[(M – C_2F_5)$^+$], 181/179 ($C_2F_4Br^+$), 119 [($C_2F_5^+$), 100], 69 (CF_3^+); ^{19}F NMR, $CF_3^ACF_2^BC(O)NHCF_2^CCF_2^DBr$ (d_6-acetone), δ_A –82.6, δ_B –122.0, δ_C –94.3 (br m), δ_D –66.7 (t), J_{CD} = 4.4 Hz; ^{1}H NMR δ 10.80.

ClCF$_2$C(O)NHCF$_2$CF$_2$Br: mp 43.5 °C; IR (gas) 3573 (w), 3458 (s, NH), 1798 (vs, C=O), 1518 (vs), 1291 (m), 1233 (m), 1170 (s), 1109 (s), 1028 (vs), 990 (m), 930 (s), 865 (w), 669 (m) cm^{-1}; MS (EI, major) m/z 274/272 [(M – Cl)$^+$], 224/222 [(M – ClCF$_2$)$^+$], 181/179 ($C_2F_4Br^+$), 131/129 (CF_2Br^+), 85/87 [($CF_2Co)^+$, 100]; ^{19}F NMR, $ClCF_2^AC(O)NHCF_2^BCF_2^CBr$ (d_6-acetone) δ_A –64.9 (s), δ_B –94.2 (br m), δ_C –66.9 (m), J_{BC} = 4.4 Hz; ^{1}H NMR δ 10.8 (br).

General Procedure for the Dehydrofluorination of R$_x$CONHCF$_2$CF$_2$Br. The amide (2.0 mmol) was condensed onto 1.0 g of KF cooled to –196 °C in a 50-mL glass reactor. The mixture was then heated at 60 °C for 1 h, after which time any volatiles were pumped off and collected in a –196 °C trap. The products were then separated from any unreacted amide by trap–trap fractionation. Yields were typically 55–60%.

CF$_3$C(O)N=CFCF$_2$Br: bp 76 °C; IR (gas) 1795 (vs, C=O), 1765 (vs, C=N), 1319 (s), 1295 (s), 1236 (vs), 1193 (vs), 1133 (vs), 1080 (vs), 942 (vs), 833 (s), 800 (w), 734 (s), 708 (s), 656 (m), 624 (s) cm^{-1}; MS (CI, major) m/z 274/272 [(M + 1)$^+$, 100], 254/252 [(M – F)$^+$], 204/202 [(M – CF_3)$^+$], 176/174 [(M – CF_3CO)$^+$], 131/129 (CF_2Br^+), (EI, major) 204/202 [(M – CF_3)$^+$], 193 [(M – Br)$^+$], 97 (CF_3CO^+), 69 [(CF_3^+), 100]; ^{19}F NMR, $CF_3^AC(O)N=CF^BCF_2^CBr$ (C_6D_6), δ_A –76.4, δ_B –34.6 (br t), δ_C –61.7 (d), J_{BC} = 11 Hz; molecular weight calcd 271.9, found 274.5.

CF$_3$CF$_2$C(O)N=CFCF$_2$Br: bp 91–93 °C; IR (gas) 1793 (s, C=O), 1764 (vs, C=N), 1336 (s), 1293 (s) 1266 (vs), 1231 (vs), 1192 (vs), 1143 (vs), 1106 (vs), 1006 (vs), 934 (s), 816 (s), 774 (w), 738 (s), 714 (m), 661 (w), 626 (m) cm^{-1}; MS (CI major) m/z 324/322 [(M + 1)$^+$, 100], 304/302 [(M – F)$^+$], 242 [(M – Br)$^+$], 204/202 [(M – C_2F_5)$^+$], 192 [(M – CF_2Br)$^+$], 147 ($C_2F_5CO^+$), 131/129 (CF_2Br^+), 119 ($C_2F_5^+$), (EI, major) 242 [(M – Br)$^+$], 204/202 [(M – C_2F_5)$^+$, 100], 69 (CF_3^+); ^{19}F NMR (C_6D_6), $CF_3^ACF_2^BC(O)N=CF^CCF_2^DBr$, δ_A –82.6, δ_B –122.4, δ_C –34.4 (br t), δ_D –61.7 (d), J_{CD} = 10 Hz; molecular weight calcd 321.9, found 318.6.

ClCF$_2$C(O)N=CFCF$_2$Br: bp 87 °C; IR (gas) 1798 (vs, C=O), 1765 (vs, C=N) 1293 (vs), 1257 (w), 1243 (w), 1171 (vs), 1128 (vs), 1086 (vs), 1052 (m), 977 (vs), 927 (s), 819 (m), 761 (m), 743 (m), 714 (w), 656 (w), 612 (m) cm^{-1}; MS (CI, major) m/z 292/290/288 [(M + 1)$^+$, 100], 291/289/287 (M$^+$), 272/270/268 [(M – F)$^+$], 204/202 [(M – $ClCF_2$)$^+$], 131/129 (CF_2Br^+), 113 ($ClCF_2CO^+$), (EI, major) 204/202 [(M – $ClCF_2$)$^+$], 87/85 [($ClCF_2^+$), 100]; ^{19}F NMR (C_6D_6), $ClCF_2^AC(O)N=CF^BCF_2^CBr$, δ_A –65.8, δ_B –34.3 (br t), δ_C –61.5 (d), J_{BC} = 10.5 Hz; molecular weight calcd 288.6, found 289.4.

