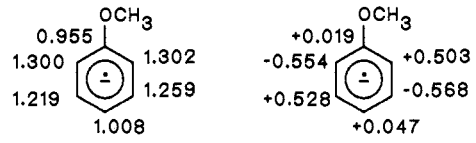

Figure 1. Total radical anion electron densities and frontier MO coefficients for the anisole radical anion.

The ratio of *m*- to *o*-deuterium content (i.e., D_m:D_o) was found to be 6.98 ± 0.67, thus establishing that the greater selectivity was at the ortho site. Hence we can conclude that the initial protonation in the Birch reduction of anisole occurs preferentially at the ortho carbon.

An alternative approach to this conclusion is algebraic. Equation 2a states that the sum of hydrogen and deuterium content accumulated in the ortho position in protonation step 1 (i.e., of radical anion **7**) is equal to the sum accumulated at the meta site in protonation step 2 (i.e., of carbanion **9o**); note path O in Scheme I. In parallel, eq 2b deals with the path M process

$$H_1^{o} + D_1^{o} = H_2^{m} + D_2^{m} \qquad H_1^{m} + D_1^{m} = H_2^{o} + D_2^{o} \quad (2a,b)$$

in Scheme I. The isotope selectivities at each site in each step are given in the following four equations, where the *R* selectivities are those encountered in the radical anion protonation, and the *C* selectivities, in the final, cyclohexadienyl carbanion protonation:

$$R_o = H_1^{o}/D_1^{o} \qquad R_m = H_1^{m}/D_1^{m} \quad (3a,b)$$

$$C_o = H_2^{o}/D_2^{o} \qquad C_m = H_2^{m}/D_2^{m} \quad (3c,d)$$

These equations are utilized to eliminate the *H* terms in eqs 2a and 2b. Additionally, eq 4a and 4b give the total deuterium contents at the ortho and meta positions acquired in the two protonation steps. These are used to eliminate the terms D_2^{o} and

$$D_o = D_1^{o} + D_2^{o} \qquad D_m = D_1^{m} + D_2^{m} \quad (4a,b)$$

D_2^{m} in eq 2a and 2b. This leads to eq 5, which gives the regioselectivity, *W*, in the initial radical anion protonation.

$$W = \frac{D_1^{o}}{D_1^{m}} = \frac{(C_m + 1)[(R_m + 1)D_m - (C_o + 1)D_o]}{(C_o + 1)[(R_o + 1)D_o - (C_m + 1)D_m]} \quad (5)$$

One might anticipate that the deuterium versus hydrogen selectivity in the radical anion protonation would be relatively independent of position, and the same should be true for the carbanion protonation. With this assumption that $C_m = C_o = C$ and $R_m = R_o = R$, we obtain the simpler expression 6. Both expressions 5 and 6 prove useful in providing the desired ortho to meta regioselectivity, *W*, in the initial, radical anion protonation. With the experimental finding that $D_m > D_o$ (i.e., 6.98:1) and the original premise that $R > C$, we conclude from eq 6 that *W*, the ortho to meta radical anion protonation ratio, is greater than unity.

$$W = \frac{D_1^{o}}{D_1^{m}} = \frac{(R + 1)D_m - (C + 1)D_o}{(R + 1)D_o - (C + 1)D_m} \quad (6)$$

Further, eq 6 reveals that as the relative isotope selectivity of the radical anion protonation increases (i.e., $R \gg C$), the ortho to meta selectivity *W* of the radical anion protonation reaches a lower limit of 6.98 (i.e., D_m/D_o).

Interestingly, an ab initio ROHF/6-31G//STO-3G computation (note Figure 1) proved to be in qualitative agreement with the early Huckel calculations published[4a] in which we noted that the site ortho to the maximum number of alkoxy groups is most electron rich.[10] It is particularly noteworthy that the frontier MO has its highest density at the meta site and thus is not controlling protonation.

(10) Note also SCF computations in ref 8.

We are continuing our research on the regioselectivity of radical anion protonation in the Birch reduction with the aim of further dissecting the two protonation steps and assessing the validity of the original premise.

Acknowledgment. Support of this research by the National Science Foundation and also in part by the Graduate School of the University of Wisconsin is gratefully acknowledged.

Registry No. Anisole, 100-66-3; anisole radical anion, 34519-87-4.

