, photoinduced electron transfer (PET)[16] with formation of solvent-separated ion pairs (SSIP) is energetically unfeasible in unpolar solvents such as benzene or cyclohexane. The oxidation potential[17] for **4** is too high to enable exergonic electron transfer (ΔG_{SSIP}[benzene, ϵ: 2.3] = +0.62 eV) from the triplet state

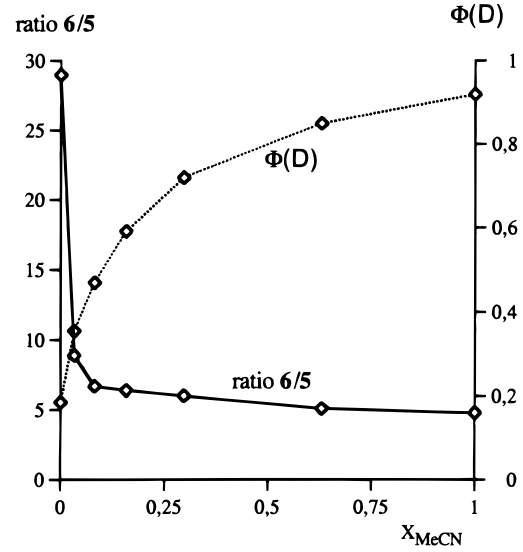


Figure 2. Correlation between solvent polarity and oxetane product ratio **6**/**5**.

of benzaldehyde.[18] This lack in driving force can be compensated by increasing the solvent polarity, which reduces the coulomb term in the Rehm−Weller equation.[19] In acetonitrile (ΔG_{SSIP}[CH_3CN, ϵ: 37.5] = −0.46 eV), 12% of the regioisomer **5**[20] was formed in addition to 50% of **6**, 18% of the carbinol **7**, and ca. 20% of 1,2-diphenylglycol. The diastereoselectivity of the formation of product **6** (88:12) did not change when switching from benzene to acetonitrile. The acetal-type regioisomer **5** also was formed with a similar degree of diastereoselectivity (15:85); in this case, however, the exo product was the preferred stereoisomer. The carbinol **7** was isolated as a 1:1 mixture of diastereoisomers.

For a mechanism where the bulk solvent polarity controls the regioselectivity, a dependence between the regioisomeric ratio and the polar solvent mole fraction x_p is expected. In ideal solvent mixtures described either by the Onsager function[21] or by the Debye function, the dielectric constant ϵ shows only little increase up to x_p = 0.4 and the "polarity" goes linear with x_p. Consequently, the relative amount of "polar" products (**5** and also **7**, *vide infra*) should also rise linear with increasing solvent polarity. We have investigated solvent mixtures consisting of benzene and acetonitrile and found a near-linear dependency between the dielectric constant ϵ and the polar solvent mole fraction x_p.[22] Consequently, when describing the solvent polarity by the Onsager or Debye functions, a strong increase in polarity results for the region of low x_p. The ratio of "polar" products against "nonpolar" products (i.e., **5** and **7** vs **6**) behaved likewise (Figure 2 for the dependence of the **6**/**5** ratio vs the Debye function Φ(D)). Already concentrations of acetonitrile in

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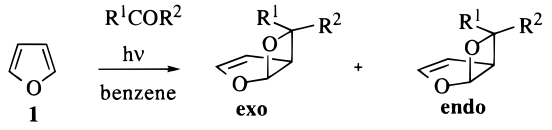
(15) Yoshida, K.; Fueno, T. *Bull. Soc. Chim. Jpn.* **1987**, *55*, 229.
(16) (a) Pandey, G. *Top. Curr. Chem.* **1993**, *168*, 175−221. (b) Mariano, P. S.; J. L. Stavinoha, J. L. In *Synthetic Organic Photochemistry*, Horspool, W. A., Ed.; Plenum Press: New York, 1984. (c) *Photoinduced Electron Transfer*; Fox, M. A., Chanon, M., Eds.; Elsevier: Amsterdam, 1988. (d) Kavarnos, G. J. *Fundamentals of Photoinduced Electron Transfer*; VCH: Weinheim, 1993. (e) Mattay, J.; Vondenhof, M. In Mattay, J., Ed. *Top. Curr. Chem.* **1991**, *159*.
(17) $E^0_{ox.}$(**4**) = 0.97 V vs SCE in CH_3CN: Mattay, J. *Tetrahedron* **1985**, *41*, 2405.
(18) $E^0_{red.}$(benzaldehyde) = −1.80 V vs SCE in DMF: Letaw, H., Jr.; Gropp, A. H. *J. Phys. Chem.* **1953**, *57*, 964. E_T = 3.17 eV: Kearns, D. R.; Case, W. A. *J. Am. Chem. Soc.* **1966**, *88*, 5087.
(19) (a) Weller, A. *Z. Phys. Chem. N. F.* **1982**, *130*, 129. (b) Weller, A. *Z. Phys. Chem. N. F.* **1982**, *133*, 93. (c) Rehm, D.; Weller, A. *Isr. J. Chem.* **1970**, *8*, 259.
(20) The exo diastereoisomer of **5** was independently synthesized from **2** by catalytic reduction with Pd−C in EtOAc, following a procedure reported in ref 11n.
(21) Onsager, L. *J. Am. Chem. Soc.* **1936**, *58*, 1486.
(22) This effect was also reported for other "non-ideal" solvent mixtures (e.g., *n*-hexane/propionitrile): Suppan, P. *J. Chem. Soc., Faraday Trans. 1* **1987**, *83*, 495.

