Stereoselectivity of Alkylidenecarbene Addition to Olefins. 2. Effect of Orbital Polarization in the Alkenes†[1]

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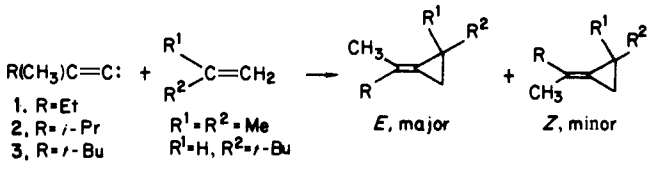
Abstract: The reactions of unsymmetrical alkylidenecarbenes $R(CH_3)C{=}C{:}$, where R = *i*-Pr (**2**) and *t*-Bu (**3**), with three unsymmetrical olefins, 1-butene, styrene, and ethyl vinyl ether, were studied. In each case, the *E* olefin adduct predominated over the *Z* adduct. Stereoselectivity was found to decrease in the order (*E*:*Z* product ratios with **3** at −20 °C) styrene (250:1) ≫ ethyl vinyl ether (11.5:1) > *tert*-butylethylene (10:1) > 1-butene (4.3:1) > isobutylene (2.0:1); with **2** stereoselectivity with all olefins was considerably lower. As previously predicted, the olefins with the more highly polarized π orbitals, styrene and ethyl vinyl ether, gave the most stereoselective reactions. Polarization of the olefinic π^* orbitals was also determined to influence the stereoselectivity of the cycloadditions. High stereoselectivity is expected only for olefins where the π and π^* orbitals are strongly polarized in *the same direction*, as in styrene. The results also are discussed relative to earlier MNDO calculations.

Recently we reported a detailed experimental and theoretical investigation of the stereoselectivity of alkylidenecarbene additions to olefins.[1] Unsymmetrical alkylidenecarbenes $R(CH_3)C{=}C{:}$ (**1–3**) were found experimentally to add to two unsymmetrical olefins, isobutylene and *tert*-butylethylene, to give a predominance of the *E* alkylidenecyclopropane over the *Z* alkylidenecyclopropane. For each alkene, stereoselectivity increased as a function

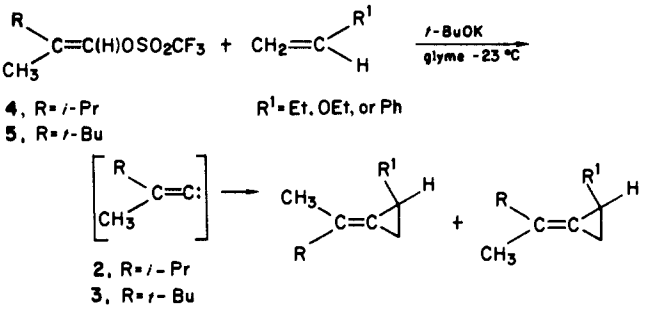


of the increasing size of R in the carbenes. The highest stereoselectivity observed was for the reaction of **3** with *tert*-butylethylene (9:1 *E*:*Z* ratio). Theoretical calculations carried out in conjunction with the experimental study were in complete harmony with the observed stereoselectivities. These earlier calculations along with arguments based on Frontier Molecular Orbital theory (FMO)[2] were used to predict that higher selectivities for carbenes **1–3** would be observed when olefins substituted with strong polarizing groups such as phenyl or methoxy were used. Here we report experimental studies that to a large extent confirm these predictions and also provide further insight into the factors that control the transition-state energies of alkylidenecarbene addition to olefins.

Results

Three new olefins, 1-butene, styrene, and ethyl vinyl ether, were utilized in this study as traps for carbenes **2** and **3**. Reactions were carried out as follows. Each of the vinyl triflates **4** and **5** (as mixtures of the *E* and *Z* isomers) was treated with 1.5 equiv of *t*-BuOK at −23 °C in a 3:1 mixture of excess alkene and glyme as solvent. Reactions were complete in 0.5 to 1 h as determined through GC analysis. After GC analysis of the original reaction mixtures and workup, alkylidenecyclopropane products[3] were isolated by preparative GC and then identified through spectral means. The alkylidenecyclopropane products, their *E*:*Z* ratios, and the conditions of the reactions are given in Table I along with pertinent results from the previous study. Stereoselectivity ranged from a low *E*:*Z* ratio of 2:1 (entries 1 and 10) to a high of 250:1 (entry 7).

In this study the reaction medium was changed from the pure alkene used previously to a 3:1 mixture of alkene and glyme. The reactions were homogeneous and were complete after 1 h at −23 °C (vs. 1–4 days at −20 °C when pure alkene was the solvent[1]).



This change had little effect upon the *E*:*Z* ratios (compare entries 3, 4, 8, and 9 in Table I) but greatly increased the reaction rates. A slight effect of glyme as cosolvent has been noted by us before for reactions of alkylidenecarbenes.[4] These small changes in *E*:*Z* ratio do not alter the basic conclusions derived from this work.

As a check on product stability in the new medium, adduct **8*E*** was subjected to standard reaction conditions and analysis. No isomerization or decomposition of **8*E*** was observed.

Alkylidenecyclopropane stereochemistry was determined through analysis of the 300-MHz ^1H NMR of products **6–8**. In these cyclopropanes, the presence of a chiral center causes the methyls of the isopropyl group to be diastereotopic. The chemical shift differences between the diastereotopic methyls are greater for the *Z* isomers than for the *E* isomers as expected[5] (see Table II). In addition, the shielding effect of the phenyl in products **8*E*** and **8*Z*** is clearly seen and is also illustrated in Table II.

With the new olefins employed here, 1-butene, ethyl vinyl ether, and styrene, *E* products in the alkylidenecarbene cycloadditions again predominate over the *Z* products. Very high stereoselectivity was found for the reaction of carbene **3** with styrene. The significance and implications of the stereoselectivity results are discussed in the following.

Discussion

Singlet alkylidenecarbenes possess an empty 2p orbital and a filled sp orbital (see **15**). Calculations[1] show that the favored

† Dedicated to Professor Cheves Walling on the occasion of his 70th birthday.

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(1) Part 1: Apeloig, Y.; Karni, M.; Stang, P. J.; Fox, D. P. *J. Am. Chem. Soc.* **1983**, *105*, 4781–4792.

(2) Fleming, I. "Frontier Orbitals and Organic Chemical Reactions"; Wiley: London, 1976.

(3) Alkynes, $RC{\equiv}CCH_3$ (R = *i*-Pr and *t*-Bu), and enol ethers, $R(CH_3)C{=}C(H)O$-*t*-Bu, were also observed as products in some of these reactions, but they were not isolated. Their formation and characterization have been detailed elsewhere.[1]

(4) Fox, D. P.; Bjork, J. A.; Stang, P. J. *J. Org. Chem.* **1983**, *48*, 3994–4002.

(5) Reference 1 and references therein.

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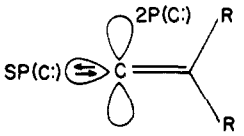
approach of **15** to olefins is determined primarily by the interaction



of the empty 2p (C:) orbital of the carbene and the π orbital of the olefin. This description is consistent with the classification of singlet alkylidenecarbenes as electrophilic species.[6] As the stabilizing overlap between these orbitals is larger in the "inward" (**16**) or the "semiperpendicular" (**17**) approaches than in the "outward" conformations (**18**, Figure 1), the former transition states are preferred.[1]

Specifically for the systems studied earlier, it was concluded that the experimentally favored *E* products were obtained through "C_2-inward" transition states for isobutylene (e.g., **16a**, Figure 1) and through "anti C_2-semiperpendicular" transition states for *tert*-butylethylene (e.g., **17a**). The *Z* products arose in both cases from "C_1-inward" transition states (e.g., **16b** and **16c**), especially when *t*-Bu(CH_3)C=C: was the reacting carbene. The energy differences between the "inward" and the "semiperpendicular" approaches were generally small, with the former being favored by better orbital overlap but disfavored by larger steric interactions between the olefinic and the carbenic substituents.

