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PYRIDYLHALOCARBENES AND PYRIDINIUMHALOCARBENES

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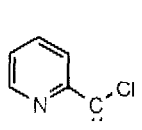
Summary. Pyridylhalocarbenes and pyridiniumhalocarbenes can be generated from diazirines. Absolute rate constants have been determined for additions of 2- and 3-pyridylchlorocarbenes to alkenes.

Recently, one of us reported the generation and alkene capture of 2-pyridylchlorocarbene (**1**, 2-Py-C-Cl) and 3-pyridylchlorocarbene (**2**, 3-Py-C-Cl) following thermolyses of the corresponding diazirines, **3** and **4**, respectively.[2] In view of the extensive literature describing the absolute reactivity of the related arylhalocarbenes,[3] it seemed appropriate to scrutinize the pyridylhalocarbenes from the same perspective.

Here, we report absolute rate constants for the reactions of 2-Py-C-Cl and 3-Py-C-Cl with a series of alkenes. The results show the carbenes to be ambiphiles, similar to, but more reactive than the "parent" phenylchlorocarbene (Ph-C-Cl). Additionally, we generated the fluorocarbene analogues of **1** and **2**, 2-Py-C-F (**5**) and 3-Py-C-F (**6**), as well as the N-methyl pyridinium derivatives of carbenes **2** and **6**, 3-MePy$^+$-C-Cl (**7**) and 3-MePy$^+$-C-F (**8**). To our knowledge, **7** and **8** are the first carbenes to carry cationic substituents.

Diazirines **3** (λ_{max}, pentane, 344, 360 nm) and **4** (λ_{max}, pentane, 356 nm) were prepared[2] from 2- or 3-pyridylcarbonitrile via conversion to the corresponding amidine hydrochlorides,[4] followed by Graham oxidation[5] of the latter with aqueous NaOCl/DMSO. 2-Py-C-Cl was generated by photolysis of **3** (200 W focused Osram XE mercury lamp, Pyrex tube, 5 h), and added to tetramethylethylene, trimethylethylene, trans-2-pentene, 1-hexene, acrylonitrile, and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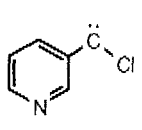
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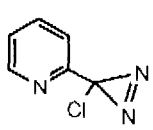
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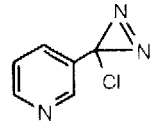
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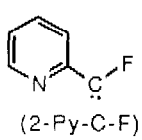
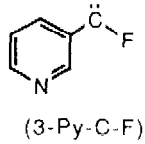
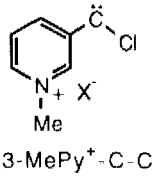
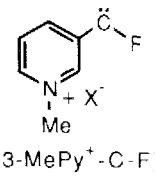

5 (2-Py-C-F)


6 (3-Py-C-F)


7 (3-MePy$^+$-C-Cl)


8 (3-MePy$^+$-C-F)

α-chloroacrylonitrile. The appropriate cyclopropanes were formed in 50-70% yields, isolated by GC (SE-30, 100°C), and characterized by NMR and elemental analysis (or mass spectrometry).[6]

3-Py-C-Cl (**2**) could be generated either thermally or photochemically from diazirine **4**, but

better yields of cyclopropanes were obtained thermolytically, in refluxing hexane containing 10-fold excesses of the above alkenes. The appropriate cyclopropanes were isolated in 6-52% yields, purified by GC or column chromatography, and characterized as above.[6]

The reactivities of 2-Py-C-Cl and 3-Py-C-Cl were ascertained by laser flash photolysis (LFP)[3,7] of diazirines 3 and 4 in isooctane solutions. LFP afforded transient UV signals within the time period of the laser pulse (351 nm, 50-80 mJ, 14 ns). The transients had λ_{max} ~310 nm, similar to the absorption of Ph-C-Cl;[8] they could be quenched by the addition of alkenes, and were accordingly assigned as the carbenes 2-Py-C-Cl and 3-Py-C-Cl. In the case of diazirine 4, LFP also gave a transient that "grew in" at 480 nm, with a rate constant dependent on [4]. The second order rate constant for the formation of this transient was 2.5×10^9 $M^{-1}s^{-1}$. From its λ_{max} and dependence on [4], we identify this species as the ylide resulting from attack of 3-Py-C-Cl on the pyridine N of diazirine 4. Similar observations have been reported for the 4-pyridyl analogue of diazirine 4,[9] and the formation of N-ylides in carbene/pyridine LFP experiments is well known.[10]

LFP of 3 or 4 in isooctane afforded 2-Py-C-Cl or 3-Py-C-Cl whose decay, monitored at 310 nm, was pseudo-first-order in the presence of alkenes. Plots of the observed decay constants as a function of [alkene] were linear, and, from the slopes of these correlations, we extracted bimolecular rate constants for the carbene/alkene additions;[3] cf., Table 1.

