Tetrahedron Letters,Vol.27,No.50,pp 6115-6118,1986 0040-4039/86 $3.00 + .00
Printed in Great Britain Pergamon Journals Ltd.

# THE SELECTIVITY OF ISOPROPYLIDENECARBENE

Yitzhak Apeloig,*[a] Miriam Karni,[a] Peter J. Stang*[b] and Stephen B. Christensen,[b]
Departments of Chemistry, Technion-Israel Institute of Technology, Haifa 32000, Israel,[a]
University of Utah, Salt Lake City, Utah 84112, U.S.A.[b]

**Abstract**: A simple FMO treatment of the selectivity of $(CH_3)_2C{=}C:$, using calculated orbital energies and neglecting orbital overlap, predicts ambiphilic behavior, in exact analogy with the known ambiphilicity of $MeO\ddot{C}Cl$. Experimental evidence indicates only electrophilic selectivity. A more complete treatment, including orbital overlap, also predicts electrophilic behavior. The failure of the simple theoretical model might result from an "early" transition state geometry for addition, as a result of only slight stabilization of unsaturated carbenes by most substituents.

The exact nature of a reactive intermediate governs its chemical behavior and reactivity. Carbenes may be electrophilic, $\underline{E}$, nucleophilic, $\underline{N}$, or ambiphilic, $\underline{A}$. An ambiphilic carbene acts as an electrophile towards electron-rich alkenes and as a nucleophile towards electron-poor olefins. This spectrum of behavior of carbenes is rationalized within the framework of frontier molecular orbital theory (FMO).[1] Thus, for an electrophilic carbene the dominant interaction is between the vacant carbene p-orbital (2p(C:), LUMO) and the filled alkene π-orbital (HOMO), and for a nucleophilic carbene it is between the filled carbene σ(sp(C:), HOMO) and the vacant alkene $\pi^*$ (LUMO).[1] The degree of interaction arising from a given frontier orbital interaction (ΔE) depends (eq. 1) on both, the extent of orbital overlaps and the differential orbital energies, Δε , where $\Delta E = (S_{HOMO-LUMO})^2 / (\varepsilon_{HOMO} - \varepsilon_{LUMO})$ (eq. 1). Neglecting orbital overlap the stabilization of the interaction is inversely proportional to Δε .

Using known experimental orbital energy values for a set of standard alkenes and styrenes[1] and calculated values (4-31G) for the carbenes, the Table shows the orbital energy differences $[(\underline{E} = \Delta\varepsilon(2p(C:) - \pi),\ \underline{N} = -\Delta\varepsilon(sp(C:) - \pi^*)]$ for three carbenes: $Cl_2C:$,[1] $MeO\ddot{C}Cl$[1] and $Me_2C{=}C:$ (calculations performed in this work).

As seen from the data (Table) this, simple but effective, FMO treatment developed by Moss, Houk *et al.*[1] elegantly and accurately predicts the actual experimental behavior of both the electrophilic $Cl_2C:$ and the ambiphilic $MeO\ddot{C}Cl$. In other words, for $Cl_2C:$ the dominant interaction is exclusively electrophilic towards **all** olefins, whereas for $MeO\ddot{C}Cl$ the interaction **switches** from a dominant electrophilic one with electron-rich olefins to a dominant nucleophilic one with electron-poor olefins, in perfect accord with experiment.

Moss and Houk's treatment of carbene philicity was supported by more recent studies and gained wide acceptance.[2] It was of interest therefore to test this simple FMO treatment on alkylidenecarbenes, species of considerable current interest and activity.[3] Calculations[4] gave the FMO energies (at 4-31G//STO-3G) of $(CH_3)_2C{=}C:$ as 2.82 eV (LUMO) and -11.48 eV (HOMO). Use of these values allow the determination, in complete analogy to the Moss procedure, of the required differential orbital energies of $CH_3C{=}C:$ with the same olefins, and these are also summarized in the Table. As these data indicate $(CH_3)_2C{=}C:$ is **predicted to be ambiphilic** with very similar selectivity to that of $MeO\ddot{C}Cl$. In fact even the olefins at which the dominant interactions switch from $\underline{E}$ to $\underline{N}$ are predicted to be the same: methyl acrylate and p-chlorostyrene.

To test this prediction relative reactivities were determined for the standard olefins in the Table, by the usual techniques.[1,3]

**Table:** Differential Orbital Energies for Carbene-Alkene and Carbene-Styrene Interactions (in eV) and Relative Rates of Addition.

