Pergamon

Tetrahedron Letters, Vol. 37, No. 3, pp. 279-282, 1996

0040-4039/96 $15.00 + 0.00

0040-4039(95)02149-3

Kinetic Isotope Effects on the 1,3-Intramolecular Insertion Reaction of t-Butylchlorocarbene

Robert A. Moss* and Weiguo Liu

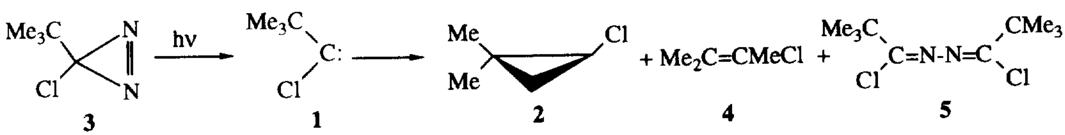
Department of Chemistry, Rutgers, The State University of New Jersey, New Brunswick, New Jersey 08903

Summary. The primary kinetic isotope effect for the 1,3-CH(D) insertion reaction of t-butylchlorocarbene-$\underline{d}_6$ ranges from 3.25 at -12 °C to 2.14 at 118 °C; tunneling is not apparent in this temperature interval.

Recent studies of the kinetic isotope effects (KIE) associated with intramolecular carbenic insertions furnish surprising results, including unexpectedly high values of $\underline{k}_H/\underline{k}_D$ (~3-5) for the ambient temperature 1,2-H(D) shifts of neopentylchlorocarbene,[1] neopentylfluorocarbene,[2] and dimethylcarbene.[3] Additionally, methylchlorocarbene and methylchlorocarbene-$\underline{d}_3$ exhibit curved Arrhenius plots of ln $\underline{k}$(1,2-H(D) shift) vs. 1/T over the temperature range 248-343 K, and a KIE that increases from 0.9-1.8 as the temperature rises.[4] Both quantum mechanical tunneling (QMT) and classical 1,2-H(D) shifts may contribute to the rearrangement of methylchlorocarbene to vinyl chloride, with QMT dominant at lower temperatures.[4,5]

Methylbromocarbene[6] and benzylchlorocarbene[7] similarly display curved Arrhenius correlations for both α-H and α-D carbenes, with QMT again a possible cause of the curvature. In the case of benzylchlorocarbene, matrix isolation studies of the α,α-$\underline{d}_2$ carbene at 10 K suggest a KIE ~ 2000, implicating QMT in the low temperature regime.[8]

Similarly, matrix isolation of t-butylchlorocarbene (t-BuCCl, **1**) in nitrogen matrices shows that the 1,3-CH insertion to 1,2-dimethyl-2-chlorocyclopropane (**2**) occurs at a finite rate ($\underline{k}$ ~ 3×10^{-5} - 4×10^{-4} s^{-1}) even at 11 K, and is temperature independent from 11-30 K.[9] In contrast, the perdeuterocarbene, **1**-$\underline{d}_9$, is persistent in the matrix; no C-D insertion occurs over 40 h at 14 K or 48 h at 30 K.[9]



(1)

The temperature independence of the insertion rate at very low temperature, together with the necessarily very large KIE, are strong evidence for QMT conversion of **1**→**2** at very low temperature.

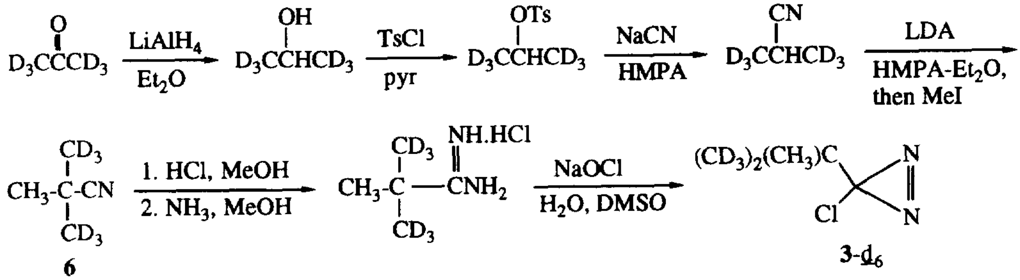
Our prior studies of carbene **1** in solution revealed that photolysis of diazirine **3** afforded cyclopropane

2, the 1,2-Me shifted alkene, **4**, and azine **5**, eq. (1).[10] Importantly, carbene trapping experiments with 2-methyl-1-butene demonstrated that the cyclopropane arose from carbene **1** by intramolecular insertion,[11] whereas alkene **4** stemmed directly from an untrappable photoexcited state of diazirine **3**. The carbene could undergo a thermally-driven 1,2-Me shift to **4** (~10%) at higher temperature (79 °C), but did not appreciably do so at ambient temperature.[10c,12]

In view of the demonstrated importance of tunneling in the low temperature reactions of 1,[9] and the unusual KIE associated with methylchlorocarbene,[4,5] we have now determined (intramolecular) KIE's for the 1,3-CH insertion reaction of **1** from -12 to 118 °C. Over this temperature regime, the KIE's are of normal magnitude, exhibit normal temperature dependence, and afford no overt evidence for QMT.

