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# Spin-Directed Stereoselectivity of Carbonyl–Alkene Photocycloadditions

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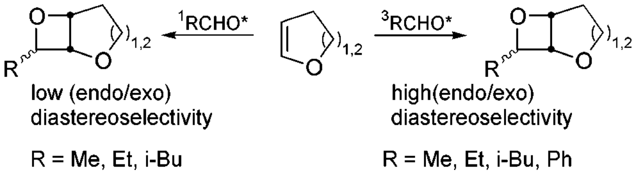
## ABSTRACT



**The concentration dependence of the Paternò–Büchi photocycloaddition of the two cyclic enolethers 2,3-dihydrofuran and 2,3-dihydropyran, respectively, with aromatic as well as aliphatic aldehydes was studied. For aliphatic aldehydes, a sharp transition from low to high diastereostereoselectivity was observed, indicating a switch from singlet to triplet photocycloaddition with different selectivity controlling mechanisms.**

The photocycloaddition of carbonyls to alkenes is known as Paternò−Büchi reaction[1] and has been intensively studied with respect to its synthetic utility.[2] A mechanistic model developed by us for the photocycloaddition of triplet excited carbonyls connects (noninduced) product diastereoselectivity with the spin−orbit coupling controlled geometry of the 1,4-biradical during the triplet−singlet crossing (ISC) process.[3] This model was successfully applied to several triplet photocycloadditions and predicts the stereochemical orientation of the radical centers during the spin−inversion process and thus also the correct product diastereoselectivity.[4] A recent MC-SCF study resulted in the prediction that ISC from triplet to singlet leads to the same biradical ground-state pathways that are entered via singlet photochemistry. Following this line of argumentation, the product-determining molecular geometry is expected to be similar from either the first excited singlet or triplet state of the carbonyl reactant.[5] The spin profile of a bimolecular photochemical reaction can be traced by variation of substrate concentrations provided that the lifetime of the excited singlet state allows diffusion-controlled processes.

To evaluate the differences in diastereoselectivity of the Paternò−Büchi reaction in the singlet and in the triplet channel, we investigated the concentration dependence of the photocycloaddition of aldehydes with electron-rich alkenes. As alkene reagents, 2,3-dihydrofuran and 2,3-dihydropyran were used. As aliphatic aldehydes we used acetaldehyde, propionaldehyde, and 3-methylbutyraldehyde. In our initial studies, aromatic aldehydes were investigated which have high intersystem crossing rates and quantum yields and thus exclusively react via their first excited *triplet* states in intermolecular photocycloadditions.[6] The concentration profile of a model reaction is shown in Figure 1. Both substrates (2,3-dihydrofuran and benzaldehyde) were applied in a 1:1 ratio over a broad concentration range, showing no significant effect on the (simple) *endo*/*exo* diastereoselectivity.

The lifetimes of the first excited *singlet* state of aliphatic aldehydes are in the 1−2 ns range.[7] Thus, trapping reagents

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[1] Paternò, E.; Chiefi, G. *Gazz. Chim. Ital.* **1909**, *39*, 431. Büchi, G.; Inman, C. G.; Lipinsky, E. S. *J. Am. Chem. Soc.* **1954**, *76*, 4327.
[2] Bach, T. *Synthesis* **1998**, 683. Bach, T. *Liebigs Ann.* **1997**, 1627. Griesbeck, A. G. *Handbook of Photochemistry and Photobiology*; Horspool, W., Song, P.-S., Eds.; CRC Press: Boca Raton, 1995; p 550 and 755.
[3] Griesbeck, A. G.; Mauder, H.; Stadtmüller, S. *Acc. Chem. Res.* **1994**, *27*, 70. Griesbeck, A. G.; Buhr, S.; Fiege, M.; Lex, J.; Schmickler, H. *J. Org. Chem.* **1998**, *63*, 3847.
[4] For example: Abe, M.; Torii, E.; Nojima, M.*J. Org. Chem.* **2000**, *65*, 3426.
[5] Palmer, I. J.; Ragazos, I. N.; Bernardi, F.; Olivucci, M.; Robb, M. *J. Am. Chem. Soc.* **1994**, *116*, 2121.
[6] Griesbeck, A. G.; Stadtmüller, *J. Am. Chem. Soc.* **1990**, *112*, 1281. Griesbeck, A. G.; Stadtmüller, *J. Am. Chem. Soc.* **1991**, *113*, 6923.

