manzamine H (**3**, 0.9 mg). A total of 0.8 mg of **2** was recovered.

DDQ Oxidation of Compound 3. To a stirred solution of **3** (4.3 mg) in EtOH (0.1 mL) and $CHCl_3$ (0.3 mL) at room temperature was added DDQ (2.8 mg). The mixture was stirred for 30 min. After evaporation of the solvent, the residue was passed through a silica gel column (0.5 × 5 cm) with $CHCl_3$ to afford manzamine J (**4**, 1.6 mg).

Treatment of Manzamine B (6) with NaH. To a stirred solution of **6** (10.0 mg) in DMF (1 mL) at room temperature was added NaH (7.1 mg). The mixture was refluxed for 12 h. To the reaction mixture was added 1 N HCl/MeOH (0.25 mL). After evaporation of the solvent, the residue was passed through a silica gel column (0.5 × 5 cm) with $CHCl_3$ to afford compound **4** (3.0 mg). A total of 4.2 mg of **6** was recovered.

Biological Assay. Antitumor activity was determined by using L1210 murine leukemia cells and KB human epidermoid carcinoma cells according to the method previously reported.[10]

Acknowledgment. We thank Mr. Z. Nagahama for his help in collecting the sponge and Dr. P. R. Bergquist, The University of Auckland, for identification of the sponge.

Supplementary Material Available: All spectra of ircinals A and B and manzamines H and J (39 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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Study of 1,2-Chlorine Migration in (α,α-Dichlorobenzyl)chlorocarbene Generated by Laser Flash Photolysis of 3-Chloro-3-(α,α-dichlorobenzyl)diazirine

Michael T. H. Liu*

Department of Chemistry, University of Prince Edward Island, Charlottetown, P.E.I., Canada C1A 4P3

Roland Bonneau

URA 348 du CNRS, Laboratoire de Chimie Physique A, Universite de Bordeaux 1, 33405 Talence Cedex, France

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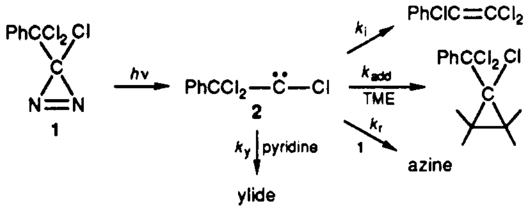
Although the literature is replete with information[1-5] on 1,2-hydrogen shifts in carbenes, few investigations involving chlorine migration to a carbene center are reported. By employing the laser flash photolysis (LFP) technique and the appropriate carbene precursors, the rates for 1,2-hydrogen shift in benzyl-[6] and alkylchorocarbenes[7] have been reported recently. We now report the LFP of 3-chloro-3-(α,α-dichlorobenzyl)diazirine. The results that we obtained lead to the rate of a 1,2-chlorine shift[8] in (α,α-dichlorobenzyl)chlorocarbene, **2**. The rate constants for the addition of carbene **2** to tetramethylethylene (TME) and diazirine **1** were obtained as well.



Results and Discussion

In the case of benzylchlorocarbene,[6] it was possible to observe directly the transient absorption (carbene) in the 280–330-nm window. However, since the extinction coefficient for diazirine **1** is very low at the exitation wavelength, we use a high concentration of diazirine (0.22 M) for the LFP experiments. As a result, the window at 280–330 nm is not transparent for the observation of the carbene. Similar to the benzylchlorocarbene, the LFP of **1** in isooctane in the presence of pyridine produces a transient species with an absorption at 370 nm. This transient is not present in the absence of pyridine and is attributed to the pyridinium ylide. Normally, the rate of formation of the ylide allows the determination of the absolute rate constant for the 1,2-shift in carbene by plotting the observed pseudo-first-order rate constants for growth of the absorption at 370 nm vs [pyridine]. The slope gives the rate constant for reaction of the carbene with pyridine, and the intercept, [pyridine] = 0, yields the rate constant for 1,2-shift. Upon the addition of a small amount (0.62 mM) of pyridine in a 0.22 M diazirine solution, the growth of the transient at 370 nm is already 20 ns. Therefore, an alternative Stern–Volmer analysis for the amount of ylide is sought for the determination of the rate constant for 1,2-chlorine shift. Also, the quenching reaction of carbene by diazirine to form azine is included in the scheme since this reaction has been recently noted by us[9] and by other investigators.[10,11] k_1 is the rate constant representing the sum of all first-order and pseudo-first-order decay pathways of the carbene in the absence of pyridine, $k_1 = k_i + k_r[1]$. The yield for ylide formation is given by $\phi_{ylide} = k_y[py]/(k_1 + k_y[py])$ and the amount of carbene produced in a single pulse is [carbene] = αE, where E is the reading of the energy meter monitoring the

