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Phenyl versus alkyl migration in the fragmentation of alkoxychlorocarbenes

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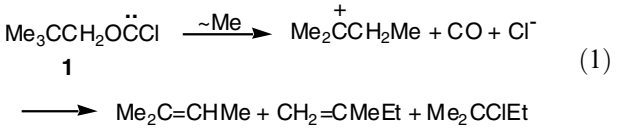
Abstract—Phenyl versus methyl (alkyl) group migration is assessed in the fragmentations of neophyloxychlorocarbene, 2,2-diphenylpropyloxychlorocarbene, and 1-phenylcyclopropylmethoxychlorocarbene. Rate constants and activation parameters of the fragmentations are also reported.

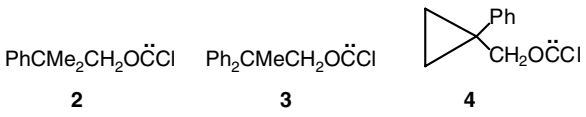
Aryl groups generally migrate in preference to alkyl groups in cationic rearrangements.[1,2] However, much of the data underlying this generalization derives from solvolysis reactions where the activation energies are high and the differential activation energies between competitive pathways are significant. What happens when the activation energies are drastically reduced, and differential energies are perforce very small? The fragmentation of alkoxychlorocarbenes to alkyl cation–chloride ion pairs is characterized by low activation energies, frequently <10 kcal/mol,[3] and can afford simple systems to answer this question.

The fragmentation of neopentyloxychlorocarbene, **1**, generated by photolysis of the corresponding diazirine in MeCN, occurs with $k_{frag} \sim 1 \times 10^6\ s^{-1}$, and the products are derived from the methyl-shifted *t*-amyl cation; cf., Eq. 1.

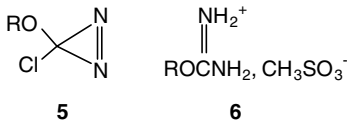


(1)

Here, we present a parallel study of the fragmentations of carbenes **2**–**4**, where the competitive 1,2-migrations of phenyl and methyl groups can be readily analyzed. Additionally, we report the kinetics and activation energies of the fragmentations. It is then possible to answer the question posed above.



Diazirines **5a**–**c** were prepared by hypochlorite oxidation[5] of *O*-alkylisouronium mesylates **6a**–**c**, with the latter obtained from reactions of the corresponding alcohols with cyanamide and methane sulfonic acid.[6] The diazirines and isouronium salts (admixed with urea) were characterized by ^1H and ^{13}C NMR spectroscopy. The diazirines each displayed UV absorptions at 348 nm in pentane.



(a) R = $PhCMe_2CH_2$; (b) R = Ph_2CMeCH_2; (c) R = *c*-$C_3H_4(Ph)CH_2$

Photolysis of **5a** in $CDCl_3$ gave 57% of dichloride **7** (from HCl trapping[4] of carbene **2**) and 43% of carbene fragmentation products **8**–**11**; cf., Eq. 2. Products **8**–**11**

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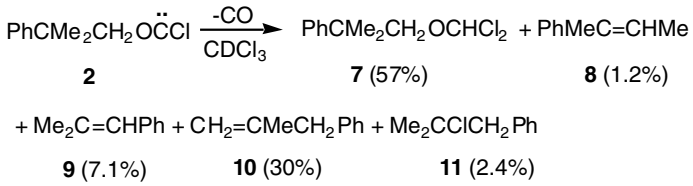
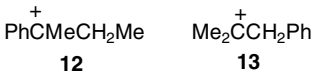