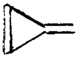
| Alkene[a] / Carbene | $Cl_2C:$[a] | | | $MeO\ddot{C}Cl$[a] | | | $Me_2C{=}C:$[b,c] | | |
|---|---|---|---|---|---|---|---|---|---|
| | E | N | $k_{rel.}$ | E | N | $K_{rel.}$ | E | N | $K_{rel.}$[c] |
| $Me_2C{=}CMe_2$ | 8.6 | 13.7 | 78.4 | 10.7 | 13.1 | 12.6 | 11.1 | 13.8 | 0.16 |
| $Me_2C{=}CH_2$ | 9.6 | 13.6 | 4.9 | 11.7 | 13.0 | 5.4 | 12.1 | 13.7 | 0.60 |
| t-MeCH=CHMe | 9.4 | 13.5 | 1.00 | 11.3 | 12.9 | 1.0 | 11.9 | 13.6 | 1.00 |
| $CH_2{=}CHCO_2Me$ | 11.0 | 12.2 | 0.06 | 13.2 | 11.6 | 29.7 | 13.5 | 12.3 | 0.18 |
| $CH_2{=}CHCN$ | 11.2 | 11.6 | 0.05 | 13.4 | 11.0 | 54.6 | 13.7 | 11.7 | — |
| $X{-}C_6H_4CH{=}CH_2$[a] | E | N | $k_{rel.}$ | E | N | $K_{rel.}$ | E | N | $K_{rel.}$[c] |
| X = p-MeO | 8.05 | 11.92 | 3.3 | 10.20 | 11.30 | 1.50 | 10.56 | 11.96 | 1.51 |
| p-Me | 8.51 | 11.78 | 1.7 | 10.66 | 11.16 | 1.07 | 11.02 | 11.82 | 1.28 |
| H | 8.74 | 11.69 | 1.0 | 10.89 | 11.07 | 1.00 | 11.25 | 11.73 | 1.00 |
| p-Cl | 9.21 | 11.17 | 0.8 | 11.36 | 10.55 | 1.04[d] | 11.72 | 11.21 | 0.63 |
| $m{-}NO_2$ | 9.42 | 11.10 | 0.46 | 11.57 | 10.48 | 1.27 | 11.93 | 11.14 | — |

[a] Using the energies in ref. 1; [b] This work; [c] Part of experimental data from: D.P. Fox, J.A. Bjork and P.J. Stang, *J. Org. Chem.*, *48*, 3994 (1984) and P.J. Stang, J.R. Madsen, M.G. Mangum, and D.P. Fox, *ibid*, *42*, 1820 (1977); [d] For the m-Cl.

Unfortunately, the known modes of alkylidenecarbene generation (most involve a base or at least $F^-$)[3] polymerize $CH_2{=}CHCN$ and $p{-}O_2NC_6H_4CH{=}CH_2$ and hence no rates could be determined for these substrates. Moreover, as expected, because of the great steric demands of alkylidenecarbene/olefin interactions[5] electron-rich, but hindered olefins, such as $Me_2C{=}CMe_2$ and $Me_2C{=}CH_2$, react slower than they should based upon electronic factors alone.[3] Nevertheless, the available data clearly contradict these simple FMO predictions. Specifically, unlike the A-$MeO\ddot{C}Cl$, where the switch in the dominant interaction from E to N is accompanied by a thirty-fold **increase** in relative reactivity, from t-2-butene to methyl acrylate, with $(CH_3)_2C{=}C:$ this change in olefin results in a six-fold **decrease** in relative reactivity,[6] comparable to the selectivity of the electrophilic $Cl_2C:$. Likewise, $MeO\ddot{C}Cl$ shows a clear A-behavior with substituted styrenes, with a Hammett plot resembling a flattened parabola, but $(CH_3)_2C{=}C:$ shows a classic E-behavior with a good linear Hammett correlation ( $\rho{=}-0.75$, $r{=}0.997$), again resembling the known E-selectivity of $Cl_2C:$.[1] Using 6,6-dimethylfulvene as an indicator substrate Moss *et al.* have also concluded that $(CH_3)_2C{=}C:$ is electrophilic.[7]

