Tetrahedron Letters,Vol.29,No.46,pp 5863-5866 1988 0040-4039/88 $3.00 + .00
Printed in Great Britain Pergamon Press plc

REACTIVITY AND SELECTIVITY IN INTERMOLECULAR INSERTION REACTIONS OF CHLOROPHENYLCARBENE

*Michael P. Doyle**‡, *Jack Taunton, and Su-Min Oon*
Department of Chemistry, Trinity University, San Antonio, Texas 78284

*Michael T.H. Liu** *and N. Soundararajan*
Department of Chemistry, University of Prince Edward Island
Charlottetown, Prince Edward Island, Canada C1A 4P3

*Matthew S. Platz** *and James E. Jackson*+
Department of Chemistry, Ohio State University, Columbus, Ohio 43210

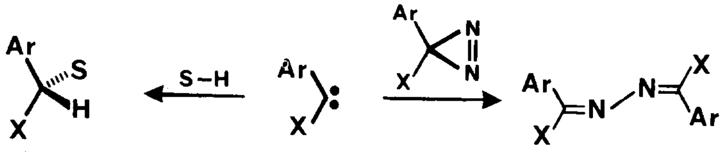
Summary: Reactivities for intermolecular C-H/Si-H/Sn-H insertion reactions of chlorophenylcarbene follow the order tri-*n*-butyltin hydride>>diphenylsilane>triethylsilane>> cumene>ethylbenzene>>toluene, and these reactions are competitive with addition to the double bond of α,β-unsaturated esters.

Although a considerable amount of information about the reactivities and selectivities of carbenes is now available,[1] the vast majority of our knowledge about these highly reactive intermediates has been obtained from olefin addition reactions. Meager attention has been given to intermolecular insertion reactions by carbenes into carbon-hydrogen and related group 4A-hydrogen bonds. Originating in early investigations of methylene insertion into hydrocarbons,[2] a general impression has existed that carbenes are relatively unselective in these transformations. Recently, however, Steinbeck and Klein have communicated that halophenylcarbenes, generated under phase-transfer conditions from the corresponding benzal halides in the presence of 18-Crown-6, undergo selective carbon-hydrogen insertion with cumene, adamantane, and 2-methyltetrahydrofuran, although in low yields.[3] Padwa and Eastman,[4] in an earlier investigation, showed that 3-chloro-3-phenyldiazirine underwent decomposition in the presence of tri-*n*-butyltin hydride to yield the Sn-H insertion product. Similar transformations with dihalocarbenes from phenyl(trihalomethyl)mercury compounds[5] or haloform solvents[6] and with unsaturated carbenes[7] have been documented, but reactivities of carbenes for insertion have not been determined.

Diazirines are effective precursors of carbenes in photochemical and thermal reactions, and 3-aryl-3-halodiazirines, which are conveniently prepared by Graham's procedure,[8] are optimum starting materials for the generation of arylhalocarbenes. Since the major competing process in carbene reactions initiated by decomposition of diazirines is azine formation (eq. 1),[9] insertion

---

‡Author to whom inquiries should be sent. +Current address: Department of Chemistry, Michigan State University, East Lansing, Michigan 48824.



P

(1)

reactions should be limited only by the relative reactivity of the carbene towards the S-H substrate. We have undertaken investigations of these transformations and now wish to report the high selectivity that can be achieved in reactions of arylchlorocarbenes with compounds containing C-H, Si-H, and Sn-H bonds.

Treatment of a series of representative substrates with 3-chloro-3-phenyldiazirine (CPD) in refluxing benzene provided the results that are reported in Table I. Both Si-H and Sn-H insertion reactions are extremely facile, providing excellent yields of the S-H insertion product even when the substrate is employed in only a 3- to 5-fold excess over the reactant diazirine. With hydrocarbons, however, the relative reactivities for insertion into a benzylic and/or tertiary C-H bond, relative to azine formation, are much lower, although selectivity is surprisingly high. In all cases where comparative data is available, yields of insertion products formed with the use of chlorophenyldiazirine are 2- to 4-times those obtained under phase-transfer conditions from benzal chloride.[3]

Table I. Insertion Reactions of Chlorophenylcarbene[a]

