

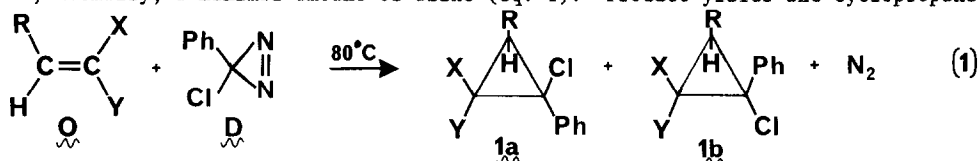
NUCLEOPHILIC CHARACTER OF AN ELECTROPHILIC CARBENE. SYNTHESIS
 OF CYCLOPROPANES BY THERMAL DECOMPOSITION OF 3-CHLORO-3-
 PHENYLDIAZIRINE

Michael P. Doyle*, Jan W. Terpstra, and Charles H. Winter
 Department of Chemistry, Hope College, Holland, Michigan 49423

Summary: Chlorophenylcarbene reacts with electrophilic olefins to form cyclopropane products in high yield through proposed ylide intermediates.

Diazirines, cyclic structural isomers of diazo compounds, are routinely employed as carbene precursors.¹ Although photolytic methods are most commonly used for dinitrogen extrusion,^{1,2} thermal decomposition of diazirines also provides entry to carbenes.^{1,3} The specific characteristics of carbenes generated from diazirines and other carbenic sources are subjects of intense current interest⁴ and, recently, the spectrum of carbene philicity has been uncovered through investigations of relative olefin reactivities with generated carbenes.⁵ According to this scheme, chlorophenylcarbene is a typically electrophilic carbene that should exhibit preferential reactivity with nucleophilic olefins.^{5,6} To our surprise, we have found that vinyl ethers and α,β -unsaturated esters exhibit similar reactivity towards chlorophenylcarbene and that chlorophenyldiazirine is exceptionally effective for cyclopropanation of the spectrum of olefins ranging from vinyl ethers to α,β -unsaturated carbonyl compounds.

3-Chloro-3-phenyldiazirine was prepared from benzamidine hydrochloride by Graham's procedure.⁷ Thermal decomposition of this diazirine (**D**) at 80°C in excess olefin (**O**) occurred with the expected evolution of dinitrogen. Following complete gas evolution, distillation of excess olefin afforded a strikingly simple composite of cyclopropane products (**1a,b**) and, normally, a minimal amount of azine (eq. 1). Product yields and cyclopropane



isomer ratios from reactions of **D** with a spectrum of olefins are reported in Table I. Reactions were performed in excess olefin without the use of a cosolvent, except with trans-stilbene where CCl_4 was employed. Various reactant ratios are effective for cyclopropane formation, but azine formation⁸ becomes increasingly important as $[\text{O}]/[\text{D}]$ approaches

Table I. Cyclopropane Yields and Stereoselectivities from Thermolysis of 3-Chloro-3-phenyldiazirine at 80°C in the Presence of Selected Olefins^a

R	X	Y	[O]/[D]	$\frac{1a,b}{\text{Yield, \%}}$	$\frac{1b}{1a^b}$	B.p., C°(Torr) ^c
H	H	COOEt	10	93	2.2	70-72 (0.5)
H	CH ₃	COOMe	10	70	3.0	78-82 (0.4)
H	CH ₃	CN	10	95	4.0	87-89 (0.4)
CH ₃	H	COOEt	5.0	77	3.3	90-91 (0.2)
COOEt	H	COOEt	3.5	85	<u>d</u>	140-5 (2.0)
	-(CH ₂) ₄ -	H	5.0	65	0.67	170-3 (33)
H	H	O-n-Bu	5.0	97	2.1	80-82 (0.3)
H	H	Ph	10	96	1.6	105-9 (0.4) ^e
Ph	H	Ph	1.1	48	<u>d</u>	(m.p. 96-102°C)