Why does the simple FMO treatment[1] work for normal carbenes but fails for alkylidene carbenes?[8] Apparently, in the alkylidenecarbene-olefin interactions the numerator in eq. 1, i.e., the orbital overlaps, control the selectivity overriding the opposing orbital energy effect, in contrast to the comparable carbene-olefin interactions. Indeed, a more complete FMO treatment, following Rondan, Houk and Moss (RHM),[9] which includes orbital overlaps, predicts $(CH_3)_2C{=}C{:}$ to be **electrophilic not ambiphilic** - in agreement with the available experimental results. Thus, the "philicity index", PI, was calculated according to the RHM formula (eq. 1 in ref. 9), using $\Delta E_{stab}$ of -37.0 kcal.mol$^{-1}$ (4-31G), where $\Delta E_{stab}$ is given by: $H_2C{:} + (CH_3)_2C{=}CH_2 \longrightarrow H_4C + (CH_3)_2C{=}C{:}$. We calculate PI=0.68,[10] a value typical for electrophilic carbenes (e.g., PI=0.85 for $:CF_2$[9]). The electrophilic orbital overlap apparently dominates the interaction, even when opposed by a nucleophilic orbital energy difference. Note, that $\Delta E_{stab}$ for $(CH_3)_2C{=}C{:}$ is relatively low, in the range typical for electrophilic carbenes (e.g., $\Delta E_{stab}$ = 29.3 kcal.mol$^{-1}$ for $Cl\ddot{C}CH_3$[9]), and significantly lower than for ambiphilic or nucleophilic carbenes (e.g. $\Delta E_{stab}$ = 83.0 kcal.mol$^{-1}$ for $((HO)_2C{:})$.[9] Low $\Delta E_{stab}$ suggests a highly exothermic cycloaddition reaction and an "early" transition state, as we indeed calculate for $CH_2{=}C{:} + H_2C{=}CH_2$, (steric effects also contribute to this "early" transition state[5a]), where the shortest intermolecular C–C distance is 1.94 Å at STO-3G,[5a] (e.g., 1.96 Å for $Cl_2C{:}$[9]). Rondan <u>et al.</u> found that "early" transition states involve more electrophilic character than "late" transition states[9] and this can be used to rationalize the failure of the FMO energy criterion for $(CH_3)_2C{=}C{:}$ in contrast to its success with regular carbenes. Houk has noted a similar behaviour for $Cl\ddot{C}CH_3$, $F\ddot{C}Ph$ and $Cl\ddot{C}SCH_3$; these carbenes are predicted to be ambiphilic on the basis of the FMO energies, but electrophilic when overlap is included.[9]

The use of other calculated criteria, following RHM's criteria and terminology,[9] to predict the "philicity" of $(CH_3)_2C{=}C{:}$ also leads to ambiguous results. Criteria which use the geometry of the cycloaddition transition state point clearly to an electrophilic carbene (we use the $CH_2{=}CH_2 + H_2C{=}C{:}$ transition structure[5a]). Thus: (1) The ratio of the newly forming bond lengths, $r_{12}/r_{23}$ =1.19 (1.18 for $Cl_2C{:}$[9]). (2) The tilt angle of the carbene with respect to the original ethylene plane is $\zeta$=35.6° (36° for $Cl_2C{:}$[9]). (3) The angle of distortion away from planarity of the ethylene $\beta$-$CH_2$ group is $\beta$=13.2° (13.9° for $Cl_2C{:}$[9]). Calculations of the "carbene selectivity index", m, using RHM's equation: $m=[0.035\,\Delta E_{stab}-0.449$[9]$]$, gives $m[(CH_3)_2C{=}C{:}]=0.85$ (0.97 for $Cl_2C{:}$[9]). On the other hand, the calculated "charge-transfer", q, from ethylene to $H_2C{=}C{:}$ is $14\times10^{-2}$ electrons, a value typical for ambiphilic carbenes ($q=10\times10^{-2}$ and $29\times10^{-2}$ electrons for HOFC: and $Cl_2C{:}$ respectively[9]).

Can ambiphilic or nucleophilic alkylidenecarbenes be generated? To achieve this goal one should significantly stabilize the carbene (i.e., increase $\Delta E_{stab}$), and push up the energies of its HOMO and LUMO. This is more difficult to achieve with alkylidenecarbenes because substituents influence their stabilities and orbital energies to a smaller extent than they do for normal carbenes.[11] However, this goal **may be** achieved with strongly hyperconjugating groups such as $Me_3Si$. For, $(H_3Si)_2C{=}C{:}$ we calculate (3-21G), $\Delta E_{stab}$= -58 kcal.mol$^{-1}$, PI= 1.0, HOMO=-11.98 eV, LUMO=2.60 eV.[12] Similarly, the strong charge polarization towards the carbenic carbon lead us to suggest that  C: might be an ambiphilic or even a nucleophilic carbene.[13]

**Acknowledgments.**

This research was supported by a U.S.-Israel Binational Science Foundation (BSF) grant in Israel and by the NSF (CHE 84-19099) and the PRF (administered by the ACS) at Utah. PJS also wishes to express his gratitude to the Lady Davis Foundation for a Visiting Professorship at the Technion that greatly facilitated this collaboration.

