17.8 mg (0.47 mmol) of sodium borohydride. After 15 min at −78 °C, the reaction was quenched by the addition of acetone. The solvent was removed under reduced pressure, and the crude product was dissolved in ethyl acetate and was washed with saturated sodium bicarbonate solution. The organic layer was dried over anhydrous magnesium sulfate and concentrated in vacuo. There was obtained 320 mg (100%) of crude alcohol **10** [R_f 0.47 (ether–hexane, 2:1)] as a homogeneous crystalline solid. Recrystallization from ether–hexane gave colorless needles: mp 180–181 °C; $[\alpha]_D$ +75.5° (*c* 0.70, $CHCl_3$); IR ($CHCl_3$) 3590, 3500, 3080, 3055, 3020, 3000, 2960, 2920, 2870, 2820, 1710, 1595, 1490, 1450, 1405, 1365, 1325, 1315, 1270, 1185, 1070, 1020, 1000, 980, 960, 895, 875, 700, 625 cm^{-1}; NMR (220 MHz, $CDCl_3$) δ 0.80 (t, 3 H, *J* = 6.5 Hz), 1.00 (d, 6 H, *J* = 6.5 Hz), 1.75 (s, 3 H), 3.34 (s, 3 H), 4.04 (dd, 1 H, *J* = 10.0, 5.0 Hz), 4.26 (br s, 1 H), 5.00 (m, 2 H), 5.56 (d, 1 H, *J* = 10.5 Hz), 5.78 (dd, 1 H, *J* = 15.8, 3.6 Hz), 6.46 (d, 1 H, *J* = 15.8 Hz). Anal. Calcd for $C_{43}H_{54}O_7$: C, 75.63; H, 7.97. Found: C, 75.83; H, 8.01.

Preparation of Seco Acid Derivative 2. A solution of 100 mg (0.15 mmol) of lactone **10** in 1.5 mL of methanol was treated with 340 μL (0.35 mmol) of 1 N sodium hydroxide solution. After 12 h at 60 °C, the methanol was removed under reduced pressure, and 10 mL of water was added. The alkaline solution was cooled to 0 °C, acidified (pH 4) with 3% phosphoric acid, and saturated with sodium chloride. The product was isolated by extraction with ethyl acetate. The combined organic extracts were dried over anhydrous magnesium sulfate and evaporated in vacuo. There was obtained 95 mg (97%) of seco acid **2** as a glass which was used directly in the next reaction. For purposes of characterization, seco acid **2** was transformed into ester **14** by treatment with an ethereal solution of diazomethane. Purification on silica gel with 4:1 ether–hexane gave analytically pure **14** as colorless needles: mp 52–54 °C: R_f 0.55 (ether); $[\alpha]_D$ +43.0° (*c* 1.00, $CHCl_3$) (lit.[3c] $[\alpha]_D$ +40.0°); IR ($CHCl_3$) 3590, 3500, 3080, 3050, 2995, 2950, 2920, 2870, 2830, 1725, 1595, 1490, 1460, 1445, 1435, 1375, 1365, 1320, 1225, 1175, 1150, 1060, 1025, 970, 895, 695, 625 cm^{-1}; NMR (360 MHz, $CDCl_3$) δ 1.72 (s, 3 H), 3.33 (s, 3 H), 3.69 (s, 3 H), 4.15 (m, 1 H), 4.20 (m, 1 H), 4.28 (dd, 1 H, *J* = 7.2, 4.0 Hz), 5.01 (d, 1 H, *J* = 4.3 Hz), 5.61 (dd, 1 H, *J* = 15.5, 6.8 Hz), 5.62 (d, 1 H, *J* = 9.4 Hz), 6.29 (d, 1 H, *J* = 15.5 Hz). Anal. Calcd for $C_{44}H_{58}O_8$: C, 73.92; H, 8.18. Found: C, 73.68; H, 8.10.

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Registry No. 1, 61219-81-6; 2, 83061-10-3; 4, 61257-02-1; 5, 84710-25-8; 8, 81132-63-0; 9, 81114-52-5; 10, 84710-26-9; 11, 84710-27-0; 14, 83114-35-6; OMT *N*-oxide, 63838-03-9; 20-*O*-methyltylonolide hemiacetal (isomer 1), 83005-90-7; 20-*O*-methyltylonolide hemiacetal (isomer 2), 83058-31-5.