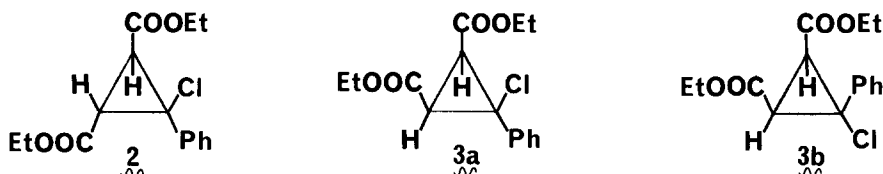
^a Reactions were generally performed with 1-2 mmol of diazirine. The combined diazirine/olefin solution was heated at 80°C in an oil bath, and gas evolution was monitored. ^b Products were identified by spectroscopic methods. Isomer ratios were determined by GC and/or NMR analyses. ^c Microanalyses for new compounds were in satisfactory agreement with calculated values. ^d Only one isomer was obtained. ^e Z-isomer: m.p. 78°C.

1.0. The high cyclopropane yields, the ease of cyclopropane isolation and purification, and the general applicability to electrophilic and nucleophilic olefins suggest that diazirine decomposition is the method of choice for many cyclopropane syntheses.

The facility of cyclopropane formation with α,β -unsaturated esters and nitriles was unexpected since, despite extensive investigations of the decomposition of 3-chloro-3-phenyldiazirine,^{1,3} there has been no reported example of its reaction with such nucleophilic olefins. We initially thought that these addition reactions might be the result of thermal isomerization of the diazirine to the corresponding diazo compound^{1a} with its subsequent dipolar addition to the α,β -unsaturated ester or nitrile and dinitrogen extrusion.⁹ However, three separate experimental observations rendered this pathway unlikely: (1) The rate of dinitrogen evolution is not markedly dependent on whether 3-chloro-3-phenyldiazirine is treated with butyl vinyl ether, styrene, ethyl acrylate, or any other of the olefins that have been employed. (2) Cyclopropane formation is remarkably free from competing reactions and occurs without formation of formal vinyl CH insertion products that are commonly observed from 1-pyrazoline decomposition.^{9,10} (3) Despite numerous attempts to trap potential 1-pyrazoline intermediates by addition of bases,¹¹ neither 2-pyrazoline nor pyrazole products were detected.

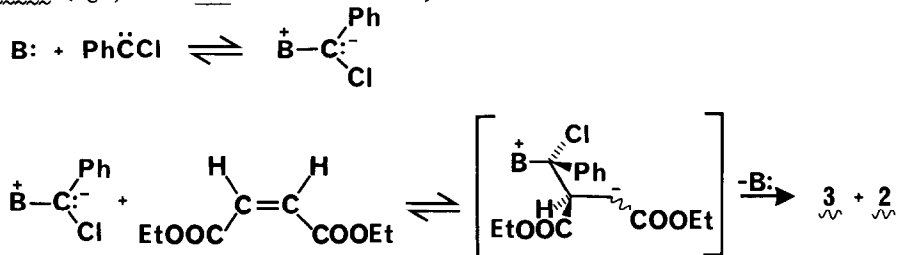
Relative reactivity studies were performed with butyl vinyl ether (BVE), styrene (STY), and ethyl acrylate (EAC). The order of relative reactivities for electrophilic addition to these three olefins was expected to be BVE>STY>EAC.¹² However, with 3-chloro-3-phenyldiazirine at 80°C, styrene was more reactive than either ethyl acrylate or butyl vinyl ether towards cyclopropanation, and individual olefin pairs gave relative reactivities of 5.18 (STY/BVE), 4.37 (STY/EAC), and 1.18 (EAC/BVE).

Interpretation of PhCCl as an electrophilic or nucleophilic carbene in addition reactions with α,β -unsaturated esters and nitriles was further complicated by results obtained from reactions with diethyl maleate. With diethyl fumarate (Table I) only one cyclopropane product is produced, and its structure retains the trans geometry of the carboethoxy groups (**2**). However, reaction with diethyl maleate under the same conditions produces three cyclopropane products: two that have retained the cis geometry of the carboethoxy groups (**3**, 79% relative yield, $\underline{3a}/\underline{3b} = 1.9$) and **2** (21% relative yield). Although product yields are low (16% of **2** + **3** when $[O]/[D] = 3.0$), the formation of **2** could not be



attributed to the amount of diethyl fumarate present in the maleate reactant (< 0.5%) or to isomerization of diethyl maleate, since diethyl fumarate was neither a product of this reaction nor was it formed in control experiments without diazirine. In addition, **3** did not isomerize under the reaction conditions or during analysis. The production of **2** in reactions of diethyl maleate with PhCCl demands a reaction intermediate whose lifetime allows bond rotation to occur.