Photocycloaddition of Benzaldehyde to Cyclic Olefins: Electronic Control of Endo Stereoselectivity

Axel G. Griesbeck* and Stefan Stadtmüller

Institut für Organische Chemie der Universität Würzburg Am Hubland, D-8700 Würzburg, FRG

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The Paternò–Büchi reaction[1] of aliphatic and aromatic carbonyl compounds with electron-rich alkenes has been shown to be an effective and versatile method for the generation of polyoxygenated and hydroxylated molecules (e.g., photo aldol reaction,[2] asymmetric induction[3]). In cases where the starting materials were acyclic olefins, only moderate regio- and stereoselectivity could be observed.[4] For reactions with electronically excited carbonyl compounds in their triplet states (aromatic ketones, aldehydes, esters), the exciplex model can be useful to explain low regiocontrol,[5] whereas the low stereoselectivity is due to bond rotation at the triplet biradical stage.[6] These triplet biradicals have been shown to be relevant intermediates in trapping experiments,[7] spectroscopy,[8] and independent generation.[9] Whereas the lifetime of these species is rather low (1–5 ns[8,10]) compared to that of their hydrocarbon analogues (50–200 ns[10]), bond rotation is fast enough to lead to stereorandomization. As we have previously shown,[11]

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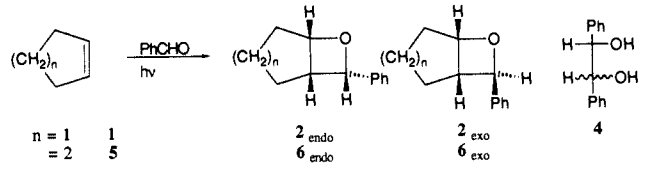
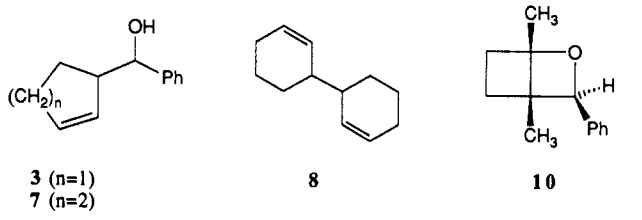
the addition of triplet aromatic aldehydes to furan as well as 2,3-dihydrofuran proceeds highly regio- and stereoselectively. In the furan case, oxetanes are formed exo selectively (>98%) as 2-alkoxy isomers; in the dihydrofuran case, the oxetanes are formed endo selectively (7:1 endo:exo for benzaldehyde) as 3-alkoxyoxetanes. We now present evidence for a general principle, which determines the stereochemistry of the photoproducts from cycloalkenes and benzaldehyde.

In the cases of the carbocyclic compounds cyclopentene (**1**), cyclohexene (**5**), and 1,2-dimethylcyclobutene (**9**), the ratio between the photoaddition and photoreduction pathways was about 1:1. The reduction product, 1,2-diol (**4**), could be isolated in all

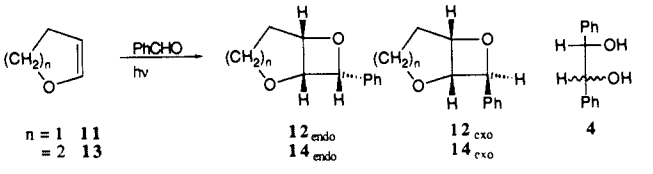


of these cases in good yield. The corresponding product from olefin dehydrogenation (**8**, diastereomeric ratio = 1:1) was detected in the cyclohexene reaction. Coupling products were formed in both the cyclopentene and cyclohexene reactions: the tertiary alcohols **3** and **7** as 1:1 mixtures of diastereomers with a yield of 33% and 17%, respectively. The oxetanes were isolated in moderate yield



and with moderate diastereoselectivity: 55% for the cyclopentano-annulated oxetane (**2**) with an endo:exo ratio of 61:39, and 34% for the corresponding oxetane (**6**) with an endo:exo ratio of 74:26. The cyclohexene reaction was already reported in the literature,[12,13] where the spectral data of the main product (35%) was "consistent with the unusual assignment of *endo*-stereochemistry".[14] The yield for the cyclobutene-derived oxetane **10** was similar (48%), surprisingly with the exo diastereomer as sole product.

