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Reactions of Diazirines with Aluminum Chloride: Lewis Acid-Mediated Carbene Generation and Friedel−Crafts Reactions

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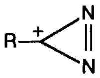
3-Substituted diazirinium ions (**1**) are possible intermediates in the Graham (hypochlorite) oxidation of amidines to 3-chloro-3-substituted diazirines (**2**).[1,2] Despite their superficial resemblance to the aromatic cyclopropenyl cations, however, computational studies of the stability of **1** are equivocal,[3] and the experimental evidence is not encouraging.[2,4] Thus, treatment of **2** (R = MeO), or the corresponding bromide, with $AgNO_3$, $AlBr_3$, SbF_5, $AlCl_3$, AgF, H_2SO_4, or FSO_3H failed to provide spectroscopic or chemical evidence for **1**.[2] Related failures were reported for diazirine **3**,[4b,c] while the "diazirine exchange" reactions[5] of, e.g., **2** and **3**, initially attributed to the intermediacy of **1**,[6] have been reinterpreted as S_N2'[4c−e,7] or $S_{RN}1$[4c,8,9] reactions.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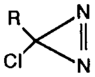
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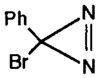
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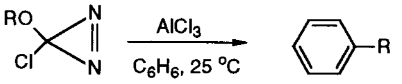
Here, we describe the chemical consequences of reacting various diazirines with $AlCl_3$ in benzene. The resulting Friedel−Crafts reactions provide new insights into the decomposition pathways available to these protean molecules.

Reactions of alkoxychlorodiazirines (**4**)[10] with ∼30% excess $AlCl_3$ in dry benzene (25 °C, dark, 20−30 min) afforded alkylbenzenes (**5**) in >95% purity; eq 1. The R groups of **4**



4 **5** (1)

included isopropyl, cyclopentyl, cyclohexyl, benzyl, neopentyl, and *n*-butyl. Rearrangements were observed in the latter two cases, where the products were *tert*-amylbenzene or a 73:27 mixture of *s*-butylbenzene and *n*-butylbenzene, respectively. In the case of R = $PhCH_2$, the absolute yield of **5** was ∼40%, based on **4**; the balance of the material was nonvolatile. Products were identified by GC and GC-MS comparisons with authentic samples, and no reactions occurred in the absence of $AlCl_3$ (UV, TLC, HPLC).

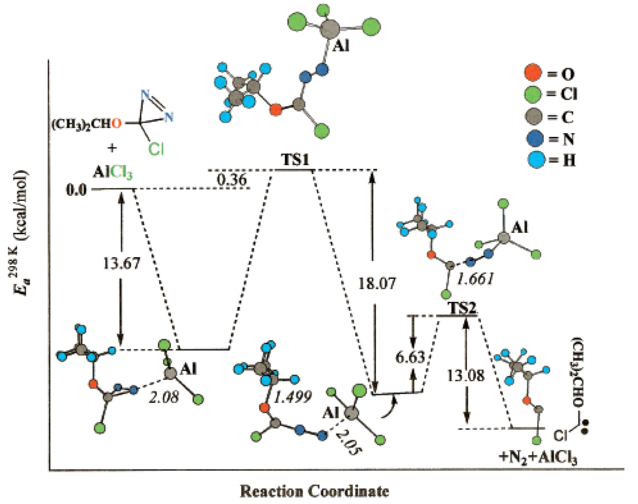


Figure 1. B3LYP/6-31G* potential energy profile for the $AlCl_3$ conversion of **4** (R = *i*-Pr) to *i*-PrOCCl. Calculations are for the gas phase with zero point energy and thermal corrections. Arabic numerals refer to energies (kcal/mol); italic numerals indicate bond lengths (Å).

An obvious formulation of these reactions involves chloride abstraction from **4** by $AlCl_3$, yielding an unstable alkoxydiazirinium ion (**1**, R = RO), which fragments to R^+, CO, and N_2, with subsequent alkylation of benzene by R^+. However, B3LYP/6-31G* computational studies[11] fail to locate a $AlCl_3$/Cl abstraction transition state for **4** (R = *i*-Pr or Me). Instead, a transition state proceeding from $AlCl_3$ attack on a diazirine *nitrogen* atom is readily found. Figure 1 illustrates the ensuing molecular processes and energy relationships for **4** (R = *i*-Pr). As computed in the gas phase, N/Al interaction affords a diazirine/$AlCl_3$ complex with 13.7 kcal/mol stabilization. C−N bond breaking then requires ∼14.0 kcal/mol of activation energy via **TS1** (transition states exhibited 1 negative vibrational frequency), leading exothermally (net, −4.0 kcal/mol) to an $AlCl_3$ complex of isopropyloxychlorodiazomethane, the linear isomer of **4**.[12] Loss of nitrogen from the latter via **TS2** (E_a = 6.6 kcal/mol) then affords isopropyloxychlorocarbene with a net exothermicity of ∼6.5 kcal/mol. A very similar sequence of steps is also computed to convert **4** (R = Me) to MeOCCl.