Reaction of CF$_3$C(O)N(Cl)CF$_2$CF$_2$Br with CsF. $CF_3C(O)NClCF_2CF_2Br$ (0.25 mmol) was condensed onto an excess of active CsF (0.45 g) contained in a 50-mL glass reactor at –196 °C. The mixture was warmed and stirred at room temperature for 2 h. Distillation of the crude mixture afforded two major products, identified as (a) $CF_3C(O)F$ and (b) $BrCF_2CF=NCl$. For $BrCF_2CF=NCl$: IR (gas) 1687 (vs, C=N), 1348 (w), 1313 (vs), 1268 (w), 1237 (w), 1189 (vs), 1145 (s), 1113 (vs), 1030 (w), 947 (vs), 912 (m), 828 (m), 789 (s), 742 (vs), 712 (w), 648 (vs), 605 (m) cm^{-1}; MS (EI, major) m/z 211/209 (M$^+$), 192/190 [(M – F)$^+$], 132/130 [(M – Br)$^+$, 100], 131/129 (CF_2Br^+), 82/80 ($FCNCl^+$), 50 (CF_2^+); ^{19}F NMR (C_6D_6), $BrCF_2^ACF^B=NCl$, δ_A –57.9 (d), δ_B –40.6 (t), J_{AB} = 12.7 Hz.

Reaction of CF$_3$C(O)N=CFCF$_2$Br with ClF. $CF_3C(O)N=CFCF_2Br$ (0.5 mmol) and ClF (0.5 mmol) were condensed into a FEP reactor (10 mL) at –196 °C. The reactor was warmed to room temperature and left for 1 h, after which time the volatile products were separated by trap-to-trap distillation. The major product was identified as **CF$_3$C(O)NClCF$_2$CF$_2$Br**: IR (gas) 1772 (vs, C=O), 1525 (w), 1341 (s), 1240 (vs), 1186 (s), 1169 (s), 1099 (vs), 1027 (m), 1001 (m), 930 (m), 909 (m), 895 (m), 828 (s), 802 (s), 777 (vs), 724 (s), 661 (w), 627 (w) cm^{-1}; MS (EI, major) m/z 248/246 [(M – Br)$^+$], 198/196 [(M – CF_2Br)$^+$], 181/179 ($C_2F_4Br^+$), 131/129 (CF_2Br^+), 97 (CF_3CO^+), 69 [(CF_3^+), 100], 50 (CF_2^+); ^{19}F NMR (C_6D_6), $CF_3^AC(O)NClCF_2^BCF_2^CBr$, δ_A –70.7 (t), δ_B –90.6 (sex.), δ_C –63.6 (t), J_{AB} = J_{BC} = 3.9 Hz.

Acknowledgment. The financial support of this research by the Army Research Office (DAAG 29-83-K-0173) and the National Science Foundation is gratefully acknowledged.

Registry No. $CF_3CONH(CF_2)_2Br$, 135041-65-5; $CF_3CF_2CONH(CF_2)_2Br$, 135041-66-6; $ClCF_2CONH(CF_2)_2Br$, 135041-67-7; $Br(CF_2)_2N=CFCF_3$, 135041-68-8; $Br(CF_2)_2N=CFCF_2CF_3$, 135041-69-9; $Br(CF_2)_2N=CFCF_2Cl$, 111223-75-7; $CF_3CON=CFCF_2Br$, 135041-70-2; $CH_3CF_2CON=CFCF_2Br$, 135041-71-3; $ClCF_2CON=CFCF_2Br$, 135041-72-4; CF_3COF, 354-34-7; $ClN=CFCF_2Br$, 135041-73-5; $CF_3CONCl(CF_2)_2Br$, 135041-74-6.

Supplementary Material Available: ^{19}F NMR spectra of all new compounds (9 pages). Ordering information is given on any current masthead page.

Synthesis of β-(Trifluoromethyl)pyrroles via the Cycloaddition of Munchnones to Electron-Deficient Trifluoromethylated Olefins

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The 1,3-dipolar cycloaddition of munchnones (1,3-oxazolium 5-olates) to β-chloro-β-(trifluoromethyl)vinyl phenyl ketone (1) and butyl β-chloro-γ,γ,γ-trifluorocrotonate (2) gave (trifluoromethyl)pyrroles. The monocyclic munchnones **3a–c** yielded the β-(trifluoromethyl)pyrroles **7a–c** and **8a–c** regiospecifically. The bicyclic and tricyclic munchnones **9a,b** and **16a,b** reacted with 1 and 2 to give mixtures of regioisomeric fused-ring trifluoromethylated pyrroles. In all instances, the unsaturated phenone 1 was more reactive than the crotonate 2. The cycloaddition of munchnones to the former occurred with a higher degree of regioselectivity.