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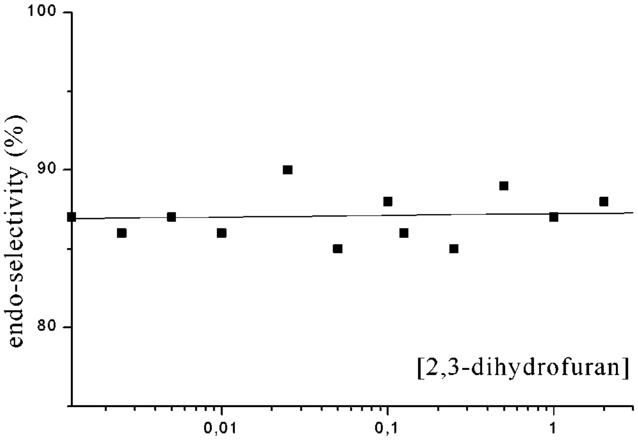


**Figure 1.** Concentration/selectivity profile of the benzaldehyde/2,3-dihydrofuran photocycloaddition.

can intercept these singlets in diffusion-controlled bimolecular processes. Figure 2 shows the effect of concentration variation on the *endo*/*exo* diastereostereoselectivity of the propionaldehyde/2,3-dihydrofuran photocycloaddition. In the low concentration region (<0.02 M), the diastereoselectivity reached a plateau with an *endo*/*exo* ratio of ca. 85:15. Likewise, in the high concentration region (>0.8 M) the diastereoselectivity became constant with a ca. 1:1 *endo*/*exo* ratio. The relative configurations of the photoproducts were established by NOE measurements and comparison with the NMR data published earlier (Scheme 1). The diastereomeric ratios were determined by GC and NMR analyses. A similar result was obtained for the photocycloaddition of acetaldehyde with 2,3-dihydrofuran (Figure 3): the transition between high and low selectivity region occurred at substrate concentrations of ca. 0.2 M. The maximum *endo*/*exo* selectivity (76:24) was lower than for the propionaldehyde case; at high concentrations the selectivity switched to 42:58. An analogous trend was observed for the dihydropyran reactions: whereas benzaldehyde gave constant stereoselectivity over the whole range, the addition of aliphatic aldehydes was strongly dependent on the substrate concentrations. In contrast to the results with 2,3-dihydrofuran, the selectivity curves were much less steeper and showed a near-linear behavior in the region between 5.0 and 0.01 M (Figure 4).

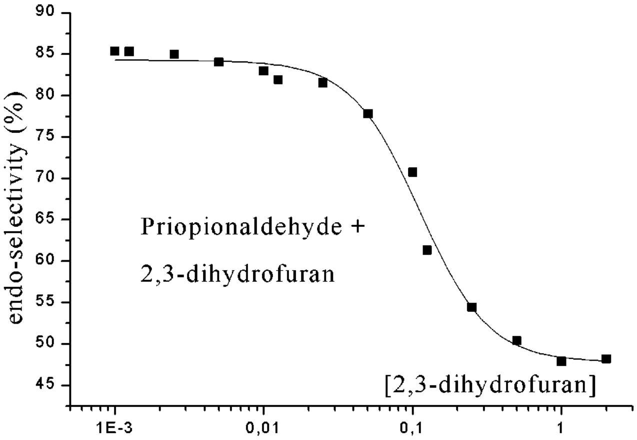
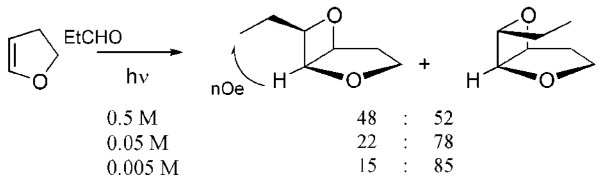