Scheme 2. *Exo/Endo* Ratios for Paternò−Büchi Reactions with Furan (1)

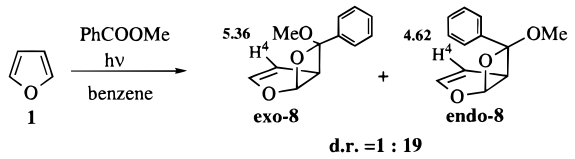


(3)

R^2 =	H	Me	CN	COOMe	OMe	COOR
R^1 = Ph	212 : 1	> 49 : 1	3.7 : 1	1 : 9	1 : 19	< 1: 49
R^1 = Mes			16 : 1			
R^1 = tBu	> 250 : 1			< 1: 49		

benzene as low as 10 mol % were sufficient to enable more than 70% of the polar pathway (i.e., products **5** and **7** and glycol).

Substituent Effects in Furan Cycloadditions. The extraordinary high stereoselectivity of the benzaldehyde/furan photocycloaddition is not a result of π-interactions with the phenyl substituent, i.e., aliphatic aldehydes do react with exo diastereoselectivities higher than 99:1.[7b,23] It was, therefore, of interest to study the influence of α-substituents in benzoyl compounds on the stereoselectivity of the Paternò−Büchi reaction with furan. Recently, it was reported by Cantrell and co-workers that methyl benzoate reacts with furan with a high degree of exo selectivity.[24] The relative configuration of the major cycloadduct was determined by comparison of the relevant ^{1}H NMR signals. When repeating this reaction, we found two diastereoisomeric products **8** in a ratio of 95:5 (eq 2). Similar as for the endo isomer **2**, which we



(2)

detected as a minor product in the cycloaddition of benzaldehyde with furan, the proton 4-H of the major isomer showed a high-field-shifted resonance line at 4.62 ppm and the corresponding signal of the minor diastereoisomer at 5.36 ppm. This already indicated that the literature assignment was not correct. Definite proof resulted from the X-ray analysis of **8** (Figure 3).[25] Thus, the exchange of the hydrogen in benzaldehyde by a methoxy group completely inverts the diastereoselectivity in the photocycloaddition with furan.

Further modification of the α-substituent in the benzoyl substrates uncovered a distinct dependence of the exo/endo ratio on the size of this substituent (Scheme 2,

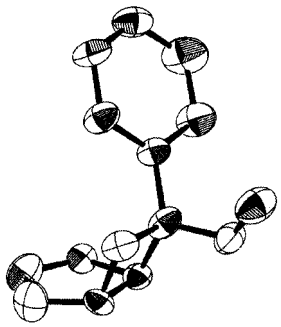


Figure 3. X-ray structure of product **8**.

eq 3). The acetophenone reaction gave only one product,[11d] whereas a 77:23 mixture of diastereoisomers resulted from the addition of benzoyl cyanide.[26] Increasing the size of the aryl group from phenyl to mesityl in aroyl cyanides led to an increase in exo diastereoselectivity from 3.9:1 up to 16:1.[26] An analogous increase was reported by us for the cycloaddition of aromatic aldehydes with 2,3-dihydrofuran; however, in contrast to the furan case, the endo diastereoisomer is always the major isomer with the enol ether substrate.[7g] Scharf and co-workers have intensively investigated Paternò−Büchi reactions of phenyl glyoxylates with furan.[27] Whereas the methyl ester of phenylglyoxylate gave a 10:90 diastereoisomeric ratio, all other esters (e.g., R = menthyl)[27c] reported in the literature or investigated by ourselves exclusively resulted in formation of the endo diastereoisomer.

Thus, by changing the α-substituent from H or Me to CN, COOMe, OMe, and eventually COOR, the direction (*exo*-phenyl vs *endo*-phenyl) of the diastereoselectivity is completely switched. Again, this cannot be a result of π-interactions with the phenyl substituent because an identical sequence is obtained when using the corresponding *tert*-butyl compounds; i.e., pivaldehyde gave solely the exo [2 + 2] cycloadduct,[7b] whereas methyl trimethylpyruvate exclusively resulted in the formation of the endo [2 + 2] cycloadduct[7a] (exo, endo with respect to the *tert*-butyl group).