Because trifluoromethyl-substituted heterocycles often show biological activity, much current activity has focused on the development of methods for the regioselective synthesis of such compounds.[1] In particular, trifluoromethyl-substituted pyrroles and other five-membered heterocycles have drawn considerable attention.[1,2] However, there exist only a few reports that deal with the synthesis of β-trifluoromethyl-substituted pyrroles.[3] We

(1) For a recent review on fluorine-containing heterocyclic compounds, see: Tanaka, K. *J. Synth. Org. Chem., Jpn.* **1990**, *48*, 16 and references cited therein.

(2) For a recent review on the synthesis of pyrroles, see: Bean, G. P. *The Chemistry of Heterocyclic Compounds*; Jones, R. A., Ed.; John Wiley & Sons: New York, 1989; Vol. 48, Part 1, pp 105 and references cited therein.

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Scheme I

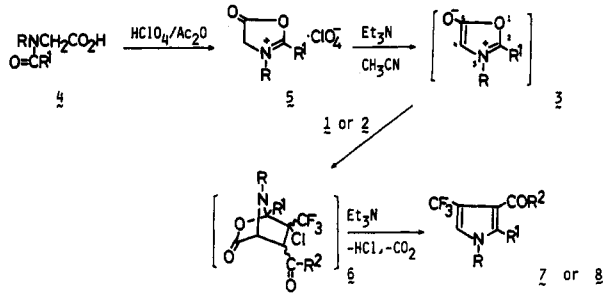
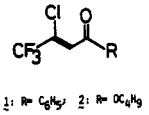


Table I. Synthesis of Pyrroles 7 and 8

perchlorate	olefin	pyrrole	R	R^1	R^2	yield (%)
5a	1	**7a**	C_6H_5	CH_3	C_6H_5	56
5b	1	**7b**	CH_3	C_6H_5	C_6H_5	88
5c	1	**7c**	C_6H_5	C_6H_5	C_6H_5	89
5a	2	**8a**	C_6H_5	CH_3	OC_4H_9	33
5b	2	**8b**	CH_3	C_6H_5	OC_4H_9	33
5c	2	**8c**	C_6H_5	C_6H_5	OC_4H_9	9

report here a synthesis of 3-(trifluoromethyl)pyrroles via the 1,3-dipolar cycloaddition of munchnones to 1 and 2.[4]



1: R= C_6H_5; 2: R= OC_4H_9

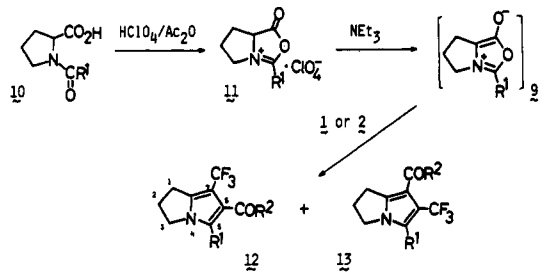
Results and Discussion

Munchnones **3** were originally prepared by Huisgen et al.[5,6] by the acetic anhydride induced dehydrative cyclization of *N*-alkyl-*N*-acyl α-amino acids **4** at high temperature. Boyd et al.[7] later described a method for generating munchnones by the deprotonation of 1,3-oxazolium perchlorate (**5**) with triethylamine at low temperature. The latter method proved advantageous in the work described here because the amine also dehydrochlorinates the bicyclic intermediate **6**. Subsequent decarboxylation yields the pyrroles **7** or **8** (Scheme I).

The reaction of 3 equiv of munchnone **3a** (generated from perchlorate **5a** and 10 equiv of triethylamine) and olefin **1** in acetonitrile solution at temperatures below 0 °C afforded pyrrole **7a** in 56% yield as the only product (Scheme I). The regiochemistry of product **7a** was inferred from that compound's ^1H NMR spectrum, which showed that the pyrrole C(5) proton was coupled with the fluorine atoms of the trifluoromethyl group (J = 1.2 Hz). Similarly, perchlorates **5b** and **5c** gave the pyrroles **7b** and **7c**, respectively, in good yield. The less reactive crotonate **2** also reacted with dipoles **3a–c** to give pyrroles **8a–c**, but in lower yields (Scheme I and Table I).

Fused-ring munchnones, which are derived from cyclic amino acids, reacted with **1** and **2** to give fused-ring pyrroles, which possess skeletons commonly found in naturally occurring alkaloids. The reaction of munchnones **9a** and **9b** (derived from *N*-acylprolines **10a** and **10b**) with ketone **1** gave the regioisomeric dihydropyrrolizines **12a** and **13a**, and **12b** and **13b**, respectively. The major products (**12a** and **12b**) had the same regiochemistry as the monocyclic pyrroles **7** and **8**, which were obtained regiospecifically. Similarly, the reaction of **9a** and **9b** with crotonate **2** gave the dihydropyrrolizines **12c** and **13c** and **12d** and **13d**, respectively. In these cases, the regioselectivity was lower (5:4 and 9:7) than for the reactions of **9a** and **9b** with **1** (3:1 and 5:1) (Scheme II, Table II). The structures of the regioisomers were inferred from the ^1H NMR spectra of **12a–d**, which showed that the C(1) methylene protons were coupled with the fluorine atoms of the trifluoromethyl group (J = 1.6–2.2 Hz). The methyl group protons of **13b** and **13d** were also coupled with the fluorine atoms of the trifluoromethyl group (J = 2.4 Hz).