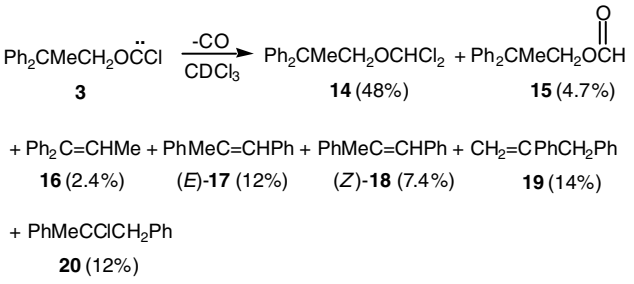
(2)

were identified by GC–MS and by ^{1}H and ^{13}C NMR comparisons with literature data. Alkene **8**[7] arises via 1,2-Me migration accompanying the fragmentation of **2**, yielding the 2-phenyl-2-butyl cation (**12**), followed by proton loss. Alkenes **9**[8] and **10**[8] stem from competitive 1,2-Ph migration to the 1-phenyl-2-methyl-2-propyl cation (**13**), followed by proton loss, whereas chloride **11**[9] represents collapse of **13** with chloride ion. The product distributions in Eq. 2, determined by ^{1}H NMR integration, indicate that Ph migration exceeds Me migration by ~66:1 (corrected for the 2:1 Me > Ph substituent advantage).



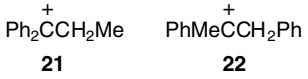
The dominance of Ph migration in the fragmentation of **2** parallels solvolytic results where the acetolysis of neophyl brosylate or tosylate (corresponding to carbene **2**) gives 34% of the acetate analogous to chloride **11**, and 66% of a mixture of alkenes **9** and **10**.[10] A careful quantitative study of the solvolysis of neophyl tosylate gave the statistically corrected ratio of Ph to Me migration as 286:1 in formic acid and 667:1 in acetic acid.[11]

Photolysis of **5b** in $CDCl_3$ gave 48% of dichloride **14**, 5% of formate **15**, 35% of alkenes **16**–**19**, and 12% of chloride **20**; cf., Eq. 3. Dichloride **14** and formate **15** are trapping products of carbene **3** with HCl or water, respectively.[4] In $CDCl_3$ with added pyridine, the formation of **14** is suppressed.

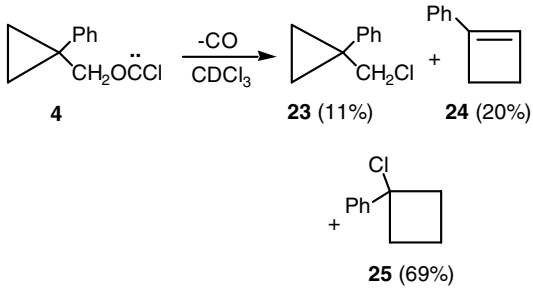


(3)

Fragmentation product alkenes **16**–**19** were identified by GC–MS and by comparisons of key ^{1}H NMR resonances to those of known compounds. Alkene **16**[12] arises by 1,2-Me migration accompanying the fragmentation of **3**, yielding the 1,1-diphenylpropyl cation **21**, followed by proton loss. Alkenes **17**,[13] **18**,[13] and **19**[14] stem from competitive 1,2-Ph migration to form the 1,2-diphenyl-2-propyl cation **22**, again followed by proton loss. Chloride **20**[15] represents chloride return to cation **22**. There was no NMR evidence for the formation of (unrearranged) 1-chloro-2,2-diphenylpropane.[16] The product distribution of Eq. 3, determined by NMR integration, indicates dominance of Ph over Me migration in the fragmentation of carbene **3** with a statistically corrected ratio of ~9.5:1. For comparison, formolysis of 2,2-diphenylpropyl tosylate (which corresponds to carbene **3**) gives alkene **17**, the product of Ph migration, in 77% yield.[17]

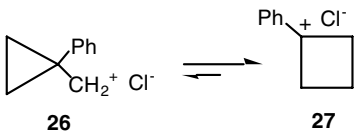


Photolysis of **5c** gave, in analogy to the examples above, 20% of dichloride and 6% of formate trapping products derived from carbene **4**. There were also 3 carbene fragmentation products: 1-chloromethyl-1-phenylcyclopropane (**23**), 1-phenylcyclobutene (**24**), and 1-chloro-1-phenylcyclobutane (**25**). These appear in Eq. 4, where their yields are normalized to 100%. They stem from the



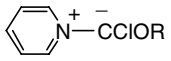
(4)

