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TRIFLUOROACETYLATION OF PYRROLO[1,2-*a*]PYRAZINES

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A study was carried out on the reaction of pyrrolo[1,2-a]pyrazines containing an alkyl, aryl, or aralkyl substituent at C-1 with trifluoroacetic anhydride. Trifluoroacetylation products may be formed either by reaction in the pyrrole ring or at the aryl or aralkyl groups at C-1. Products of electrophilic substitution at C-6 are formed in the trifluoroacetylation of pyrrolo[1,2-a]pyrazines containing at C-1 a substituent bulkier than a methyl group but lacking substituents at C-6 (the α-position of the pyrrole ring).

Keywords: pyrrolo[1,2-*a*]pyrazine, trifluoroacetic anhydride, trifluoroacetylation.

The pyrrolo[1,2-*a*]pyrazine bicyclic aromatic system has not been studied extensively, perhaps due to the difficulties in its preparation and its relatively low reactivity. The relative stability of the pyrrolo[1,2-*a*]pyrazine system to the action of weak electrophilic agents is indicated, for example, by the formation of the 6-acetyl derivative in only 16% yield upon heating 1,7-dimethylpyrrolo[1,2-*a*]pyrazine with excess acetic anhydride at reflux for 24 h [1]. The bromination of unsubstituted pyrrolo[1,2-*a*]pyrazine leads to a 1:1 mixture of 8-bromo and 6,8-dibromo derivatives [2, 3], while formylation of this model leads to 8-formylpyrrolo[1,2-*a*]pyrazine in 60% yield as the authors [2] affirm, although the ^{1}H NMR spectrum given for this compound leaves doubt concerning its structural identification. Paudler and Dunham [3] were unable to formylate unsubstituted pyrrolo[1,2-*a*]pyrazine by the Vilsmeier-Haack procedure. Attempts to obtain nitroso or azo derivatives of pyrrolo[1,2-*a*]pyrazines in reactions with nitrous acid and phenyldiazonium chloride also proved unsuccessful [4].

Hence, we undertook a systematic study of the behavior of pyrrolo[1,2-*a*]pyrazines **1-10** in reactions with electrophiles such as acylation with trifluoroacetic anhydride, which is a stronger acylating agent than acetic anhydride. The trifluoroacetyl cation is a rather strong electrophile. Thus, the acylation of pyrroles by trifluoroacetic anhydride proceeds rapidly at 0°C [5]. In previous work [6], we showed that dipyrrolo[1,2-*a*:2',1'-*c*]pyrazines form ditrifluoroacetyl derivatives as the major reaction products with excess trifluoroacetic anhydride even at room temperature. On the other hand, much more complicated behavior is found for 3,4-dihydropyrrolo[1,2-*a*]pyrazines, for which the direction of the reaction depends on the structure of the starting compounds and substrate/reagent ratio [7].

The α-position of the pyrrole ring in 1-methylpyrrolo[1,2-*a*]pyrazine (**1**) is unoccupied and we might expect that the most likely product in its reaction with trifluoroacetic anhydride would be 6-trifluoroacetylpyrrolo[1,2-*a*]pyrazine by analogy to acylation by acetic anhydride [1]. However, the reaction of **1** with a 2.5-fold excess of trifluoroacetic anhydride in benzene (method A) yielded three products. NMR spectroscopy and mass spectrometry indicated the formation of 1-(3,3,3-trifluoro-2-oxopropylidene)-

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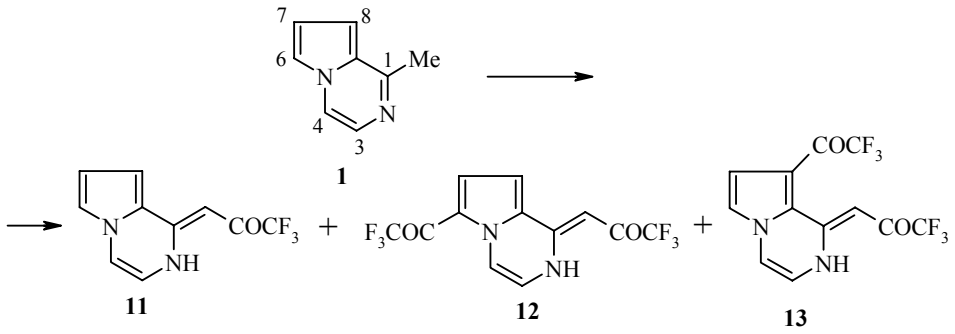
1,2-dihydropyrrolo[1,2-*a*]pyrazine (**11**), 1-(3,3,3-fluoro-2-oxopropylidene)-6-(trifluoroacetyl)-1,2-dihydropyrrolo-[1,2-*a*]pyrazine (**12**), and 1-(3,3,3-trifluoro-2-oxopropylidene)-8-(trifluoroacetyl)-1,2-dihydropyrrolo[1,2-*a*]-pyrazine (**13**).