$$\text{carbene (2)} \rightarrow \text{styrene}, k_i$$

$$\text{carbene (2)} + \text{diazirine} \rightarrow \text{azine}, k_r$$

$$\text{carbene (2)} + \text{pyridine} \rightarrow \text{ylide}, k_y$$

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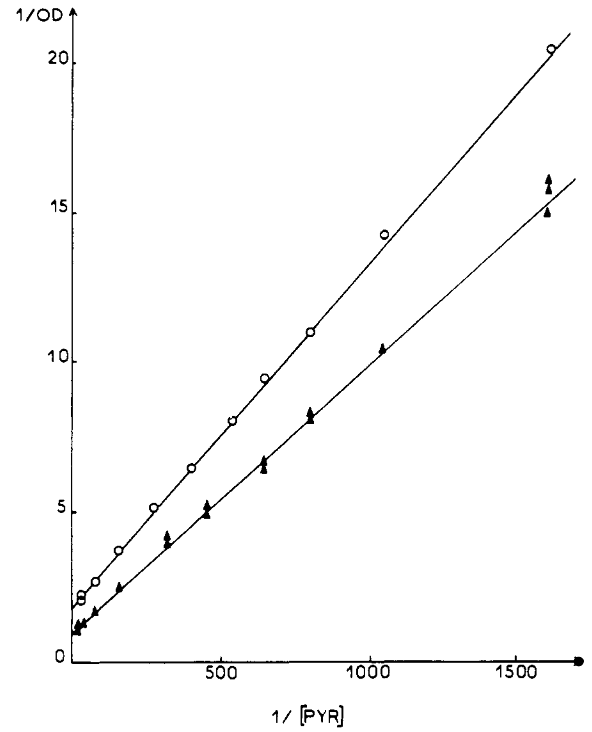

Figure 1. Plots of 1/OD vs 1/[pyridine] at 25 °C. Upper line, [1] = 0.22 M; lower line, [1] = 0.60 M.

laser pulse intensity and α is a proportionality factor. The ylide absorption is OD = [ylide]ϵl, and it follows that

$$\frac{1}{OD} = \frac{1}{\alpha E}\left(\frac{1}{\epsilon l} + \frac{k_1}{\epsilon l k_y}\cdot\frac{1}{[py]}\right)$$

For each initial concentration of diazirine, we performed LFP experiments (298 K) at 10 different concentrations of pyridine (0.5–40 mM). The straight line plot 1/OD vs 1/[pyridine] at 25 °C for [1] = 0.22 M is given in Figure 1 in which the slope and intercept are 11.6×10^{-3} and 1.9, respectively. Thus, the ratio of the slope/intercept leads to a value of 6.1×10^{-3} for k_1/k_y, and if k_y is taken[7] as 8×10^9 M^{-1} s^{-1}, then $k_1 = 4.8 \times 10^7$ s^{-1}. For [1] = 0.60 M, LFP experiments yielded 1.0×10^{-2} for the ratio of the slope/intercept; hence, $k_1 = 8.0 \times 10^7$ s^{-1}. Notice that the intercepts for the two plots are different since they depend on energy absorbed which in turn depends on the concentration of diazirine. With the two known concentrations of diazirine, the values for k_i (3.0×10^7 s^{-1}) and k_r (8.4×10^7 M^{-1} s^{-1}) can be calculated at 25 °C. The present k_r value is in excellent agreement with the rate constant for the reaction of benzylchlorocarbene with diazirine (3.6×10^8 M^{-1} s^{-1}) as determined by direct observation of the carbene quenching by diazirine.[9] As well, the lifetime of 33 ns for 1,2-chlorine shift in carbene is comparable to the 18-ns lifetime for 1,2-H shift in benzylchlorocarbene.[6] In both instances, the introduction of a methyl substituent on the α-carbon for $PhCH_2\ddot{C}Cl$ and $PhCCl_2\ddot{C}Cl$ reduces the lifetime of these carbenes to ~1 ns. In this respect, the 1,2-H migration and 1,2-Cl migration to a carbene center are similar. Thus, for 1,2-H migration: $PhC(CH_3)H\ddot{C}Cl$[7] (τ = 1 ns) > $PhCH_2\ddot{C}Cl$[6] (τ = 18 ns) > $CH_3\ddot{C}Cl$[12] (τ = 330 ns) and for 1,2-Cl migration $PhC(CH_3)ClC\ddot{C}l$[8] (τ ~ 1 ns) > $PhCCl_2\ddot{C}Cl$ (τ = 33 ns) > $CCl_3\ddot{C}Cl$ (τ = ?). The τ for $CCl_3\ddot{C}Cl$ has yet to be determined, but considering these reactivities it is expected to have a long lifetime. It appears much to our surprise that the rate constant, $k = 1/\tau$, does not appear to vary significantly with the nature of the migrating species.