Scheme II



Scheme III

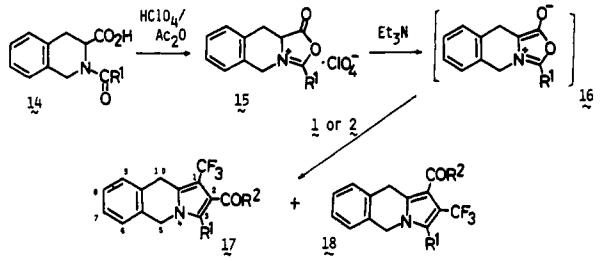


Table II. Synthesis of Dihydropyrrolizines 12 and 13

perchlorate	olefin	R^1	R^2	products (yield, %)	
11a	1	C_6H_5	C_6H_5	**12a** (49)	**13a** (15)
11b	1	CH_3	C_6H_5	**12b** (56)	**13b** (12)
11a	2	C_6H_5	OC_4H_9	**12c** (49)	**13c** (36)
11b	2	CH_3	OC_4H_9	**12d** (9)	**13d** (7)

Table III. Synthesis of Dihydropyrrolo[1,2-*b*]isoquinolines 17 and 18

perchlorate	olefin	R^1	R^2	products (yield, %)	
15a	1	C_6H_5	C_6H_5	**17a** (71)	
15b	1	CH_3	C_6H_5	**17b** (65)	**18b** (21)
15a	2	C_6H_5	OC_4H_9	**17c** (50)	**18c** (24)

The tricyclic 5,10-dihydropyrrolo[1,2-*b*]isoquinolines **17a–c** and **18b** and **18c** were produced by the reactions of munchnones **16a** and **16b** (derived from the *N*-acyl-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acids **14a** and **14b**) with **1** and **2**. Again, the regiochemistry of the products was inferred from the ^1H NMR spectra. The spectra of the major products (compounds **17**) showed that the C(10) methylene protons were coupled with the fluorine atoms of the trifluoromethyl group. Unexpectedly, the 1,3-dipolar cycloaddition of the more crowded of the two olefins, phenone **1**, to the most crowded munchnones, phenyl derivative **16a**, was regiospecific (Scheme III, Table III).

(3) (a) Ogoshi, H.; Homma, M.; Yokota, K.; Toi, H.; Aoyama, Y. *Tetrahedron Lett.* **1983**, *24*, 929. (b) Aoyagi, K.; Toi, H.; Aoyama, Y.; Ogoshi, H. *Chem. Lett.* **1989**, 1891. (c) Jones, R. A.; Rustidge, D.; Cushman, S. *Synth. Commun.* **1984**, *14*, 575.

(4) (a) Okano, T.; Uekawa, T.; Sawaki, H.; Eguchi, S. *Synlett* **1990**, 403. (b) Okano, T.; Uekawa, T.; Eguchi, S. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 2575.

(5) For a recent review, see: Gingrich, H. L.; Baum, J. S. *The Chemistry of Heterocyclic Compounds*, Turichi, I. J., Ed.; John Wiley & Sons: New York, 1986; Vol. 45, pp 731 and references cited therein.

(6) (a) Huisgen, R.; Gotthardt, H.; Bayer, H. O. *Angew. Chem., Int. Ed. Engl.* **1964**, *3*, 135. (b) Huisgen, R.; Gotthardt, H.; Bayer, H. O.; Schaefer, F. C. *Ibid.* **1964**, *3*, 136. (c) Bayer, H. O.; Gotthardt, H.; Huisgen, R. *Chem. Ber.* **1970**, *103*, 2356. (d) Gotthardt, H.; Huisgen, R. *Ibid.* **1970**, *103*, 2625.

(7) Boyd, G. V.; Wright, P. H. *J. Chem. Soc., Perkin Trans. 1* **1972**, 909, 914.