Similar trifluoroacetylation results leading to trifluoroacetonyl derivatives were obtained previously for methyl-substituted azines such as pyridine or pyrimidine [8]. Pyridine was shown to promote this reaction.

The yield of product **11** is enhanced while the yields of **12** and **13** were reduced to trace amounts when the acylation of **1** was carried out with a 2.5-fold excess of trifluoroacetic anhydride in the presence of pyridine (method B). Increasing the amount of reagent to a 10-fold excess and the acylation reaction time to 72 h (methods C and D) led to the exclusive formation of ditrifluoroacetyl derivatives **12** and **13** (Tables 1-3).

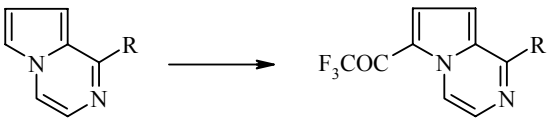
TABLE 1. Characteristics ot Compounds Synthesized

Com-pound	Empirical formula	Found, % / Calculated, %			mp,°C	Yield, % (method)
		C	H	N		
11	$C_{10}H_7F_3N_2O$	52.22 / 52.64	2.84 / 3.09	12.06 / 12.28	145-146	32 (A), 44 (B)
12	$C_{12}H_6F_6N_2O_2$	44.52 / 44.46	1.65 / 1.87	8.84 / 8.64	240-250 (dec.)	11 (A), 2 (B), 31 (C), 78 (D)
13	$C_{12}H_6F_6N_2O_2$	44.15 / 44.46	1.94 / 1.87	8.35 / 8.64	230-240 (dec.)	12 (A), 3 (B), 34 (C), 14 (D)
14	$C_{11}H_9F_3N_2O$	53.97 / 54.55	3.67 / 3.75	11.89 / 11.57	82-84	37 (A), 60 (B)
15	$C_{12}H_{11}F_3N_2O$	55.69 / 56.25	4.18 / 4.33	11.12 / 10.93	108-110	51 (A), 59 (B)
16	$C_{12}H_{11}F_3N_2O$	55.89 / 56.25	4.27 / 4.33	10.54 / 10.93	88-90	87 (A), 98 (B)
17	$C_{15}H_9F_3N_2O$	61.87 / 62.07	3.25 / 3.13	9.59 / 9.65	112-114	94 (A), 64 (B)
18	$C_{13}H_7F_3N_2OS$	52.58 / 52.70	2.45 / 2.38	9.38 / 9.46	116-117	50 (A), 70 (B)
19	$C_{14}H_{13}F_3N_2O$	59.65 / 59.57	4.50 / 4.64	9.85 / 9.92	40-42	63 (B)
20	$C_{16}H_{11}F_3N_2O$	63.57 / 63.16	3.46 / 3.64	9.26 / 9.21	86-88	69 (B)
21	$C_{18}H_{10}F_6N_2O_2$	52.54 / 54.01	2.58 / 2.52	6.72 / 7.00	176-180 (dec.)	9 (B)
22	$C_{11}H_9F_3N_2O$	54.19 / 54.55	3.63 / 3.75	11.62 / 11.57	214-215	4 (A), 46 (B)
23	$C_{13}H_8F_6N_2O_2$	47.25 / 46.17	3.10 / 2.38	7.06 / 8.28	212-214 (dec.)	6 (A), traces (B), 67 (C), 66 (D)
24	$C_{11}H_{11}F_3N_2O_2$	49.25 / 50.77	4.09 / 4.64	10.55 / 10.77	144-146	64 (A)
25	$C_{12}H_{11}F_3N_2O$	55.89 / 56.25	4.44 / 4.33	10.74 / 10.93	126-128	5 (B)