Addition Reactions of *N*-Bromoperfluoromethanamine with Some Olefins

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Perfluoro compounds containing nitrogen–bromine bonds are very rare. Only a few examples are known in the literature including *N*-bromoperfluorosuccinimide,[2] $SF_2{=}NBr$,[3] F_2NBr,[4] $(CF_3)_2C{=}NBr$,[5] and $(CF_3)_2NBr$.[6] Only the latter compound has been investigated in any detail regarding its chemistry.[7] As expected, the N–Br bond in $(CF_3)_2NBr$ is very labile, the bromine atom is electrophilic, and a variety of useful photochemical and thermal reactions can be carried out, e.g., see Scheme I.

Scheme I

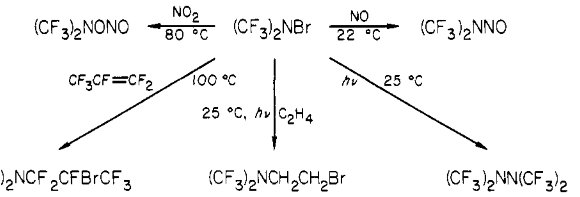

Table I. Addition Reactions of CF_3NBrF

olefin[a]	temp/time, °C/h	product (%)[c]
$CH_2{=}CH_2$	110/12	$CF_3NFCH_2CH_2Br$ (37)
$CH_2{=}CH_2$	110/5, 110/13, 125/18[b]	$CF_3NFCH_2CH_2Br$ (~90)
$CF_2{=}CH_2$	110/12	$CF_3NFCH_2CF_2Br$ (25)
$CF_2{=}CH_2$	93/10, 108/9, 150/12[b]	$CF_3NFCH_2CF_2Br$ (40)
$CF_2{=}CF_2$	122/9, 125/18[b]	$CF_3NFCF_2CF_2Br$ (90)
$CF_2{=}CF_2$	105/18	$CF_3NFCF_2CF_2Br$ (80)
$CF_2{=}CFCl$	100/9	$CF_3NFCF_2CFClBr$ (73)
$CF_2{=}CBr_2$	105/10	$CF_3NFCF_2CBr_3$ (85)
$CF_2{=}CCl_2$	109/13	$CF_3NFCF_2CCl_2Br$ (52

[a] Reactions were carried out with ~1 mmol each of olefin and CF_3NBrF. [b] Product was removed and unreacted starting materials were recycled after each temperature/time given. [c] Yield is based on starting amount of CF_3NBrF.

Recently, an excellent synthesis for CF_3NBrF from CF_2NF was found.[8]

$$CF_2{=}NF + Br_2 + KF \xrightarrow{22\ ^\circ C} CF_3NBrF + KBr$$

The surprising thermal stability of this compound facilitates an investigation of its reaction chemistry. Herein we report the thermal addition of CF_3NBrF to several olefins, which proceed in good yield with high regioselectivity.

Results and Discussion

The addition reactions of CF_3NBrF to olefins are summarized in Table I. The temperature necessary for reaction in every case was very near 100 °C. All the olefins except $CF_2{=}CBr_2$ and $CF_2{=}CCl_2$ were checked for reactivity at 22 °C, and the reactants were recovered after 1 day. In addition, $CF_2{=}CH_2$ was recovered after 10 h at 93 °C and similarly $CF_2{=}CFCl$ after 6 h at 80 °C. Even at 100 °C, the reactions are slow. Very little product was observed with $CF_2{=}CF_2$ after only 3 h at 105 °C. The yields of the reactions are not optimized, and it is clear from this survey that the yields vary with pressure and temperature. Also, side reactions were evident with $CH_2{=}CH_2$ and $CH_2{=}CF_2$, resulting in lower yields. Improved yields in these cases by removing the product after a period of time and recycling the reactants suggest that

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the addition product may decompose by HF elimination. However, no confirmation of this was attempted.