The regioselectivity of the 1,3-dipolar cycloaddition reaction of munchnones to electron-deficient dipolarophiles like unsymmetrical acetylenic esters has been described.[6,8-21] In general, such dipolarophiles, upon reaction with monocyclic munchnones, afford mixtures of regioisomers. Furthermore, in contrast to the reactions of 1 and 2, the cycloaddition of polycyclic dipoles to such dipolarophiles are regiospecific.[5] Huisgen et al.[6] reported that the 1,3-dipolar cycloaddition of the C(4)-substituted munchnone proceeded with reverse regioselectivity. The same regioselectivity was also observed in the cycloadditions of proline-derived munchnones.[13,15,16] However, Padwa et al.[8] demonstrated that the regioselectivity depended on the nature of the substituents on the dipole. Recently, the regioselectivity of the cycloaddition of munchnones to electron-deficient olefins was investigated in detail[19] and was found to depend on the nature of the substituent on C(2) or C(4) of the monosubstituted munchnone 3. However, the controlling MO interaction was HOMO(dipole)–LUMO(dipolarophile), which leads to the preferential formation of 2,3-disubstituted pyrroles (the electron-withdrawing substituent is located at C(3)). The presence of a trifluoromethyl group makes the olefins more dipolarophilic by lowering the level of the LUMO. However, bond polarization is only slightly affected by such substitution.[22] Thus, a high degree of regioselectivity is observed in the reactions of 1 and 2 with monocyclic munchnones 3.

Because 1 and 2 are trisubstituted olefins, considerable steric hindrance to cycloaddition exists. Also, the presence of a substituent on C(4) of the munchnone changes the frontier orbital polarization and inhibits the regioselective formation of cycloadducts. Thus, the reactions of 9 and 16 gave, for the most part, mixtures of regioisomers. The presence of a benzoyl group increases the reactivity of the olefin. Thus, a higher degree of regioselectivity was observed in the reactions of phenone 1 than in those of crotonate 2. The regioselectivity that is observed is also a result of the greater steric hindrance, which destabilizes the electronically less favored transition states.

Experimental Section

^{1}H NMR spectra of $CDCl_3$ solutions were recorded at 200 MHz. ^{19}F NMR spectra of $CDCl_3$ solutions were recorded at 84.67 MHz. Chemical shifts in the ^{19}F NMR spectra were reported in ppm (δ) relative to internal $CFCl_3$. Fuji Gel BW-300 was used for column chromatography.

Oxazolinonium perchlorates 5, 11, and 15 were prepared from the corresponding *N*-acyl-*N*-alkyl α-amino acids by the method of Boyd et al.[7] The crystalline perchlorates 5 and 15 were hygroscopic and were used without purification. The liquid perchlorates **11a** and **11b** were used after overnight drying in vacuo over P_2O_5.

3-Benzoyl-2-methyl-1-phenyl-4-(trifluoromethyl)pyrrole (7a). To a solution of Et_3N (505 mg, 5.0 mmol) in CH_3CN (5 mL) under N_2 was added ketone 1 (117 mg, 0.5 mmol) drop by drop at 0 °C. Then a solution of perchlorate **5a** (413 mg, 1.5 mmol) in CH_3CN (1 mL) was slowly added while the temperature was maintained below 0 °C. The mixture was stirred at 0 °C for 3 h and then at room temperature overnight. After evaporation of the solvent in vacuo, the residue was purified by column chromatography on silica gel (*n*-hexane/EtOAc (5:1 then 5:2)). Pyrrole **7a** was obtained as a pale yellow solid (93 mg, 56%): mp 73–5 °C; IR (KBr) 1643, 1600 cm^{-1}; ^{1}H NMR δ 7.9–7.84 (m, 2 H), 7.64–7.84 (m, 6 H), 7.36–7.30 (m, 2 H), 7.163 (q, J = 1.2 Hz, 1 H), 2.002 (s, 3 H); ^{19}F NMR δ –56.1. Anal. Calcd for $C_{19}H_{14}F_3NO$: C, 69.30, H, 4.28, N, 4.25. Found: C, 69.15, H, 4.56, N, 4.12.

Compounds **7b,c, 8a–c, 17a–c, and 18b,c** were prepared in a similar manner.

3-Benzoyl-2-phenyl-1-methyl-4-(trifluoromethyl)pyrrole (7b) was obtained from ketone 1 (148 mg, 0.63 mmol), Et_3N (606 mg, 6.0 mmol), and perchlorate **5b** (521 mg, 1.89 mmol) as a colorless solid (185 mg, 89%): mp 105–7 °C; IR (KBr) 1748, 1664 cm^{-1}; ^{1}H NMR δ 7.64–7.57 (m, 2 H), 7.35–7.11 (m, 9 H), 3.589 (s, 3 H); ^{19}F NMR δ –56.4. Anal. Calcd for $C_{19}H_{14}F_3NO$: C, 69.30, H, 4.28, N, 4.25. Found: C, 69.48, H, 4.21, N, 4.13.

3-Benzoyl-1,2-diphenyl-4-(trifluoromethyl)pyrrole (7c) was obtained from ketone 1 (117 mg, 0.5 mmol), Et_3N (505 mg, 5.0 mmol), and perchlorate **5c** (507 mg, 1.5 mmol) as a colorless solid (170 mg, 88%): mp 95–6 °C; IR (KBr) 1647 cm^{-1}; ^{1}H NMR δ 7.71–7.65 (m, 2 H), 7.367 (q, J = 1.2 Hz, 1 H), 3.35–7.29 (m, 4 H), 7.23–7.09 (m, 4 H), 7.06–6.91 (m, 5 H); ^{19}F NMR δ –56.6. Anal. Calcd for $C_{24}H_{16}F_3NO$: C, 73.65, H, 4.12, N, 3.58. Found: C, 73.42, H, 4.18, N, 3.75.