According to FMO theory, attack of the carbene should preferentially occur at the atom with the largest coefficient in the relevant molecular orbital—in this case the olefinic π orbital.[2] In agreement with this simple description, both calculations and experiment show that attack on both isobutylene and *tert*-butylethylene occurs mainly at C_2—the unsubstituted carbon and the site with the larger π coefficient (Figure 2 and Table III). The polarizing effect of alkyl groups, as measured by the ratio of the coefficients at the two olefinic centers ($C_{HO} = C_2/C_1$, HO = HOMO), is small[7] and this leads to a low stereoselectivity for alkyl-substituted olefins (except when the substituent is large, i.e., *tert*-butyl). In the previous report,[1] we suggested that the stereoselectivity of alkylidenecarbene addition to other olefins could be qualitatively predicted on the basis of their C_{HO} values.[7] The experiments described here allow the examination of the validity of this analysis.

The following discussion will focus on the reactions of carbene **3**, *t*-Bu(CH_3)C=C:. Carbene **2**, *i*-Pr(CH_3)C=C:, was expected to be less stereoselective than **3** because a "C_2-inward" approach with the isopropyl group pointing toward the olefin (leading to *Z* adduct) can effectively compete with the "C_2-inward" approach (methyl pointing toward olefin) that leads to *E* adduct.[8] With carbene *3*, such a "C_2-inward" approach that has the large *tert*-butyl group pointing toward the olefin and that leads to *Z* product is sterically hindered and should not contribute much to the formation of *Z* alkylidenecyclopropane. Indeed, as expected, the stereoselectivity of **2** was lower than that of **3** and was of similar magnitude for all the olefins utilized here (Table I). The addition of **2** to the olefins was primarily carried out to assist in assigning product stereochemistry (see before) and also to qualitatively check the stereoselectivity in reactions of carbene **3**. As with carbene **3**, the most stereoselective reaction of **2** was with styrene (Table I), but the stereoselectivity was much lower.

Consider first the stereoselectivity of the addition of *t*-Bu(CH_3)C=C: to the alkyl-substituted olefins: 1-butene, isobutylene, and *tert*-butylethylene. As the C_{HO} values for these alkenes are close to unity (Table III),[9] low stereoselectivity was expected[8] and was generally observed for these olefins. The highest selectivity was seen with *tert*-butylethylene (*E*:*Z* ratio of 10.1:1). The stereoselectivity was lower for 1-butene (4.3:1) and was the lowest for isobutylene (2.0:1). These ratios correspond to energy differences between the transition states leading to the *E* and *Z* products of 1.2, 0.7, and 0.3 kcal mol^{-1}, respectively, at −20 °C. According to our previous MNDO calculations,[1] the stereoselectivity of alkylidenecarbene addition was expected to decrease as follows: *tert*-butylethylene > isobutylene > propene (theoretical model for 1-butene[10]), while the actual order was found to be *tert*-butylethylene > 1-butene > isobutylene. The relatively high stereoselectivity for *tert*-butylethylene was found to arise from steric repulsion between the bulky *tert*-butyl group[11] and the carbenic carbon in the "C_1-inward" transition state **16c**.[8]

The failure of MNDO to predict the correct stereoselectivity order for 1-butene and isobutylene is not surprising in light of the small energy differences which are involved. Thus, our previous study has shown that MNDO considerbly overestimates the energy differences between the "C_2-inward" and the "C_1-inward" transition states.[1] For example, for isobutylene MNDO finds an energy difference of 3.8 kcal mol^{-1} between these transition states while the experimental energy difference is only 0.3 kcal mol^{-1}.[1] Recent ab initio calculations support this conclusion. Thus, for the cycloaddition of CF_2 to propene, Rondan and Houk[12] have calculated that attack at C_2 is favored over attack at C_1 by only 0.1 kcal mol^{-1}, which is much smaller than the 3.0 kcal mol^{-1} energy difference that we have calculated using MNDO for the cycloaddition of CH_3CH=C: to propene.[1,13]

The new experiments for 1-butene provide further insight into the limitations of the MNDO method for this particular problem. We suggested previously that MNDO underestimates the importance of steric effects.[1] This suggestion was based on the observation that according to ab initio calculations, the carbene–olefin separations (*d*) at the transition state are significantly shorter than those derived from MNDO. For example, *d* is 1.83 Å at 3-21G,[13b] 1.95 Å at STO-3G, but 2.20 Å at MNDO for H_2C=C: + C_2H_4. The fact that 1-butene gives higher *E*:*Z* product ratios than isobutylene supports the shorter ab initio separations. Thus, the incorrect MNDO prediction probably results from an underestimation of the steric interactions between the carbenic methyl group of *t*-Bu(CH_3)C=C: and the *gem*-dimethyl substituents of isobutylene in the "C_2-inward" transition state **16a**. The higher polarity of the π bond in isobutylene relative to that in the monoalkyl-substituted olefins argues for a higher stereoselectivity in the former. The steric effect apparently offsets this small electronic advantage.

Note that steric factors play a different role in the reactions of **3** with 1-butene or *tert*-butylethylene than with isobutylene. Steric effects are minimized in the anti "C_2-semiperpendicular" transition states **17a** and **17b** that lead to the *E* products. Close proximity between the methyl of *t*-Bu(CH_3)C=C: and the olefinic substituent is avoided in these transition states, in contrast to the corresponding transition state for isobutylene (**16a**). However, in the "C_1-inward" transition states that proceed to *Z* products (e.g., **16c**), steric interactions between the carbenic carbon and the olefinic substituent raise the energy level of these transition states. As these steric interactions are larger for *tert*-butyl than for ethyl, the stereoselectivity observed with *tert*-butylethylene is higher than with 1-butene.

A more crucial test of our qualitative model is the stereoselectivity of alkylidenecarbene addition to more polarized olefins such as styrene and ethyl vinyl ether. Both phenyl and ethoxy strongly polarize the π bond toward C_2 (Figure 2); at MNDO,

(6) Stang, P. J. *Chem. Rev.* **1978**, *78*, 383–405.

(7) For comprehensive discussions of substituent effects on the coefficients of frontier orbitals see: (a) Sauer, J.; Sustmann, R. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 779–807. (b) Eisenstein, O.; Lefour, J. M.; Anh, N. T.; Hudson, R. F. *Tetrahedron* **1977**, *33*, 523–531. (c) Minot, C.; Anh, N. T. *Ibid.* 533–537. (d) Houk, K. N.; Sims, J.; Duke, R. E., Jr.; Strozier, R. W.; George, J. K. *J. Am. Chem. Soc.* **1973**, *95*, 7287–7301. (e) Houk, K. N. In "Pericyclic Reactions"; Marchand, A. P., Lehr, R. E., Eds.; Academic Press: New York, 1977; Vol. II. (f) Zhixing, C. *Theor. Chim. Acta.* **1983**, *62*, 293–299.

(8) See ref 1 for a more detailed explanation.