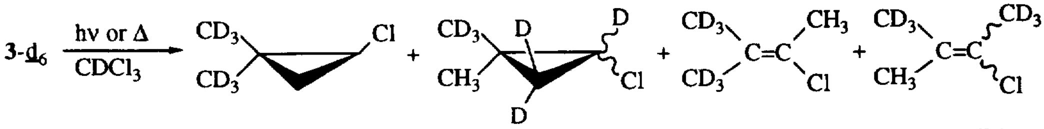
The requisite carbene precursor [3-(t-butyl-d_6)-3-chlorodiazirine, **3-d_6**] was prepared from pivalonitrile-d_6 as outlined in Scheme 1. Reduction of acetone-d_6 (>99%) d_6) with $LiAlH_4$ (25 °C, 1 h, 63%) gave isopropanol-d_6, which was converted to the tosylate (TsCl, pyr, 20 °C, 3 h, 71%), and thence to isobutyronitrile-d_6 (NaCN, HMPA,[13] 100 °C, 3 h, 18%). Methylation (LDA,[14] Et_2O, N_2 atm., -78 °C, 40 min, then MeI, to 25 °C, 3 h, 93%) then gave pivalonitrile-d_6, **6**. Finally, nitrile **6** was converted to diazirine **3-d_6** by Pinner reaction (HCl, MeOH) to the iminoester, ammonolysis to the amidine hydrochloride (31%) and Graham oxidation to the diazirine (~50%).[10,15,16]

Scheme 1



Photochemical decomposition of **3-d_6** was carried out in $CDCl_3$,[17] with product analysis by 200 MHz ^1H NMR on $CDCl_3$ solutions that were first concentrated by careful fractional distillation, and then flash distilled to rid the samples of azine. The products[10] obtained from **3-d_6** are shown in eq. (2), where the cyclopropanes **2a** and (isomers) **2b**, **2b′** stem from C-H or C-D insertion, respectively, whereas the alkenes **4a** and (isomers) **4b**, **4b′** arise from CH_3 or CD_3 shifts. Only the cyclopropanes are considered to be products of the carbene when it is generated photochemically.[10c] Thermal decompositions of **3-d_6** yield the same products as photolysis, with cyclopropanes and alkenes both attributable to the carbene.[10c]

Cyclopropane **2a** exhibits ^1H NMR multiplets for its 3 cyclopropyl protons that are centered at (δ) 0.54, 0.84, and 2.88. The isomeric pair of cyclopropanes **2b**, **2b′** display CH_3 singlets at 1.07 and 1.23. From



2a **2b, 2b'** **4a** **4b, 4b'** (2)

the appropriate ratio of integral areas, corrected for the 2:1 CD_3/CH_3 bias in carbene **1**-$\underline{d}_6$, 200 MHz NMR analysis of the reaction product mixture affords $\underline{k}_H/\underline{k}_D$ for the 1,3-insertions of **1**-$\underline{d}_6$. Data appear in Table 1 for decompositions of **3**-$\underline{d}_6$ under varied conditions.

The CH_3 resonances of the methyl shift alkene products **4a** and **4b**, **4b′** appear at 2.08 and 1.81, 1.72, respectively, so that NMR integration also affords the **4a**/(**4b** + **4b′**) ratio. Statistical correction then yields the secondary KIE for CH_3 vs. CD_3 shifts of carbene **1**-$\underline{d}_6$. These data also appear in Table 1, where the KIE's are seen to be small.

If we neglect the secondary KIE on the CH_3 migration of **1**-$\underline{d}_6$, then the primary KIE's for the 1,3-insertion reactions can also be derived from $(\underline{k}_{ins}/\underline{k}_{-Me})_{1\text{-}\underline{d}_0}/(\underline{k}_{CD\ ins}/\underline{k}_{-Me})_{1\text{-}\underline{d}_6}$, where we compare the ratio of C-H insertion to CH_3 migration of carbene **1** with the ratio of C-D insertion (**2b**, **2b′**) to CH_3 migration (**4a**) of carbene **1**-$\underline{d}_6$. Appropriate NMR integrations give these data (shown in parentheses in Table 1), which are in good agreement with the KIE's derived from the insertion products **2a** and **2b**, **2b′**.

The data are consistent with a classical primary KIE operative during the 1,3-CH(D) insertions of **1**-$\underline{d}_6$ in the temperature range -12 to 118 °C (261-391 K). The tunneling mechanism, so strongly evident at 30 K,[9] is not readily detectable at the higher temperatures,[18,19] where the KIE decreases with increasing temperature, as expected for a classical insertion mechanism.[20]

The "normal" behavior of the 1,3-CH insertion KIE of carbene **1** resembles that observed for the 1,2-H(D) shift primary KIE's of the neopentylhalocarbenes,[1,2] but markedly contrasts to that reported for methylchlorocarbene.[4] In this latter case, the (small) KIE increases from 0.9 - 1.8 as the temperature rises from 248-343 K, and it is at least conceivable that tunneling may significantly contribute even at ambient temperatures.[4] More to the point, the "blends" of classical and QMT contributions to the 1,2-H migration of methylchlorocarbene and the 1,3-CH insertion of $\underline{t}$-butylchlorocarbene differ, so that the associated KIE's and their temperature dependences diverge. Apparently, the influence of QMT persists at higher temperatures in the 1,2-H shift more than in the 1,3-CH insertion.