According to this scenario, the function of the $AlCl_3$ is simply to catalyze the loss of nitrogen from **4**, affording the alkoxychlorocarbene, ROCCl. When R provides a moderately stable R^+, ROCCl readily fragments to R^+, CO, and Cl^-.[13] Therefore, the

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[1] Graham, W. H. *J. Am. Chem. Soc.* **1965**, *87*, 4396.

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[4] (a) Padwa, A.; Eastman, D. *J. Org. Chem.* **1969**, *34*, 2728. (b) Creary, X.; Sky, A. F. *J. Org. Chem.* **1988**, *53*, 4637. (c) Creary, X. *Acc. Chem. Res.* **1992**, *25*, 31. (d) Dailey, W. P. *Tetrahedron Lett.* **1987**, *28*, 5801. (e) Bainbridge, K. E.; Dailey, W. P. *Tetrahedron Lett.* **1989**, *20*, 4901.

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[10] Diazirines **4** were produced from the appropriate isouronium salts, see ref 1, and: Moss, R. A.; Ge, C.-S.; Maksimovic, L. *J. Am. Chem. Soc.* **1996**, *118*, 9792. Moss, R. A.; Johnson, L. A.; Merrer, D. C.; Lee, G. E., Jr. *J. Am. Chem. Soc.* **1999**, *121*, 5940. For isouronium salts, see: Moss, R. A.; Kaczmarczyk, G. M.; Johnson, L. A. *Synth. Commun.* **2000**, *30*, 3233.

[11] (a) All optimizations utilized Gaussian94 Revision E.2 using default convergence criteria: Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Robb, M. A.; Cheeseman, J. R.; Keith, T.; Petersson, G. A.; Montgomery, J. A.; Raghavachari, K.; Al-Laham, M. A.; Zakrezewski, V. G.; Ortiz, J. V.; Foresman, J. B.; Cioslowski, J.; Stefanov, B. B.; Nanayakkara, A.; Challacombe, M.; Peng, C. Y.; Ayala, P. Y.; Chen, W.; Wong, M. W.; Andres, J. L.; Replogle, E. S.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Binkley, J. S.; Defrees, D. J.; Baker, J.; Stewart, J. P.; Head-Gordon, M.; Gonzalez, C.; Pople, J. A. Gaussian, Inc.: Pittsburgh, PA, 1995. (b) DFT calculations used Becke's three-parameter hybrid method using the LYP correlation functional: Becke, A. D. *J. Chem. Phys.* **1993**, *98*, 5648.

[12] This step is supported by an intrinsic reaction coordinate calculation which connects the diazirine/$AlCl_3$ complex, **TS1**, and the diazoalkane/$AlCl_3$ complex. Note the rehybridization of N(1) in this process.

[13] (a) Moss, R. A. *Acc. Chem. Res.* **1999**, *32*, 969. (b) Yan, S.; Sauers, R. R.; Moss, R. A. *Org. Lett.* **1999**, *1*, 1603 and references therein.

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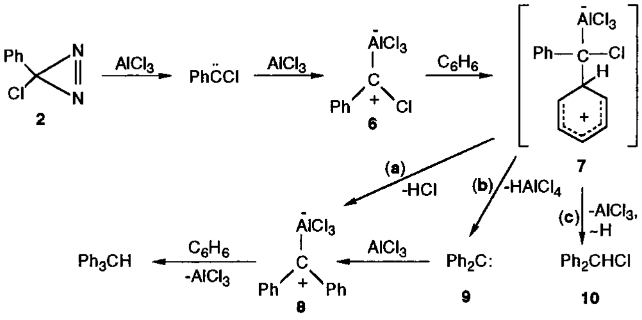
simplest overall mechanism envisions the alkylation of benzene by R^+ derived from **4** via ROCCl. A more complicated variant includes $AlCl_3$ assistance (at C or Cl) in the carbene fragmentation, but given the low activation energies (<10 kcal/mol in vacuo) computed for the fragmentations of **4** (R = *i*-Pr or $PhCH_2$),[13b] $AlCl_3$ assistance is probably not required. Note that the possible formation of RCl or alkenes from ROCCl is moot in the present instance; controls show that these products simply alkylate benzene in the presence of $AlCl_3$.

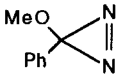
When **2** or **4** afford RCCl or ROCCl that cannot readily fragment to R^+, $AlCl_3$-catalyzed decompositions follow a very different course. Thus, **2** (R = Ph or *p*-tolyl) or **4** (R = Me or Ph)[14] with $AlCl_3$ in benzene yield *triphenylmethane* in >90% purity.[15,16] The origin of the methine proton in $Ph_3C\mathit{H}$ is the benzene substrate; reactions in C_6D_6 give $(C_6D_5)_3C\mathit{D}$. The $AlCl_3$ catalyzes phenyl exchange with solvent C_6D_6, but the methine proton does not exchange;[17] it is irreversibly derived from C_6D_6.