(9) C_{HO} value (MNDO): CH_2=C$(CH_3)_2$, 1.05.[1]

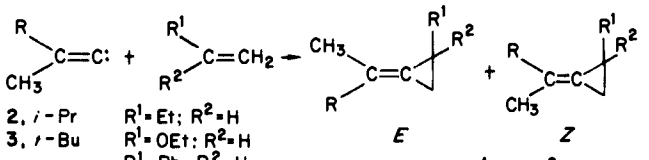
(10) 1-Butene and propene should be very similar both electronically and sterically.[15] C_{HO} values (MNDO): 1-butene, 1.03 (Table III); propene, 1.03.[1]

(11) Lowry, T. H.; Richardson, K. S. "Mechanism and Theory in Organic Chemistry", 2nd ed.; Harper and Row: New York, 1981.

(12) Rondan, N. G.; Houk, K. N. *Tetrahedron Lett.* **1984**, *25*, 5965–5968.

(13) (a) 3-21G calculations for CH_3CH=C: + propene are in progress and will be reported separately. (b) Apeloig, Y.; Karni, M., unpublished results.

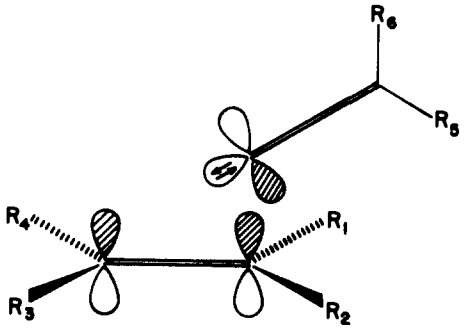
Table I. Alkylidenecyclopropanes from Reactions of Alkylidenecarbenes **2** and **3** with 1-Butene, Ethyl Vinyl Ether, Styrene, *tert*-Butylethylene, and Isobutylene



6, R=*i*-Pr; R¹=Et; R²=H
7, R=*i*-Pr; R¹=OEt; R²=H
8, R=*i*-Pr; R¹=Ph; R²=H
9, R=*t*-Bu; R¹=Et; R²=H
10, R=*t*-Bu; R¹=OEt; R²=H
11, R=*t*-Bu; R¹=Ph; R²=H
12, R=*t*-Bu; R¹=*t*-Bu; R²=H
13, R=*t*-Bu; R¹=R²=Me

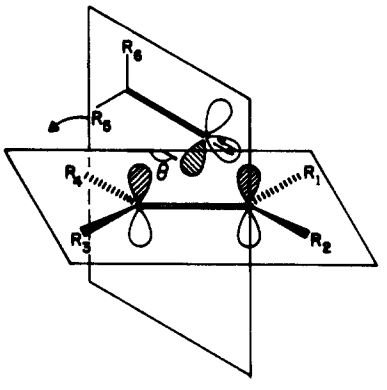
entry	triflate	alkene	conditions[a]	products[b]	*E*:*Z* ratio[c]	reference
1	**4**, R = *i*-Pr	1-butene	A	**6*E*,6*Z***	68:32 (2.1:1)	this work
2	**4**, R = *i*-Pr	ethyl vinyl ether	A	**7*E*,7*Z***	75:25 (3.0:1)	this work
3	**4**, R = *i*-Pr	styrene	A	**8*E*,8*Z***	78:22 (3.95:1)	this work
4	**4**, R = *i*-Pr	styrene	B	**8*E*,8*Z***	76:24 (3.2:1)	this work
5	**5**, R = *t*-Bu	1-butene	A	**9*E*,9*Z***	81:19 (4.3:1)	this work
6	**5**, R = *t*-Bu	ethyl vinyl ether	A	**10*E*,10*Z***	92:8 (11.5:1)	this work
7	**5**, R = *t*-Bu	styrene	A	**11*E*,11*Z***	99.6:0.4[d] (250:1)	this work
8	**5**, R = *t*-Bu	*tert*-butylethylene	A	**12*E*,12*Z***	91:9 (10.1:1)	*e*
9	**5**, R = *t*-Bu	*tert*-butylethylene	B	**12*E*,12*Z***	90:10 (9.0:1)	1
10	**5**, R = *t*-Bu	isobutylene	B	**13*E*,13*Z***	67:33 (2.0:1)	1

[a] A: triflate, *t*-BuOK, −23 °C, 3:1 alkene/glyme as solvent. B: triflate, *t*-BuOK, −20 °C, pure alkene as solvent. [b] See ref 3. [c] Range/2 for %'s from duplicate runs was 0.2%. [d] Range/2 was 0.01%. [e] Fox, D. P. Ph.D. Dissertation, The University of Utah, Salt Lake City, Utah, 1982.



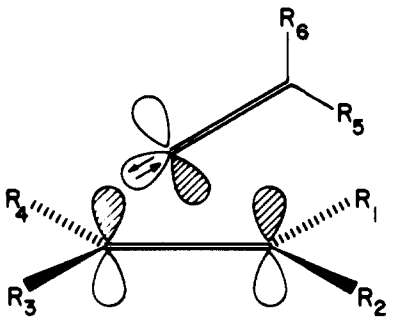
16

16a, $R_1 = R_2 = R_5 = Me$; $R_3 = R_4 = H$; $R_6 = t$-Bu
16b, $R_1 = R_2 = H$; $R_3 = R_4 = R_5 = Me$; $R_6 = t$-Bu
16c, $R_1 = R_2 = R_3 = H$; $R_5 = Me$; $R_4 = R_6 = t$-Bu



17

17a, $R_1 = R_2 = R_4 = H$; $R_5 = Me$; $R_3 = R_6 = t$-Bu; $\theta < 90°$
17b, $R_1 = R_2 = R_4 = H$; $R_3 = Et$; $R_5 = Me$; $R_6 = t$-Bu; $\theta < 90°$



(18)

Figure 1. "Inward" (**16**), "semiperpendicular" (**17**), and "outward" (**18**) conformations of transition states in alkylidenecarbene additions to olefins. For each specific case, the unsubstituted carbon is designated C_2 and the substituted carbon C_1.

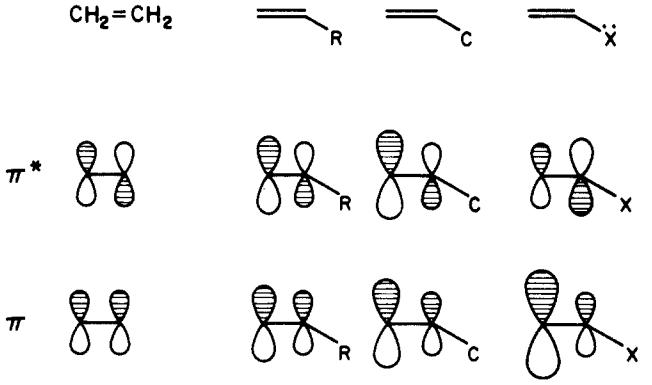


Figure 2. Estimated π frontier orbital coefficients for alkenes.[7d] (R = alkyl, C = vinyl, Ph, etc.; X = OR, NR_2, etc.).

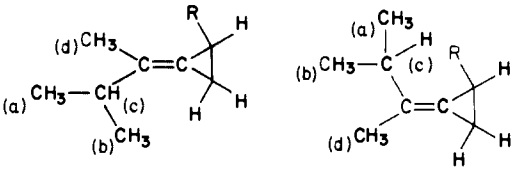
C_{HO} = 1.39 for both styrene and H_2C=CHOMe (model for H_2C=CHOEt). Similar C_{HO} values are obtained with other computational methods such as CNDO/2 and the Hückel method (Table III). Although the absolute values of the coefficients are dependent on the computational method, the trends are not and therefore have predictive value.[7,14] Thus, the simple FMO model presented above predicts high stereoselectivity for the reactions of carbene **3** with both olefins.