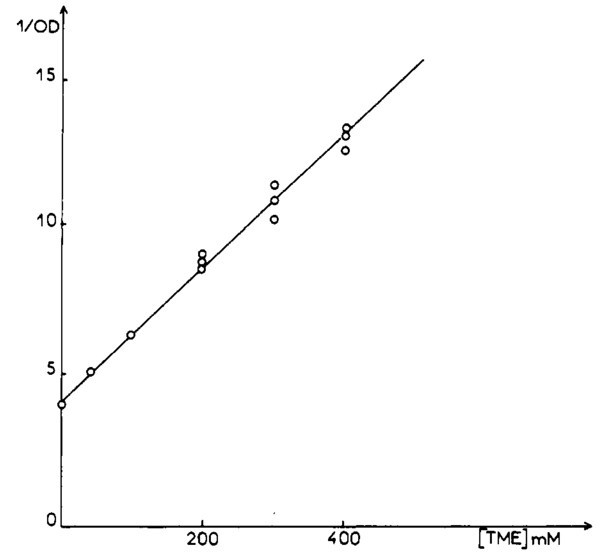

Figure 2. Plot of 1/OD vs [TME] at 25 °C. [1] = 0.22 M and [pyridine] = 6.2×10^{-3} M.

The reactivity of carbene 2 toward alkene substrates such as tetramethylethylene can also be measured according to the above method. The yield of ylide formation is now given by $\phi_{ylide} = k_y[py]/(k_1 + k_y[py] + k_{add}[TME])$.

$$\frac{1}{OD} = \frac{1}{\alpha E}\left(\frac{k_1 + k_y[py]}{\epsilon l k_y[py]} + \frac{k_{add}}{\epsilon l k_y[py]}[TME]\right)$$

For [diazirine 1] = 0.22 M and a constant concentration of pyridine, 6.2×10^{-3} M, we performed LFP experiment (298 K) at five different concentrations of TME 40–400 mM). The variation of the OD for ylide absorption at 370 nm was measured as a function of TME concentrations and the linear plot for 1/OD vs [TME] is displayed in Figure 2. The slope and intercept are 22.6 ± 2 and 4.1 ± 0.2, respectively. Hence, the ratio of slope/intercept yielded a value of 5.5 for $k_{add}/(k_1 + k_y[py])$. Substituting the values for k_1 and k_y[py], the rate constant for the addition of carbene 2 to TME at 25 °C is $(5.5 \pm 1.0) \times 10^8$ M^{-1} s^{-1}, in agreement with the rate constant for the reaction of benzylchlorocarbene[6] with TME (6.0×10^8 M^{-1} s^{-1}).