Substrate (S-H)	[S-H]/[CPD]	Product (P)[b]	Yield, %	P/Azine
n-Bu_3SnH	5.0	n-$Bu_3SnCH(Cl)Ph$	85	>100
Et_3SiH	8.0 (4.0)	$Et_3SiCH(Cl)Ph$	91 (74)	>100
Ph_2SiH_2	3.4	$Ph_2SiHCH(Cl)Ph$	80	>100
$PhCH_3$	10	$PhCH_2CH(Cl)Ph$	21	0.31
$PhCH_2CH_3$	10	$PhCH(CH_3)CH(Cl)Ph$[c]	61	2.2
$PhCH(CH_3)_2$	10	$PhC(CH_3)_2CH(Cl)Ph$	62	3.2
Ph_2CH_2	5.0	$Ph_2CHCH(Cl)Ph$	40	1.0
Adamantane (AdH)	2.8	AdCH(Cl)Ph	46	3.0

[a] Reactions were performed in refluxing benzene at reaction times of 3 h. [b] Only insertion product observed. Other reaction products included azine and benzal chloride. [c] Two diasterioisomers in a 1.1:1.0 ratio.

As anticipated from parallel competing reactions (eq. 1), the ratio of the insertion product to azine increases linearly with increasing [S-H] at constant diazirine concentration in thermal decomposition reactions. Thus increasing the molar reactant ratio of S-H to CPD effectively minimizes azine formation. Similar results are obtained in photochemical decompositions of CPD at room temperature. However, at -196°C photochemical decomposition of CPD in the glass matrix of either toluene or cumene results in only the corresponding insertion products, and the azine is not observed. Under these conditions chlorophenylcarbene is generated in close proximity to the hydrocarbon substrate, and effective reaction with an intact diazirine is restricted.

Relative reactivities were determined from product ratios obtained by decomposition of CPD in the presence of a minimum 10-fold molar excess of substrate pairs with suitable cross-checks using mixed pairs and varying S-H/S'-H ratios. For example, product ratios from the thermal decomposition of CPD in refluxing benzene were 1.7 for cumene/ethylbenzene, 9.1 for ethylbenzene/toluene, and 15.4 for cumene/toluene. These results, which are given in Table II, clearly establish the reactivity scale for benzylic C-H insertion as methine>methylene>>methyl. Photolytic decomposition of CPD provides slightly greater selectivities for C-H/Si-H insertion than those observed for the thermal reactions. However, carbene insertion into the methylene C-H bonds of pentane, which is employed as the solvent, is competitive with benzylic C-H insertion into toluene, ethylbenzene, and cumene.[10]

Laser flash photolysis (LFP) studies of the quenching of chlorophenylcarbene by representative substrates[11] established their absolute rate constants which, by extrapolation through the hydrocarbon relative reactivity series, provides the values for k_{calcd} that are reported in Table II. The carbene generated from CPD by LFP decays slowly in the absence of quenchers. However, addition of S-H or olefinic quenchers accelerates the carbene decay kinetics and produces a time course described by a single exponential rate process from which the reported values of k_{obs} are obtained through kinetic determinations at various concentrations of quencher.

Table II. Relative and Absolute Reactivities of Chlorophenylcarbene in Intermolecular Insertion Reactions

	relative reactivity[a]			
Substrate	thermal[b]	photochemical[c]	k_{obs}, $M^{-1}s^{-1}$	k_{calcd}, $M^{-1}s^{-1}$[d]
Toluene	0.065	0.044	-	7.5×10^3
Ethylbenzene	0.61	0.48	-	8.2×10^4
Cumene	1.00	1.00	1.7×10^5	(1.8×10^5)[e]
Diethyl maleate	0.48	*f*	1.5×10^5	
Triethylsilane	7.8	14	2.5×10^6	2.4×10^6
Diethyl fumarate	15	*f*	3.5×10^6	
Diphenylsilane	13	31	5.7×10^6	
Tri-*n*-butyltin hydride	1.9×10^2	*g*	1.0×10^8	

[a]Based on molar amounts of substrates from competitive experiments; not calculated with adjustments for number of equivalent hydrogens. [b]Reactions performed in refluxing benzene. [c]Reactions performed in pentane with 350 nm excitation at room temperature. [d]Calculated from relative reactivities using k_{obs} for cumene. [e]Calculated from k_{obs} for triethylsilane. [f]Olefin isomerization prevented determination. [g]Radical reactions prevented determination; hexa-*n*-butyldistannane was a major product.