The addition of *t*-Bu(CH_3)C=C: to styrene is indeed *highly* stereoselective with an observed *E*:*Z* product ratio of 250:1, which corresponds to an energy difference of 2.8 kcal mol^{-1} between the two respective transition states at −20 °C. As a phenyl group is smaller than a *tert*-butyl group,[15] this greatly enhanced stereoselectivity clearly arises from an electronic effect.[16] Interestingly,

(14) A recent study has concluded that Hückel and CNDO/2 coefficients are more stable than MNDO coefficients for predicting regioselectivity in Diels–Alder reactions.[7f] However, this conclusion applies mostly to electron-withdrawing substituents such as CN and COOR which were not used in this study.

(15) Relevant *A* values are as follows (kcal·mol^{-1}): OEt, 0.9; Me, 1.7; Et, 1.8; Ph, 3.1; *t*-Bu, 5.[11] In this case the phenyl probably exhibits even a smaller size than in cyclohexane, because styrene is a planar molecule. See: Allinger, N. L.; Eliel, E. L.; Eds. "Topics in Stereochemistry"; Interscience: New York, 1967; Vol. 1.

Table II. 300-MHz ^{1}H NMR Data for Alkylidenecyclopropanes **6–8** and **14**



6*E*, R = Et
7*E*, R = OEt
8*E*, R = Ph
14*E*, R = *t*-Bu

6*Z*, R = Et
7*Z*, R = OEt
8*Z*, R = Ph
14*Z*, R = *t*-Bu

cyclopropane	resonance a	resonance b	chemical shift difference[a]	resonance c	resonance d	reference
6*E*	1.052 (d)		0			this work
6*Z*	1.032 (d)	1.053 (d)	0.021			this work
7*E*	1.082 (d)		0			this work
7*Z*	1.084 (d)	1.102 (d)	0.018			this work
8*E*	1.142 (d)	1.146 (d)	0.004	2.56 (m)	1.73 (m)	this work
8*Z*	0.964 (d)	0.980 (d)	0.016	2.46 (m)	1.87 (m)	this work
14*E*	1.042 (d)	1.050 (d)	0.008			1
14*Z*	1.008 (d)	1.034 (d)	0.026			1

[a] Resonance b − resonance a.

Table III. MNDO, CNDO/2, and Hückel Coefficients for the π and π^* Orbitals of Various Substituted Olefins $RCH^{(1)}=C^{(2)}H_2$[a]

	π orbital									π^* orbital[b]								
	MNDO			CNDO/2			Hückel			MNDO			CNDO/2			Hückel		
R	C_1	C_2	C_{HO}[c]	C_1	C_2	C_{HO}[c]	C_1	C_2	C_{HO}[c]	C_1	C_2	C_{LU}[d]	C_1	C_2	C_{LU}[d]	C_1	C_2	C_{LU}[d]
H	0.71	0.71	1.00	0.71	0.71	1.00	0.5	0.5	1.00	0.71	0.71	1.00	0.71	0.71	1.00	0.5	0.5	1.00
CH_3CH_2	0.67	0.69	1.03	0.56	0.67	1.20				0.68	0.71	1.04	0.65	0.67	1.03			
i-Pr	0.66	0.69	1.04							0.68	0.71	1.04						
t-Bu	0.66	0.69	1.04							0.68	0.71	1.04						
OCH_3	0.51	0.71	1.39	0.39	0.61	1.56	0.64	0.73	1.14[e]	0.71	0.66	0.93	0.72	0.66	0.92	0.72	0.68	0.94[f]
C_6H_5	0.33	0.46	1.39	0.32	0.49	1.53	0.39	0.59	1.51	0.27	0.42	1.55	0.33	0.48	1.45	0.39	0.59	1.51

[a] CNDO/2 values from ref 7d and 7e. Hückel values from ref 7b. [b] The absolute values of the coefficients are given. [c] $C_{HO} = C_2/C_1$. [d] $C_{LU} = C_2/C_1$. [e] $C_{HO} = 1.42$ at the extended Hückel level. [f] $C_{LU} = 0.87$ at the extended Hückel level.

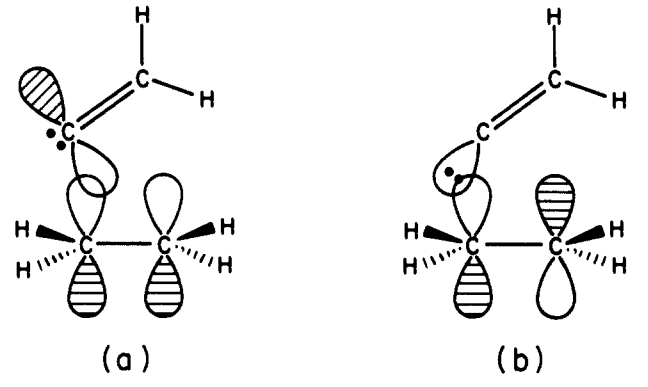


Figure 3. Schematic representation of orbital interactions in the cycloaddition of $H_2C{=}C{:}$ to $H_2C{=}CH_2$. (a) The electrophilic π–2p(C:) interaction. (b) The nucleophilic sp(C:)–π^* interaction.

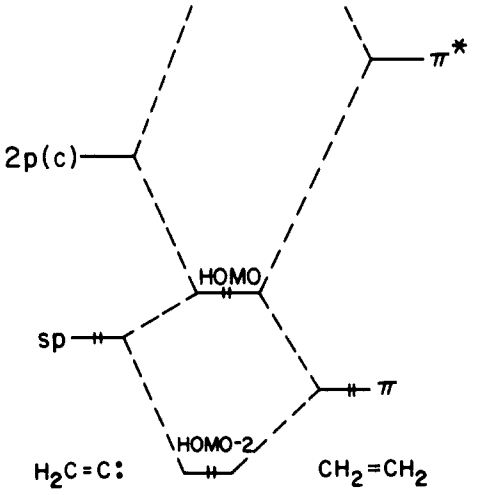


Figure 4. A schematic interaction diagram for the frontier orbitals of $H_2C{=}C{:}$ and of $H_2C{=}CH_2$.

even though their C_{HO} values are very similar, ethyl vinyl ether exhibited a significantly lower stereoselectivity as a carbene trap than styrene (*E*:*Z* ratio of 11.5:1, Table I). This lower selectivity cannot be directly attributed to steric factors as ethoxy is the smallest substituent in the olefins studied.[15] Why, then, does ethyl vinyl ether give rise to lower stereoselectivity than styrene?

One strong possibility for the discrepancy is the lack of consideration of nucleophilic interaction in the model that we have suggested above for the addition transition states. Alkylidenecarbenes, as well as saturated carbenes, possess both an electrophilic (the empty 2p(C:) orbital) and a nucleophilic site (the sp lone pair). In the previous analysis the nucleophilic interaction between the carbene and the olefin was neglected and the stereochemical model was based entirely on the electrophilic interaction, as it is believed to play the major role at the early stages of the reaction,[17–19] in particular for electrophilic carbenes such as alkylidenecarbenes.[6] The two interactions are illustrated schematically in Figure 3. A fragment analysis[20] of the inter-

(16) Based on qualitative steric considerations, the addition of **3** to styrene should have resulted in an *E*:*Z* ratio between 4:1 and 10:1 (i.e., between the value for 1-butene and that for *tert*-butylethylene).[11]

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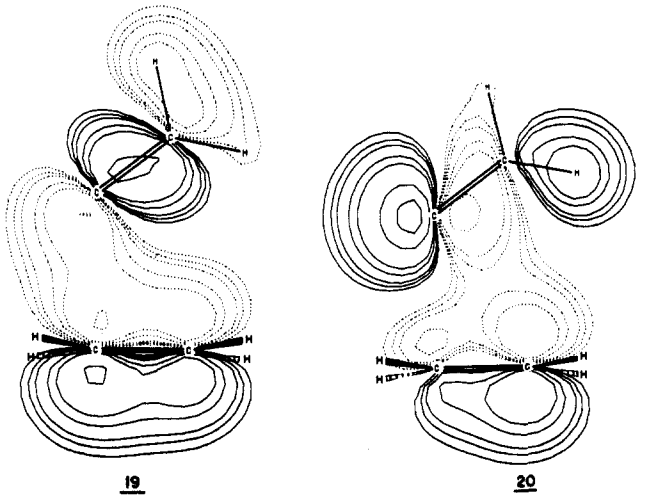
(18) Hoffmann, R.; Hayes, D. M.; Skell, P. S. *J. Phys. Chem.* **1972**, *76*, 664–669. Hoffmann, R. *J. Am. Chem. Soc.* **1968**, *90*, 1475–1485.
(19) (a) Schoeller, W. W.; Brinker, U. H. *Z. Naturforsch. B* **1980**, *35B*, 475–476. (b) Schoeller, W. W. *Tetrahedron Lett.* **1980**, 1505–1508, 1509–1510.



