EXCHANGE REACTIONS OF DIAZIRINES: 3-X-3-METHYLDIAZIRINES
AND DERIVED CARBENES

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Summary. 3-Bromo-3-methyldiazirine readily undergoes exchange reactions with F⁻, MeO⁻, CN⁻,
or N₃⁻. New carbene precursors can thus be prepared.

3-Halo-3-aryldiazirines undergo synthetically useful exchange reactions with strong
nucleophiles that proceed via tight diazirinium halide ion pairs and provide convenient
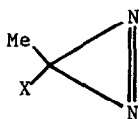precursors for carbenes; eq (1).[1] As anticipated, these reactions are enhanced by
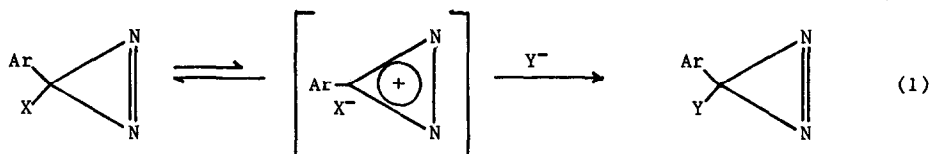
substitution of cation stabilizing groups on Ar. Similarly, 3-bromo-3-methoxydiazirine
readily exchanges with fluoride ion, affording 3-fluoro-3-methoxydiazirine, presumably via
the 3-methoxydiazirinium cation.[2]

For simple carbocations, the stabilizing effects of substituents clearly fall in the
order MeO>Ph>Me, so that one might expect exchange reactions of 3-halo-3-methyldiazirine to
occur with difficulty or not at all. However, in the cyclopropenium cation series, Me is
known to be superior to Ph as a stabilizing group; the pK_R+ values of trimethyl and
triphenylcyclopropenium cations are 7.4[3] and 3.1-3.4,[4] respectively. If this order of
stability were also to hold for the isoelectronic diazirinium (diazacyclopropenium) cations,
then the exchange reactions of 3-bromo-3-methyldiazirine, might be more facile than
expected. This, in fact, appears to be the case.

3-Bromo-3-methyldiazirine, 1, was prepared in 40-70% yield by Graham oxidation of
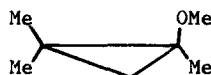
acetamidine hydrochloride with freshly prepared, excess aqueous sodium hypobromite solution.[5] The diazirine was removed under vacuum (<1 mm-Hg) as formed, pumped through 2 traps [KOH pellets at 25°C; empty trap at -50°C], and then condensed in ~2 ml of acetonitrile or pentane at 77 K.

$\underline{1}$, X = Br; $\underline{2}$, X = F $\underline{5}$, X = F $\underline{7}$
$\underline{3}$, X = OMe; $\underline{4}$, X = CN $\underline{6}$, X = CN
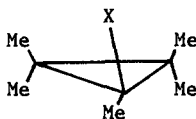
The uv and ir spectra of $\underline{1}$ agreed with literature descriptions,[5,6] and CH$_3$CN solutions of the diazirine were used in exchange reactions without further purification.

Diazirine $\underline{1}$ was converted to the novel 3-fluoro-, 3-methoxy-, or 3-cyano-3-methyldia-zirines 2-4, respectively, by exchange with appropriate nucleophiles. For example, the bromodiazirine from 20 mmol of acetamidine in ~2 ml of dry CH$_3$CN was added to a solution of "anhydrous" $\underline{n}$-Bu$_4$N$^+$F$^-$ (prepared from 20 mmol of the trihydrate)[1,7] in 3 ml of dry CH$_3$CN at -25°C. The combined solution, which turned brown at once, was stirred for several minutes, and then stored at -20°C for 24 hrs. Product diazirine $\underline{2}$ was isolated by distillation at -25°C/0.1 mm-Hg through a train of traps (0°, -78°, -196°C). The final trap contained 2-3 ml of an appropriate solvent in which $\underline{2}$ was captured in 40% yield, based on acetamidine. 3-Fluoro-3-methyldiazirine was characterized by uv, ir, and nmr spectra (Table I), and by its behavior as a precursor for fluoromethylcarbene; see below. Diazirine $\underline{2}$ was stable in pentane solution for ~24 hrs at 25°C in the dark.

3-Methoxy-3-methyldiazirine, $\underline{3}$, and 3-cyano-3-methyldiazirine, $\underline{4}$, were prepared and isolated by similar procedures, utilizing exchange reactions between diazirine $\underline{1}$ in CH$_3$CN and $\underline{n}$-Bu$_4$N$^+$OMe$^-$,[8] or $\underline{n}$-Bu$_4$N$^+$CN$^-$,[9] respectively, both in $\underline{o}$-dichlorobenzene solution. Characterizations again depended on spectroscopy (Table I), and on conversions to MeOCMe or NCCMe. Diazirine $\underline{3}$ is unstable in pentane solution at 25°C, whereas $\underline{4}$ survives for 24 hrs.

