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# REACTIVITY OF AN AMBIPHILIC CARBENE - A NONLINEAR HAMMETT CORRELATION

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Summary. Methoxychlorocarbene behaves as an ambiphile in addition reactions with styrene derivatives.

Methoxychlorocarbene ($CH_3OCCl$) exhibits electrophilic selectivity toward electron-rich alkenes ($Me_2C{=}CMe_2$, $Me_2C{=}CH_2$) and nucleophilic selectivity toward electron-poor alkenes ($CH_2{=}CHCOOMe$, $CH_2{=}CHCN$).[1] This unique carbenic reactivity has been usefully rationalized in terms of frontier molecular orbital (FMO) theory.[1,2] In our previous studies, the electronic properties of the substrate alkenes were altered by substituent variations directly at the olefinic carbon atoms (e.g., C=C-Me → C=C-CN), which generated rather large changes in alkene HOMO and LUMO orbital energies.[1] A much more demanding test of $CH_3OCCl$ ambiphilicity is possible with styrene substrates, where the (remote) substituent variation elicits smaller FMO energy and carbene selectivity changes. We now demonstrate ambiphilic selectivity in the additions of $CH_3OCCl$ to styrene derivatives.

Methoxychlorodiazirine[3] was thermally decomposed[4] (25°, 24 h) in each of five styrene substrates (see Table I) to afford syn/anti mixtures of the expected 1-chloro-1-methoxy-2-arylcyclopropanes. Products were generally obtained in 20-25% isolated yields (based on the diazirine precursor, o-methylisourea p-toluenesulfonate), and purified by fractional distillation in vacuo. The m-$NO_2$ product (12.5%) required chromatographic separation on silica gel. Product identities were established by structurally-consonant ir and nmr spectra, and by satisfactory elemental analyses.

The relative reactivities of $CH_3OCCl$ toward the styrenes could not be generally obtained by the usual cyclopropane product analysis method,[5] because the p-$CH_3O$ and p-$CH_3$ products were unstable to a variety of gc and hplc analytical conditions. We therefore used Sadler's method[6] to determine a consistent set of relative reactivities. A hexane solution of competing styrenes A and B, and an internal standard, was analyzed by gc to give $A_o/B_o$, the initial alkene ratio. A $N_2$-purged portion of this solution was stirred in the dark (25°, 24 h) with sufficient methoxychlorodiazirine (in pentane) to consume about 60% of the total alkene. Gc analysis then afforded $A_f/B_f$,[7] the final alkene ratio, while gc analysis of the reserved initial alkene solution demonstrated the quantitative stability of the alkenes to the reaction conditions. Relative reactivity ratios were then calculated from: $k_A/k_B = [\log A_o/A_f]/[\log B_o/B_f]$.[6,8] The experimental requirements for application of Sadler's method were carefully observed;[6] results appear in Table I.

Table I. Experimental Relative Reactivities for $CH_3OCCl$ + X-$C_6H_4CH{=}CH_2$, 25°

| Competing alkenes | | |
|---|---|---|
| A[a] | B[a] | $k_A/k_B$[b] |
| *p*-$CH_3$ | H | 1.07 ± 0.01[c] |
| *p*-$CH_3O$ | *p*-$CH_3$ | 1.40 ± 0.02[d] |
| *m*-$NO_2$ | *m*-Cl | 1.22 ± 0.02[e] |
| *m*-Cl | H | 1.04 ± 0.01[f] |

[a] X in X-$C_6H_4CH{=}CH_2$. [b] Errors are average deviations of 2 independent competitions. [c] Gc on 12'x0.25" 10% Carbowax 20M, 125°; int. std., *p*-chlorotoluene. [d] Gc on 12'x0.25" 15% SF-96, 145°; int. std., naphthalene. [e] Gc on 11.5'x0.25" 2.5% SE-30 + 3.5% Carbowax 20M, 150°; int. std., naphthalene. [f] Gc on preceding column, 110°; int. std., *p*-chlorotoluene.

Not only are the reproducibilities excellent, but several satisfactory "cross-check" competitions[5] interrelated the "primary" relative reactivities shown in the Table.[9] Normalizing the experimental data of Table I to styrene (*i.e.*, $k_{sty}^{rel}$ = 1.00), we obtain the relative reactivities shown in Table II. Also included are comparable data for $CCl_2$ and $CF_2$.