Stereoselectivity Effects in 1,3-Cyclodiene Cycloadditions. As already mentioned, not only furan and substituted furans but also other heteroaromatic substrates show highly stereoselective [2 + 2] photocycload-

(23) For the propionic aldehyde photocycloaddition to furan an exo/endo ratio of 82:1 was determined: Fiege, M. University of Cologne, unpublished results.

(24) Cantrell, T. S.; Allen, A. C.; Ziffer, H. *J. Org. Chem.* **1989**, *54*, 140.

(25) The crystals of **8** $C_{12}H_{12}O_3$, M = 204.22 from CH_2Cl_2 are monoclinic, space group $P2_1/n$, a = 1515.7(5) pm, b = 550.0(1) pm, c = 1242.8(3) pm; β = 93.15(2)°; V = 1034.5(5) Å^3; Z = 4; d_{calc} = 1.311 g/cm^3; μ = 0.094. Data Collection: Enraf-Nonius-CAD4 diffractometer; Mo Kα; graphite monochromator; Wyckoff-scan; θ range (deg) 2.06−26.97; crystal dimensions 0.2 × 0.2 × 0.15 mm^3; number of reflections measured, 796; number of unique reflections, 796; number of reflections $I > 2\sigma(I)$, 528. Structural Analysis and Refinement: solution by direct phase determination; method of refinement, full-matrix LSQ; hydrogen positions of riding model with fixed isotropic U, data-to-parameter ratio, 4.29; R_1, 0.048 (for $I > 2\sigma(I)$); R_1, 0.048 (all reflexes); weighting scheme, $w = 1/[\sigma^2(F_o^2) + (0.100P)^2]$; largest differential peak/hole, 0.11 and −0.11 e Å^{-3}; program used, Siemens SHELXTL-93.

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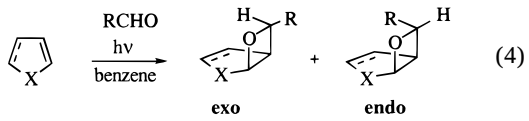
(27) (a) Koch, H.; Scharf, H.-D.; Runsink, J.; Leismann, H. *Chem. Ber.* **1985**, *118*, 1485. (b) Weuthen, M.; Scharf, H.-D.; Runsink, J.; Vassen, R. *Chem. Ber.* **1988**, *121*, 971. (c) Pelzer, R.; Scharf, H.-D.; Buschmann, H.; Runsink, J. *Chem. Ber.* **1989**, *122*, 2, 1187. (d) Pelzer, R.; Jütten, P.; Scharf, H.-D. *Chem. Ber.* **1989**, *122*, 487. (e) Buschmann, H.; Scharf, H.-D.; Hoffmann, N.; Plath, M.; Runsink, J. *J. Am. Chem. Soc.* **1989**, *111*, 5367.

Scheme 3. *Exo/Endo* Ratios: Comparing Cycloalkenes with 1,3-Cyclodienes

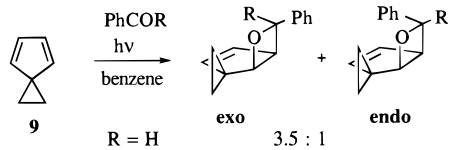


(4)

cyclopentene[7d]	*1 : 1.5* [a]	cyclopentadiene[28]	*5 : 1* [b]
cyclohexene[7d]	*1 : 2.8* [a]	cyclohexadiene[29]	*6 : 1* [c]
dihydrofuran[7g]	*1 : 7.3* [a]	furan	*212 : 1* [a]

ditions with benzaldehyde and other triplet excited aldehydes. Comparison of the cycloaddition stereoselectivity of cycloalkenes with the corresponding cyclo-1,3-dienes (Scheme 3, eq 4) shows the pertinent effect of an extra double bond in conjugation with the reactive alkene moiety. In all these cases, the direction of the diastereoselectivity was inverted when going from the monoalkene (endo selectivity) to the corresponding 1,3-diene (exo selectivity); however, the magnitude of this effect is strongly reduced for pure hydrocarbons in comparison with the dihydrofuran/furan couple.

To test the influence of spiroannulation for these types of reactions, we also investigated the Paternò–Büchi reaction of spiro[4.2]heptadiene **9** (eq 5). In constrast to



(5)

other 1,3-dienes that have been investigated earlier, the endo side of substrate **9** is additionally shielded by the spirocyclopropane ring. The exo diastereoselectivity for the benzaldehyde cycloaddition was substantially reduced (from 212:1 for the furan adduct **2** to 3.5:1 for **10**), whereas the regioselectivity remained higher than ca. 500:1. Perfectly in line with the effects observed in the furan series was the result that we obtained with the methyl ester of phenyl pyruvate: exclusively the endo diastereoisomer **11** was formed. To unambiguously establish the relative configuration of this cycloadduct we also performed an X-ray analysis (see Figure 4).[30] In both reactions, no products were observed that derive from a ring-opening process of the spiroannulated cyclopropane ring.