TABLE 2. Mass Spectra of Compounds **11-25**

Compound	*m/z* (I_{rel}, %)
11	228 $[M]^+$ (79.55), 160 (10.79), 159 (100), 132 (7.95), 131 (59.66), 104 (27.84), 103 (9.09), 78 (14.77), 77 (18.18)
12	324 $[M]^+$ (71.40), 255 (100), 227 (19.28), 158 (27.64), 130 (17.22)
13	324 $[M]^+$ (86.07), 255 (100), 227 (77.27), 177 (53.98), 158 (48.57), 130 (19.99), 103 (19.95), 79 (19.62)
14	242 $[M]^+$ (94.34), 241 (59.82), 173 (100), 145 (24.53), 144 (22.37), 117 (17.65), 91 (24.15), 86 (21.76), 69 (12.26), 64 (14.77), 63 (17.94)
15	256 $[M]^+$ (33.14), 255 (16.51), 241 (42.69), 229 (18.91), 228 (100), 187 (15.87), 159 (29.26), 158 (19.92), 144 (17.48), 131 (28.17), 117 (10.49), 103 (10.93), 90 (12.03), 77 (19.19)
16	256 $[M]^+$ (100), 241 (77.63), 228 (53.22), 214 (12.04), 187 (31.79), 158 (6.00), 144 (15.16), 89 (5.62)
17	290 $[M]^+$ (74.50), 221 (100), 193 (32.15), 192 (29.28), 168 (36.44), 140 (20.29), 139 (20.27), 70 (21.36), 63 (25.93), 51 (18.52)
18	297 (14.06), 296 $[M]^+$ (73.05), 227 (100), 199 (21.88), 159 (18.72), 155 (10.59), 114 (12.56), 69 (19.39), 64 (18.37), 57 (18.28), 44 (91.90)
19	282 $[M]^+$ (26.30), 253 (25.49), 242 (19.75), 241 (100), 156 (31.45), 144 (25.48), 58 (22.77), 44 (24.34), 43 (51.08)
20	304 $[M]^+$ (43.48), 303 (100), 235 (13.66), 207 (25.13), 206 (35.25), 205 (21.45)
21	400 $[M]^+$ (83.19), 331 (100), 303 (43.69), 206 (60.60), 205 (78.90), 117 (21.88)
22	242 $[M]^+$ (72.17), 173 (100), 145 (64.88), 118 (31.86), 91 (12.57), 77 (14.14), 73 (16.52), 72 (20.40), 63 (18.19), 51 (18.07)
23	338 $[M]^+$ (46.69), 269 (100), 241 (75.72), 191 (39.20), 172 (54.41), 171 (26.75), 86 (29.65), 69 (30.80), 63 (41.70)
24	147 (32.64), 146 (96.11), 145 (100), 104 (16.58), 69 (44.95), 51 (19.33), 45 (25.15)
25	256 $[M]^+$ (27.88), 188 (15.20), 187 (100), 159 (15.49), 93 (20.22), 78 (25.17), 63 (30.01)

The trifluoroacetylation of pyrrolo[1,2-*a*]pyrazines with the pyrrole ring free in the α-position when the substrate has a substituent at $C_{(1)}$ other than a methyl group proceeds selectively at the α-position of the pyrrole ring. Thus, compounds **2-7** give 1-ethyl-, 1-propyl-, 1-(2-propyl)-, 1-phenyl-, 1-(2-thienyl)-, and 1-cyclopentyl-6-(trifluoroacetyl)pyrrolo[1,2-*a*]pyrazines **14-19**. Carrying out this reaction in the presence of pyridine leads to enhanced yields of the reaction products (Table 1).