Experimental Section

3-Chloro-3-(α,α-dichlorobenzyl)diazirine 1, was prepared by the oxidation of the α,α-dichlorobenzylamidine according to Graham's method[13] and purified by chromatography on 60–200-mesh silica gel. 1: IR 1560 cm^{-1} (N=N); UV 328 (ϵ = 31 L mol^{-1} cm^{-1}), 344 (ϵ = 29), 355 nm (ϵ = 2). After photolysis or thermolysis of 1, the solvent was removed under reduced pressure, followed by column chromatography (hexane + 2% ethyl acetate) on silica, and the product(s) was subjected to ^1H NMR, GC, and GCMS analyses. An internal standard, dibenzyl ether, was employed to obtain product yields. Photolysis or thermolysis of 0.1 M of 1 in isooctane yielded α-chloro-β,β-dichlorostyrene (95%): MS *m/e* 210 (24), 208 (75), 206 (81), 171 (60), 136 (100). Photolysis (300 nm, 10 h at 25 °C) of 0.1 M of 1 in isooctane in the presence of a 10-fold excess of tetramethylethylene (TME) yielded α-chloro-β,β-dichlorostyrene (30%) and the 1-chloro-1-(α,α-dichlorobenzyl)-2,2,3,3-tetramethylcyclopropane (60%): MS *m/e* 212 (2), 210 (16), 208 (50), 206 (51), 175 (8), 173 (45), 171 (70),

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136 (100), 84 (23); ^{1}H NMR (CDCl$_3$) δ 7.3-8.0 (m, Ph, 5 H), 0.7-1.5 (m, CH$_3$, 12 H). Pyridine was distilled over CaH$_2$.

The laser flash photolysis setup uses a crossed-beam arrangement. The sample, in a 10- × 10-mm cell, was excited at 355 nm by single light pulses (200 ps; 5-30 mJ) provided by a frequency tripled mode-locked Nd-YAG laser (Quantel). The detection system (pulsed Xe arc, monochromator, photomultiplier, and Tektronix 7912 transient recorder) has a response time around 4 ns.

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Registry No. 1, 139409-05-5; 2, 139409-06-6; TME, 563-79-1; (trichloroethenyl)benzene, 700-60-7; 1-chloro-1-(α,α-dichlorobenzyl)-2,2,3,3-tetramethylcyclopropane, 139409-07-7; pyridine, 110-86-1; (α,β,β-trichlorophenethyl)pyridinium ylide, 139409-08-8.

Tandem-Addition Rearrangements in the Reaction of 2-Butenoic Acid and *N*-(4-Methoxyphenyl)-2-butenamide with Methyl-Substituted Benzynes

A. Rakeeb Deshmukh, Hongming Zhang, Long duc Tran, and Ed Biehl*

Department of Chemistry, Southern Methodist University, Dallas, Texas 75275

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We[1] showed recently that *N*-(4′-methoxyphenyl)-2-butenamide dianion (**1**) and 2-butenoic acid (crotonic acid) dianion (**2**) react with various methoxy-substituted arynes to yield the corresponding 4-aryl derivatives of 3-butenoic acid, presumably by the usual aryne arylation mechanism. We report herein that these dianions also react with the methyl-substituted benzynes, i.e., 3,6-dimethylbenzyne (**3a**) and 3,4,5,6-tetramethylbenzyne (**3b**), to give predominantly rearranged cyclic products. Thus, treatment of 1 equiv of **1** in THF, prepared from equivalent molar amounts of *N*-(4′-methoxyphenyl)-2-butenamide and LDA, with aryne **3a**, generated from LDA (2 equiv) and 2-chloro-1,4-dimethylbenzene (1 equiv) (−50 °C to room temperature) yields the *N*-(4′-methoxyphenyl)-2-carboxamide of 4,7-dimethyl-1-(2′,5′-dimethylphenyl)indan **5a** (51%) and an inseparable 1:1 mixture of propenamide **6a** and *N*-(4′-methoxyphenyl)-3-butenamide (6% overall yield), after proton quench. Additionally, **1** reacts with 3,4,5,6-tetramethylbenzyne (**3b**) to give the rearranged 2-propenamide (**6b**) (55%); however, no indan derivative analogous to **5a** was observed. The IR, ^{1}H NMR, ^{13}C NMR, and mass spectra of rearranged products are consistent with proposed structures. Single-crystal X-ray crystallography[2] further supports the structure of indane **5a** whose ORTEP[3] plot is shown in Figure 1.

