furnace. After an appropriate reaction time, the reactor was cooled to -196 °C, any gases noncondensables at this temperature were removed, and the products were distilled through a series of cold traps. Further purification when needed was carried out by GLC using 35-40% halocarbon oil on Chromosorb P. The reactions are summarized in Table I, and details for each reaction and the characterization of the new compounds follow.

Ethene. The reaction mixture was separated through traps cooled to -90 and -196 °C. The -196 °C trap contained unreacted CH_2=CH_2, CF_4, CF_3NBrF, and other unidentified products. The -90 °C trap contained the addition compound, some $(CH_2Br)_2$, and small amounts of other unidentified products. Pure $CF_3NFCH_2CH_2Br$ was isolated by GLC. $CF_3{}^ANF^BCH_2{}^CCH_2{}^DBr$: mp -63 °C; mol wt 209.2, calcd 209.96; NMR δ A -77.5 (d), B -73.6 (t, q), C and D ~4.3 and 4.2 (A_2B_2X system), J_{AB} = 14.0, J_{BC} = 38.5, $J_{BD} \simeq 0.5$, $J_{CD} \simeq 7.0$ Hz; IR 2995 (w), 1434 (w), 1336 (w), 1311 (s), 1272 (s), 1250 (s), 1203 (s), 1167 (s), 1091 (w), 1070 (w), 1050 (w), 1000 (w), 924 (m), 885 (w), 820 (w), 773 (w), 733 (vw), 642 (m), 600 (w), 582 (w), cm^{-1}; major m/z [EI] 107/109 ($C_2H_4Br^+$), 93/95 (CH_2Br^+), 69 (CF_3^+), [CI] 210/212 (MH^+), 190/192 ($C_3F_3H_4NBr^+$), 130 ($C_3F_4H_4N^+$), 107/190 ($C_2H_4Br^+$).

CF_2=CH_2. The reaction mixture was separated through traps cooled to -108 and -196 °C. The -196 °C trap contained CF_4, CF_2=CH_2, and small amounts of other unidentified products. The -108 °C trap contained a mixture of $BrCF_2CH_2Br$ and the addition compound, with minor amounts of other unidentified products. Pure $CF_3NFCH_2CF_2Br$ was obtained by GLC. $CF_3{}^ANF^BCH_2{}^CCF_2{}^DBr$: glass at -97 °C; mol wt 242, calcd 245.96; NMR δ A -77.1 (d), B -60.2 (br, s), C 4.3 (d, t), D -53.2 (d, t), J_{AB} = 13.0, J_{BC} = 37.2, J_{BD} = 9.0, J_{CD} = 11.0 Hz; IR 1410 (w), 1375 (w), 1312 (s), 1270 (s), 1245 (m), 1205 (s), 1180 (m), 1135 (m), 1090 (sh), 1018 (s), 980 (sh), 945 (m), 885 (w), 830 (w), 778 (w), 705 (w), 665 (m), 650 (sh), 590 (w), 553 (w) cm^{-1}; major m/z [EI] 166 ($C_3F_6H_2N^+$), 143/145 ($C_2F_2H_2Br^+$), 129/131 (CF_2Br^+), 116 ($C_2F_4H_2N^+$), 96 ($C_2F_3HN^+$), 79/81 (Br^+), 78 ($C_2F_2H_2N^+$), 69 (CF_3^+), 64 (CF_2N^+), 51 (CF_2H^+), 50 (CF_2^+), [CI] 246/248 (MH^+), 226/228 ($C_3F_5H_2Br^+$), 166 ($C_3F_6H_2N^+$), 143/145 ($C_2F_2H_2Br^+$), 116 ($C_2F_4H_2N^+$).

CF_2=CF_2. The reaction mixture was separated through traps cooled to -90 and -196 °C. The -196 °C trap contained CF_2=CF_2 and CF_4. The addition product collected in the -90 °C trap and was purified by GLC. $CF_3{}^ANF^BCF_2{}^CCF_2{}^DBr$: bp 42.9 °C; glass at -110 °C; mol wt 280.1, calcd 281.93; log P(torr) = 6.5371 - 787.05/T - 114 664/T^2; ΔH_{vap} = 6.93 kcal/mol; ΔS_{vap} = 22.0 eu; NMR δ A -68.6 (m), B -89.9 (br, m), C -108.2 (m), D -65.8 (t, t, q), J_{AB} = 13.0, J_{AC} = 13.0, J_{AD} = 1.0, $J_{BC} \simeq 23$, J_{BD} = 19.0, J_{CD} = 4.5 Hz; IR 1304 (s), 1275 (vs), 1250 (vs), 1205 (sh), 1181 (vs), 1112 (s), 1029 (m), 981 (sh), 955 (m), 863 (m), 809 (m), 762 (m), 700 (w), 668 (m), 606 (w), 577 (w) cm^{-1}; major m/z [EI] 179/181 ($C_2F_4Br^+$), 152 ($C_2F_6N^+$), 129/131 (CF_2Br^+), 69 (CF_3^+), 50 (CF_2^+), [CI] 281/283 (MH^+), 261/263 ($C_3F_7NBr^+$), 179/181 ($C_2F_4Br^+$), 104 ($CF_4NH_2^+$), 84 (CF_3NH^+).