The mechanism for these reactions is probably free radical in nature, but the possibility of a concerted addition or a process involving the initial addition of Br^+ cannot be ruled out. A free radical process may be represented by the following idealized scheme representing initiation, addition, chain transfer, and propagation

$$CF_3NBrF \rightleftarrows CF_3NF\cdot + Br\cdot$$

$$CF_3NF\cdot + H_2C{=}CH_2 \rightarrow CF_3NFCH_2CH_2\cdot$$

$$CF_3NFCH_2CH_2\cdot + CF_3NBrF \rightarrow CF_3NF(CH_2)_2Br + CF_3NF\cdot$$

$$CF_3\text{-}NFCH_2CH_2\cdot + H_2C{=}CH_2 \rightarrow CF_3NF(CH_2)_3CH_2\cdot$$

The relatively weak N-Br bond and the reaction conditions clearly favor the chain-transfer step over propagation because very little telomerization products were observed. Similar results have been observed for $(CF_3)_2NBr$ reactions with olefins.[9]

The very high regioselectivity of these reactions with $CF_2{=}CH_2$, $CF_2{=}CFCl$, $CF_2{=}CBr_2$, and $CF_2{=}CCl_2$ (none of the other regioisomers could be detected by ^{19}F NMR) is consistent with attack of the $CF_3NF\cdot$ radical at the least sterically hindered carbon of the olefin.[10] It also consistent with the expected stabilization of the intermediate free-radical $CF_3NFCF_2CX_1X_2\cdot$, when X_1 is Cl or Br, compared to the intermediate for the formation of the other possible regioisomer, where X = F. An attempt to add CF_3NBrF to a 5:4 mixture of *cis* and *trans*-CFCl=CFCl containing ~10% $CF_2{=}CCl_2$ was also informative. After a few hours at 107 °C, the major product by ^{19}F NMR was $CF_3NFCF_2CCl_2Br$ with only weak signals that could be attributed to *erythro* and *threo*-$CF_3NFCFClCFClBr$. This result is consistent with an expected decrease in reactivity for an olefin with a large halogen on both carbons.

The identity of the new compounds is strongly supported by the data given in the experimental section. The mass spectra, vapor density, molecular weight, and IR are all consistent with those expected for each compound, and the ^{19}F NMR serves to confirm the regioisomer formed. In $CF_3NFCH_2CH_2Br$ the large J_{HF} value of 38.5 Hz must be $^3J_{HF}$ and the large J_{HF} (37.2 Hz) in the adduct with $CF_2{=}CH_2$ must therefore be the same $^3J_{HF}$ in $CF_3NFCH_2CF_2Br$. These $^3J_{HF}$ coupling constants are consistent with previously observed values for compounds containing an FN-CH moiety.[11] Similarly, $^5J_{FF}$ in the latter is very small, and this serves to identify the CF_2Br group in $CF_3NFCF_2CF_2Br$, where $^5J_{FF}$ = 1.0 Hz and $^4J_{FF}$ is 13.0 Hz. Similar $^4J_{FF}$ values of 13 Hz in $CF_3NFCF_2CCl_2Br$, $CF_3NFCF_2CBr_3$, and $CF_3NFCF_2CFClBr$ support the proposed regioisomers. Identical conclusions can also be reached on the basis of the chemical shift of the difluoromethylene group vs. that of a terminal difluoromethyl group. For a variety of examples of the latter from the addition of CF_3SO_3X (X = Cl, Br), CF_3CO_2Cl, and $C_4F_9SO_3$ (X = Cl, Br) to related olefins, the chemical shift of CCF_2X (X = Cl, Br) always appears at much lower field (-60 to -70 ppm) than for the observed products with $CF_2{=}CBr_2$, $CF_2{=}CCl_2$, or $CF_2{=}CFCl$ (-100 ppm), eliminating the alternative regioisomer.[12]

Two additional comments regarding the NMR are needed. For $CF_3{}^ANF^BCF_2{}^CCF^DClBr$, the signal for the fluorines labeled C is a basic overlapping q-d-d. However, at least 32 lines are visible in the multiplet, indicating the presence of different rotational isomers resulting from the presence of the terminal CFClBr group undergoing slow rotation on the NMR time scale. In $CF_3NFCH_2CH_2Br$, the A_2B_2X spin system for the protons was examined by computer simulation, and the coupling constants and chemical shifts reported were estimated by this procedure. However, an iterative fit was not attempted.

