port from the National Institutes of Health through Research Grant CA 14378-04.

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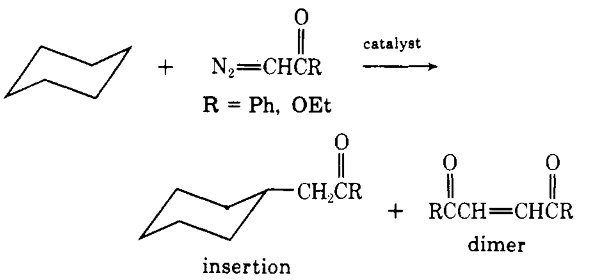
Received September 22, 1973

Intermolecular Carbon–Hydrogen Insertion of Copper Carbenoids

Sir:

Free carbenes, generated by the photolysis or thermolysis of aliphatic diazo compounds, have enjoyed little popularity in the cyclopropanation of olefins because insertion of the reactive intermediate into carbon–hydrogen bonds often competes effectively with olefin addition.[1] Catalysis of the decomposition by copper metal or its salts generally suppresses C–H insertion,[2] however, except in favorable intramolecular cases,[3,4] and this observation has led to the widely held tenet[2] that copper carbenoids lack the necessary reactivity to insert into C–H bonds. It has never been clearly established whether carbenoids or adventitious free carbenes account for the C–H insertion by-products occasionally reported[5,6] from the decomposition of diazo compounds in the presence of copper catalysts; consequently, the only authenticated case of intermolecular copper carbenoid C–H insertion to date appears to be that of CH_2 into the relatively special carbon–hydrogen bonds of hexamethyldisilane and tetramethylsilane[7] (5–10% yield). We have now demonstrated by the experiments described below that certain copper carbenoids, when deprived of alternative reaction pathways, can and do insert intermolecularly into unactivated, aliphatic C–H bonds.

Cyclohexane, a solvent often employed for carbenoid reactions[4,8] and commonly regarded as inert, was chosen as the substrate for our studies to ensure that C–H insertion would produce only a single, easily identifiable product (eq 1). High dilution techniques were used to minimize the formation of "dimers" arising from attack of the carbenoid on excess diazo compound. Thus a dilute solution of the diazo compound in 20 ml of dry cyclohexane was added dropwise with vigorous stirring to a refluxing suspension of the catalyst in 100 ml of cyclohexane over a standard period of time. In the absence of catalyst, the diazo compounds remain >90% unchanged, and glc indicates no more than a trace of the insertion product. With cupric sulfate or cuprous chloride catalysis, however, none of the diazo compound survives, and the C–H insertion product appears in 9–24% yield together with varying amounts of dimer (see Table I).



(1)

Table I

——Starting materials——		——% products——		
Diazo	Catalyst	Diazo[c]	Insertion[d]	Dimer[e]
$N_2{=}CHCO_2Et$[a]	None	98	<1	0
	$CuSO_4$	0	24	40
	CuCl	0	15	61
$N_2{=}CH\overset{O}{\overset{\|}{C}}Ph$[b]	None	92	0	0
	$CuSO_4$	0	17	9
	CuCl	0	9	29

[a] The reactions of ethyl diazoacetate were run with 4.4 mmol each of catalyst and diazoester for 1 hr as described in the text. [b] The reactions of diazoacetophenone were run with 2.2 mmol each of catalyst and diazoketone for 0.5 hr as described in the text. [c] The amount of recovered ethyl diazoacetate was determined by quantitative uv; recovered diazoacetophenone was determined by nmr with an internal standard. [d] The insertion products were purified by preparative glc and identified by nmr, ir, and mass spectroscopy. Yields were determined by glc with an internal standard, making the appropriate adjustments for detector response factors. [e] Yields of diethyl maleate and diethyl fumarate were determined by quantitative nmr; dibenzoylethylene was analyzed by quantitative glc.