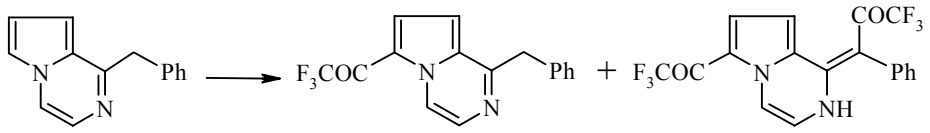


2–7 **14–19**

2, **14** R = Et, **3**, **15** R = Pr, **4**, **16** R = *i*-Pr, **5**, **17** R = Ph, **6**, **18** R = 2-Th, **7**, **19** R = *c*-C_5H_{11}

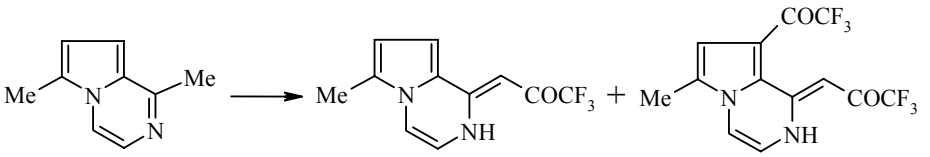
We should note that acylation of 1-benzylpyrrolo[1,2-*a*]pyrazine (**8**) with trifluoroacetic anhydride is more ambiguous and leads to the formation both of the predominant 6-trifluoroacetyl derivative, 1-(phenylmethyl)-6-(trifluoroacetyl)pyrrolo[1,2-*a*]pyrazine (**20**) in 69% yield and the ditrifluoroacetyl derivative, (3,3,3-trifluoro-2-oxo-1-phenylpropylidene)-6-(trifluoroacetyl)-1-pyrrolo[1,2-*a*]pyrazine (**21**), in 9% yield.

A similar dependence for the result of trifluoroacetylation on the structure of the substituent at $C_{(1)}$ of the pyrrolo[1,2-*a*]pyrazine system is found for these compounds substituted in the α-position of the pyrrole ring.



8 **20** **21**

Thus, the reaction of 1,6-dimethylpyrrolo[1,2-*a*]pyrazine (**9**) with trifluoroacetic anhydride by method A gave two products analogous to **12** and **13** in low yields: 1-(3,3,3-trifluoro-2-oxopropylidene)-6-methyl-1,2-dihydropyrrolo[1,2-*a*]pyrazine (**22**) in 4% yield and 1-(3,3,3-trifluoro-2-oxopropylidene)-6-methyl-8-(trifluoroacetyl)-1,2-dihydropyrrolo[1,2-*a*]pyrazine (**23**) in 6% yield.

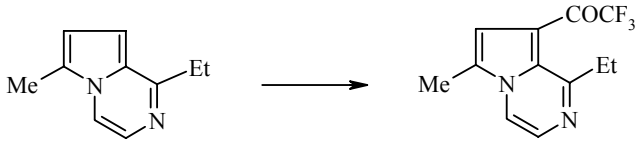


9 **22** **23**

In addition to **22** and **23**, 1,6-dimethylpyrrolo[1,2-*a*]pyrazinium trifluoroacetate (**24**) was isolated from the reaction mixture. Trifluoroacetate **24** is probably the result of the reaction of starting pyrrolopyrazine **9** and trifluoroacetic acid formed during the reaction. The formation of an analogous by-product, 2-methyl-3H-indolizinium trifluoroacetate, has been observed in the trifluoroacetylation of 2-methylindolizine [9]. The formation of **24** is not observed when the reaction is carried out in the presence of pyridine, which binds the acid.

The acylation of pyrrolo[1,2-*a*]pyrazine **9** by trifluoroacetic anhydride in the presence of pyridine (method B) leads predominantly to the formation of monotrifluoroacetyl derivative **22** in 46% yield, while significantly increasing the excess of anhydride and the reaction time (methods C and D) leads to the formation of **23** in good yields (66-67%).

A mixture of acylation products is formed in the reaction of 1-ethyl-6-methylpyrrolo[1,2-*a*]pyrazine (**10**) with trifluoroacetic anhydride. Only one compound could be isolated with low yield from this reaction mixture. ^{1}H NMR spectroscopy and mass spectrometry indicated that this product was 1-ethyl-6-methyl-8-(trifluoroacetyl)pyrrolo[1,2-*a*]pyrazine (**25**).