CF_2=$CFCl$. The reaction mixture was passed through traps at -100 and -196 °C. Essentially pure addition compound collected in the -100 °C trap, and a mixture CF_4, CF_2=$CFCl$, and other unidentified products collected in the -196 °C trap. $CF_3{}^ANF^BCF_2{}^CCF^DClBr$: mp -116 °C; mol wt 295.6, calcd 298.38; NMR (see discussion) δ A -68.5 (basic q), B - 84 (br, m), C -105 (m), D -73.2 (d, t, m), J_{AB} = 13, J_{AC} = 13, J_{BC} = 10, $J_{BD} \simeq 24$, $J_{CD} \simeq 10$ Hz; IR 1295 (s), 1280 (s), 1250 (vs), 1195 (s), 1109 (m), 1090 (w), 1030 (m), 960 (w), 940 (w), 885 (m), 870 (m), 842 (w), 790 (w), 750 (w), 660 (w), 585 (w) cm^{-1}; major m/z [EI] 218/220 ($C_3F_7NCl^+$), 195/197/199 ($C_2F_3ClBr^+$), 152 ($C_2F_6N^+$), 145/147/149 ($CFClBr^+$), 69 (CF_3^+), [CI] 298/300/302 (MH^+), 278/280/282 ($C_3F_6NClBr^+$), 262/264 ($C_3F_7NBr^+$), 218/220 ($C_3F_7NCl^+$), 195/197/199 ($C_2F_3ClBr^+$), 183 ($C_2F_7N^+$).

CF_2=CBr_2. The reaction products were separated by -45 and -196 °C traps. The latter contained a mixture CF_2=CBr_2, CF_3NBrF, and small amounts of other unidentified products. The addition product collected in the -45 °C trap. $CF_3{}^ANF^BCF_2{}^CCBr_3$: bp 152 °C; mp -37 °C; log P(torr) = 7.9812 - 2170.8/T; ΔH_{vap} = 9.93 kcal/mol; ΔS_{vap} = 23.3 eu; NMR δ A -68.1 (d, t), B -72.2 (t, q), C -97.9 (d, q), J_{AB} = 13.0, J_{AC} = 13.0, J_{BC} = 15.0 Hz; IR 1283 (s), 1240 (vs), 1192 (m), 1160 (m), 1025 (m), 931 (w), 807 (w), 774 (m), 752 (m), 727 (w), 643 (m), 607 (w), 581 (w) cm^{-1}; major m/z [EI] 322/324/326 ($C_3F_6NBr_2^+$), 220/222/224 ($C_2F_2Br_2^+$), 170/172/174 (CBr_2^+), 152 ($C_2F_6N^+$), 141/143 ($C_2F_2Br^+$), 129/131 (CF_2Br^+), 122/124 (C_2FBr^+) 91/93 (CBr^+), 79/81 (Br^+), 69 (CF_3^+), [CI, 350-500] 402/404/406/408 (MH^+), 382/384/386/388 ($C_3F_5NBr_3^+$).

CF_2=CCl_2. The reaction mixture was separated through traps at -85 and -196 °C. The -196 °C trap contained a mixture of CF_3NBrF, CF_2=CCl_2, and small amounts of other unidentified products. Essentially pure addition product collected in the -85 °C trap. $CF_3{}^ANF^BCF_2{}^CCCl_2Br$: mol wt 312.4, calcd 314.84; NMR δ A -68.2 (d, t), B -75.6 (br q, t), C -101.1 (q, d), J_{AB} = 13.5, J_{AC} = 13.5, J_{BC} = 16.8 Hz; IR 1285 (vs), 1251 (vs), 1235 (vs), 1200 (s), 1170 (s), 1030 (s), 1000 (w), 940 (w), 855 (s), 810 (s), 790 (m), 766 (w), 741 (m), 695 (vw), 670 (m), 610 (vw), 585 (w); major m/z [EI] 234/236/238 ($C_3F_6NCl_2^+$), 211/213/215/217 ($C_2F_2BrCl_2^+$), 152 ($C_2F_6N^+$), 132/134/136 ($C_2F_2Cl_2^+$), 85/87 (CF_2Cl^+), 82/84/86 (CCl_2^+), 69 (CF_3^+), 50 (CF_2^+), 47/49 (CCl^+), [CI, 150-450] 314/316/318/320 (MH^+), 211/213/215/217 ($C_2F_2Cl_2Br^+$).