**Figure 2.** Concentration/selectivity profile of the propionaldehyde/2,3-dihydrofuran photocycloaddition.

## Scheme 1



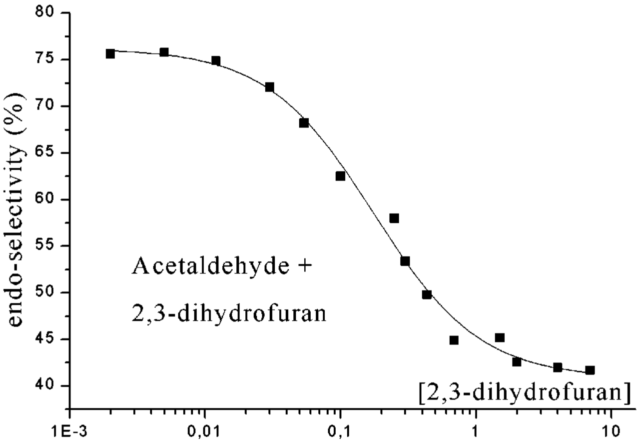


**Figure 3.** Concentration/selectivity profile of the acetaldehyde/2,3-dihydrofuran photocycloaddition.

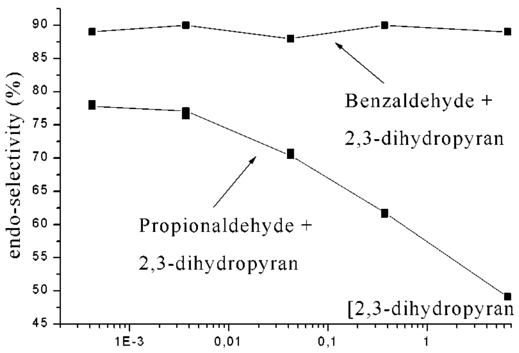


**Figure 4.** Concentration/selectivity profile of the benzaldehyde versus propionaldehyde/2,3-dihydropyran photocycloaddition.

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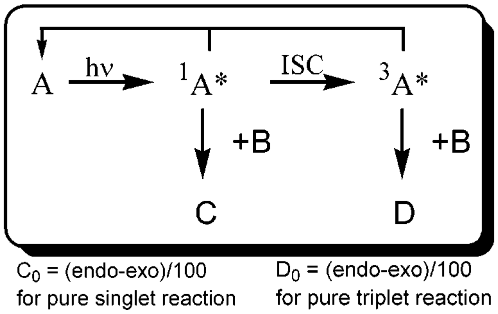
(7) Kossanyi, J.; Sabbah, S.; Chaquin, P.; Ronfart-Haret, J. C. *Tetrahedron* **1981**, *37*, 3307.

Other alkene−carbonyl combinations measured over a smaller concentration range showed also nonlinear behavior strongly depending on the reactivity of the alkene and of the singlet lifetime of the electronically excited carbonyl addend. In light of these results, recent reports on hydrogen-bonding interactions as stereoselectivity-determining factors in Paternò−Büchi reactions become relevant because these interactions should be active for the singlet as well as the triplet excited state of the carbonyl reactant.[8]