Discussion of Triplet 1,4-Biradical Geometries. I. Cyclic Monoalkenes. [2 + 2] cycloaddition reactions of electronically excited triplet carbonyl compounds pro-

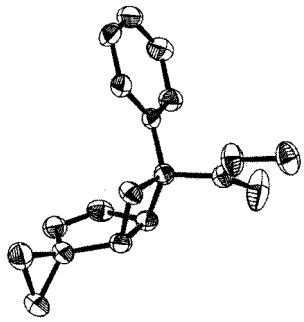


Figure 4. X-ray structure of product **10**.

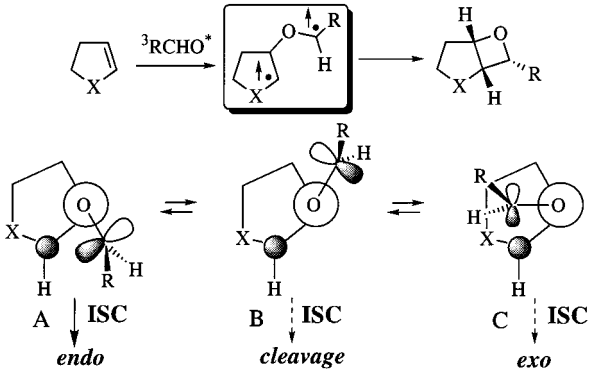
ceed via triplet 1,4-biradicals (2-oxatetramethylenes). To progress from these intermediates to ground-state singlet products, spin-inversion is necessary. The spin-imposed barrier for triplet to singlet intersystem crossing leads to a dramatic increase in lifetime (1–10 ns) when compared with the corresponding singlet biradicals. Because of the enhanced lifetimes, stereochemical information originating from the starting materials is expected to be wiped out during the phototransformation. The most important mechanism for the interaction between singlet and triplet biradicals with shorter distances between the radical centers is spin–orbit coupling (SOC). In contrast to electron–nuclear hyperfine coupling and spin–lattice relaxation, SOC is strongly dependent on the geometry of the triplet biradical. An important geometrical prerequisite for strong SOC, as postulated by Salem and Rowland[5] and confirmed by theoretical[3] and spectroscopical[4] work, concerns the orthogonality of the p-orbitals at the spin-bearing carbon atoms.[31] Conservation of the total angular momentum can be achieved when the axes of the p-orbitals at the radical centers are oriented perpendicular to each other. If the distance between the radical centers is less crucial for facilitating ISC, there is not only one conformational arrangement responsible for the triplet/singlet transition, but many. After transition from the triplet to the singlet potential energy surface, immediate product formation is expected. Thus, the *ISC is expected to be concerted with the formation of a new bond or the cleavage of the primarily formed single bond*. With other words, the stereochemistry of the products from [2 + 2] cycloaddition reactions reflects the molecular ISC geometry.

We have published this SOC geometry model in order to explain the stereochemical results of the photocycloadtion reactions of aromatic aldehydes with cyclic monoalkenes.[7e] These results can be visualized using the relevant Newman projections **A**–**C** of the intermediary 1,4-triplet biradicals (Scheme 4).

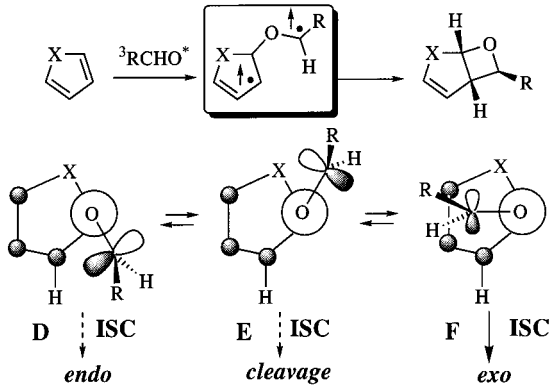
The conformers **A** and **B** are expected to be similarly populated; however, ISC from **A** results in product formation, whereas ISC from **B** leads to cleavage of the singlet biradical and formation of starting material. Spin inversion is coupled with a torque, which in the case of conformers **A** and **C** leads to an immediate formation of the new C–C bond. Thus, the torque induced in conformer **A** rotates the large substituent ("large" with respect to H) over the ring plane and results in the formation of the endo diastereoisomer. From conformer