Table II. Relative Reactivities for Additions of CZY to X-$C_6H_4CH{=}CH_2$

| X in X-$C_6H_4CH{=}CH_2$ | ($k_X/k_H$) | | |
|---|---|---|---|
| | $CCl_2$[a] | $CF_2$ | MeOCCl[c] |
| *p*-$CH_3O$ | 3.3 | 3.00 | 1.50 ± 0.03 |
| *p*-$CH_3$ | 1.7 | 1.72 | 1.07 ± 0.01 |
| H | 1.0 | 1.00 | 1.00 |
| *m*-Cl | (0.8)[d] | 0.69 | 1.04 ± 0.01 |
| *m*-$NO_2$ | | 0.43 | 1.27 ± 0.02 |
| $\rho$ ($\sigma^+$) | -0.69[a]<br>-0.62[e] | -0.57[b] | |

[a] $Cl_3CCOOEt$ + NaOMe, 0°; ref. 10. [b] $PhHgCF_3$ + NaI, $C_6H_6$, 80°; ref. 11. [c] From Table I; this work. Errors taken from Table I or calculated by standard propagation of error methods where necessary. [d] *p*-Cl substituent. [e] $PhHgCCl_2Br$, $C_6H_6$, 80°; ref. 12.

The carbenic selectivity trends in Table II are very clear: $CF_2$ and $CCl_2$ behave as classical electrophiles, selecting between styrenes with negative rho values of moderate magnitude. $CH_3OCCl$, however, behaves as an ambiphile, adding to *p*-$CH_3O$-styrene with electrophilic selectivity, but to *m*-$NO_2$-styrene with nucleophilic selectivity.[13] Although we do not contend that the experimental differences between the *p*-$CH_3$, H and *p*-Cl reactivities are real, the differences between these and the *p*-$CH_3O$ or *p*-$NO_2$ data *are* significant. The ambiphilic $CH_3OCCl$ Hammett behavior thus resembles a "flattened parabola", and stands in marked contrast to the "normal" behavior of $CF_2$ or $CCl_2$.

There is an interesting, though non-rigorous, FMO treatment of this system which provides an excellent parallel to the experimental results. We took the measured first ionization potential[14] and electron affinity[15] of styrene as indicative of its FMO energies; $E^{HO} = -8.43$ eV and $E^{LU} = 0.25$ eV. We then calculated (STO-3G basis set[16]) HOMO and LUMO energies for four substituted styrenes (*m*-$NO_2$, *m*-Cl, *p*-$CH_3$, *p*-$CH_3O$) and for styrene itself. The differences between the experimental and calculated orbital energies of styrene were used to scale or "correct" the calculated FMO energies of the substituted styrenes.[17] We thus obtained the following sets of scaled FMO energies (in eV): [HOMO or $\pi$] *p*-$CH_3O$, -7.74; *p*-$CH_3$, -8.20; styrene, -8.43; *m*-Cl, -8.90; *m*-$NO_2$, -9.11 and [LUMO or $\pi^*$] *p*-$CH_3O$, 0.48; *p*-$CH_3$, 0.34; styrene, 0.25; *m*-Cl, -0.27; *m*-$NO_2$, -0.34.

Using these substrate orbital energies and calculated values (4-31G basis set, with geometry optimization at the STO-3G level[2]) for the HOMO ($\sigma$) and LUMO (p) orbital energies of $CH_3OCCl$, $CCl_2$, and $CF_2$,[18,19] we obtained *differential* orbital energies, $\underline{E} = (E^{LU}_{CXY} - E^{HO}_{X\text{-}sty})$ and $\underline{N} = (E^{LU}_{X\text{-}sty} - E^{HO}_{CXY})$ for the FMO interactions of each carbene with each styrene derivative; see Table III. These results parallel the finding that $CCl_2$ and $CF_2$, which behave[1b,c,5] as typical electrophiles toward various alkenes, extend this electrophilic pattern to the styrenes. Thus, their calculated *E* differential energies are uniformly less than the corresponding *N* terms. The *E* orbital interactions therefore dominate in the $CCl_2$ (or $CF_2$) + X-styrene additions. Moreover, for either carbene, *E* increases as X becomes increasingly electron-withdrawing ($\sigma_X$ increases), so that, to the extent that *E* parallels the activation energy for these carbenic additions, Table III shows that $CCl_2$ and $CF_2$ should display electrophilic Hammett behavior ($\rho<0$) in correlations of log $\underline{k}^{rel}_{addn}$ vs. $\sigma_X$.