Scheme 1



We formulate these reactions as shown in Scheme 1 (illustrated with **2**, R = Ph). Reaction of $AlCl_3$ with diazirine **2** generates the carbene (here PhCCl) by the *N*-attack mechanism described above. Next, the carbene reacts with $AlCl_3$ to give the aluminocarbocation **6**,[18] which alkylates benzene via the Wheland intermediate, **7**. Three likely continuations include the following: (a) loss of HCl from **7** affording diphenylaluminocarbocation **8**, which alkylates benzene to give Ph_3CH; (b) loss of $HAlCl_4$ from **7** to give diphenylcarbene (**9**) which, upon capture by $AlCl_3$, also yields **8**, and thence Ph_3CH; or (c) loss of $AlCl_3$ from **7**, (effectively) coupled with a proton shift, to give benzhydryl chloride (**10**). The latter then alkylates benzene in a classic Friedel−Crafts process, affording Ph_3CH.[19]

The *N*-attack mechanism for $AlCl_3$ conversion of a diazirine into a carbene (Figure 1) implies that a *chloro*diazirine is not required; any diazirine should serve. Indeed, methoxyphenyldiazirine (**11**)[20] with $AlCl_3$ in benzene affords triphenylmethane (96%), while phenyldiazirine (**12**)[21] leads to diphenylmethane (Ph_2CH_2, 96%). We can rationalize these reactions according to Scheme 1, noting (for **11**) that MeO plays an equivalent role to Cl in **2**,[19] and also that one fewer benzene alkylation is possible when starting with **12**, so that Ph_2CH_2 rather than Ph_3CH becomes the sequence terminus. Moreover, in accord with these ideas are the findings that, with C_6D_6 as substrate, **11** gives $(C_6D_5)_3CD$, but **12** affords $(C_6D_5)_2CHD$.



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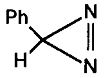

12

$PhCH{=}N_2$

13

$Ph_2C{=}N_2$

14

Irradiation of **12** in benzene gives a ~5/95 mixture of diphenylmethane (PhCH insertion) and phenylcycloheptatriene (PhCH addition). Treatment of the product mixture with $AlCl_3$/benzene yields ~27% of Ph_2CH_2 and ~73% of Ph_3CH, quite different from the 96% of Ph_2CH_2 obtained from the direct reaction of **12** with $AlCl_3$/benzene. The latter reaction proceeds via the aluminocarbocation derived from PhCH and $AlCl_3$, not via free PhCH.

Finally, we note that the $AlCl_3$ diazirine to carbene conversion of Figure 1 transits an $AlCl_3$ complex of the isomeric linear diazoalkane. Not surprisingly, therefore, phenyldiazomethane (**13**)[22] or diphenyldiazomethane (**14**)[23] yield Ph_2CH_2[24] or Ph_3CH,[25] respectively, with $AlCl_3$/benzene. These conversions can also be rationalized with aluminocarbocations as outlined in Scheme 1.

Although the new reactions of diazirines **2** and **4** provide no evidence for the intermediacy of diazirinium ions, they do afford unanticipated mechanistic insights into diazirine chemistry.[4−9] We are extending our studies of Lewis acid-catalyzed diazirine decompositions to fluorodiazirines and additional catalysts.

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[14] Computed E_a's in a vacuum for the fragmentations of MeOCCl and PhOCCl are 33.2 and 32.7 kcal/mol, respectively.[13b]

[15] About 8% of Ph_2CH_2 is also formed, but controls suggest that it comes from $AlCl_3$-mediated phenylation of benzene by Ph_3CH.[16]

[16] Thomas, C. A. *Anhydrous Aluminum Chloride in Organic Chemistry*; Rheinhold, New York, 1941; p 721.

[17] $(C_6H_5)_3C\mathit{H}$ with $AlCl_3$ and C_6D_6 yields $(C_6D_5)_3C\mathit{H}$.

[18] B3LYP/6-31G* calculations indicate that the reaction of PhCCl with $AlCl_3$ gives **6** with 46.2 kcal/mol of exothermicity. Aluminocarbocation **6** is near-trigonal and planar at "C^+", with a computed charge of +0.39 on this carbon. MeOCCl and $AlCl_3$ are computed to react analogously, with $\Delta E = -32.8$ kcal/mol and $\delta^+ = +0.35$.

[19] With **4** (R = Me or Ph) in Scheme 1, one penultimately arrives at $ROCHPh_2$. Attack of $AlCl_3$ on an oxygen lone pair then initiates a final Friedel−Crafts reaction with benzene, affording Ph_3CH.

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[24] With C_6D_6, **13** gave $(C_6D_5)_2CHD$ in 95−98% purity.

[25] The product mixture contained 77% Ph_3CH, 22% $Ph_2C{=}CPh_2$, and 1% Ph_2CH_2. With substrate C_6D_6, the two major products were perdeuterated.