Butyl 1-phenyl-2-methyl-4-(trifluoromethyl)pyrrole-3-carboxylate (8a) was obtained from ester 2 (50 mg, 0.22 mmol), Et_3N (222 mg, 2.2 mmol), and perchlorate **5a** as a colorless oil (23 mg, 33%): IR (neat film) 1712 cm^{-1}; ^{1}H NMR δ 7.54–7.45 (m, 3 H), 7.31–7.26 (m, 2 H), 7.065 (q, J = 1.0 Hz, 1 H), 4.280 (t, J = 6.6 Hz, 2 H), 2.418 (s, 3 H), 1.81–1.66 (m, 2 H), 1.56–1.37 (m, 2 H), 0.963 (t, J = 7.0 Hz, 3 H); ^{19}F NMR δ –58.2. Anal. Calcd for $C_{17}H_{18}F_3NO_2$: C, 62.76, H, 5.58, N, 4.31. Found: C, 62.55, H, 5.70, N, 4.33.

Butyl 2-phenyl-1-methyl-4-(trifluoromethyl)pyrrole-3-carboxylate (8b) was obtained from ester 2 (130 mg, 0.56 mmol), Et_3N (566 mg, 5.6 mmol), and perchlorate **5b** (467 mg, 1.69 mmol) as a colorless solid (59 mg, 33%): mp 79–80 °C; IR (KBr) 1712 cm^{-1}; ^{1}H NMR δ 7.48–7.41 (m, 3 H), 7.35–7.28 (m, 2 H), 7.048 (q, J = 1.2 Hz, 1 H), 4.041 (t, J = 6.4 Hz, 2 H), 3.411 (s, 3 H), 1.48–1.03 (m, 2 H), 0.801 (t, J = 7.0 Hz, 3 H); ^{19}F NMR δ –58.0. Anal. Calcd for $C_{17}H_{18}F_3NO_2$: C, 62.76, H, 5.58, N, 4.31. Found: C, 62.63, H, 5.64, N, 4.19.

Butyl 1,2-diphenyl-4-(trifluoromethyl)pyrrole-3-carboxylate (8c) was obtained from ester 2 (115 mg, 0.5 mmol), Et_3N (505 mg, 5.0 mmol), and perchlorate **5c** (507 mg, 1.5 mmol) as a colorless solid (17 mg, 9%): mp 70–2 °C; IR (KBr) 1722 cm^{-1}; ^{1}H NMR δ 7.32–7.15 (m, 9 H), 7.08–7.01 (m, 2 H), 4.113 (t, J = 6.5 Hz, 2 H), 1.56–1.40 (m, 2 H), 1.28–1.09 (m, 2 H), 0.826 (t, J = 7.2 Hz, 3 H); ^{19}F NMR δ –58.1. Anal. Calcd for $C_{22}H_{20}F_3NO_2$: C, 68.21, H, 5.20, N, 3.62. Found: C, 68.43, H, 5.23, N, 3.61.

6-Benzoyl-5-phenyl-7-(trifluoromethyl)-2,3-dihydro-1*H*-pyrrolizine (12a) and 7-Benzoyl-5-phenyl-6-(trifluoromethyl)-2,3-dihydro-1*H*-pyrrolizine (13a). A solution of *N*-benzoylproline[23] (260 mg, 1.186 mmol) and Ac_2O (2.5 mL) under N_2 was cooled in ice/water. Then 70% aqueous $HClO_4$ was slowly added. The mixture was stirred for 10 min at 0 °C. Anhydrous Et_2O (10 mL) was added. Two liquid layers formed. The Et_2O layer was decanted, and the residual viscous oil was washed with anhydrous Et_2O. The oily material was dried overnight in vacuo over P_2O_5. The perchlorate **11a** so obtained was dissolved in CH_3CN (1 mL). From the reaction of 1 (117 mg, 0.5 mmol), Et_3N (505 mg, 5.0 mmol), and perchlorate **11a**, performed in the manner described above, was obtained an inseparable mixture (112 mg,

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64%) of **12a** (49%) and **13a** (15%) as a colorless solid after column chromatography on silca gel: mp 92–113 °C; IR (KBr) 1649 cm^{-1}; ^1H NMR δ 7.92–7.86 (m, 0.23 × 2 H), 7.68–7.64 (m, 0.77 × 2 H), 7.53–7.10 (m, 8 H), 4.008 (t, J = 7.0 Hz, 0.77 × 2 H), 3.632 (t, J = 7.2 Hz, 0.23 × 2 H), 3.119 (tq, J = 7.0, 1.6 Hz, 0.77 × 2 H), 2.946 (t, J = 7.2 Hz, 0.23 × 2 H), 2.570 (tt, J = 7.0, 7.0 Hz, 0.77 × 2 H), 1.920 (tt, J = 7.2, 7.2 Hz, 0.23 × 2 H); ^{19}F NMR δ −55.0 (unseparated peak). Anal. Calcd for $C_{21}H_{16}F_3NO$: C, 70.98, H, 4.54, N, 3.94. Found: C, 71.22, H, 4.68, N, 3.66.