In the case of the more electron rich olefins 2,3-dihydrofuran (**11**) and 2,3-dihydropyran (**13**), the rates of photocycloaddition as well as the observed diastereoselectivities increased. Compound **11** was the most reactive olefin, and no hydrogen-abstraction product could therefore be isolated. The sole product was the oxetane **12** with an endo:exo ratio of 82:18. The stereochemistry was confirmed via NOE spectroscopy for a set of endo stereoisomers ($\mathbf{6}_{endo}$, $\mathbf{12}_{endo}$, and $\mathbf{14}_{endo}$). A common feature of the NOE measurements was the enhancement of both oxetane-ring hydrogen resonances during saturation of the third hydrogen. Additionally, the exo isomers $\mathbf{6}_{exo}$ and $\mathbf{12}_{exo}$, which could be separated by chromatographic methods, showed corresponding NOE properties. Saturation of hydrogen resonances of the five-membered ring led to signal enhancement of the α oxo hydrogen of the oxetane ring.



In contrast to this clean reaction, the irradiation of 2,3-dihydropyran (**13**) with benzaldehyde gave a multitude of products,

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Table I. Photoreaction of Benzaldehyde with Cyclic Monoolefins[a]

alkene	photoaddn, % (endo:exo)	photoredn,[b] %
1	55 (61:39) **2**	45
5	34 (74:26) **6**	66
9	48 (<2:98) **10**	52
11	>98 (82:18) **12**	
13	45 (90:10) **14**[c]	45

[a] Irradiation in benzene, 5 °C, N_2, Pyrex, alkene: PhCHO = 5:1. [b] Sum of percent of formed **4** and percent coupling product (**3**, **7**). [c] Additionally 10% of the regioisomeric 2-alkoxyoxetane.

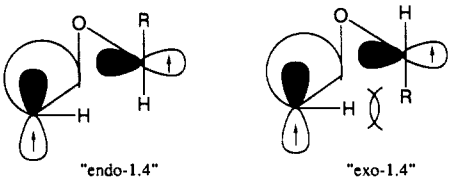

Figure 1.

with the 3-alkoxyoxetane **14** as the main product (45%, endo:exo = 90:10). The regioisomeric 2-alkoxyoxetane also appeared in the crude reaction mixture (ca. 10%), but decomposed during workup. At least four different coupling products of **13** were formed from hydrogen transfer to benzaldehyde (45% **4**), the stereochemistry of which could not be determined in detail. Table I summarizes the results of our investigations.

Mechanistic Discussion. The formation of thermodynamically unfavored products in cycloaddition reactions is well-known from thermal reactions as, for example, the Diels–Alder reaction (endo selectivity). In most cases, these effects could be rationalized by application of the secondary orbital interaction concept.[15] In our investigation of Paternò–Buchi reactions with cycloalkenes, a similar stereoselectivity phenomenon could be observed. Secondary orbital interactions cannot be responsible for these effects. In contrast to thermal reactions, triplet biradicals (oxatetramethylenes) play a role as intermediates here. For the formation of photoproducts, an intersystem crossing (ISC) into the singlet manifold is therefore necessary. Several mechanisms are known enhancing the (first order strictly forbidden) ISC. The most important one for flexible triplet 1,4-biradicals is spin–orbit coupling (SOC).[16] The strength of SOC is proportional to the distance of the radical centers R and the angle ϕ between the p orbitals localized at these positions (Salem rules,[17] for the numerical equation: [SOC = $B(R)|S|\sin\phi$]; see ref 18). Because of the very short lifetime (some picoseconds, if any[19]) of the singlet 1,4-biradicals formed, the product stereochemistry should represent to a certain extent the geometry of the triplet 1,4-biradical during ISC.

According to the Salem rules, there are two conformers for effective SOC (Figure 1, ϕ = 90°).[20] Steric interaction between the R group (R = phenyl in our case) and the α ring hydrogen disfavors the "exo-1,4" conformer. Therefore ISC should occur preferentially from the "endo-1,4" conformer and lead to the formation of the endo photoproduct from the short-lived singlet 1,4-biradical. Following this argumentation, increasing size of R should lead to a corresponding increase of the endo:exo ratio. This we could show[11] for the reaction between 2,3-dihydrofuran (**11**) and mesitylenecarbaldehyde (R = Mes), where the endo:exo ratio is higher than 20:1.

This explanation corresponds perfectly with the concept of conformational memory in singlet biradicals, as postulated by

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Scaiano.[21] The high exo selectivity observed in the photocycloaddition of benzaldehyde to 1,2-dimethylcyclobutene (9) could be due to fast retrocleavage from the energetically disfavored singlet 1,4-biradical stage. In this case, the endo diastereomer should less likely be formed because of the high strain of the bicyclo[2.2.0]hexane skeleton.