Pyridylchlorocarbenes 1 and 2 are ambiphilic[11] toward the set of alkenes. Their selectivity patterns are mutually similar, and analogous to that of Ph-C-Cl; their reactivities are highest toward electron-rich or electron-poor alkenes, but minimal toward alkenes of intermediate electronic character. The arylhalocarbenes are known to be ambiphiles,[3,12,13] and detailed discussions have appeared.[13] The data in Table 1 indicate a carbenic reactivity order of 2-Py-C-Cl > 3-Py-C-Cl > Ph-C-Cl where the absolute rate constants for the alkene additions of 1 and 2 range from ~6×10^6 to ~1×10^9 $M^{-1}s^{-1}$, roughly 4-10 times (2-Py-C-Cl) or 2-3 times (3-Py-C-Cl) greater than the analogous rate constants determined for Ph-C-Cl.[3,12,14]

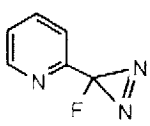
The higher reactivity of the pyridylchlorocarbenes can be attributed to the greater electron-withdrawing power of the pyridyl vs. the phenyl group,[15] that destabilizes the pyridylcarbenes and augments their reactivity. Electron withdrawing groups placed on phenyl rings also enhance the reactivity of arylhalocarbenes.[13,16] As one might expect, the reactivity of 2-Py-C-Cl, where the electronegative nitrogen atom is closer to the carbenic carbon, exceeds that of 3-Py-C-Cl. Indeed, the reactivity of 2-Py-C-Cl is similar to that of p-CF_3Ph-C-Cl, a very reactive arylchlorocarbene.[16]

Diazirines 3 and 4 are susceptible to the diazirine exchange reaction;[17] excess anhydrous $Bu_4N^+F^-$ in dry DMF[18] (25°C, 15-20 h) converted them to the corresponding 2-pyridyl (9) and 3-pyridylfluorodiazirines (10). These were purified by short column silica gel chromatography (CH_2Cl_2 or pentane), and obtained in 62% (9) or 48% (10) yields.[19] Photolyses of 9 and 10 afforded pyridylfluorocarbenes 5 and 6, that were readily intercepted by isobutene to give

cyclopropanes **11** (90%) and **12** (50%). The cyclopropane structures were secured by ^{1}H and ^{19}F NMR spectroscopy, and elemental analysis or mass spectrometry.

Most intriguingly, 3-pyridylhalodiazirines **4** and **10** could be quaternized to afford pyridinium diazirines **13** and **14**. Thus, **4** and excess MeI ($CHCl_3$, 25°, 24 h) gave >90% of **13**, whereas **10** and MeI (MeOH, 50°, 3 days) gave 44% of **14**. Obviously, the fluorodiazirine is much less reactive toward MeI than its chloro analogue; only the thermal stability of **10** permits its quaternization.

Pyridinium chlorodiazirine **13** was converted to its BF_4^- salt ($AgBF_4$/MeCN or ion exchange over Amberlite IRA-35); **13-BF$_4$** had λ_{max} 356, 362, and 372 nm in MeCN. The pyridinium



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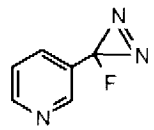

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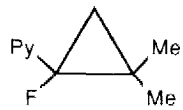
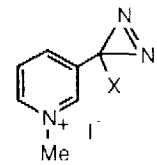
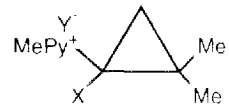


11 (2-Py)
12 (3-Py)



13 (X = Cl)
14 (X = F)



15 (X = Cl)
16 (X = F)

fluorodiazirine, **14**, was characterized both as the iodide,[20] and in the BF_4^- form after ion exchange (λ_{max}, MeCN, 350, 362 nm).