19 20

Figure 5. Extended Hückel contour diagrams of the HOMO-2 (orbital **19**) and the HOMO (orbital **20**) in the $H_2C{=}C{:} + H_2C{=}CH_2$ complex at the STO-3G calculated geometry of the transition state (d = 1.95 Å).[1] The contours are plotted in a plane containing the four carbon atoms and the two carbenic hydrogens and are at values of ±0.03, ±0.04, ±0.05, ±0.075, ±0.1, ±0.2, and ±0.3.

actions between the molecular orbitals of $H_2C{=}C{:}$ and of ethylene, at separation distances of 1.9–2.2 Å, indeed shows that the electrophilic 2p(C:)–π interaction is 6–8 times larger than the nucleophilic sp–π^* interaction. The nucleophilic portion is, however, significant[21] (e.g., the sp(C:)–π^* overlap population is 0.20 at d = 1.95 Å) and probably cannot be ignored in all cases.

A closer examination of these orbital interactions may assist our understanding of the carbene addition mechanism. Four frontier orbitals, π, π^*, 2p(C:), and sp(C:), are involved in forming the molecular orbitals of the $H_2C{=}CH_2 + H_2C{=}C{:}$ activated complex (Figure 4).

It is convenient to analyze the interaction in Figure 4 in the following way. The filled π and sp(C:) orbitals interact to form two new orbitals, one of higher and one of lower energy than the π or sp(C:) orbitals, respectively. Due to the low symmetry of the transition state (i.e., C_s) the empty 2p(C:) and π^* orbitals can mix into these orbitals forming the more stabilized orbitals **19** and **20**. The 2p(C:) orbital which lies considerably lower in energy than the π^* orbital is expected (and found, see below) to contribute more strongly to the formation of both **19** and **20**, in agreement with the predominant electrophilic character of the carbene.[6] Contour plots of orbitals **19** and **20** which were calculated at a separation distance of 1.95 Å by using the extended Hückel method[20] are shown in Figure 5.

Examination of the contour plot of orbital **19** (HOMO-2) reveals its bonding π + sp(C:) character and shows that it is strongly polarized toward the carbon that is being attacked. Orbital fragment analysis[20] shows that orbital **19** also contains contributions from the 2p(C:) and the π^* orbitals (ca. 15% and 6%, respectively). Orbital **20** (which is the HOMO of the activated complex)[22] is formed from the antibonding combination of π and sp(C:) orbitals (Figure 4), and as expected it is strongly polarized away from the attacked carbon (Figure 5). Despite this strong antibonding interaction, the energy of orbital **20** does not rise much above that of the sp(C:) orbital because it is strongly stabilized by substantial mixing in a bonding fashion of the empty 2p(C:) and π^* orbitals (i.e., by ca. 28% and 11%, respectively[20]). The most important conclusion from this analysis is that the π^* *orbital contributes significantly* (as much as ca. 40% of the contribution of the 2p(C:) orbital) to the total wave function and thus to the energy of the cycloaddition complex. Let us return now to the problem of stereoselectivity.

In ethyl vinyl ether, the π^* orbital is polarized toward the substituted carbon C_1 ($C_{LU} < 1$; $C_{LU} = C_2/C_1$, LU = LUMO), while the π orbital is polarized toward C_2 (Figure 2 and Table III). The electrophilic interaction directs the attack to C_2 which would lead to *E* adduct, but the nucleophilic interaction directs the attack to C_1 which would give the *Z* adduct. The electrophilic and nucleophilic interactions therefore guide carbene **3** to *opposing* sites in ethyl vinyl ether. In styrene, on the other hand, the HOMO and the LUMO are polarized in the *same direction* so that both C_{HO} and C_{LU} are considerably larger than 1. The nucleophilic and electrophilic interactions are, therefore, *reinforcing* and both direct the carbene to the unsubstituted carbon C_2. The steric effect of the phenyl group[15] also directs the carbene to C_2 (see before). As a result of these interactions, very high stereoselectivity was observed in the reaction of **3** with styrene. With ethyl vinyl ether, the reduced stereoselectivity (when compared to styrene) is then due, we believe, to the contribution of the nucleophilic sp(C:)–π^* interaction. Experimentally, the *E* isomer was found to be the major olefin adduct (92%), so the electrophilic 2p(C:)–π interaction is still dominant.[23] Even though the stereoselectivity with ethyl vinyl ether as a carbene trap is lower than that seen with styrene, the *E*:*Z* ratio of 11.5:1 was nevertheless greater than that observed with any alkyl-substituted olefin tested, again indicating the predominant importance of the electrophilic 2p(C:)–π interaction and thus of the relative coefficient sizes (C_{HO}) in the π orbital, as predicted earlier. With respect to the alkyl-substituted olefins, the polarization of both π and π^* is small and a slightly larger coefficient is present at C_2 in both orbitals. The *E* isomer was the major product, but the stereoselectivity was, as expected, more modest than that seen with ethyl vinyl ether and styrene.

Finally we note that actual MNDO calculations are probably not superior to the simple FMO guidelines presented above in predicting the *E*:*Z* product ratios in the cycloaddition of alkylidenecarbenes to various olefins. MNDO calculations for the cycloaddition of $CH_3CH{=}C{:}$ (model for *3*)[1] to $H_2C{=}CH(OH)$ (model for $H_2C{=}CHOEt$) predict correctly that attack should occur preferably at C_2, but the activation barrier for attack at C_1 is higher by only 0.4 kcal mol^{-1}.[13b] Similar results were reported recently with MINDO/3 for the addition of methylene to hydroxyethylene.[24] For the addition of $CH_3CH{=}C{:}$ to isobutylene, we calculated an energy difference of 3.8 kcal mol^{-1} between the "C_1-" and the "C_2-inward" transition states.[1] Thus, MNDO predicts, contrary to experiment, that isobutylene (the same applies to 1-butene and *tert*-butylethylene) should exhibit a higher stereoselectivity than ethyl vinyl ether. Further studies now being carried out in our laboratory are directed toward the identification of a theoretical method that can reproduce the experimental trend (hopefully even quantitatively) in the stereoselectivity of alkylidenecarbene addition to olefins.