1-phenylcyclopropylmethyl cation chloride ion pair (**26**), formed by fragmentation of carbene **4**. Collapse of **26** with chloride provides unrearranged **23**, while ring expansion to the more stable 1-phenylcyclobutyl cation (**27**) leads to **24** and **25** by proton loss or recombination with chloride. Products **23**–**25** were identified by GC–MS and by comparisons of key NMR resonances to those of known materials.[18–20] The 89:11 dominance of ring-expanded products over unrearranged products can be compared to acetolysis, hydrolysis, or methanolysis of 1-phenylcyclopropylcarbinyl tosylate, where only ring-expanded products are formed.[21] We note that with cyclopropylmethyl cation **26**, and in contrast to the phenylpropyl systems above, 1,2-alkyl ring expansion trumps 1,2-phenyl migration (which is not observed).



Absolute rate constants for the fragmentations of carbenes **2**–**4** were determined by ns laser flash photolysis

(LFP) using the pyridine ylide method.[1,22] Thus, LFP at 351 nm (10 ns pulse width) and 25 °C of diazirine **5a** in 1,2-dichloroethane (DCE) containing pyridine gave an absorption due to pyridine ylide **28a**, at 420 nm. A correlation of the apparent rate constants for ylide formation, k_{obs} ($1.34–6.34 \times 10^6\ s^{-1}$) versus pyridine concentration (0.80–8.0 M) was linear (10 points, $r = 0.998$) with a slope of $6.8 \times 10^5\ M^{-1}\ s^{-1}$, equivalent to the rate constant for ylide formation, k_y, and a *Y*-intercept of $9.9 \times 10^5\ s^{-1}$ (see Supplementary data, Fig. S-1). We take the latter value to approximate k_{frag} for carbene **2**. Even though HCl capture of **2** to give dichloride **7** accounts for 57% of the carbene's disappearance in $CDCl_3$ (Eq. 2), this pathway is suppressed in the presence of pyridine (under the kinetics conditions) in favor of fragmentation.[1]



28 (**a-c** as above)

Similarly, LFP of diazirine **5b** in DCE–pyridine revealed ylide **26b** at 428 nm. A correlation of k_{obs} for ylide formation with pyridine concentration was linear ($r = 0.999$) with a slope, $k_y = 1.34 \times 10^6\ M^{-1}\ s^{-1}$, and a *Y*-intercept $= 1.98 \times 10^6\ s^{-1}$ (see Supplementary data, Fig. S-2). We take the latter value to approximate k_{frag} for carbene **3**. Carbene **3** also gives the HCl trapping product (**14**) as the major product in $CDCl_3$. Again, however, pyridine suppresses this pathway; in its presence, fragmentation accounts for ~60% of the carbene's reactions. In precisely the same way, LFP of diazirine **5c** in DCE–pyridine afforded ylide **28c** at 424 nm, leading to a determination of $k_{frag} = 1.50 \times 10^5\ s^{-1}$ for carbene **4** (see Supplementary data, Fig. S-3).

We also measured the activation energies associated with the fragmentations of carbenes **2**–**4**. Arrhenius LFP studies were conducted in DCE from −30 to +30 °C; see Figures S4–S6 in the Supplementary data. For carbene **2**, $E_a = 2.1$ kcal/mol, $\log A = 7.74\ s^{-1}$, and $\Delta S^{\ddagger} = -26.5$ e.u. For carbene **3**, $E_a = 1.2$ kcal/mol, $\log A = 7.06\ s^{-1}$, and $\Delta S^{\ddagger} = -28.2$ e.u. For carbene **4**, $E_a = 3.4$ kcal/mol, $\log A = 7.70\ s^{-1}$, and $\Delta S^{\ddagger} = -25.3$ e.u. Recalling that only ~50–60% of the carbenes fragment, while the remainder is captured by HCl, we consider these activation energies to be lower limits for the fragmentations. Nevertheless, E_a is clearly minimal and the transition states are 'early'. Were it not for the very negative activation entropies, the carbenes would fragment too rapidly to be trapped by pyridine.[23]