Many 3-alkyldiazirines[10] and 3-X-3-phenyldiazirines (X=F,[1,11] OMe,[12] CN[11,13]) are known, but this is the first report in which 3-X-3-methyldiazirines are described with these uncommon X substituents. Accordingly, we now have convenient, clean precursors for the carbenes XCMe. Thus, photolysis (4-6 hrs. λ > 300 nm) of $\underline{2}$ or $\underline{4}$ in tetramethylethylene gave cyclopropanes $\underline{5}$ or $\underline{6}$, respectively, in 10-20% isolated yields. Similarly, $\underline{7}$ was obtained in 14% yield by thermal decomposition of diazirine $\underline{3}$ in isobutene (25°C, 12 hrs). In each case, the product was isolated by preparative gc (20% SF-96 on Chromosorb W, teflon column), and characterized by appropriate nmr and ir spectra, and by elemental analysis. The

isolated yields were low due to the inefficiency of the gc trapping, but the product mixtures were very clean, with the cyclopropanes the dominant components.

The mild generative methods for FCMe and MeOCMe described here are to be compared with previously reported methods for FCMe that include pyrolysis of 1,1-difluoroethyltrifluorosilane at 140°C,[14] or treatment of CCl_2F_2 or $CHClF_2$ with MeLi at low temperature (where mixtures of FCMe, CF_2, ClCMe, or Me_2C products are obtained).[15] MeOCMe has been generated by pyrolysis (100-150°C) of 1,1-difluoroethyltrimethoxysilane,[14] or by thermolysis (80°C) of 2-methoxy-2,5,5-trimethyl-Δ^3-1,3,4-oxadiazoline.[16] In these procedures, the efficiency of carbene generation and trapping is unclear.

We showed recently that the exchange of 3-bromo-3-aryldiazirines with azide ions afforded unstable azidodiazirines that rapidly lost 2 moles of nitrogen to give arylnitriles; eq. (2, R=Ar).[1] With excess azide, k_1 was limiting and the rate of nitrogen

$$\text{8} \quad \xrightleftharpoons[k_{-1}]{k_1} \quad \text{9} \quad \xrightarrow[k_2]{n\text{-}Bu_4N^+N_3^-} \quad \xrightarrow[-2N_2]{k_3} RCN \quad (2)$$
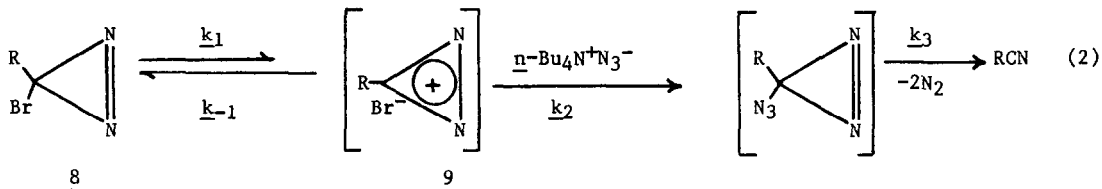
evolution was equivalent to the rate of formation of azidodiazirine.[1] Now we have compared the reactions of 3-bromo-3-methyldiazirine (1) and 3-bromo-3-phenyldiazirine (8, R=Ph) with 6.6 equiv. of n-Bu$_4$N$^+$N$_3^-$ in anhydrous DMF at -1.3 ± 0.1°C. As expected, the product from 1 was acetonitrile (95%). The observed pseudo-first-order rate constants, measured manometrically on evolved nitrogen, were 1.08 ± 0.09 x 10^{-5} s^{-1} for 1 and 0.54 ± 0.02 x 10^{-5} s^{-1} for 8 (R=Ph). Azide/bromide exchange is thus ~2 times faster with the methyl than with the phenyl substituted diazirine, suggesting that ion pair 9 may indeed be more stabilized with R=Me, instead of Ph.[17]

In conclusion, 3-bromo-3-methyldiazirine readily undergoes halide exchange reactions with strong nucleophiles affording novel diazirines that can be used as carbene precursors. Moreover, the methyl group appears to potentiate the exchange, relative to phenyl, so that the presumed intermediate 3-methyldiazirinium cation may be more stable than originally anticipated.[1,18]

Table I. Properties of 3-X-3-methyldiazirines

Structure	X	Yield, %[a]	UV[b]	IR[c]	NMR[d]
<u>2</u>	F	40	340, 350, 358	1560, 1200[e] 1060[e], 1040[e]	1.64, d, J_{HF} = 12.5 Hz[f] 133.1, q, J_{HF} = 12.5 Hz[g]
<u>3</u>	OMe	45-55	348, 358sh, 366	1555, 1240[h] 1165[h]	1.20, s, 2.90, s[i]
<u>4</u>	CN	20	314sh, 330, 338, 346	1570, 2235[j]	k

[a]For 2 steps, from acetamidine. [b]λ_{max} (nm) in pentane. [c]ν_{max}, gas phase for <u>2</u>; CCl_4 solution elsewhere. The characteristic N=N band is listed first. [d]Chemical shifts in δ. [e]Two of these bands are C-F vibrations. [f]^{1}H spectrum in $CDCl_3$. [g]^{19}F spectrum, $CDCl_3/CFCl_3$ (standard). [h]C-O bands. [i]δ, CCl_4/Me_4Si. [j]CN band. [k]Not determined.

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(17) Electron donating groups stabilize <u>9</u>. With R=Ar, a Hammett study of azide exchange gave ρ = -1.03 (vs. σ$^+$).[1]

(18) CAUTION. Diazirines are explosive in concentrated solution or when neat. Care should be taken during cold trap procedures when crystalline diazirines are present. Thawing should be done so as to dissolve the diazirines at the lowest possible temperature. All operations should be carried out behind safety shields.