Conclusion

This study illustrates that the polarization of *both* the π and π^* orbitals of the olefins affects the stereoselectivity of cycloaddition of alkylidenecarbenes to olefins. The π orbital exerts a larger effect than the π^* and its polarization determines the stereochemistry of the major product. Of the olefins employed, styrene and ethyl vinyl ether yielded the most stereoselective reactions as predicted from FMO theory and earlier calculations. However, ethyl vinyl ether is much less stereoselective than styrene because in the former the π and π^* orbitals are polarized in *opposite* directions while in styrene these orbitals are polarized in the *same* direction. With alkyl-substituted olefins, *E* alkylidenecyclopropanes effects were found to play a significant role in the degree of stereoselectivity observed for the alkyl-substituted alkenes. MNDO calculations fail to predict the exact magnitude

(20) The fragment analysis approach[18] is based on the extended Hückel method: Hoffmann, R. *J. Chem. Phys.* **1963**, *39*, 1397–1412.

(21) Recent calculations on electrophilic, saturated carbenes such as $:CCl_2$ found that the nucleophilic character of their cycloaddition transition states was greater than previously thought.[17]

(22) The HOMO-1 orbital is the π orbital of the carbene which by symmetry cannot be involved in the interactions which form the activated complex (see Figure 4).

(23) Extended Hückel calculations[20] showed that the electrophilic interaction is dominant over the nucleophilic for the case of ethyl vinyl ether.

(24) Moreno, M.; Lluch, J. M.; Oliva, A.; Bertran, J. *J. Chem. Soc., Perkin Trans. 2* **1985**, 131–134.

of these steric effects or of the directive electronic effect of OR substituents. Stereoselectivity ranged from a very high 250:1 in the reaction of *t*-Bu(CH_3)C=C: with styrene to a low 2:1 when isobutylene was employed as the carbene acceptor.

Experimental Section

General. All boiling points are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 298 infrared spectrometer and are reported in wave numbers (cm^{-1}). ^1H NMR spectra were recorded on a Varian EM-390 (90 MHz) or SC 300 (300 MHz) spectrometer, and all values are given in δ (ppm) relative to internal tetramethylsilane (Me_4Si, δ 0). A VG Micromass 7070 Double Focusing High Resolution Mass Spectrometer with VG Data System 2000 was utilized to obtain both low-resolution mass spectra and accurate mass determinations. Analytical GC columns employed in the following reactions were also used to obtain the low-resolution mass spectra. Accurate mass determinations are reported for the molecular ion (M^+) or for M^+ - Me when M^+ was not discernible. Mass spectra are recorded as *m/z* (relative intensity). Analytical GC was carried out on a Hewlett-Packard 5710A flame ionization gas chromatograph connected to a Hewlett-Packard 3380A integrator. Preparative GC was accomplished with a Varian Aerograph 90-P or 920 gas chromatograph. Columns used are as follows: A, 0.125 in. × 15 ft 15% QF-1 on 100–120 Chromosorb W; B, 0.125 in. × 20 ft 10% Apiezon J on 100–120 Chromosorb W; C, 0.125 in. × 25 ft 15% Carbowax 20M on 100–120 Chromosorb W; D, 0.375 in. × 15 ft 15% QF-1 on 45–60 Chromosorb W; E, 0.25 in. × 25 ft 20% Apiezon J on 60–80 Chromosorb W; F, 0.375 in. × 25 ft 20% Carbowax 20M on 30–60 Chromosorb W.

Materials. The preparation of triflate **4** has been previously reported.[1] Triflate **5** has also been described[1] but was prepared for this study in the following manner. Treatment of 2,3,3-trimethylbutanal with triflic anhydride and *N,N*-diisobutyl-2,4-dimethyl-3-pentylamine in CH_2Cl_2 for 4 h at 0 °C and 3 h at room temperature gave triflate **5** in 50% yield after workup.[4] Styrene (Aldrich) was fractionally distilled under vacuum from $LiAlH_4$, degassed with argon, and stored under argon. Ethyl vinyl ether (Aldrich) was fractionally distilled from CaH_2. 1-Butene (Phillips research grade) was condensed through use of a dry ice–isopropyl alcohol bath and then fractionally distilled with an ice bath into the reaction flask. 1,2-Dimethoxyethane (glyme, Ansul) was freshly distilled from potassium benzophenone ketyl. Potassium *tert*-butoxide (Alfa) was sublimed twice and stored under argon.

General Procedure for the Reaction of Triflates 4 and 5 with KO-*t*-Bu. Into a round-bottom flask equipped with a stirring bar and a wired-on serum stopper were added under argon KO-*t*-Bu (50% excess) and a 3:1 mixture of olefin and glyme. When 1-butene was used, it was introduced as described above. The nearly homogeneous solution was cooled to −23 °C by means of a dry ice–CCl_4 bath, and triflate was added dropwise via syringe. Reaction appeared to be rapid as the reaction solution quickly became light yellow and a white solid precipitated. After 0.5 to 1 h of reaction at −23 °C, GC analysis of the solution showed no starting triflate remained. Analytical reactions (0.2 mmol of triflate in 2 mL of olefin–glyme mixture) and preparative reactions (1–4 mmol of triflate in 10–40 mL of olefin–glyme mixture) were directly analyzed by GC. Product ratios were determined through multiple injections of duplicate reactions. Unless indicated otherwise, range/2 for product percentages in the duplicate runs was between 0.0 and 0.2%. Workup of the preparative reactions was carried out as follows. An equal volume of hexanes was added, and the resulting solution was extracted once with water and once with brine and then dried over K_2CO_3. Solvent was removed either with a rotary evaporator or by vacuum distillation (styrene). Alkylidenecyclopropane products were then isolated from the residue through preparative GC.[3] In the 1-butene reactions, the 1-butene was distilled from the reaction mixture with an ice bath and an equal volume of hexanes was added before GC analysis or workup. In several reactions, product ratios were again determined after workup and were found to be identical with the values determined before workup.

(*E*)- and (*Z*)-1-Ethyl-2-(1,2-dimethylpropylidene)cyclopropane (6*E* and 6*Z*). Reaction of triflate **4** (70% *E*:30% *Z*) in 1-butene–glyme mixture produced adducts **6*E*** and **6*Z*** in a 67.6% *E*:32.4% *Z* ratio (column C, 90 °C). The adducts were separated and isolated with column F at 80 °C. For **6*E***: IR (neat) 3027 (cyclopropyl H), 2960, 2930, 2875, 1768 (C=C), 1460, 1380, 1370, 1360, 1138 cm^{-1}; 300-MHz ^1H NMR ($CDCl_3$) δ 2.44 (m, 1, $HCMe_2$), 1.76 (m, 3, CH_3C=C), 1.46 (m, 1, CHEt), 1.1–1.3 (m, 3, CH_2 of Et and cyclopropyl), 1.052 (d, 6, ^3J = 6.8 Hz, Me_2C), 0.96 (t, 3, ^3J = 7.1 Hz, CH_3 of Et), 0.70 (m, 1, cyclopropyl); mass spectrum, 138 (M^+, 6), 123 (18), 109 (36), 96 (37), 95 (38), 81 (73), 70 (80), 69 (22), 67 (97), 55 (100), 53 (33), 43 (33), 42 (31), 41 (81); exact mass calcd for $C_{10}H_{18}$ 138.1408, found 138.1449; calcd for C_9H_{15} (M - Me) 123.1174, found 123.1179. For **6*Z***: IR (neat) 3030 (cyclopropyl H), 2962, 2933, 2875, 1769 (C=C), 1460, 1380, 1370, 1360, 994 cm^{-1}; 300-MHz ^1H NMR ($CDCl_3$) δ 2.48 (m, 1, $HCMe_2$), 1.75 (m, 3, CH_3C=C), 1.68 (m, 1, HCEt), 1.40 (m, 1, cyclopropyl), 0.9–1.14 (m, 5, Et), 1.053 (d, 3, ^3J = 6.9 Hz, *i*-Pr Me), 1.032 (d, 3, ^3J = 6.8 Hz, *i*-Pr Me), 0.52 (m, 1, cyclopropyl); mass spectrum, 138 (M^+, 7), 123 (25), 109 (40), 96 (40), 95 (44), 81 (92), 70 (87), 69 (20), 67 (99), 55 (100), 53 (39), 43 (35), 42 (30), 41 (90); exact mass calcd for $C_{10}H_{18}$ 138.1408, found 138.1425.