The concept of electronic control of stereoselectivity described here can be useful to explain a number of unusual results in photocycloaddition reactions. Further work for synthetic applications is in progress.

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Probing Macrocycle Flexibility: Ligand Binding to Zinc and Nickel Tetraphenylhydroporphyrins

Warren A. Kaplan,[†] Robert A. Scott,*[,‡] and Kenneth S. Suslick*[,†]

School of Chemical Sciences
University of Illinois at Urbana-Champaign
Urbana, Illinois 61801
Departments of Chemistry and Biochemistry and the Center for Metalloenzyme Studies
University of Georgia, Athens, Georgia 30602

Received August 10, 1989

Metallohydroporphyrins have been identified as being essential in a variety of biological systems including nitrite and sulfite reductases[1,2] and *S*-methyl coenzyme M reductase.[3] Of special note is the highly reduced nickel-containing macrocyclic tetrapyrrole F_{430}, found in the latter enzyme of methanogenic bacteria.[3,4] The relative rigidity of the macrocycle is expected to be important in metallohydroporphyrin enzymes for metal ions that undergo changes in either spin state or oxidation state during the course of catalytic activity. Such reactions can induce metal ion size changes of up to 0.2 Å (in the case of nickel).[5] The reduction of the macrocycle is generally thought to be responsible for an enhanced reactivity in these systems.[6-9] It has been argued that ring reduction gives the macrocycle greater flexibility: the expected reduction in aromaticity (based on decreased ring-current effects in the NMR spectra)[10-12] and observed S_4 ruffling both in solids[10,13,14] and in solution[15-17] serve as the basis of these arguments. From ligand binding experiments, however, we find no evidence for such increased flexibility.

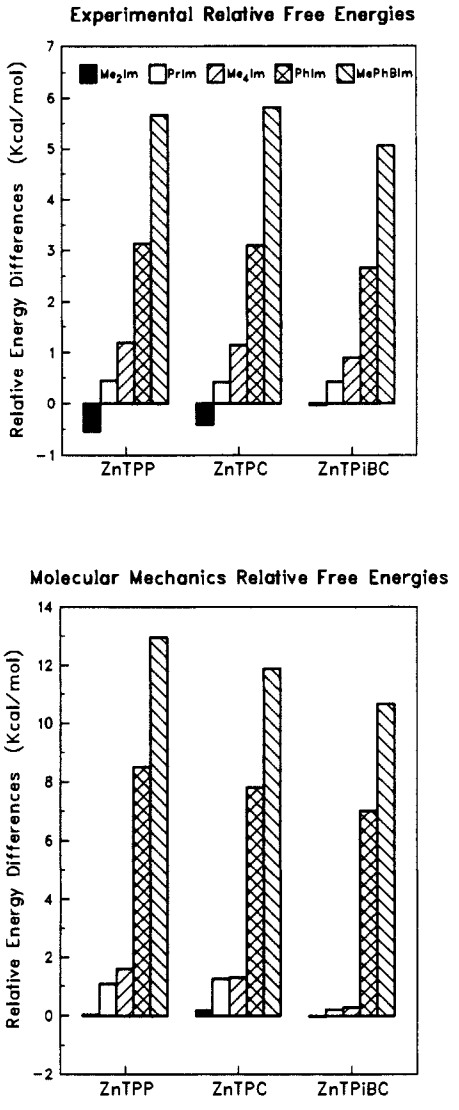

Figure 1. Experimental and molecular mechanics free energies of ligand binding, relative to the binding of 1MeIm.

To probe the role of porphyrin ring reduction in metal reactivity, we have measured the equilibrium binding constants of a series of sterically hindered bases with both zinc[18] and nickel[16,17] tetraphenylhydroporphyrins. The use of zinc allows examination of a well-defined equilibrium between four- and five-coordination without added complications of spin- or oxidation-state changes. The series of sterically hindered imidazoles allows us to probe the flexibility of the macrocycle with minimal electronic changes. If the more reduced hydroporphyrins had greater flexibility, then the steric hindrance of the incoming ligand would have less effect on the equilibrium constant for the metallohydroporphyrins than for the fully unsaturated metalloporphyrin. In contrast, the use of nickel allows examination of a biologically relevant system with a four- to six-coordination equilibrium. Titrations with the more

* Authors to whom correspondence should be addressed.
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‡ University of Georgia.

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