## References and Notes

1. R.A. Moss, Acc. Chem. Res., 13, 58 (1980).
2. E.g.;(a) M.P. Doyle, J.W. Terpstra and C.H. Winter, Tetrahedron Lett., 901 (1984); (b) M. Moreno, J.M. Lluch, A. Oliva, and J. Bertran, J. Chem. Soc., Perkin Trans. II, 183 (1986); Chem. Phys., 100, 33 (1985); (c) W.W. Schoeller, N. Aktekin and H. Friege, Angew. Chem. Int. Ed., 21, 932 (1982); W.W. Schoeller, ibid., 20, 698 (1981); (d) S.-I. Murahashi, K. Okumura, T. Naota, and S. Nagase, J. Am. Chem. Soc., 104, 2466 (1982); (e) H. Tomioka, K. Ohno, Y. Izawa, R.A. Moss, and R.C. Munjal, Tetrahedron Lett., 5415 (1984); (f) R.A. Moss, W. Guo and K. Krogh-Jespersen, Tetrahedron Lett., 15 (1982); (g) R.A. Moss and L.A. Perez, ibid., 2719 (1983); (h) R.A. Moss, W. Guo, D.Z. Denney, K.N. Houk, and N.G. Rondan, J. Am. Chem. Soc., 103, 6164 (1981).
3. Reviews: P.J. Stang, Acc. Chem. Res., 15, 348 (1982), Chem. Rev., 78, 383 (1978).
4. The Gaussian 80 series of programs was used: J.S. Binkley, R.A. Whiteside, R. Krishnan, R. Seeger, D.J. DeFrees, H.B. Schlegel, S. Topiol, L.R. Kahn and J.A. Pople, QCPE, 13, 406 (1980).
5. (a) Y. Apeloig, M. Karni, P.J. Stang, and D.P. Fox, J. Am. Chem. Soc., 105, 4781 (1983); (b) D.P. Fox, P.J. Stang, Y. Apeloig, M. Karni, J. Am. chem. Soc., 108, 750 (1986).
6. Reactions were carried out at -20°C, significantly lower than the common isoselective temperatures of carbenes, see: B. Giese, Acc. Chem. Res., 17, 438 (1984). This factor is important because the FMO analysis does not account for entropy effects.
7. R.A. Moss, C.M. Young, L.A. Perez, and K. Krogh-Jespersen, J. Am. Chem. Soc., 103, 2413 (1981).
8. On the other hand, extended unsaturated carbenes are predicted, in agreement with experiment,[3] to be electrophilic. For example with $H_2C=C=C:$, $E<N$ for both $(CH_3)_2C=C(CH_3)_2$, $E=8.90$, $N=14.1$; and $H_2C=CHCN$, $E=11.5$, $N=12.1$ (4-31G, eV).
9. N.G. Rondan, K.N. Houk and R.A. Moss, J. Am. Chem. Soc., 102, 1770 (1980).
10. We have evaluated PI via $\Delta E_{stab}$ rather than by a direct calculation of the nucleophilic and electrophilic orbital overlaps because of ambiguities regarding the procedure for their direct evaluation. Our calculations for $Cl_2C: + H_2C=CH_2$ gave $S_E=0.144$ and $S_N=0.021$ compared with $S_E=0.131$ and $S_N=0.095$ reported by Rondan et al.[9] The differences between our and Rondan's[9] calculations may result from our use of Gaussians in place of Slatter orbitals, different procedures for separation of the orbital overlaps into $\sigma$ and $\pi$ components, etc.
11. Y. Apeloig and R. Schreiber, Tetrahedron Lett., 4555 (1978).
12. Recently, $(Me_3Si)_2C=C:$ was generated by thermolysis: R.W. Hoffmann, Acc. Chem. Res., 18, 248 (1985).
13. Y. Apeloig, R. Schrieber and P.J. Stang, Tetrahedron Lett., 411 (1980).

(Received in UK 28 July 1986)