10 **25**

TABLE 3. ^{1}H NMR Spectra of Compounds Sinthesized

Compound	Solvent	Chemical shifts, δ, ppm (*J*, Hz)
1	2	3
11	$CDCl_3$	5.99 (1H, s, C<u>H</u>COCF$_3$); 6.80 (1H, d, $J_{3,4}$ = 5.4, H-3); 6.82 (1H, dd, $J_{7,6}$ = 2.6, $J_{7,8}$ = 4.3, H-7); 7.10 (1H, d, $J_{8,7}$ = 4.3, H-8); 7.34 (1H, d, $J_{4,3}$ = 5.4, H-4); 7.38 (1H, dd, $J_{6,7}$ = 2.6, $J_{6,8}$ = 1.0, H-6)
	Acetone-d_6	6.04 (1H, s, C<u>H</u>COCF$_3$); 6.86 (1H, dd, $J_{7,6}$ = 2.6, $J_{7,8}$ = 4.2, H-7); 7.24 (1H, d, $J_{3,4}$ = 5.6, H-3); 7.33 (1H, d, $J_{8,7}$ = 4.2, H-8); 7.74 (1H, dd, $J_{6,7}$ = 2.6, $J_{6,8}$ = 1.3, H-6); 7.84 (1H, d, $J_{4,3}$ =5.6, H-4)
12	Acetone-d_6	6.31 (1H, s, C<u>H</u>COCF$_3$); 7.57 (1H, dd, $J_{7,8}$ = 4.8, $J_{8,4}$ = 0.55, H-8); 7.64 (1H, d, $J_{3,4}$ = 5.6, H-3); 7.77 (1H, dq, $J_{7,8}$ = 4.8, J_{H-F} = 2.1, H-7); 8.83 (1H, dd, $J_{4,3}$ = 5.6, $J_{4,8}$ = 0.6, H-4)

TABLE 3. (continued)