Spin-directed stereoselectivity has been already reported for the photolyses of azoalkanes[9] as well as for Yang cyclization processes following intramolecular hydrogen abstractions.[10] In these cases, however, high diastereoselectivities were observed for singlet reactions and low selectivities for sensitized (triplet) processes. The inverse behavior, as described herein for the cycloalkene photocycloadditions to aliphatic aldehydes, can be rationalized as follows: in triplet Paternò−Büchi reactions 1,4-triplet biradicals are generated, which have to undergo intersystem crossing in order to convert into closed-shell products. Obviously, this process requires severe geometrical restrictions and, following the model published earlier,[4] leads to high *endo* selectivity. The surprising result is the stereoselectivity of the singlet process: very low selectivities were determined even for the reaction of pivaldehyde with 2,3-dihydrofuran (ca. 1:1 at high concentrations), which gave a 95:5 diastereoisomeric ratio in the triplet channel.[4]

Thus, the stereoselectivity of the Paternò−Büchi reaction of singlet excited aldehydes which most likely involves *conical intersections* is not sensitive with respect to carbonyl substituents. The reaction sequence behind the concentration/selectivity plots is given in Scheme 2: the bimolecular photocycloaddition steps resulting in the "spin-characteristic" products C and D competes with two unimolecular processes, the ISC to give the triplet excited carbonyl (ca. 0.3−0.5 for aliphatic aldehydes) and the photophysical deactivation of the triplet state. From the correlations shown in Figure 2, 3, or 4, $C_0$ and $D_0$ were estimated and the $D/(C + D)$ ratio plotted versus the concentration of the trapping reagent B. Nonlinear curve fitting led to the equation $y = [D_0 - C_0/1 + (x/x_0)^p] + C_0$ with $y = D/(C + D)$ and $x = B$. For the photocycloaddition of propionaldehyde with 2,3-dihydrofuran, the values $x_0 = 0.09$ and $p = 1.9$ were determined (Figure 5). The concentration $B_0$ ($x_0$) corresponds to a spin (singlet/triplet) selectivity of zero. These values were characteristic for every substrate combination and represent the specific kinetic data. Qualitatively, for carbonyls with shorter-lived excited singlets (e.g., aromatic aldehydes), the $B_0$ value shifts to higher concentrations, whereas a change in bimolecular rate constants of the cycloaddition steps alters the sigmoidal behavior of the curve. Investigations on the quantitative relationships are underway.

**Scheme 2**



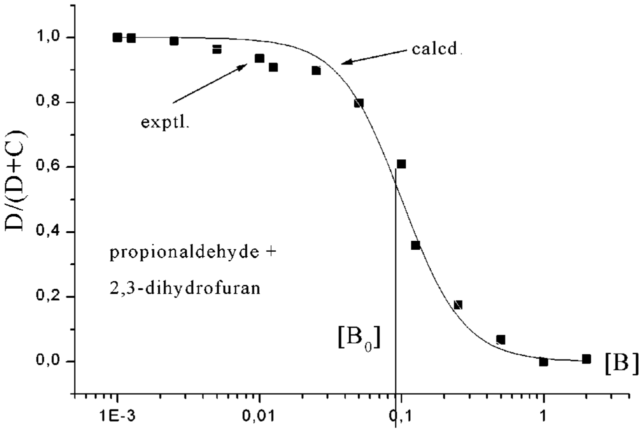


**Figure 5.** Experimental and calculated concentration/selectivity profile of the propionaldehyde/2,3-dihydrofuran reaction.

In conclusion, ISC from the triplet to the singlet 1,4-biradical in Paternò−Büchi reactions does not lead to the same biradical ground-state pathways that are entered via singlet photochemistry. Excited singlet carbonyls react with low *endo*/*exo* diastereoselectivity whereas triplet reactions proceed with high diastereoselectivities even with sterically less demanding α-substituents.

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[9] Also named spin-correlation effect: Engel, P. S. *Chem. Rev.* **1980**, *80*, 99. Engel, P. S.; Nalepa, C. J. *Pure Appl. Chem.* **1980**, *52*, 2621.

[10] Giese, B.; Wettstein, P.; Stahelin, C.; Barbosa, F.; Neuburger, M.; Zehnder, M.; Wessig, P. *Angew. Chem., Int. Ed.* **1999**, *38*, 2586.