All of the *N*-fluoro-*N*-(trifluoromethyl)-*N*-alkylamines are stable colorless liquids at 22 °C and are stable in the presence of $H_2O(l)$. They are also unreactive toward Hg at 22 °C and were recovered unchanged after 10 h. A brief attempt was made to dehydrofluorinate $CF_3NFCH_2CH_2Br$, and with active KF, no reaction was observed after 3 h at 22 °C. With powdered KOH, the compound was absorbed, and a very small amount of volatile material was identified as $CH_2{=}CHBr$ by IR and mass spectrometry.

In conclusion, the thermal addition of CF_3NBrF to olefins provides a facile route to a variety of new *N*-fluorodialkylamines. Such compounds are very rare, and the few examples known have usually been obtained by low yield, direct fluorination reactions.[13] In contrast, large numbers of *N*,*N*-difluoroalkylamines are known via direct fluorination of appropriate nitrogen-containing compounds and via reactions of NF_2 reagents such as HNF_2, $ClNF_2$, and N_2F_4.[13-15]

Experimental Section

General Procedures. All volatile compounds were manipulated in a glass or stainless steel (series 304 and 316) vacuum line. The glass line employed glass-Teflon valves throughout. Pressures were measured with a Wallace and Tiernan differential pressure gauge (series 1500). Temperatures were measured with a digital indicating iron-constantan thermocouple. Amounts of materials were measured by direct weighing or by PVT measurements assuming ideal gas behavior.

Infrared spectra were taken on Perkin-Elmer Model 337, 180, and 1330 spectrometers using a 10-cm glass cell fitted with AgCl or KCl windows. Mass spectra were taken on a Finnigan 4021C GC/MS at 70 eV for EI and CI with methane as the reagent gas for CI. Samples were introduced into the mass spectrometer source via direct gas inlet. NMR spectra were taken on Varian XL-100-15 (^{19}F) and T-60 (^1H) spectrometers using $CFCl_3$ as a solvent and internal standard for ^{19}F and Me_4Si as external standard for ^1H. Concentrations were normally ~15 mol %. High-frequency chemical shifts relative to the standard are positive.

Vapor pressures as a function of temperature were determined by the method of Kellogg and Cady[16] or by a small-volume isoteniscope.[17] A least-squares fit of the data to linear and quadratic equations was employed to determine the extrapolated boiling point and the ΔH_{vap} and ΔS_{vap} values. Melting points were taken by a modified Stock procedure.

Reagents. The olefins $CF_2{=}CF_2$, $CF_2{=}CFCl$, $CF_2{=}CCl_2$, $CF_2{=}CBr_2$, and $CF_2{=}CH_2$ were obtained from PCR, Inc. Their purity was sufficiently high so as to require no purification before use. Ethylene was 99.5% purity. The synthesis of CF_3NBrF was carried out by reaction of $CF_2{=}NF$ with Br_2 over KF or CsF.[8,18]

Reactions. Reactions of CF_3NBrF with olefins were carried out in a 20-mL glass reactor fitted with a glass-Teflon valve. The reactants were condensed into the reactor at -196 °C by vacuum transfer, and the vessel was then heated up to the valve in a

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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. $CF_3{}^{A}NF^{B}CH_2{}^{C}CH_2{}^{D}Br$: 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. $CF_3{}^{A}NF^{B}CH_2{}^{C}CF_2{}^{D}Br$: 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. $CF_3{}^{A}NF^{B}CF_2{}^{C}CF_2{}^{D}Br$: bp 42.9 °C; glass at −110 °C; mol wt 280.1, calcd 281.93; $\log P(\text{torr}) = 6.5371 - 787.05/T - 114664/T^2$; $\Delta H_{vap} = 6.93$ kcal/mol; $\Delta S_{vap} = 22.0$ 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. $CF_3{}^{A}NF^{B}CF_2{}^{C}CF^{D}ClBr$: 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. $CF_3{}^{A}NF^{B}CF_2{}^{C}CBr_3$: bp 152 °C; mp −37 °C; $\log P(\text{torr}) = 7.9812 - 2170.8/T$; $\Delta H_{vap} = 9.93$ kcal/mol; $\Delta S_{vap} = 23.3$ 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. $CF_3{}^{A}NF^{B}CF_2{}^{C}CCl_2Br$: 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.

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