1	2	3
13	Acetone-d_6	7.51 (1H, m, H-7); 7.52 (1H, s, C<u>H</u>COCF$_3$); 7.63 (1H, d, $J_{3,4}$ = 5.4, H-3); 7.93 (1H, d, $J_{6,7}$ = 3.2, H-6); 8.06 (1H, d, $J_{4,3}$ = 5.4, H-4)
	DMSO-d_6	7.35 (1H, s, C<u>H</u>COCF$_3$); 7.46 (1H, m, H-7); 7.56 (1H, d, $J_{3,4}$ = = 5.4, H-3); 7.95 (1H, d, $J_{6,7}$ = 3.3, H-6); 8.03 (1H, d, $J_{4,3}$ = 5.4, H-4)
14	$CDCl_3$	1.44 (3H, t, J = 7.5, CH$_2$C<u>H</u>$_3$); 3.14 (2H, q, J = 7.5, C<u>H</u>$_2$CH$_3$); 6.91 (1H, d, $J_{8,7}$ = 5.2, H-8); 7.70 (1H, m, H-7); 8.05 (1H, d, $J_{3,4}$ = 5.0, H-3); 9.40 (1H, d, $J_{4,3}$ = 5.0, H-4)
	Acetone-d_6	1.40 (3H, t, J = 7.4, CH$_2$C<u>H</u>$_3$); 3.16 (2H, q, J = 7.5, C<u>H</u>$_2$CH$_3$); 7.16 (1H, d, $J_{8,7}$ = 5.0, H-8); 7.78 (1H, m, H-7); 8.12 (1H, d, $J_{3,4}$ = 4.7, H-3); 9.36 (1H, d, $J_{4,3}$ = 4.7, H-4)
15	Acetone-d_6	1.01 (3H, t, J = 7.5, CH$_3$); 1.88 (2H, m, CH$_2$C<u>H</u>$_2$CH$_3$); 3.08 (2H, t, J = 7.5, C<u>H</u>$_2$CH$_2$CH$_3$); 7.16 (1H, dd, $J_{8,7}$ = 5.0, $J_{8,4}$ = 0.8, H-8); 7.77 (1H, dq, $J_{7,8}$ = 5.0, J_{H-F} = 2.10, H-7); 8.09 (1H, d, $J_{3,4}$ = 4.7, H-3); 9.34 (1H, d, $J_{4,3}$ = 4.7, H-4)
16	$CDCl_3$	1.43 (6H, d, J = 6.8, CH(C<u>H</u>$_3$)$_2$); 3.55 (1H, m, J = 6.8, C<u>H</u>(CH$_3$)$_2$); 6.96 (1H, dd, $J_{8,7}$ = 5.0, $J_{8,4}$ = 0.8, H-8); 7.71 (1H, dq, $J_{7,8}$ = 5.0, J_{H-F} = 1.9, H-7); 8.03 (1H, d, $J_{3,4}$ = 4.8, H-3); 9.42 (1H, d, $J_{4,3}$ = 4.8, H-4)
17*	$CDCl_3$	7.08 (1H, dd, $J_{8,7}$ = 5.0, $J_{8,4}$ = 0.8, H-8); 7.55-7.58 (3H, m, H-*p,m* Ph); 7.74 (1H, dq, $J_{7,8}$ = 5.0, J_{H-F} = 2.0, H-7); 7.92 (2H, m, H-*o* Ph); 8.21 (1H, d, $J_{3,4}$ = 4.7, H-3); 9.53 (1H, dd, $J_{4,3}$ = 4.7, $J_{4,8}$ = 0.8, H-4)
18	Acetone-d_6	7.30 (1H, dd, $J_{\alpha,\beta}$ = 5.1, $J_{\beta,\beta'}$ = 3.9, H-β Th); 7.54 (1H, dd, $J_{8,7}$ = 5.0, $J_{8,4}$ = 0.9, H-8); 7.81 (1H, dd, $J_{\alpha,\beta}$ = 5.0, $J_{\alpha,\beta'}$ = 1.0, H-α Th); 7.91 (1H, dq, $J_{7,8}$ = 5.0, J_{H-F} = 2.0, H-7); 8.09 (1H, dd, $J_{\beta,\beta'}$ = 3.9, $J_{\alpha,\beta'}$ = 1.0, H-β' Th); 8.20 (1H, d, $J_{3,4}$ = 4.7, H-3); 9.49 (1H, dd, $J_{4,3}$ = 4.7, $J_{4,8}$ = 0.9, H-4)
19	$CDCl_3$	1.74–2.19 (8H, m, –(CH$_2$)$_4$); 3.67 (1H, q, J = 8.4, –C<u>H</u> cyclopentyl); 6.96 (1H, d, $J_{8,7}$ = 5.1, H-8); 7.70 (1H, m, H-7); 8.06 (1H, d, $J_{3,4}$ = 4.7, H-3); 9.40 (1H, d, $J_{4,3}$ = 4.7, H-4)
20	$CDCl_3$	4.44 (2H, s, –C<u>H</u>$_2$Ph); 6.86 (1H, dd, $J_{8,7}$ = 4.8, $J_{8,4}$ = 0.5, H-8); 7.23–7.36 (5H, m, Ph); 7.65 (1H, dq, $J_{7,8}$ = 4.8, J_{H-F} = 1.9, H-7); 8.07 (1H, d, $J_{3,4}$ = 4.7, H-3); 9.43 (1H, dd, $J_{4,3}$ = 4.7, H-4)
21	$CDCl_3$	5.01 (1H, d, $J_{8,7}$ = 5.2, H-8); 7.22 (1H, d, $J_{3,4}$ = 5.7, H-3); 7.27 (1H, dq, $J_{7,8}$ = 5.2, J_{H-F} = 2.0, H-7); 7.35-7.53 (5H, m, C$_6$H$_5$); 9.00 (1H, dd, $J_{4,3}$ = 5.7, H-4)
22	$CDCl_3$	2.49 (3H, s, 6-CH$_3$); 5.95 (1H, s, C<u>H</u>COCF$_3$); 6.61 (1H, d, $J_{7,8}$ = 4.3, H-7); 6.85 (1H, d, $J_{3,4}$ = 5.5, H-3); 7.05 (1H, d, $J_{8,7}$ = 4.3, H-8); 7.20 (1H, d, $J_{4,3}$ = 5.5, H-4)
	Acetone-d_6	2.54 (3H, s, 6-CH$_3$); 5.98 (1H, s, C<u>H</u>COCF$_3$); 6.69 (1H, dd, $J_{8,7}$ = 4.3, $J_{8,4}$ = 0.5, H-7); 7.26 (1H, d, $J_{3,4}$ = 5.8, H-3); 7.28 (1H, d, $J_{7,8}$ = 4.3, H-8); 7.62 (1H, d, $J_{4,3}$ = 5.8, H-4)
23	Acetone-d_6	2.61 (3H, d, J = 0.8, 6-CH$_3$); 7.32 (1H, m, H-7); 7.44 (1H, s, C<u>H</u>COCF$_3$); 7.64 (1H, d, $J_{3,4}$ = 5.5, H-3); 7.80 (1H, d, $J_{4,3}$ = 5.5, H-4)
24	Acetone-d_6	2.70 (3H, s, 6-CH$_3$); 2.93 (3H, s, 1-CH$_3$); 7.15 (1H, d, $J_{7,8}$ = 4.3, H-7); 7.64 (1H, d, $J_{8,7}$ = 4.3, H-8); 7.68 (1H, d, $J_{4,3}$ = 5.5, H-4); 8.26 (1H, d, $J_{3,4}$ = 5.5, H-3)
25	$CDCl_3$	1.30 (3H, t, J = 7.4, CH$_2$C<u>H</u>$_3$); 2.52 (3H, s, 6-CH$_3$); 3.46 (2H, q, J = 7.4, C<u>H</u>$_2$CH$_3$); 7.22 (1H, m, H-7); 7.68 (1H, d, $J_{3,4}$ = 4.4, H-3); 8.00 (1H, d, $J_{4,3}$ = 4.4, H-4)

