METHOXYCHLOROCARBENE

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Carbenes are commonly described as electrophilic or nucleophilic, depending on their expressed preferences for addition to electron-rich or electron-poor olefinic π-bonds.[1] Determination of the selectivities of carbenes toward a common standard set of alkenes allows the derivation of "carbene selectivity indices", $\underline{m}_{CXY}$, which can be correlated with the electronic properties of the carbenic substituents, X and Y.[2] Currently, the "electrophilic" carbene of highest selectivity on this scale is CF_2[3] ($\underline{m}^{obsd} = 1.48$).[2] Dimethoxycarbene ($\underline{m}^{calcd} = 2.22$)[2], on the other hand, appears to be a nucleophilic species which adds readily to electron-poor olefins such as diethylfumarate,[4] but not to electron-rich olefins such as ketene diethylacetal or cyclohexene.[5]

Carbenes with $1.48 < \underline{m}_{CXY} < 2.22$ are therefore of special interest because the transition between predominantly electrophilic or predominantly nucleophilic behavior should occur in this region.[6] Appropriate candidate carbenes include CH_3OCF ($\underline{m}^{calcd} = 1.85$)[2], C_6H_5OCF ($\underline{m}^{calcd} 1.74$)[2] and CH_3OCCl ($\underline{m}^{calcd} = 1.59$). Difficulties attending the generation of the first two species have been discussed.[2] Previous reports of CH_3OCCl production include the action of isopropoxide ion on α,α-dichlorodimethyl ether,[7] and of methyllithium on α,α,α-trichlorodimethyl ether.[8] In the former case,[7] the carbene was not (and probably could not have been[2]) added to alkenes, whereas, in the latter instance,[8] cyclopentadiene did intercept "CH_3OCCl", but under the strongly basic conditions rearrangement and elimination reactions of the presumed initial adduct afforded anisole as the isolable product. Accordingly, we are pleased to report the generation and olefinic capture under very mild conditions of CH_3OCCl,[9] a carbene which exhibits a broad range of reactivity in the cyclopropanation of alkenes.

O-methylisourea p-toluenesulfonate was converted to 3-methoxy-3-chlorodiazirine,[10] which was condensed into alkenes Ia-Id[11] at -77°. Subsequent thermolysis (25°, ca. 1 day) afforded the expected cyclopropanes IIa-IIf, cf., eq. (1) and Table I.

$$ \text{(1)} $$

Ia - If   IIa - IIf
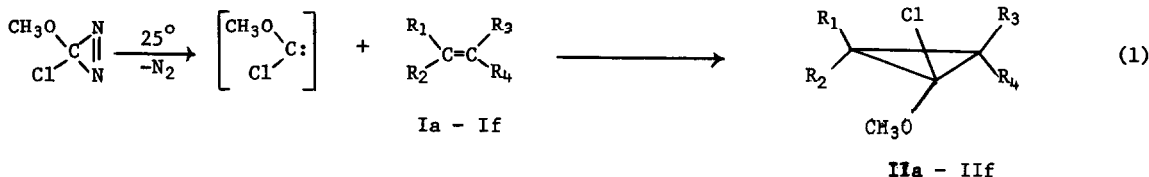
Table I.   Additions of Methoxychlorocarbene to Alkenes

Alkene	Adduct	R_1	R_2	R_3	R_4	Yield(%)[a]
Ia	IIa	CH_3	CH_3	CH_3	CH_3	72[b]
Ib	IIb	CH_3	CH_3	H	H	41[c]
Ic	IIc	CH_3	H	H	CH_3	25[c]
Id	IId	$COOCH_3$	H	H	H	73[b,d]
Ie	IIe	CN	H	H	H	-[d,e]
If	IIf	$COOCH_3$	H	H	$COOCH_3$	-[e]

[a]Yields of II were determined by nmr integration of crude reaction products, relative to an internal CH_2Cl_2 or $CHCl_3$ standard, and are referred either to [b]N_2 evolution observed during the thermolysis (i.e., moles of diazirine converted to carbene), or [c]to the initial O-methylisourea p-toluenesulfonate, assuming that this was converted to diazirine in 60% yield.[9] [d]A mixture of stereoisomeric adducts was formed. [e]Not determined; Smith and Stevens[9] report 40% (IIe) and 21% (IIf).

Adducts IIb-IIe, from isobutene, trans-butene, methyl acrylate,[12] and acrylonitrile,[12] respectively, were isolated by gc on SF-96 at 100°. Cyclopropanes IIe[12] were identical (nmr) to the compounds described by Smith and Stevens;[9] the structures of IIb-IId were established by nmr spectroscopy and by satisfactory exact mass determinations of their parent molecular ions. In particular, nmr spectra of IIb-IId revealed no vinyl protons, but did exhibit methoxy singlets in the region δ3.4-3.5. Additionally, IIb and IIc displayed methyl signals (δ1.1-1.3) and cyclopropyl proton resonances (δ0.6-1.1). The isomers of IId (and IIe) exhibited cyclopropyl protons at δ1.4-2.4 (δ1.6-2.2), as well as appropriate functional group ir absorptions.