Compounds **12b–d and 13b–d** were prepared in a similar manner.

6-Benzoyl-5-methyl-7-(trifluoromethyl)-2,3-dihydro-1*H*-pyrrolizine (12b) and 7-Benzoyl-5-methyl-6-(trifluoromethyl)-2,3-dihydro-1*H*-pyrrolizine (13b). Treatment of *N*-acetylproline **10b**[24] (235 mg, 1.5 mmol), **1** (100 mg, 0.43 mmol), and Et_3N (505 mg, 5.0 mmol), in the manner described above, gave an inseparable mixture (85 mg, 68%) of **12b** (56%) and **13b** (12%) as a pale yellow amorphous solid: mp 71–101 °C; IR (KBr) 1705, 1628 cm^{-1}; ^1H NMR δ 7.80–7.69 (m, 2 H), 7.58–7.37 (m, 3 H), 3.876 (t, J = 7.0 Hz, 2 H), 3.008 (tq, J = 7.0 Hz, 2.0 Hz, 0.83 × 2 H), 2.64–2.44 (m, 2 H), 2.44–2.36 (m, 0.17 × 2 H), 2.335 (q, J = 2.0 Hz, 0.17 × 3 H), 2.001 (s, 0.83 × 3 H); ^{19}F NMR δ −54.6 (0.18 × 3 F), −54.7 (0.82 × 3 F). Anal. Calcd for $C_{16}H_{14}F_3NO$: C, 65.54, H, 4.81, N, 4.78. Found: C, 65.82, H, 4.92, N, 4.39.

Butyl 5-Phenyl-7-(trifluoromethyl)-2,3-dihydro-1*H*-pyrrolizine-6-carboxylate (12c) and Butyl 5-Phenyl-6-(trifluoromethyl)-2,3-dihydro-1*H*-pyrrolizine-7-carboxylate (13c). From acid **10a** (738 mg, 3.37 mmol), ester **2** (115 mg, 0.5 mmol), and Et_3N (1.01 g, 10.9 mmol) were obtained **12c** (86 mg, 49%) and **13c** (47 mg, 27%) as colorless solids. **12c**: mp 74–6 °C; IR (KBr) 1726 cm^{-1}; ^1H NMR δ 7.44–7.35 (m, 6 H), 4.079 (t, J = 6.5 Hz, 2 H), 3.819 (t, J = 7.2 Hz, 2 H), 3.069 (tq, J = 7.2, 2.0 Hz, 2 H), 2.478 (tt, J = 7.2, 7.2 Hz, 2 H), 1.54–1.39 (m, 2 H), 1.29–1.07 (m, 2 H), 0.814 (t, J = 7.2 Hz, 2 H); ^{19}F NMR δ −55.8. Anal. Calcd for $C19H_{20}F_3NO_2$: C, 64.95, H, 5.74, N, 3.99. Found: C, 64.84, H, 5.74, N, 4.00.

13c: mp 108–9 °C; IR (KBr) 1697 cm^{-1}; ^1H NMR δ 7.51–7.30 (m, 5 H), 4.257 (t, J = 6.6 Hz, 2 H), 2.793 (t, J = 7.3 Hz, 2 H), 3.177 (t, J = 7.3 Hz, 2 H), 2.487 (tt, J = 7.3, 7.3 Hz, 2 H), 1.78–1.63 (m, 2 H), 1.52–1.37 (m, 2 H), 0.925 (t, J = 7.2 Hz, 3 H); ^{19}F NMR δ −54.3. Anal. Calcd for $C_{19}H_{20}F_3NO_2$: C, 64.95, H, 5.74, N, 3.99. Found: C, 64.82, H, 5.88, N, 3.98.

Butyl 5-Methyl-7-(trifluoromethyl)-2,3-dihydro-1*H*-pyrrolizine-6-carboxylate (12d) and Butyl 5-Methyl-6-(trifluoromethyl)-2,3-dihydro-1*H*-pyrrolizine-7-carboxylate (13d). From acid **10b** (314 mg, 2.0 mmol), ester **2** (115 mg, 0.5 mmol), and Et_3N (505 mg, 5.0 mmol) was obtained an inseparable mixture (23 mg, 16%) of **12d** (9%) and **13d** (7%) as a colorless solid: mp 53–55 °C; IR (KBr) 1713 cm^{-1}; ^1H NMR δ 4.225 (t, J = 6.8 Hz, 0.56 × 2 H), 4.208 (t, J = 6.6 Hz, 0.44 × 2 H), 3.883 (t, J = 7.2 Hz, 0.44 × 2 H), 3.870 (t, J = 7.2 Hz, 0.56 × 2 H), 3.100 (t, J = 7.2 Hz, 0.44 × 2 H), 2.990 (tq, J = 7.2, 2.2 Hz, 0.56 × 2 H), 2.513 (tt, J = 7.2, 7.2 Hz, 0.44 × 2 H), 2.497 (tt, J = 7.2, 7.2 Hz, 0.56 × 2 H), 2.461 (s, 0.56 × 3 H), 2.305 (q, J = 2.4 Hz, 0.44 × 3 H), 1.77–1.61 (m, 2 H), 1.53–1.34 (m, 2 H), 0.945 (t, J = 7.2 Hz, 3 H); ^{19}F NMR δ −55.0 (0.44 × 3 F), −55.8 (0.56 × 3 F). Anal. Calcd for $C_{14}H_{18}F_3NO_2$: C, 58.12, H, 6.27, N, 4.84. Found: C, 57.92, H, 6.31, N, 4.68.