* ^{13}C NMR spectrum ($CDCl_3$), δ, ppm: 107.56, 119.06, 132.84 (C-3,4,8); 116.90 (q, J = 289, CF_3); 125.28 (q, J = 3.9, C-7); 128.65, 128.86 (*o,m*-C_6H_5); 130.33 (*p*-C_6H_5); 136.91 (C-9); 154.06 (C-1); 170.14 (q, J = 35.8, C=O).

Thus, the trifluoroacetylation of pyrrolo[1,2-*a*]pyrazines with various substituents at $C_{(1)}$ is a ambiguous reaction. The structure of the reaction products is a function of the substituents. The formation of substitution products at the alkyl or aralkyl group is possible in the case of alkyl or aralkyl substituents at $C_{(1)}$.

EXPERIMENTAL

The ^{1}H and ^{13}C NMR spectra of all the products were taken on a Varian VXR-400 spectrometer at 400 MHz with TMS as the internal standard. The mass spectra were taken on a Kratos mass spectrometer with 70 eV ionization energy. The reaction course was monitored by thin-layer chromatography on Silufol UV-254 plates. Starting pyrrolo[1,2-*a*]pyrazines **1-10** were prepared according to our previous procedure [10].

Trifluoroacetylation of Pyrrolo[1,2-*a*]pyrazines (General Method). A. A solution of pyrrolo[1,2-*a*]pyrazine (3 mmol) in dry ether (10 ml) was cooled with ice and then a solution of trifluoroacetic anhydride (7.5 mmol) in ether (10 ml) was added dropwise with stirring. The reaction mixture was stirred for 5-7 h at room temperature, then poured into cold water, and extracted with chloroform. The extract was dried over 3 Å sieves and evaporated in vacuum. The residue was subjected to chromatography on a column packed with silica gel (100/160). The eluent was benzene or 1:3 ethyl acetate-petroleum ether. The products were recrystallized from heptane.

B. A mixture of pyrrolo[1,2-*a*]pyrazine (3 mmol) and pyridine (7.5 mmol) in dry ether (10 ml) was cooled with ice and a solution of trifluoroacetic anhydride (7.5 mmol) in ether (10 ml) was added dropwise with stirring. The reaction mixture was stirred for 5-7 h and then treated as in method A.

C. A solution of trifluoroacetic anhydride (30 mmol) in ether (15 ml) was added dropwise with stirring to pyrrolo[1,2-*a*]pyrazine (3 mmol) in dry ether (10 ml) with ice cooling. The reaction mixture was stirred at room temperature for 72 h and then treated as in method A.

D. A solution of trifluoroacetic anhydride (30 mmol) in ether (15 ml) was added dropwise to an ice-cooled mixture of pyrrolo[1,2-*a*]pyrazine (3 mmol) and pyridine (30 mmol) in dry ether (15 ml). The reaction mixture was stirred at room temperature for 72 h and then treated as in method A.

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