The high recovery of diazo compound from the uncatalyzed control reactions demands that the significant amounts of C–H insertion products formed in the catalyzed reactions be copper–carbenoid derived and not a consequence of thermally generated, free carbenes. Accordingly, the characteristic suppression of C–H insertion normally associated with copper catalysis seems to reflect an enhanced selectivity of the reactive intermediate rather than an incapability of the carbenoid to participate in otherwise competitive processes. It should be noted in this connection that copper catalysis normally suppresses also the Wolff rearrangement of ketocarbenes generated by diazoketone decomposition[2] but that exceptions have been found.[9]

Although glc revealed no other products in our experiments, the poor material balance suggests polymer formation in spite of the high dilution. At even higher dilution with more catalyst the yield of insertion product increases slightly at the expense of dimer formation; the material balance fails to improve, however. Both glc and nmr comparision of the crude reaction

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(1) W. Kirmse, "Carbene Chemistry," 2nd ed, Academic Press, New York, N. Y., 1971.

(2) Reference 1, pp 85–88.

(3) F. Greuter, J. Kalvoda, and O. Jeger, *Proc. Chem. Soc., London*, 349 (1958); J. K. Chakrabarti, S. S. Szinai, and A. Todd, *J. Chem. Soc. C*, 1303 (1970).

(4) E. Wenkert, B. L. Mylari, and L. L. Davis, *J. Amer. Chem. Soc.*, **90**, 3870 (1968); R. C. Cambie and R. A. Franich, *Chem. Commun.*, 725 (1969).

(5) See, for example, B. W. Peace and D. S. Wulfman, *Synthesis*, 137 (1973).

(6) H. O. House and C. J. Blankley, *J. Org. Chem.*, **33**, 53 (1968).

(7) R. T. Conlin, P. P. Gaspar, R. H. Levin, and M. Jones, Jr., *J. Amer. Chem. Soc.*, **94**, 7165 (1972).

(8) G. Stork and J. Ficini, *J. Amer. Chem. Soc.*, **83**, 4678 (1961); M. M. Fawzi and C. D. Gutsche, *J. Org. Chem.*, **31**, 1390 (1966); H. O. House, S. G. Boots, and V. K. Jones, *ibid.*, **30**, 2519 (1965). Additional examples may be found in the table on pp 340–342 in ref 1.

(9) H. Erlenmeyer and M. Aeberli, *Helv. Chim. Acta*, **31**, 28 (1948); R. Casanova and T. Reichstein, *ibid.*, **33**, 417 (1950); P. Yates and J. Fugger, *Chem. Ind.* (*London*), 1511 (1957); P. Yates and R. J. Crawford, *J. Amer. Chem. Soc.*, **88**, 1562 (1966).

mixture with an authentic sample of triethyl 1,2,3-cyclopropanetricarboxylate[10] confirm the absence of this anticipated "trimer" of carboethoxycarbene.

Diphenyldiazomethane gives no detectable insertion product when decomposed catalytically in cyclohexane with cupric sulfate or cuprous chloride. Gaspar and Jones, *et al.*, likewise report[7] that the cuprous chloride catalyzed decomposition of unsubstituted diazomethane in cyclohexane fails to produce any detectable methylcyclohexane. Thus the conjugation of copper carbenoids with a carbonyl group appears to play a crucial role in determining the feasibility of intermolecular C–H insertion. The mechanism of C–H insertion by copper carbenoids is not known but may involve dissociation of the carbenoid to free carbene.[6]

Acknowledgments. Financial support from the National Science Foundation, the donors of the Petroleum Research fund, administered by the American Chemical Society, and the Research Committee of the University of California, Los Angeles, is gratefully acknowledged.

(10) G. Bonavent, M. Causse, M. Guitard, and R. Fraisse-Jullien, *Bull. Soc. Chim. Fr.*, 2462 (1964).