(*E*)- and (*Z*)-1-Ethoxy-2-(1,2-dimethylpropylidene)cyclopropane (7*E* and 7*Z*). Treatment of triflate **4** (70% *E*:30% *Z*) with base in ethyl vinyl ether–glyme mixture produced adducts **7*E*** and **7*Z*** in a 75.2% *E*:24.8% *Z* ratio (column A, 80 °C). Column D at 95 °C was employed to isolate the individual adducts. For **7*E***: IR (neat) 3030 (cyclopropyl H), 2960, 2870, 1768 (C=C), 1443, 1392, 1370, 1322, 1194, 1118, 1048 cm^{-1}; 300-MHz ^1H NMR ($CDCl_3$) δ 3.61 (m, 1, CHOEt), 3.61 (m, 2, OCH_2), 2.49 (m, 1, $HCMe_2$), 1.86 (m, 3, CH_3C=C), 1.23 (t, 3, ^3J = 7.1 Hz, CH_3 of Et), 1.2–1.4 (m, 2, cyclopropyl), 1.082 (d, 6, ^3J = 6.9 Hz, Me_2C); mass spectrum, 154 (M^+, 2), 139 (10), 125 (51), 111 (45), 93 (27), 83 (42), 69 (21), 67 (30), 55 (100), 53 (31), 43 (61), 41 (100); exact mass calcd for $C_9H_{15}O$ (M - Me) 139.1123, found 139.1124. For **7*Z***: IR (neat) 3030 (cyclopropyl H), 2960, 2870, 1768 (C=C), 1443, 1323, 1190, 1127, 1112, 1062, 1048 cm^{-1}; 300-MHz ^1H NMR ($CDCl_3$) δ 3.71 (m, 1, CHOEt), 3.60 (m, 2, OCH_2), 2.54 (m, 1, $HCMe_2$), 1.80 (m, 3, CH_3C=C), 1.22 (t, 3, ^3J = 7.0 Hz, CH_3 of Et), 1.13 (m, 1, cyclopropyl), 1.102 (d, 3, ^3J = 6.9 Hz, *i*-Pr Me), 1.084 (d, 3, ^3J = 6.9 Hz, *i*-Pr Me), 1.01 (m, 1, cyclopropyl); mass spectrum, 154 (M^+, 2), 139 (8), 125 (41), 111 (39), 93 (23), 83 (30), 67 (21), 55 (100), 53 (23), 45 (23), 43 (41), 41 (70); exact mass calcd for $C_9H_{15}O$ (M - Me) 139.1123, found 139.1157.

(*E*)- and (*Z*)-1-Phenyl-2-(1,2-dimethylpropylidene)cyclopropane (8*E* and 8*Z*). Reaction of triflate **4** (70% *E*:30% *Z*) in styrene–glyme mixture gave adducts **8*E*** and **8*Z*** in a 77.8% *E*:22.2% *Z* ratio (column A, 140 °C). The adducts were separated and isolated with column D at 140 °C. For **8*E***: IR (neat) 3025, 2960, 2870, 1767 (C=C), 1603, 1495, 1452, 757, 700 cm^{-1}; 300-MHz ^1H NMR ($CDCl_3$) δ 7.0–7.3 (m, 5, phenyl), 2.56 (m, 1, $HCMe_2$), 2.45 (m, 1, HCPh), 1.77 (m, 1, cyclopropyl), 1.73 (m, 3, CH_3C=C), 1.19 (m, 1, cyclopropyl), 1.146 (d, 3, ^3J = 6.9 Hz, *i*-Pr Me), 1.142 (d, 3, ^3J = 6.9 Hz, *i*-Pr Me); mass spectrum, 186 (M^+, 10), 171 (41), 143 (90), 130 (22), 129 (44), 128 (39), 116 (100), 115 (98), 91 (31), 55 (23), 51 (24), 41 (40); exact mass calcd for $C_{14}H_{18}$ 186.1408, found 186.1395. For **8*Z***: IR (neat) 3025, 2960, 2870, 1766 (C=C), 1603, 1495, 1452, 758, 700 cm^{-1}; 300-MHz ^1H NMR ($CDCl_3$) δ 7.0–7.3 (m, 5, phenyl), 2.59 (m, 1, HCPh), 2.46 (m, 1, $HCMe_2$), 1.87 (m, 3, CH_3C=C), 1.59 (m, 1, cyclopropyl), 1.02 (m, 1, cyclopropyl), 0.980 (d, 3, ^3J = 6.9 Hz, *i*-Pr Me), 0.964 (d, 3, ^3J = 6.9 Hz, *i*-Pr Me); mass spectrum, 186 (M^+, 9), 171 (48), 143 (90), 130 (26), 129 (47), 128 (39), 116 (100), 115 (93), 91 (27), 55 (23), 41 (34); exact mass calcd for $C_{14}H_{18}$ 186.1408, found 186.1425.

(*E*)- and (*Z*)-1-Ethyl-2-(1,2,2-trimethylpropylidene)cyclopropane (9*E* and 9*Z*). Reaction of triflate **5** (81% *E*:19% *Z*) in 1-butene–glyme mixture produced adducts **9*E*** and **9*Z*** in a 81.4% *E*:18.6% *Z* ratio (column B, 130 °C). The adducts were separated and isolated with column E at 130 °C. For **9*E***: IR (neat) 3025 (cyclopropyl H), 2960, 2867, 1760 (C=C), 1477, 1460, 1370, 1359, 1134 cm^{-1}; 90-MHz ^1H NMR ($CDCl_3$) δ 1.80 (m, 3, CH_3C=C), 0.7–1.6 (m, 8, Et and cyclopropyl), 1.12 (s, 9, *t*-Bu); mass spectrum, 152 (M^+, 12), 137 (8), 109 (38), 96 (24), 95 (30), 84 (52), 81 (67), 69 (100), 67 (45), 57 (30), 55 (31), 53 (22), 41 (68); exact mass calcd for $C_{11}H_{20}$ 152.1565, found 152.1582. For **9*Z***: IR (neat) 3027 (cyclopropyl H), 2960, 2870, 1728 (C=C), 1477, 1460, 1370, 1360, 1160, 1145 cm^{-1}; 90-MHz ^1H NMR ($CDCl_3$) δ 1.9 (m, 1, CHEt), 1.77 (m, 3, CH_3C=C), 1.43 (m, 1, cyclopropyl), 0.65–1.2 (m, 5, Et), 1.08 (s, 9, *t*-Bu), 0.45 (m, 1, cyclopropyl); mass spectrum, 152 (M^+, 15), 137 (9), 109 (36), 96 (22), 95 (35), 84 (47), 81 (66), 69 (100), 67 (41), 57 (55), 55 (38), 53 (21), 43 (22), 41 (86); exact mass calcd for $C_{11}H_{20}$ 152.1565, found 152.1570.