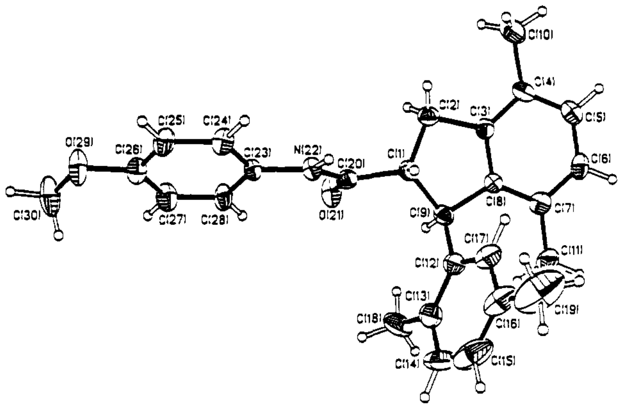

Figure 1. ORTEP plot of compound **5a**.

A possible mechanism for the formation of the rearranged products **5** and **6** is shown in Scheme I. Accordingly, dianion **1** adds to aryne **3** to give the usual aryne-nitrile anion adduct **8**. This initially formed adduct then undergoes a 5-*exo-trig*[3] cyclization to the benzocyclobutane intermediate **9**, which yields the rearranged benzyl dianion **10** upon ring opening. This tandem-addition rearrangement (TAR) sequence is similar to that proposed by Meyers[4] and extensively studied by our group.[5] The rearranged dianions are converted either exclusively (in the case of **10b**) or partly (in the case of **10a**) to the appropriate 3-aryl-2-propenamide **6**, after proton quench. The dianion **10a** undergoes a 5-*endo-trig*[3] cyclization to yield indan dianion **11**,[6] which upon addition of another molecule of **3** and proton quench supplies indan **5a**. The inability of **10b** to yield an indan derivative similar to **5a** probably reflects the decreased stability of the CH$_2$Li group in **10b** when compared to that in **10a** which is brought about by the greater number of electron-donating methyl groups in former when compared with the latter. Furthermore, the greater propensity of the methyl-substituted arynes **3a** and **3b**, when compared with the methoxy-substituted arynes, to participate with dianion **1** in the tandem-addition rearrangement pathway most likely reflects the greater nucleophilicity of the 2-lithiated cyclization site of the initially formed adduct **8**, engendered by the electron-donating methyl groups on the benzene ring.

2-Butenoic dianion **2** also reacted readily with aryne **3a** to give predominantly 5,8-dimethyl-2-naphthol (**12a**) (50%) and trace amounts (<3%) of 4-(2,5-dimethylphenyl)-3-butenoic acid; neither an indane derivative analogous to **5a** nor a 3-(2,3,6-trimethylphenyl) derivative of 2-propenoic acid was obtained. The reaction of **2** with **3b** gave mainly intractible tars from which a small quantity of 5,6,7,8-tetramethyl-2-naphthol (**12b**) (8%) could be extracted. The formation of the 2-naphthols indicates that the benzocyclobutane intermediates **13a** and **13b** open directly to the dihydronaphthalenes **14a** and **14b**, respectively, which are converted to the respective 2-naphthols **12a** and **12b** by well-established pathways (Scheme II). The greater tendency for the ring intermediates derived from crotonic acid dianions (**13a** and **13b**) to form naphthalene derivatives when compared with those derived from *N*-(4-methoxyphenyl)-2-butenamide (**10a** and **14b**) most likely reflects the greater electrophilicity of the carbonyl group of the acid when compared with that of the amide. Attempts to isolate the conjugate acid of indane **11** by periodic trapping were unsuccessful.

In conclusion, we have extended the TAR reaction to include α,β-unsaturated amides and acids and have uncovered novel chemistry of the key benzocyclobutane ring

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(2) Crystal data for C$_{27}$H$_{29}$NO$_2$ (**5a**): monoclinic $P2_1/c$, a = 9.429 (2) Å, b = 26.588 (7) Å, c = 9.705 (3) Å, β = 110.32 (2)°, V = 2282 Å^3, Z = 4, D_c = 1.16 g cm^{-3}, R = 0.052, R_w = 0.060 for 1281 reflections [$I \geq 3\sigma(I)$] collected on a Nicolett $R3m/\nu$ diffractometer with graphite-monochromated Mo Kα radiation.

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