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Received September 18, 1973

Assignment of ^{13}C Nuclear Magnetic Resonance Signals. Fingerprints in Off-Resonance $^{13}C,\{^1H\}$ Nuclear Magnetic Double Resonance Spectra[1]

Sir:

One of the most widely used techniques for the assignment of ^{13}C nmr signals is off-resonance continuous wave spin decoupling.[2] Not only can the resonances of quaternary carbons, CH–, CH_2–, and CH_3– groups, be readily identified[3–5] but, in a more refined stage, the residual one bond $^{13}C,^1H$ coupling constant J_R measured in these partially decoupled spectra may frequently be used to interrelate carbon and proton chemical shifts, since J_R is given[2] by

$$J_R = J_0\Delta\nu/\bar{\gamma}H_2 \qquad (\bar{\gamma} = \gamma/2\pi) \qquad (1)$$

where J_0 is $^1J(^{13}C,^1H_i)$, $\Delta\nu$ is the frequency difference between the proton resonance ν_i and the decoupler frequency ν_2, and $\bar{\gamma}H_2$ is the power of the decoupling field.[6] Chemically different carbons that bear the same number of protons may thus be discriminated, provided that: (1) the ^1H nmr spectrum is correctly assigned, (2) the $^1J(^{13}C,^1H)$ data are known, and (3) the difference in the $\Delta\nu$ values for individual protons yields variations in J_R that are larger than the experimental error.

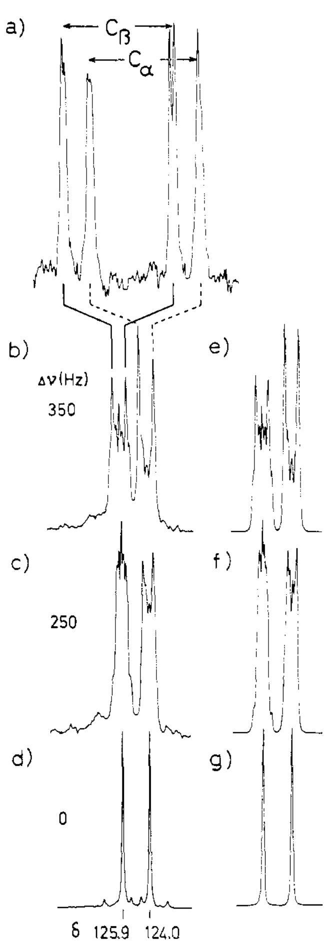
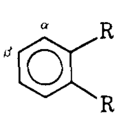


Figure 1. ^{13}C nmr spectrum of the methine carbons of indan at 22.63 MHz: (a) ^1H undecoupled; (b), (c) ^1H off-resonance decoupled with ν_2 at high field from the proton resonances; (d) ^1H decoupled, δ values refer to internal tetramethylsilane; (e)–(g) calculated spectra (see text).

Recently we have shown[8] that characteristic splitting patterns or fingerprints in the ^1H-undecoupled ^{13}C nmr spectra of compounds of types **1–3**, which have in common a C_4H_4 fragment of four methine groups and a plane of symmetry (**4**), allow an unequivocal assignment of the C_α and C_β resonances, even in cases where off-resonance decoupling fails.



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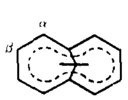

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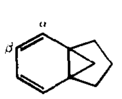

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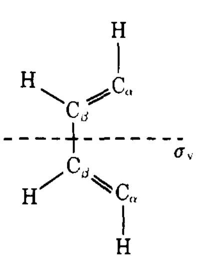

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We now report that these fingerprints are also retained in the off-resonance decoupled spectra of **1–3**, thereby eliminating certain restrictions imposed on this assignment technique.

As an example, Figure 1 shows the experimental ^{13}C nmr spectra of the α- and β-carbons of indan, where $\delta(C_\alpha) = 124.0$ and $\delta(C_\beta) = 125.9$ ppm have been firmly

(1) Applications of Carbon-13 Resonance Spectroscopy. XIII; for part XII see U. Ewers, H. Günther, and L. Jaenicke, *Chem. Ber.*, in press.

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(6) The more rigorous relation $J_R = \Delta\nu J_0/(\Delta\nu^2 + \bar{\gamma}^2 H_2^2)^{1/2}$ has been derived by Pachler.[7]

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