Photolysis of **13-BF$_4$** in excess isobutene/MeCN (sealed tube) gave the pyridinium chlorocyclopropane, **15** (BF_4 salt), presumably via the addition of 3-MePy$^+$-C-Cl (**7**). Product **15** was isolated in 36% yield by preparative TLC (silica gel, MeOH). Its structure was firmly established by comparison with a sample that had been independently synthesized. Thus, carbene **2** was added to isobutene, affording the chlorocyclopropane analogue of **12**. This compound was purified by TLC, characterized by NMR and elemental analysis, and quaternized with MeI ($CHCl_3$, 60°, 4 h) to give **15-I** that was identical by NMR[21] to the **15-BF$_4$** that had been formed directly by the addition of **7** to isobutene.

Similarly, photolysis of pyridinium fluorodiazirine **14** (I^- or BF_4^- salt) in isobutene/MeCN generated MePy$^+$-C-F (**8**) that added to the alkene, affording 68% of pyridinium cyclopropane **16**. Again, the structure was secured by independent synthesis. Photolysis of **10** in isobutene/pentane gave 3-Py-C-F (**6**) that added to the alkene yielding cyclopropane **12**. After NMR and GC-MS characterization, **12** was quaternized (MeI, MeOH, 60°, 12 h) to give **16-I**, identical by NMR[22] to the material previously obtained from **8** and isobutene. It remains to determine the reactivities of the pyridiniumhalocarbenes.

Acknowledgement. We are grateful to the National Science Foundation and the Busch Memorial Fund of Rutgers University for financial support.

Table 1. Absolute Rate Constants ($M^{-1}s^{-1}$) for Carbene/Alkene Additions[a]

	Carbene		
Alkene	2-Py-C-Cl[b]	3-Py-C-Cl[b]	Ph-C-Cl[c]
$Me_2C{=}CMe_2$	1.1×10^9	4.2×10^8	2.8×10^8
$Me_2C{=}CHMe$	7.2×10^8	1.8×10^8	1.3×10^8
trans-MeCH=CHEt	9.0×10^7	1.9×10^7	5.5×10^6
$CH_2{=}CH$-n-Bu	2.0×10^7	6.2×10^6	2.2×10^6
$CH_2{=}CHCN$	5.7×10^7	1.9×10^7	7.0×10^6
$CH_2{=}CClCN$	4.6×10^8	1.9×10^8	2.1×10^8

[a]Rate constants were determined by laser flash photolysis in isooctane at 23-25°C. Reproducibilities were ±10%. [b]This work. [c]Reference 3.

References and Notes

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(7) For a description of our LFP apparatus, see R.A. Moss, S. Shen, L.M. Hadel, G. Kmiecik-Ławrynowicz, J. Włostowska, and K. Krogh-Jespersen, J. Am. Chem. Soc., **109**, 4341 (1987).
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(15) For example, σ_I of 2-pyridyl is 0.20, vs. 0.12 for phenyl; cf., M. Charton in "Correlation Analysis in Chemistry," N.B. Chapman and J. Shorter, Ed., Plenum, New York, 1978, pp. 175f.
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(19) **9**: λ_{max} (pentane) 328, 344, 360 nm; ^1H NMR (δ, $CDCl_3$) 7.33 (m, 1H), 7.80 (m, 2H), 8.51 (m, 1H); ^{19}F NMR ($CDCl_3$) 162.9 ppm upfield from $CFCl_3$. **10**: λ_{max} (pentane) 348, 366, 384 nm; ^1H NMR (δ, $CDCl_3$) 7.33 (m, 2H), 8.33 (s, 1H), 8.68 (m, 1H); ^{19}F NMR ($CDCl_3$) 154.8 ppm upfield from $CFCl_3$.
(20) λ_{max} (MeCN) 350, 362 nm; ^1H NMR (δ, CD_3CN) 4.52 (s, 3H, Me), pyridinium protons at 8.25 ("s", 2H), 8.87 (s, 1H), 9.01 ("s", 1H); ^{19}F NMR (CD_3CN) 137.8 ppm upfield from $CFCl_3$.
(21) ^1H NMR (δ, D_2O) 0.73 and 1.38 (s, 3H each, C-Me's), 1.22 and 8.45, 8.55 (m, 1H each), 8.85 (s, 1H).
(22) ^1H NMR (δ, D_2O) 0.86 and 1.40 (d, 3H each, J_{HF} = 2 Hz, C-Me's), 1.29-1.52 (m, 2H, CH_2), 4.41 (s, 3H, N-Me),[4] pyridinium protons at 8.07 (t, J = 7 Hz), 8.52 (d, J=8 Hz), 8.75 (d, J=6 Hz), 8.95 (s).

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