Acknowledgment. We are grateful to the National Science Foundation for financial support.

Table 1. Isotope Effects in the Reactions of t-Butylchlorocarbene-d_6[a]

Decomposition of **3**-d_6[b]	k_H/k_D, 1,3-insertion[c]	k_H/k_D, ~CH_3/~CD_3
hν (-12)	3.25	----
hν (22)	2.92	1.10
Δ (61)	2.72 (2.74)	1.07
Δ (88)	2.48 (2.49)	1.07
Δ (100)	2.52 (2.52)	1.09
Δ (118)	2.14 (2.19)	1.02

[a] Errors in the isotope effects are ±10%; decomposition temperatures were held to ±2 °C. [b] Temperatures (°C) are shown in parenthesis. [c] Data in parentheses are derived from the ratios of C-H (C-D) insertion to CH_3 migration; see text.

References and Notes

(1) Moss, R.A.; Ho, G-J.; Liu, W.; Sierakowski, C. Tetrahedron Lett. **1993**, 34, 927.
(2) Moss, R.A.; Ho, G-J.; Liu, W.; Sierakowski, C. Tetrahedron Lett. **1992**, 33, 4287.
(3) Modarelli, D.A.; Morgan, S.; Platz, M.S. J. Am. Chem. Soc. **1992**, 114, 7034. It was suggested that a tunneling contribution might be partly responsible for the "high" KIE (3.2).
(4) Dix, E.J.; Herman, M.S.; Goodman, J.L. J. Am. Chem. Soc. **1993**, 115, 10424.
(5) Storer, J.W.; Houk, K.N. J. Am. Chem. Soc. **1993**, 115, 10426.
(6) Dix, E.J.; Goodman, J.L. Res. Chem. Int. **1994**, 20, 149.
(7) Liu, M.T.H.; Bonneau, R.; Wierlacher, S.; Sander, W. J. Photochem. Photobiol. A: Chem. **1994**, 84, 133.
(8) Wierlacher, S.; Sander, W.; Liu, M.T.H. J. Am. Chem. Soc. **1993**, 115, 8943.
(9) Zuev, P.S.; Sheridan, R.S. J. Am. Chem. Soc. **1994**, 116, 4123.
(10) (a) Moss, R.A.; Munjal, R.C. Chem. Commun. **1978**, 775. (b) Moss, R.A.; Ho, G-J. J. Am. Chem. Soc. **1990**, 112, 5642. (c) Moss, R.A.; Liu, W. Chem. Commun. **1993**, 1597.
(11) Laser flash photolysis gave the **1**→**2** rate constant as ~9×10^5 s^{-1} in isooctane at 25 °C.[10b,c]
(12) Not surprisingly, carbene **1** does not significantly rearrange to **4** in low temperature matrices.[9]
(13) Stephenson, B.; Solladié, G.; Mosher, H.S. J. Am. Chem. Soc. **1972**, 94, 4184.
(14) Cregge, R.J.; Herrmann, J.L.; Lee, C.S.; Richman, J.E.; Schlessinger, R.H. Tetrahedron Lett. **1973**, 2425.
(15) Graham, W.H. J. Am. Chem. Soc. **1965**, 87, 4396.
(16) ^{1}H NMR analysis of the amidine salt indicated >98% d_6.
(17) Conditions: focused Osram XE UV lamp, λ > 320 nm, A_{346} of **3**-d_6=0.8, 7 h.
(18) Attempts to study the insertion KIE in solution at temperatures much lower than -12 °C were frustrated by large scale formation of azine **5** (d_{12}).
(19) An Arrhenius treatment of the data in Table 1 gives ΔE_a ~0.56 kcal/mol for the C-H vs. C-D insertions of **1**-d_6. Extrapolation to 30 K generates a very large KIE, consistent with the observed persistence[9] of perdeutero-**1**.
(20) The magnitude and temperature dependence of the KIE's for the conversion of **1**-d_6 to cyclopropanes **2a** and **2b**, **2b′** are similar to those for conversion of α-iodoneopentyllithium-d_6 [$CH_3(CD_3)_2CCHILi$] to the corresponding isomeric d_6-dimethylcyclopropanes.[21] The latter (carbenoid) C-H/C-D insertions afford KIE's of 2.76 and 2.43 at -90 and -44 °C, respectively.
(21) Goldstein, M.J.; Dolbier, W.R., Jr.; J. Am. Chem. Soc. **1965**, 87, 2293.

(*Received in USA* 30 *October* 1995; *revised* 7 *November* 1995; *accepted* 9 *November* 1995)