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Registry No. CF_3NBrF, 82241-76-7; CH_2=CH_2, 74-85-1; CF_2=CH_2, 75-38-7; CF_2=CF_2, 116-14-3; CF_2=$CFCl$, 79-38-9; CF_2=CBr_2, 430-85-3; CF_2=CCl_2, 79-35-6; $CF_3NFCH_2CH_2Br$, 84642-47-7; $CF_3NFCH_2CF_2Br$, 84642-48-8; $CF_3NFCF_2CF_2Br$, 84642-49-9; $CF_3NFCF_2CFClBr$, 84642-50-2; $CF_3NFCF_2CBr_3$, 84642-51-3; $CF_3NFCF_2CCl_2Br$, 84642-52-4.

Synthesis of 1*H*-5-Acetyl-2-alkylimidazoles

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Interest in the pharmacology of histamine and histidine has resulted in a number of synthetic methods for the preparation of substituted imidazoles. However, C-acylation of imidazole and its derivatives is a long-standing problem. Recent work has alleviated this problem to a certain extent. Suitably N-protected 2-lithioimidazoles readily add electrophiles to the 2-position, thereby affording, after deprotection, 2-acylated imidazoles.[1,2] A one-pot aroylation of imidazole has also been described in which N-benzoylation is followed by 2-benzoylation. An aqueous workup affords a good yield of 2-benzoylimidazole.[3] Both of these approaches, however, give only the 2-acylated species, and none of the 4(5)-acylated material is formed. Furthermore, a general synthesis of 2-substituted 1*H*-5-acetylimidazoles does not exist. In fact, little information has appeared in the literature on compounds of this general type.

A number of methods were considered for the synthesis of these compounds. The most attractive route was based on the work of Iwasaki, who found that photolysis of *N*-acetylimidazole leads to a mixture of 1*H*-2-acetylimidazole and 1*H*-5-acetylimidazole in 20% and 30% yield, respectively.[4] From this work, it appeared that starting with a 2-substituted imidazole, N-acylation followed by photolysis should afford the desired compounds, since the 2-position is now blocked, and isomer formation is no longer possible. In fact, this has been found to be the case, and a number of 1*H*-5-acetyl-2-alkylimidazoles have been prepared by this route. The results appear in Table I.

(1) Kirk, K. L. *J. Org. Chem.* **1978**, *43*, 4381.
(2) Curtis, N. J.; Brown, R. S. *J. Org. Chem.* **1980**, *45*, 4038.
(3) Bastiaansen, L. A. M.; Godefroi, E. F. *Synthesis* **1978**, 675.
(4) Iwasaki, S. *Helv. Chim. Acta* **1976**, *59*, 2738.
(5) Krebs, E.-P.; Bondi, E. *Helv. Chim. Acta* **1979**, *62*, 497.

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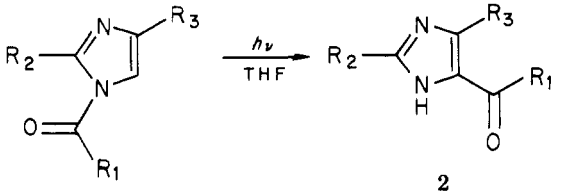
Table I. Photolysis of *N*-Acyl-2-alkylimidazoles[a]



1 2

compd	R_1	R_2	R_3	yield, %	mp, °C (solvent)[b]
2a	CH_3	CH_3	H	48	127-129 (A)
2b	CH_3	CH_3	CH_3	41	87-88 (B)
2c	CH_3	C_2H_5	H	50	120-121 (C)
2d	CH_3	C_3H_7-*n*	H	45	112-113 (C)
2e	CH_3	$CH_2C_6H_5$	H	30	154-157 (C)
2f	CH_3	$(CH_2)_2C_6H_5$	H	34	130-132 (C)
2g	CH_3	$(CH_2)_3C_6H_5$	H	48	90-91 (C)
2h	C_2H_5	CH_3	H	45	158-159 (A)
2i	CH_3	H	CH_3	39	140-142 (lit.[5] 146-149) (C)

[a] Satisfactory ^1H NMR data and analytical values (±0.4% for C, H, and N) were reported for all compounds in the table. [b] Recrystallization solvents: A, acetonitrile; B, isopropyl ether; C, ethyl acetate.