(28) Hoye, T. R.; Richardson, W. S. *J. Org. Chem.* **1989**, *54*, 688.
(29) Shima, K.; Kubota, T.; Sakurai, H. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 2567.
(30) The crystals of **11** $C_{16}H_{16}O_3$, M = 256.29 from acetone are monoclinic, space group $P2_1/c$, a = 880.6(2) pm, b = 1148.6(2) pm, c = 1345.5(3) pm; β = 104.34(2)°, V; 1318.5(5) Å^3, Z = 4; d_{calc} = 1.291 g/cm^3; μ = 0.088. Data Collection: Enraf-Nonius-CAD4 diffractometer; Mo Kα; graphite monochromator; Wyckoff-scan; θ range (deg) 2.36–26.97; crystal dimensions 0.4 × 0.4 × 0.35 mm^3; number of reflections measured, 2319; number of unique reflections, 2143; number of reflections $I > 2\sigma(I)$, 1598. Structural analysis and refinement: solution by direct phase determination; method of refinement, full-matrix LSQ; hydrogen positions of riding model with fixed isotropic U, data-to-parameter ratio, 8.78; R_1, 0.047 (for $I > 2\sigma(I)$); R_1, 0.068 (all reflexes); weighting scheme, $w = 1/[\sigma^2(F_o^2) + (0.0575P)^2 + 0.3681P]$; largest differential peak/hole, 0.198 and −0.174 e Å^{-3}; program used, Siemens SHELXTL-93.
(31) (a) Carlacci, L.; Doubleday: C., Jr.; Furlani, T. R.; King, H. F.; McIver, J. W. *J. Am. Chem. Soc.* **1987**, *109*, 5323. (b) Doubleday: C., Jr.; Turro, N. J.; Wang, J.-F. *Acc. Chem. Res.* **1989**, *22*, 199.

Scheme 4



Scheme 5



C, preferentially the exo diastereoisomeric products are formed. Assuming that **A** is lower in energy compared with **C** for unsubstituted cycloalkenes as substrates, a pronounced endo selectivity is expected that is confirmed by the experiments. Increasing steric repulsions between the substituents at the exo- and endocyclic radical centers depopulates conformer **A**, and more exo product is formed via **C**. This effect has been described in detail for several methylated cycloalkenes.[7d]

II. Cyclic 1,3-Dienes. When comparing these results with the reactions of triplet excited aldehydes with 1,3-cyclodienes (furan, cyclopentadiene, and 1,3-cyclohexadiene), two important differences become apparent: besides the complete change in *regioselectivity*, the *diastereoselectivity* is highly increased *and* the direction of stereocontrol is inverted (from endo to exo). Similar as for cycloalkenes, three 1,4-biradical conformations **D**−**F** are relevantly discussed (Scheme 5).

As already described for the cycloalkene case, ISC from **D** and **F** are expected to lead to endo and exo diastereoisomers, respectively. Using density functional theory (DFT)[32]−B3LYP/6-31G** from the Gaussian 94 package[33]—we determined whether structure **F**(**F′**) with an orthogonal arrangement of the two spin-bearing orbitals corresponds to an energy minimum (Figure 5). As a model reaction, we chose the 1,4-biradical from furan and triplet acetaldehyde. Structure **D** represents the global energy minimum (fully optimized); the restricted conformation **F** is 9.9 kJ/Mol higher in energy, separated by an activation barrier of 28 kJ/mol. This activation energy is obviously too high due to the conformational restriction for rotation about the exocyclic O−C(H,Me) bond. The alternative arrangement **F′** with the methyl group pointing toward the ring plane is much higher in energy and should be less significant in this reaction. If structure **F** (and not **D**) represents the main contribution to product formation, a high exo selectivity is expected due the nearly exclusive formation of the "methyl-up" conformation **F**. The torque induced in conformer **F** rotates the large substituent (Me or any other substituent) in the opposite direction with respect to the ring plane and results in the formation of the major (exo) diastereoisomer.

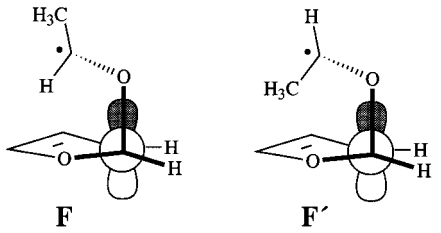


Figure 5. Calculated triplet 1,4-biradical structures for the furan/acetaldehyde reaction.