Activation energies for the fragmentations of carbenes **2**–**4** are very low, the associated transition states are early, and the k_{frag} values are $\sim 10^5$–$10^6\ s^{-1}$. Apparently, the identity of these carbenes' alkyl substituents has little effect on k_{frag} or E_a. Nevertheless, alkyl group rearrangement (Ph or Me migration), though not far advanced at the transition state, must be concerted with fragmentation because simple cleavage of carbenes **2** or **3** (or **1**[4]) to primary carbocations is improbable. Despite the low activation energies and early transition states, Ph migration markedly dominates Me migration in the fragmentations of **2** and **3**. The dominance is weaker than in the comparable solvolytic processes, where the activation energies are ~10 times greater, but the Ph > Me migration paradigm persists. An exception is carbene **4**, where a cyclopropylmethyl cation is formed and the well-known ring expansion of this 'special' cation dominates; competitive 1,2-phenyl migration is bypassed, just as it is in the solvolytic system.[21]

Acknowledgement

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2006.11.043.

References and notes

1. Smith, M. B.; March, J. *March's Advanced Organic Chemistry*, 5th ed.; Wiley: New York, 2001; p 1384f.
2. Hedaya, E.; Winstein, S. *J. Am. Chem. Soc.* **1967**, *89*, 1661.
3. (a) Yan, S.; Sauers, R. R.; Moss, R. A. *Org. Lett.* **1999**, *1*, 1603; (b) Moss, R. A.; Johnson, L. A.; Merrer, D. C.; Lee, G. E., Jr. *J. Am. Chem. Soc.* **1999**, *121*, 5940.
4. Moss, R. A.; Ge, C.-S.; Maksimovic, L. *J. Am. Chem. Soc.* **1996**, *118*, 9792.
5. Graham, W. H. *J. Am. Chem. Soc.* **1965**, *87*, 4396.
6. Moss, R. A.; Kaczmarczyk, G. M.; Johnson, L. A. *Synth. Commun.* **2000**, *30*, 3233.
7. Kawai, Y.; Inaba, Y.; Tokitoh, N. *Tetrahedron: Asymmetry* **2001**, *12*, 309.
8. Arnold, D. R.; Mines, S. A. *Can. J. Chem.* **1989**, *67*, 689.
9. Shevlin, P. B.; Hansen, H. J. *J. Org. Chem.* **1977**, *42*, 3011.
10. (a) Heck, R.; Winstein, S. *J. Am. Chem. Soc.* **1957**, *79*, 3342; (b) Sera, A.; Yamada, H.; Masaki, H. *Chem. Lett.* **1980**, 1533.
11. Saunders, W. H., Jr.; Paine, R. H. *J. Am. Chem. Soc.* **1961**, *83*, 882.
12. Clennan, E. L.; Pan, G. I. *Org. Lett.* **2003**, *5*, 4979.
13. Dabbagh, H. A.; Salehi, J. M. *J. Org. Chem.* **1998**, *63*, 7619.
14. Cho, C. S.; Uemura, S. *J. Organomet. Chem.* **1994**, *465*, 85.
15. Dabbagh, A. H.; Faghihi, K. *Tetrahedron* **2000**, *56*, 3611.
16. This material was prepared as described by Zimmerman, H. E.; Zweig, A. *J. Am. Chem. Soc.* **1961**, *83*, 1196.
17. Anet, F. A. L.; Bavin, P. M. G. *Can. J. Chem.* **1957**, *35*, 1084.
18. Doyle, M. P.; Raynolds, P. W.; Barents, R. A.; Bade, T. R.; Danen, W. C.; West, C. T. *J. Am. Chem. Soc.* **1973**, *95*, 5988.
19. Leigh, W. J.; Postigo, J. A. *Can. J. Chem.* **1995**, *73*, 191.
20. (a) Hahn, R. C.; Corbin, T. F.; Shechter, H. *J. Am. Chem. Soc.* **1968**, *90*, 3404; (b) Brown, H. C.; Rei, M. H. *J. Org. Chem.* **1966**, *31*, 1090.
21. Roberts, D. D. *J. Org. Chem.* **1965**, *30*, 23.
22. Jackson, J. E.; Soundararajan, N.; Platz, M. S.; Liu, M. T. H. *J. Am. Chem. Soc.* **1988**, *110*, 5595.
23. $\Delta G^{\ddagger} \sim 9$–11 kcal/mol for the fragmentations of **2**–**4**.