(*E*)- and (*Z*)-1-Ethoxy-2-(1,2,2-trimethylpropylidene)cyclopropane (10*E* and 10*Z*). Treatment of triflate **5** (81% *E*:19% *Z*) with base in ethyl vinyl ether–glyme mixture produced adducts **10*E*** and **10*Z*** in a 91.8% *E*:8.2% *Z* ratio (column A, 90 °C). Individual adducts were isolated through use of column D at 110 °C. For **10*E***: IR (neat) 3025 (cyclopropyl H), 2960, 2865, 1760 (C=C), 1370, 1360, 1322, 1175, 1135, 1113 cm^{-1}; 90-MHz ^1H NMR ($CDCl_3$) δ 3.58 (m, 2, CH_2O), 3.53 (m, 1, HCO), 1.88 (m, 3, CH_3C=C), 1.12–1.35 (m, 5, CH_3 of Et, cyclopropyl CH_2), 1.12 (s, 9, *t*-Bu); mass spectrum, 153 (M^+ - 15, 13), 139 (38), 125 (35), 97 (33), 84 (34), 69 (100), 67 (22), 57 (32), 55 (62), 53 (20), 43 (27), 41 (88); exact mass calcd for $C_{10}H_{17}O$ (M - Me) 153.1279, found 153.1291. For **10*Z***: IR (neat) 3027 (cyclopropyl H), 2960, 2870, 1758 (C=C), 1324, 1179, 1112, 1080, 1050 cm^{-1}; 90-MHz ^1H NMR ($CDCl_3$) δ 3.66 (m, 1, HCO), 3.58 (m, 2, CH_2O), 1.82 (m, 3, CH_3C=C), 0.8–1.3 (m, 5, CH_3 of Et and cyclopropyl CH_2), 1.13 (s, 9, *t*-Bu); mass spectrum, 153 (M^+ - 15, 11), 139 (44), 125 (41), 97 (32),

84 (30), 69 (100), 57 (26), 55 (58), 53 (20), 45 (44), 43 (22), 43 (36), 41 (77); exact mass calcd for $C_{10}H_{17}O$ (M - Me) 153.1279, found 153.1282.

(*E*)- and (*Z*)-1-Phenyl-2-(1,2,2-trimethylpropylidene)cyclopropane (11*E* and 11*Z*). Reaction of triflate **5** (81% *E*:19% *Z*) in styrene–glyme mixture gave adducts **11*E*** and **11*Z*** in a 99.63 ± 0.01% *E*:0.37 ± 0.01% *Z* ratio (column A, 150 °C). Adduct **11*E*** and a sample enriched in adduct **11*Z*** for GC/MS analysis (**11*Z*** and **11*E*** in a 14% *Z*:86% *E* ratio) were obtained through use of column D at 150 °C. For **11*E***: IR (neat) 3025, 2962, 2865, 1758 (C=C), 1602, 1452, 1372, 1359, 753, 700 cm^{-1}; 300-MHz ^1H NMR ($CDCl_3$) δ 7.0–7.3 (m, 5, phenyl), 2.39 (m, 1, HCPh), 1.89 (m, 1, cyclopropyl), 1.74 (m, 3, CH_3C=C), 1.31 (m, 1, cyclopropyl), 1.19 (s, 9, *t*-Bu); mass spectrum, 200 (M^+, 12), 185 (18), 157 (24), 144 (44), 143 (87), 129 (67), 128 (26), 116 (55), 115 (35), 91 (27), 84 (100), 69 (91), 57 (27), 41 (67); exact mass calcd for $C_{15}H_{20}$ 200.1565, found, 200.1571. Adduct **11*Z*** was characterized through its mass spectrum which was virtually identical with that of **11*E***. For **11*Z***: mass spectrum, 200 (M^+, 13), 185 (18), 157 (27), 144 (43), 143 (87), 129 (68), 128 (23), 116 (51), 115 (41), 91 (28), 84 (100), 69 (98), 57 (25), 41 (61).

Analytical Reaction of Triflates 4*E* and 4*Z* in Styrene as Sole Solvent. Treatment of triflate **4** (70% *E*:30% *Z*) with base in styrene (no glyme present) for 1 day at -23 °C resulted in a 75.5% **3*E***:24.5% **3*Z*** ratio (column A, 140 °C).

Stability of Alkylidenecyclopropane 8*E*. Treatment of **17** mg (0.091 mmol) of **8*E*** under standard reaction conditions did not lead to isomerization or decomposition of **8*E*** as determined through GC analysis with an internal standard (tridecane).

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Kinetic and Thermodynamic Parameters for the Formation of 3,5,5-Trimethyl-2-oxomorpholin-3-yl (TM-3). A Negative Activation Energy for Radical Combination[1,2]

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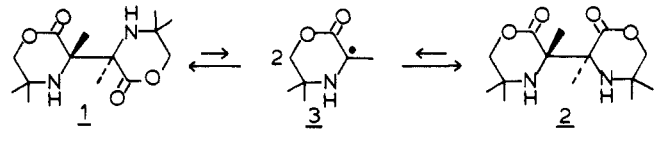
Abstract: Thermodynamic parameters for the bond homolysis of *meso*- and *dl*-bis(3,5,5-trimethyl-2-oxomorpholin-3-yl) (**1** and **2**) to 3,5,5-trimethyl-2-oxomorpholin-3-yl (**3** TM-3) in ethanol, 1,2-dimethoxyethane, and benzene solvents and in ethanol solvent containing Na^+ and Mg^{2+} at an ionic strength of 0.3 μ are reported. The equilibrium constant varies by more than 6 orders of magnitude, 1.3×10^{-9}–5.8×10^{-16} mol/L, as a function of the medium, being largest in a polar solvent containing Mg^{2+}. The solvent effect is consistent with a polar radical structure most likely resulting from a captodative resonance interaction. In the solvent sequence ethanol to benzene, $\Delta H°$ and $\Delta S°$ vary from 21.5 to 35.9 kcal/mol and 24.1 to 50.6 cal/(mol·K), respectively. The free energy of formation of TM-3 is linearly related to the methyl hyperfine coupling constants and Kosower *Z* values, also consistent with the captodative resonance interaction. The effect of Mg^{2+} on radical concentration appears to be entropically derived. The kinetic parameters for bond homolysis of the *dl* dimer of TM-3 are also reported; $\Delta H^‡$ varies from 20.4 to 28.1 kcal/mol, being smallest in polar solvent. The kinetic and thermodynamic parameters for bond homolysis give kinetic parameters for radical combination. In 1,2-dimethoxyethane and benzene solvents, $\Delta H^‡$ for the radical combination is substantially negative, -6.1 and -7.8 kcal/mol, respectively. The negative enthalpies of activation are discussed in terms of the intermediacy of a H-bonded TM-3-TM-3 complex and in terms of a rapidly rising $-T\Delta S$ term.

We have reported that *meso*- and *dl*-bis(3,5,5-trimethyl-2-oxomorpholin-3-yl) (**1** and **2**) exist in equilibrium with the persistent free radical 3,5,5-trimethyl-2-oxomorpholin-3-yl (**3**).[3] Radical **3**, to which we have assigned the acronym TM-3, is an important example of a class of radicals now described as merostabilized,[4] captodative,[5] or push-pull-stabilized.[6] Recent calculations suggest that TM-3 has an unusually high stabilization energy within this class of radicals.[7] The importance of TM-3 also stems from its effective use as a mild nontoxic reducing agent[8] for the study[9] and in vivo control[10] of the redox chemistry of quinone antitumor drugs such as adriamycin.



Earlier we reported enthalpies of bond homolysis of a mixture of the meso and *dl* dimers **1** and **2** as a function of solvent from measurements of TM-3 EPR signal intensities as a function of temperature.[3] These enthalpies have now been redetermined with improved instrumentation by double integration of the EPR signal relative to a spin concentration standard as a function of temperature in three solvents. The earlier measurements were qualitatively correct in terms of the observed effect of solvent on bond homolysis, but they underestimated the enthalpies most likely because of errors resulting from variation in the cavity quality factor *Q* as a function of temperature especially in lossy solvents such as ethanol[11] and errors associated with signal saturation. The

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