What happens if the hydrogen in structure **F** is exchanged by a substituent larger than methyl; i.e., if ketones are used as triplet carbonyl substrates? Following the arguments from above, both structures **F** and **F′** are no longer relevant and only structure **D** remains as the SOC-controlling arrangement for the ISC process. Thus, all triplet carbonyl substrates whose substituents exceed a limiting degree of steric interaction are expected to give endo-selective C−C bond formation.[34] This model offers an explanation for the dichotomy that some carbonyl substrates (e.g., phenyl glyoxylates) give idential diastereoselectivity with cyclo-1,3-dienes *and* with the corresponding cycloalkenes, whereas other carbonyls (e.g., aldehydes or acetophenone) show a completely different selectivity pattern. An alternative explanation for the high exo selectivity in furan−aldehyde photocycloadditions that we have suggested previously was the extended lifetime of the singlet 1,4-biradical that is formed after ISC.[7g] This concept, however, predicts thermodynamic control for the formation of *all* cycloaddition products, whether they are formed from triplet excited aldehydes or ketones, esters, etc. Obviously, this is not the case (see eqs 3 (Scheme 2) and 5). Thus, an interaction between the allylic and the exocyclic radical in the 1,4-triplet biradical (as depicted in structures **F**) must be crucial for the dominance of this biradical geometry for rapid ISC. This effect can be described as

(32) Bartolotti, L. J.; Flurchick, U. *Rev. Comput. Chem.* **1996**, *7*, 187.

(33) Gaussian 94, Revision B.1: Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Robb, M. A.; Cheeseman, J. R.; Keith, T.; Petersson, G. A.; Montgomery, J. A.; Raghavachari, K.; Alaham, M. A.; Zakrzewski, V. G.; Ortiz, J. V.; Foresman, J. B.; Cioslowski, J.; Stefanov, B. B.; Nanayakkara, A.; Challacombe, M.; Peng, C. Y.; Ayala, P. Y.; Chen, W.; Wong, M. W.; Andres, J. L.; Replogle, E. S.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Binkley, J. S.; Derees, D. J.; Baker, J.; Stewart, J. P.; Head-Gordon, M.; Gonzalez, C.; Pople, J. A. Gaussian Inc., Pittsburgh, PA, 1995.

(34) One reviewer remarked that the endo/exo ratios (described, for example, in eq 3) do not vary in the same order as *A* values, which are often used to quantify the steric demand of a specific group. This is definitely true, and other contributions also have to be considered, e.g., spin dilution effects by the (conjugated or notconjugated) substituent. For cyclic monoalkenes, we have shown that steric effects are truly decisive (ref 7b−e), and *A* values are useful parameters to correlate with stereoselectivities. In our opinion, *A* values are, however, not applicable for description of steric interactions in biradicals such as **F′**. The cyano group (*A* value ca. 1.0) is expected to interact much stronger in the pseudoperpendicular conformation **F′** than does a methyl group (*A* value 7.5).

a secondary orbital interaction that facilitates intersystem crossing by means of an increase in spin−orbit coupling.

III. Solvent Effects. The solvent effect simultaneously on the regio- and stereoselectivity of the 2,3-dihydrofuran photocycloaddition with benzaldehyde described above can be explained by assuming intermediate contact or solvent-separated radical ion pairs (CIP, SSIP) of the aldehyde radical anion and the enol ether radical cation formed via photoinduced electron transfer (PET). In unpolar solvents, this pathway is unfavorable, and an increase in solvent polarity leads to effective competition between biradical (via ^{3}BR) and PET (via ^{3}CIP) pathway (see Scheme 1). The nonlinear correlation between PET-product formation and x_p resembles that of excited-state properties such as fluorescence lifetimes, quantum yields, or solvatochromic shifts in solvent mixtures.[35] The radical coupling product **7**, which was observed under all conditions as the major side product, could be formed by a hydrogen abstraction reaction (which is often observed in unpolar solvents) and subsequent combination of the geminate radical pair. An alternative way involves the contact ion pair (**CIP**) and leads to **7** by a sequence of proton transfer and radical combination. Compound **7** was already present in minor quantities in unpolar solvents, and its relative appearance shows a similar nonlinear behavior in solvent mixtures. Thus, product **7** is also preferentially formed by a photoinduced electron-transfer mechanism. The product stereoselectivity for **7** is determined at the second reaction step and is only marginal, as expected from the relatively symmetric structure of the allyloxy radical formed from **4**. Another hint for the assumption of contact or solvent separated radical ion pair formation in polar solvents was the increasing amount of pinacol formation (ca. 20% in acetonitrile), which normally accompanies radical-coupling processes via the hydroxybenzyl radical. To form diphenyl glycol via the PET pathway, the radical anion has to escape from the radical ion cage, which is an important competing process. In summary, competing biradical and PET processes can be differentiated using solvent effects on the product ratio. The stereoselectivity of the photocycloaddition with **4** is controlled by different parameters for both pathways: SOC geometries in the case of the biradical path and radical combination geometries for the PET path. Combination of the two dominantly spin-bearing carbon centers results in a 1,4-zwitterion that subsequently could undergo the second bonding event to give **5**. Whereas for **6** the diastereoselectivity is determined at the *second* reaction step (C−C bond formation between two prostereogenic carbon radicals), the stereochemistry of product **5** corresponds to the relative configuration of the 1,4-zwitterion (see Scheme 1). Obviously, Coulombic interaction must already exist for the radical ion pair, allowing the radical anion and radical cation to orientate in such a way that the product configuration is matched.