Scheme I, which proposes the involvement of nucleophilic ylides for reactions with Scheme I (eg., B: = cis-EtOOCCH=CHCOOEt):



α,β -unsaturated esters and nitriles, is consistent with results that we have reported. Ylide formation is a characteristic carbene reaction¹³ whose role in cyclopropane-forming reactions¹⁴ has been overlooked. As expected from this interpretation, PhCCl addition to cis-stilbene is stereospecific although, like addition to diethyl maleate, the yield of cyclopropane products is low (< 10% yield when $[O]/[D] = 1.1$).

Acknowledgment. We thank the National Science Foundation for support of this research and for funding provided for the purchase of the GC/mass spectrometer and capillary GC employed for product determinations.

REFERENCES AND NOTES

1. (a) M.T.H. Liu, J. Chem. Soc., Perkin Trans. 2, 127 (1982). (b) E. Schmitz, Adv. Heterocyclic Chem., 24, 63 (1979). (c) P.S. Engel, Chem. Rev., 80, 99 (1980). (d) H. Meier and K.-P. Zeller, Angew. Chem., Int. Ed. Engl., 16, 835 (1977).
2. H.M. Frey, Adv. Photochem., 4, 225 (1966).
3. (a) M.T.H. Liu and K. Toriyama, J. Phys. Chem., 76, 797 (1972). (b) M.T.H. Liu and D.H.T. Chien, J. Chem. Soc., Perkin Trans. 2, 937 (1974).
4. (a) R.A. Moss and M. Jones, Jr., in "Reactive Intermediates", Vol. 2, M. Jones, Jr., and R.A. Moss, Ed., Wiley, New York, 1981, Chapter 3. (b) R.A. Moss, L.A. Perez, N.J. Turro, I.R. Gould, and N.P. Hacker, Tetrahedron Lett., 24, 685 (1983). (c) B. Giese, W.B. Lee, and C. Stiehl, ibid., 24, 881 (1983). (d) K.N. Houk, N.G. Rondan, M.N. Paddon-Row, C.W. Jefford, P.T. Huy, P.D. Burrow, and K.D. Jordan, J. Am. Chem. Soc., 105, 5563 (1983).
5. R.A. Moss, Acc. Chem. Res., 13, 58 (1980).
6. (a) N.J. Turro, J.A. Butcher, Jr., R.A. Moss, W. Guo, R.C. Munjal, and M. Fedorynski, J. Am. Chem. Soc., 102, 7576 (1980). (b) R.A. Moss, J.R. Whittle, and P. Freidenreich, J. Org. Chem., 34, 2220 (1969).
7. W.H. Graham, J. Am. Chem. Soc., 87, 4396 (1965).
8. M.T.H. Liu and K. Ramakrishnan, Tetrahedron Lett., 3139 (1977).
9. M.P. Doyle, R.L. Dorow, and W.H. Tamblin, J. Org. Chem., 47, 4059 (1982).
10. The only exception occurs in the reaction of 3-chloro-3-phenyldiazirine with cyclohexene where, in addition to the two cyclopropane isomers, products from CH insertion at the 3- and 4-positions are observed 7% and 8% yield, respectively. See also: M.T.H. Liu and K. Toriyama, Can. J. Chem., 50, 3009 (1972).
11. M.P. Doyle, M.R. Colman, and R.L. Dorow, J. Heterocyclic Chem., 20, 943 (1983).
12. F. Freeman, Chem. Rev., 75, 439 (1975).
13. M. Berkazi and J. Warkentin, J. Am. Chem. Soc., 105, 1289 (1983).
14. Y. Apeloig, M. Karni, and Z. Rappoport, J. Am. Chem. Soc., 105, 2784 (1983).

(Received in USA 1 November 1983)