Table III. Differential Orbital Energies (eV) for CZY + $X\text{-}C_6H_4CH{=}CH_2$[a]

| X in $X\text{-}C_6H_4CH{=}CH_2$ | $CCl_2$ *E* | $CCl_2$ *N* | $CF_2$ *E* | $CF_2$ *N* | MeOCCl *E* | MeOCCl *N* |
|---|---|---|---|---|---|---|
| *p*-$CH_3O$ | 8.05 | 11.92 | 9.63 | 13.86 | $\underline{10.20}$ | 11.30 |
| *p*-$CH_3$ | 8.51 | 11.78 | 10.09 | 13.72 | $\underline{10.66}$ | 11.16 |
| H | 8.74 | 11.69 | 10.32 | 13.63 | $\underline{10.89}$ | 11.07 |
| *m*-Cl | 9.21 | 11.17 | 10.79 | 13.11 | 11.36 | $\underline{10.55}$ |
| *m*-$NO_2$ | 9.42 | 11.10 | 11.00 | 13.04 | 11.57 | $\underline{10.48}$ |

[a] See text for definitions of *E* and *N*.

The case of $CH_3OCCl$, however, is quite different. Here, $\underline{E}<\underline{N}$ for X = *p*-$CH_3O$ or *p*-$CH_3$, but $\underline{N}<\underline{E}$ for X = *m*-Cl or *m*-$NO_2$; for X = H, $\underline{E}\sim\underline{N}$. In additions to $X\text{-}C_6H_4CH{=}CH_2$, therefore, the selectivity of $CH_3OCCl$ changes from (predominantly) electrophilic to nucleophilic as the styrene substituents change from electron-donating to electron-withdrawing, describing a *parabolic* Hammett correlation between log $\underline{k}^{rel}_{addn}$ and $\sigma_X$. However, *E* and *N* are similar in magnitude; both sets of orbital interactions contribute to $CH_3OCCl$/X-styrene transition state stabilization, leading to a rather "flat" parabolic Hammett correlation, with a much smaller substituent dependence than is observed when substrate substituents are altered directly at C=C.[1a,c]

Although it is clearly arbitrary to mix experimental alkene orbital energies with calculated carbene orbital energies,[19] the resulting remarkable congruence of the calculated differential orbital energies and the experimental results is surely striking, and seems to be rather general.[20] Most importantly, the persistence of experimentally demonstrable ambiphilicity in the reactions of $CH_3OCCl$ with styrenes satisfactorily completes a very sensitive test of our previously presented concept of a unified "carbenic selectivity spectrum" which embraces electrophiles, ambiphiles, and nucleophiles.[1]

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(7) Alkene pairs and internal standards were selected so that all peaks of interest were separable from carbene dimer and azine $[(MeOCCl{=}N-)_2]$ under gc conditions.

(8) See reference 5, pp. 154-156.

(9) For example, the data in Table I can be manipulated to afford $k_{NO_2}/k_H = 1.27$. A *direct* competition between these two styrenes (using *product* analysis by hplc) gave $k_{NO_2}/k_H = 1.29$.

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(13) It is important to note that *absolute* rate constants for the thermolytic decomposition (30°) of methoxychlorodiazirine display little solvent dependence in $Me_2C{=}CMe_2$, $CH_2{=}CHCOOMe$, $CH_2{=}CHCN$, or $CH_3CN$,[1a,4] indicating that cyclopropanations with this diazirine result from decomposition to $CH_3OCCl$ followed by carbene addition, rather than by decomposition of an initially-formed pyrazoline, or by reactions of other nitrogen-containing precursors with the alkenes. See also N.P. Smith and I.D.R. Stevens, *J. Chem. Soc. Perkin Trans. II*, 213 (1979).

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(17) The corrections were $E^{HO}_{calc} - 1.86\ eV = E^{HO}_{\text{"exptl"}}$ and $E^{LU}_{calc} - 5.88\ eV = E^{LU}_{\text{"exptl"}}$.

(18) Carbene orbital energies[2] (eV): [HOMO (σ)] $CH_3OCCl$, -10.82; $CCl_2$, -11.44; $CF_2$, -13.38 and [LUMO (p)] $CH_3OCCl$, 2.46; $CCl_2$, 0.31; $CF_2$, 1.89.

(19) Experimental carbene orbital energies are unavailable, so that the calculated energies cannot be readily scaled.

(20) For successful applications of this approach, see references 1a, 1c, and R.A. Moss, C.M. Young, L.A. Perez, and K. Krogh-Jespersen, *J. Am. Chem. Soc.*, *103*, 2413 (1981).

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