As is evident from the data, C-H insertion by chlorophenylcarbene can be a facile process. The rate constant for insertion into the methine C-H bond of cumene is comparable to that observed for addition to the double bond of diethyl maleate, but methylene and, even more so, methyl insertion are substantially slower. Organosilanes are comparable to diethyl fumarate in their ability to quench chlorophenylcarbene. With tri-*n*-butyltin hydride, however, the rate constant for Sn-H insertion is even greater than those for addition to the carbon-carbon double bond of most alkenes, including 2,3-dimethyl-2-butene and 2-methyl-2-butene.[12]

Acknowledgement. Financial support from the Robert A Welch Foundation (M.P.D.), the N.S.E.R.C. of Canada (M.T.H.L.), and the National Science Foundation (CHE-8513498 to M.S.P.) is gratefully achnowledged.

References and Notes

(1) (a) Moss, R.A.; Jones, M., Jr. In "Reactive Intermediates", Vol. 3; Jones, M., Jr.; Moss, R.A., Eds.; John Wiley & Sons: New York, 1985; Chapter 3. (b) Doyle, M.P. In "Chemistry of Diazirines"; Liu, M.T.H., Ed.; CRC Press: Boca Raton, FL, 1987; Chapter 8. (c) Soundararajan, N. Platz, M.A., Jackson, J.E., Doyle, M.P., Oon, S.-M., Liu, M.T.H., and Anand, S.M.*J. Am. Chem. Soc.*, in press.

(2) Kirmse, W. "Carbene Chemistry"; Academic Press: New York, 1964.

(3) Steinbeck, K.; Klein, J. *Angew. Chem. Int. Ed. Engl.* **1981**, *20*, 773.

(4) Padwa, A.; Eastman, D. *J. Org. Chem.* **1969**, *34*, 2728.

(5) (a) Seyferth, D.; Burlitch, J.M.; Dertouzos, H.; Simmons, H.D., Jr. *J. Organometal. Chem.* **1967**, *7*, 405. (b) Seyferth, D.; Damrauer, R.; Mui, J. Y.-P.; Jula, T.F. *J. Am. Chem. Soc.* **1968**, *90*, 2944. (c) Seyferth, D.; Burlitch, J.M.; Yamamoto, K.; Washburne, S.S.; Attridge, C.J. *J. Org. Chem.* **1970**, *35*, 1989 (d) Seyferth, D.; Cheng, Y.M. *J. Am. Chem. Soc.* **1973**, *75*, 6763.

(6) Steinbeck, K.; Klein, J. *Tetrahedron Lett.* **1978**, 1103.

(7) Stang, P.J.; Learned, A.E. *J. Am. Chem. Soc.* **1987**, *109*, 5019.

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

(9) Doyle, M.P.; Devia, A.H.; Bassett, K.E.; Terpstra, J.W.; Mahapatro, S.N. *J. Org. Chem.* **1987**, *52*, 1619.

(10) The ratio of products from insertion into the methylene C-H bonds of pentane was 1:1 which suggest a 4-fold greater reactivity of the methylene group at the 3-position.

(11) Samples of diazirines were dissolved in spectral grade solvents to give absorbances of *ca.* 0.1 at 351 nm, placed in 1 cm^2 suprasil cells, degassed by N_2 bubbling, and irradiated with the pulses of a lumonics TE-861-4 Excimer laser (Xe, F_2, He gas mix, 351 nm, 10 ns, *ca.* 80 mj). Kinetic studies were performed on 11 static samples containing verying concentrations of the quenching reagent to be studied. Three k_{obs} measurements were made at each quencher concentration. For more details see reference 1c.

(12) (a) Gould, I.R.; Turro, N.J.; Butcher, J., Jr.; Doubleday, C., Jr.; Hacker, N.P.; Lehr, G.F.; Moss, R.A.; Cox D.P.; Guo, W.; Munjial, R.C.; Perez, L.A.; Fedorynski, M. *Tetrahedron* **1985**, *41*, 1587. (b) Moss, R.A.; Lawrymowicz, W.; Turro, N.J.; Gould, I.R.; Cha, Y. *J. Am. Chem. Soc.* **1986**, *108*, 7028.

(Received in USA 28 July 1988)