2-Benzoyl-3-phenyl-1-(trifluoromethyl)-5,10-dihydropyrrolo[1,2-*b*]isoquinoline (17a). From perchlorate **15a**[25] (327 mg, 0.9 mmol), ketone **1** (70 mg, 0.3 mmol), and Et_3N (303 mg, 3.0 mmol) was obtained **17a** as a colorless solid (89 mg, 71%): mp 206–9 °C; IR (KBr) 1655 cm^{-1}; ^1H NMR δ 7.73–7.68 (m, 2 H), 7.42–7.13 (m, 12 H), 4.964 (s, 2 H), 4.288 (br q, 2 H); ^{19}F NMR δ −53.4. Anal. Calcd for $C_{26}H_{18}F_3NO$: C, 74,81, H, 4.35, N, 3.35. Found: C, 74.65, H, 4.35, N, 3.53.

2-Benzoyl-3-methyl-1-(trifluoromethyl)-5,10-dihydropyrrolo[1,2-*b*]isoquinoline (17b) and 1-Benzoyl-3-methyl-2-(trifluoromethyl)-5,10-dihydropyrrolo[1,2-*b*]isoquinoline (18b). From perchlorate **15b**[26] (453 mg, 1.5 mmol), ketone **1** (115 mg, 0.5 mmol), and Et_3N (505 mg, 5.0 mmol) were obtained **17b** (116 mg, 65% and **18b** (37 mg, 21%) as colorless solids. **17b**: mp 144–5 °C; IR (KBr) 1642 cm^{-1}; ^1H NMR δ 7.86 (m, 2 H), 7.61–7.28 (m, 7 H), 4.984 (s, 2 H), 4.209 (q, J = 1.4 Hz, 2 H), 2.209 (s, 3 H); ^{19}F NMR δ −53.1. Anal. Calcd for $C_{21}H_{16}F_3NO$: C, 70.98, H, 4.54, N, 3.94. Found: C, 70.75, H, 4.32, N, 4.00.

18b: mp 173–5 °C; IR (KBr) 1637 cm^{-1}; ^1H NMR δ 7.85–7.80 (m, 2 H), 7.61–7.13 (m, 7 H), 4.991 (s, 2 H), 3.907 (s, 2 H), 2.478 (q, J = 1.4 Hz, 3 H); ^{19}F NMR δ −52.7. Anal. Calcd for $C_{21}H_{16}F_3NO$: C, 70.98, H, 4.54, N, 3.94. Found: C, 70.71, H, 4.59, N, 4.16.

Butyl 3-Phenyl-1-(trifluoromethyl)-5,10-dihydropyrrolo-[1,2-*b*]isoquinoline-2-carboxylate (17c) and Butyl 3-Phenyl-2-(trifluoromethyl)-5,10-dihydropyrrolo[1,2-*b*]isoquinoline-1-carboxylate (18c). From perchlorate **15a** (450 mg, 1.24 mmol), ester **2** (95 mg, 0.41 mmol), and Et_3N (404 mg, 4.0 mmol) was obtained an inseparable mixture (125 mg, 73%) of **17c** (50%) and **18c** (24%) as a pale yellow oil: IR (neat film) 1720 cm^{-1}; ^1H NMR δ 7.65–7.07 (m, 9 H), 4.753 (s, 0.68 × 2 H), 4.698 (s, 0.32 × 2 H), 4.466 (s, 0.32 × 2 H), 4.263 (q, J = 1.4 Hz, 0.68 × 2 H), 4.036 (t, J = 6.5 Hz, 0.68 × 2 H), 1.44–1.31 (m, 2 H), 1.20–1.05 (m, 2 H), 0.796 (t, J = 7.4 Hz, 3 H); ^{19}F NMR δ −55.8 (0.68 × 3 F), −56.6 (0.32 × 3 F). Anal. Calcd for $C_{24}H_{22}F_3NO_2$: C, 69.72, H, 5.36, N, 3.39. Found: C, 69.43, H, 5.25, N, 3.53.

Supplementary Material Available: Tables of the FMO energy levels and coefficients of acrolein, crotonal, 4,4,4-trifluorocrotonal, and 3,4,4,4-tetrafluorocrotonal calculated by use of CNDO/2 and IR and mass spectra (2 pages). Ordering information is given on any curent masthead page.

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