The yields in this reaction are diminished by the fact that a side reaction in this procedure is cleavage of the *N*-acetyl bond, thereby generating the original 2-substituted imidazole. This byproduct poses no severe difficulty in that it is readily removed by chromatography. Although most of the examples are straightforward, a few deserve special comment. Disubstituted imidazoles should prove to be suitable substrates as exemplified by **2b**. Example **2h** is consistent with Iwasaki's results in that other alkyl (and presumably aryl) ketones can also be utilized in this procedure. Finally, in example **2i**, only one isomer was isolated despite previous precedence which would lead one to expect formation of the 2-acetylimidazoles as well.[6]

This method may be limited to alkylimidazoles and aralkylimidazoles since, when this reaction was attempted with 1-acetylimidazole-2-carboxaldehyde, a myriad of products were detected by TLC. It is unclear as to whether this is due to the electron-withdrawing effect of the aldehyde or to complications involving homolysis of its carbonyl. Despite this drawback, this method should prove to be of value. The ease of operation, as well as the availability of a number of 2-substituted imidazoles either by classical[7] or modern methods,[1,2] make this approach attractive for the synthesis of 1*H*-5-acetyl-2-alkylimidazoles.

Experimental Section[8]

N-Acetylation of Imidazoles. The method reported by Iwasaki[4] was followed by using a 50/50 chloroform–toluene solution as the solvent in place of benzene. The following procedure is typical. A solution of 9.6 g (0.10 mol) of 2,4-dimethylimidazole in 50 mL of chloroform and 50 mL of toluene was stirred at room temperature, and 3.6 mL (0.05 mol) of acetyl chloride was added over a 1-min period. After the mixture was stirred at room temperature for 1 h, the 2,4-dimethylimidazole hydrochloride which precipitated was removed by filtration. Concentration of the filtrate left 5.9 g (100%) of 1-acetyl-2,4-dimethylimidazole as a crystalline solid: NMR ($CDCl_3$) δ 7.00 (s, 1 H), 2.68 (s, 3 H), 2.57 (s, 3 H), 2.21 (s, 3 H). This material was used directly in the photolysis reaction.

In general, the yields of the acylations were >75%. The crude product was analyzed by NMR and then used directly without further purification.

Photolysis of 1-Acetylimidazoles. A solution of 5–6 g of the *N*-acetylimidazole in 600 mL of dry THF was placed in a quartz vessel and photolyzed under nitrogen in a Rayonet reactor at 254 nm for 24 h. The mixture was then concentrated, and the residue was chromatographed over 25 times its weight of silica gel with 19:1 chloroform–methanol as the eluant. The product, which proved less polar than the imidazole byproduct, was of sufficient purity to use directly, although further purification can be achieved by recrystallization. A summary of the physical data of **2a–i** appears in Table I.

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Registry No. **1a**, 3720-89-6; **1b**, 52757-00-3; **1c**, 84694-85-9; **1d**, 84694-86-0; **1e**, 84694-87-1; **1f**, 84694-88-2; **1g**, 84694-89-3; **1h**, 84694-90-6; **1i**, 61553-60-4; **2a**, 78210-66-9; **2b**, 56536-44-8; **2c**, 84694-91-7; **2d**, 84694-92-8; **2e**, 84694-93-9; **2f**, 84694-94-0; **2g**, 84694-95-1; **2h**, 84694-96-2; **2i**, 23328-91-8; 2-methylimidazole, 693-98-1; 2,4-dimethylimidazole, 930-62-1; 2-ethylimidazole, 1072-62-4; 2-*n*-propylimidazole, 50995-95-4; 2-benzylimidazole, 14700-62-0; 2-phenethylimidazole, 84694-97-3; 2-(3-phenylpropyl)imidazole, 13682-31-0; 4-methylimidazole, 822-36-6.

(6) It is possible that <5% of this material is formed, but if so, it was not detected.

(7) For example, 2-benzyl-, 2-phenethyl-, and 2-(3-phenylpropyl)-imidazole were all prepared by using the method of: Lawson, J. K. *J. Am. Chem. Soc.* **1953**, *75*, 3398.

(8) ^1H NMR spectra were obtained on a Varian T-60 spectrometer. Melting points are uncorrected and were obtained in open capillaries on a Thomas-Hoover melting point apparatus. Solvents and reagents were commercially available unless otherwise noted and were used directly. Tetrahydrofuran (THF) was dried over 4A molecular sieves before use.

π Route to 3-Substituted Noriceanes

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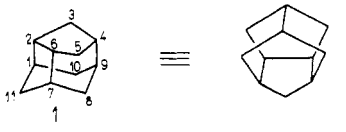
Noriceane[1] (1) is an interesting rigid and symmetrical



1

molecule, consisting of two cyclopentane and three cyclo-

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