Tetramethylethylene adduct IIa rearranged slowly in CCl_4 at 25°, rapidly in Ia at 100°, and completely during gc on SF-96 at 100° to methoxydiene III, cf., eq. (2).[13] Diene III had m/e

$$\text{(2)}$$
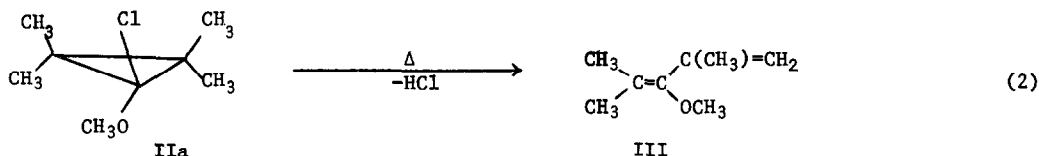
(calcd.) 126.1045, m/e (obsd.) 126.1067; δ(CCl_4) 5.20, 4.86 (m's, 2H, = CH_2), 3.33 (s, 3H, OCH_3), 1.77 (d, J = 1 Hz, 3H,CH_3CR=),   1.65 (s, 6H, $(CH_3)_2$C=). Nevertheless, intact cyclopropane IIa could readily be discerned in fresh, crude product mixtures, δ(CCl_4) 3.43 (s, 3H, OCH_3), 1.14 (s, 6H, CH_3), 1.10 (s, 6H, CH_3).

Finally, the adduct of dimethyl fumarate, IIf, was isolated by channel layer chromatography (silica gel G, 10:90 tetrahydrofuran/petroleum ether) and identified by its characteristic nmr spectrum: δ(CCl_4) 3.78 (s, 6H, $COOCH_3$), 3.52 (s, 3H, OCH_3), 2.82 (s, 2H, $CHCOOCH_3$).[9]

In a brief study of the kinetics of reaction (1), we collected absolute rate data for the decay of methoxychlorodiazirine (observing its uv absorption at 362 nm[9,10]) and for the accompanying evolution of nitrogen (manometry). For dilute diazirine solutions, both processes were first

order and yielded the following rate constants ($\times 10^4$, sec^{-1}, 30°): 0.87 (uv) and 1.2 (N$_2$) in Ia, 1.1 (uv) and 1.4 (N$_2$) in Id, and 1.5 (uv) in acetonitrile. The similarity of rate constants for N$_2$ loss or diazirine disappearance in either a nucleophilic or an electrophilic alkene, and in an inert polar solvent, suggests that adducts II are formed by alkene capture of CH$_3$OCCl and not (e.g.) by decomposition of an initially-formed pyrazoline.

Methoxychlorocarbene can thus be generated under mild conditions and added in fair to good yields to a variety of alkenes, ranging from electron-rich to electron-poor. We note, however, that a broad range of cyclopropanation reactivity does not, by itself, adequately characterize the reactivity of a carbene; required is the quantitative examination of carbenic selectivity over the entire substrate spectrum. Such experiments are now in process. We add that the wide reactivity range of CH$_3$OCCl is not unique; CCl$_2$ also adds to Ia,[2] Id,[14] Ie,[14] and diethylfumarate (31% from C$_6$H$_5$HgCCl$_2$Br).[15] Examination of the selectivity of CCl$_2$ (and of CF$_2$) toward electron-poor alkenes is under study.

References and Notes

(1) Review: R. A. Moss in "Carbenes", Vol. I, M. Jones, Jr., and R. A. Moss, Ed., Wiley-Interscience, New York, 1973, pp. 153ff.

(2) R. A. Moss, C. B. Mallon, and C. T. Ho, J. Am. Chem. Soc., 99, 4105 (1977); the correlation equation is $m_{CXY} = -1.10 \sum_{X,Y} \sigma_R^+ + 0.53 \sum_{X,Y} \sigma_I - 0.31$.

(3) CF$_2$ also discriminates electrophilically between ring-substituted styrenes, $\rho = -0.57$; R. A. Moss and C. B. Mallon, J. Am. Chem. Soc., 97, 344 (1975).

(4) R. W. Hoffmann, W. Lilienblum, and B. Dittrich, Chem. Ber., 107, 3395 (1974).

(5) D. M. Lemal, E. P. Gosselink, and S. D. McGregor, J. Am. Chem. Soc., 88, 582 (1966).

(6) Any singlet carbene is inherently both an electrophile and a nucleophile; behaviorally decisive is whether, in the transition state for addition to an alkene, the LUMO$_{carbene}$-HOMO$_{alkene}$ or the HOMO$_{carbene}$-LUMO$_{alkene}$ interaction dominates; cf., W. M. Jones, R. A. LaBar, U. H. Brinker, and P. H. Gebert, J. Am. Chem. Soc., 99, 6379 (1977), note (27). A carbene might exhibit ambiphilic behavior when these interactions are of comparable energy, and the available spectrum of alkenes makes it likely that demonstrably ambiphilic carbenes will reside in the m_{CXY} range cited above.

(7) J. Hine, R. J. Rosscup, and D. C. Duffey, J. Am. Chem. Soc., 82, 6120 (1960).

(8) U. Schöllkopf and J. Paust, Chem. Ber., 98, 2221 (1965).

(9) See also N. P. Smith and I.D.R. Stevens, accompanying communication, and N. P. Smith, Ph.D. Dissertation, University of Southampton, 1972.

(10) W. H. Graham, J. Am. Chem. Soc., 87, 4396 (1965).

(11) In the case of olefin Ie, the diazirine was condensed into n-pentane at -77°, and the resulting solution was then added to an ethereal solution of Ie; with alkene If, the diazirine was condensed into CH$_2$Cl$_2$ at -77°, and the solution was then added to a CH$_2$Cl$_2$ solution of If.

(12) Gc-separable syn/anti stereoisomeric cyclopropane mixtures were obtained [isomer ratios 3:1
      (IId) and 1.8:1 (IIe)], but we wish to defer configurational assignments at this time.

(13) The synthetic potential of this and related rearrangements is under investigation.

(14) D. Seyferth, J. M. Burlitch, R. J. Minasz, J. Y-P. Mui, H. D. Simmons, Jr., A.J.H. Treiber,
      and S. R. Dowd, J. Am. Chem. Soc., 87, 4259 (1965).

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