Experimental Section

General Methods. ^{1}H NMR: AC 200 (200 MHz), Bruker AC 250 (250 MHz), Bruker AC 300 (300 MHz) Bruker AC 500 (500 MHz). ^{13}C NMR: Bruker AC 200 (50.3 MHz), Bruker AC 250 (63.4 MHz), carbon multiplicities were determined by DEPT. UV−vis: Hitachi U-3200. Column chromatography: silica gel (Merck) 60−230 mesh; petroleum ether (PE, 40−60 °C), ethyl acetate (EA). All melting points were determined with a Büchi melting point apparatus (type Nr. 535) and are uncorrected. Combustion analyses: Institut für Anorganische Chemie der Universität zu Köln. Dielectric constants: dipolmeter DM 01. Rayonet−chamber photoreactors RPR-208 (8 × 3000 Å lamps, ca. 800 W, $\lambda = 300 \pm 10$ nm) and immersion-well reactors ($\lambda > 280$ nm) were used for irradiations. Gas chromatography: Hewlett-Packard 5890, series II, capillary column HP-5 (30 m × 0.32 mm × 0.25 μm cross-linked 5% PH ME silicone), temperature program: 60−250 °C in 20 °C/min steps (1 min initial time), flow gas, nitrogen.

General Procedure for Photocycloaddition Reactions. A solution of 5 mmol of carbonyl substrate in 100 mL of solvent in the presence of 50 mmol of 1,3-diene (furan, spiro-[2,4]heptadiene[36]) was irradiated until quantitative conversion of the carbonyl addend was detected by TLC and/or GC. After evaporation of the solvent, the crude product mixture was analyzed by high-field NMR. Purification was performed by bulb-to-bulb distillation, by flash chromatography, or by repeated crystallization.

Determination of Solvent Polarity Effects on the Paternò−Büchi Reaction of 4 with PhCHO. A solution of 1.0 g (9.43 mmol) of benzaldehyde and 7.0 g (100 mmol) of 2,3-dihydrofuran in a mixture of benzene and acetonitrile was irradiated until complete conversion of the aldehyde. The product composition was determined directly from the crude mixture by gas chromatogrphy. GC retention times (min): **6** (7.3), **7** (7.4), **5** (7.6), 1,2-diphenylglycol (9.8).

***exo*-6-Phenyl-2,7-dioxabicyclo[3.2.0]heptane (*exo*-5).**[20] ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.82 (m, 1H, 4-H), 2.08 (m, 1H, 4′-H), 3.24 (ddd, J = 3.8, 4.0, 4.0 Hz, 1H, 5-H), 4.35 (m, 2H, 3,3′-H), 5.05 (d, J = 4.0 Hz, 1H, 6-H), 6.08 (d, J = 3.8 Hz, 1H, 1-H), 7.10−7.38 (m, 5H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 28.8 (t), 49.7 (d), 67.7 (t), 82.5 (d), 106.3 (d), 125.2 (d), 128.4 (d), 128.7 (d), 142.1 (s). Anal. Calcd for $C_{11}H_{12}O_2$: C, 75.00; H, 6.87. Found: C, 75.10; H, 7.40.

***endo*-6-Phenyl-2,7-dioxabicyclo[3.2.0]heptane (*endo*-5).** ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.06 (d, J = 3.7 Hz, 1H, 1-H), no other signals were detectable.

3-(2,3-Dihydrofuranyl)-1-phenylmethanol (7). Diastereomeric ratio 71:29 after preparative thick-layer chromatography (cyclohexane/ethyl acetate 3:1, silica). *Major* diastereoisomer. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.55 (br s, 1H, OH), 3.37 (m, 1H, 3-H), 4.26 (m, nonresolved AB system, 2H, 2-H), 4.54 (d, J = 6.9 Hz, 1H, C*H*OH), 4.58 (dd, J = 2.5, 2.5 Hz, 1H, 4-H), 6.39 (dd, J = 2.1, 2.5 Hz, 1H, 5-H), 7.21−7.45 (m, 5H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 50.5 (d), 72.0 (t), 77.2 (d), 100.4 (d), 126.2 (d), 127.8 (d), 128.5 (d), 142.5 (s), 147.9 (d). *Minor* diastereoisomer. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.55 (br. s, 1H, OH), 3.37 (m, 1H, 3-H), 4.43 (m, nonresolved AB system), 4.54 (d, J = 6.9 Hz, 1H, C*H*OH), 4.92 (dd, J = 2.5, 2.5 Hz, 1H, 4-H), 6.43 (dd, J = 2.1, 2.5 Hz, 1H, 5-H), 7.21−7.45 (m, 5H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 50.1 (d), 72.2 (t), 76.1 (d), 99.2 (d), 126.1 (d), 127.9 (d), 128.7 (d), 142.5 (s), 148.3 (d). Anal. Calcd for $C_{11}H_{12}O_2$: C, 75.00; H, 6.87. Found: C, 74.84; H, 7.16.

6-Methoxy-*endo*-6-phenyl-2,7-dioxabicyclo[3.2.0]hept-3-ene (*endo*-8).[25] Irradiation time: 43 h, rt. Yield: 62%. dr = 95:5. ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.18 (s, 3H, OMe), 4.01 (ddd, J = 1.2, 2.9, 3.9 Hz, 1H, 5-H), 4.64 (dd, J = 2.9, 2.9 Hz, 1H, 4-H), 6.41 (ddd, J = 0.8, 1.2, 2.9 Hz, 1H, 3-H), 6.43 (dd, J = 0.8, 3.9 Hz, 1H, 1-H), 7.32−7.43 (m, 5H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 50.2 (q), 56.4 (d), 101.5 (d), 105.0 (d), 114.5 (s), 126.7 (d), 128.0 (d), 128.4 (d), 136.8 (s), 148.3 (d).

6-Methoxy-*exo*-6-phenyl-2,7-dioxabicyclo[3.2.0]hept-3-ene (*exo*-8). ^{1}H NMR (300 MHz, $CDCl_3$): δ 3.85 (m, 1H, 5-H), 5.36 (dd, J = 2.9, 2.9 Hz, 1H, 4-H), no other signals were detectable.

Spiro[cyclopropane-1,2′-(*exo*-6-phenyl-7-oxabicyclo-[3.2.0]hept-3-ene)] (*exo*-10). Irradiation time: 20 h, rt.

(35) (a) Ghoneim, N.; Suppan, P. *Pure Appl. Chem.* **1993**, *65*, 1739. (b) Nitsche, K.- S.; Suppan, P. *Chimia* **1982**, *36*, 346.

(36) Wilcox, C. F.; Craig, R. A. *J. Am. Chem. Soc.* **1961**, *83*, 3866.

Conversion: 20%. Due to the low degree of conversion, the two diastereoisomeric oxetanes were not isolated; the dr value (78:22) was determined from the crude product mixture. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.58−0.92 (m, 2H), 1.02−1.20 (m, 2H), 3.55 (m, 1H, 5-H), 4.84 (dd, J = 1.0, 5.5 Hz, 1H, 1-H), 5.25 (d, J = 3.3 Hz, 1H, 6-H), 5.53 (ddd, J = 1.0, 1.0, 5.6 Hz, 1H, 3-H), 5.91 (dd, J = 2.5, 5.6 Hz, 1H, 4-H), 7.13−7.86 (m, 5H, ArH). ^{13}C NMR (75 MHz, $CDCl_3$): δ 6.8 (t), 15.0 (t), 29.6 (s), 35.3 (d), 89.2 (d), 90.1 (s), 125.2 (d), 128.5 (d), 128.9 (d), 129.7 (d), 134.4 (s), 139.9 (d).

Spiro[cyclopropane-1,2′-(*endo*-6-phenyl-7-oxabicyclo[3.2.0]hept-3-ene)] (*endo*-10). ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.47 (d, J = 5.4 Hz, 1H, 1-H), 5.96 (dd, J = 2.5, 5.6 Hz, 1H, 4-H), no other signals were detectable.

Spiro[cyclopropane-1,2′-(6-phenyl-7-oxabicyclo-[3.2.0]hept-3-en-6-carboxylic acid methyl ester)] (11). Irradiation time: 65 h, rt. Yield: 50%. dr = >95:5. Purification by column chromatography (silica, EtOAc−PE 1:5), colorless needles. Mp: 120−121 °C. ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.70−0.85 (m, 2H), 1.25−1.32 (m, 2H), 3.80 (s, 3H), 4.42 (ddd, J = 1.0, 2.5, 5.2 Hz, 1H, 5-H), 4.82 (d, J = 5.2 Hz, 1H, 1-H), 5.27 (dd, J = 2.5, 5.7 Hz, 1H, 4-H), 5.37 (ddd, J = 1.0, 1.0, 5.7 Hz, 1H, 4-H), 7.26−7.46 (m, 5H, ArH). ^{13}C NMR (50 MHz, $CDCl_3$): δ 6.6 (t), 14.2 (t), 34.8 (s), 52.8 (s), 54.5 (d), 86.6 (d), 90.3 (s), 125.2 (d), 125.4 (d), 127.6 (d), 127.9 (d), 137.9 (s), 140.9 (d), 175.2 (s). Anal. Calcd for $C_{16}H_{16}O_3$: C, 74.98; H, 6.29. Found: C, 74.72; H, 6.55.

Acknowledgment. Financial support came from the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. The DFT calculations were performed by K. Malsch from the research group of Prof. G. Hohlneicher, University of Cologne.

Supporting Information Available: X-ray data for compounds **8** and **11** (6 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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