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

V. I. Terenin[1], M. A. Butkevich[1], and A. P. Pleshkova[2]

We have synthesized nitro derivatives of pyrrolo[1,2-a]pyrazines using a nitrating mixture and acetyl nitrate. We have obtained the products of oxidation of the side chain of 1,6-substituted pyrrolo[1,2-a]-pyrazines.

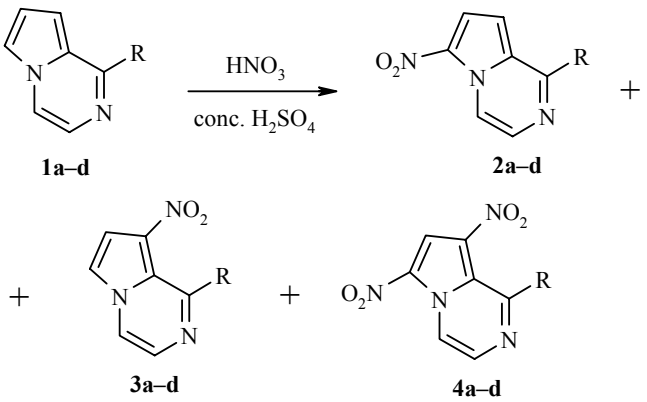
Keywords: pyrrolo[1,2-*a*]pyrazines, nitration, oxidation.

Pyrrolodiazine derivatives have attracted the attention of researchers because they have a broad spectrum of physiological activity. Azole and azine moieties are encountered in many natural biologically active compounds such as alkaloids and biogenic amines.

The bicyclic aromatic system of pyrrolo[1,2-*a*]pyrazine has been poorly studied due to the relative difficulty of obtaining it, its low reactivity relative to electrophiles, and also the ambiguous reaction pathways of these compounds [1]. The relative stability of the pyrrolo[1,2-*a*]pyrazine system with respect to treatment with weak electrophilic reagents is suggested by the fact that the unsubstituted pyrrolo[1,2-*a*]pyrazine, when boiled with excess acetic anhydride for 24 h, forms 6-acetylpyrrolo[1,2-*a*]pyrazine in only 16% yield [2].

Earlier we studied the nitration reaction for asymmetrically substituted dipyrrolo[1,2-*a*;2',1'-*c*]pyrazine systems. Nitration was carried out by treatment with a mixture of nitric acid (d = 1.42 g/ml) and acetic anhydride at -10°C. The nitronium ion attacks the free α-position of the pyrrole ring to form the mononitro and dinitro derivatives [3].

We have studied nitration reactions of pyrrolo[1,2-*a*]pyrazines containing alkyl and aralkyl substituents at the 1 and 6 positions of the heterocycle when treated with a nitrating mixture, with acetyl nitrate, and with nitric acid.



1a–d **2a–d** **3a–d** **4a–d**

1-4 a R = Me; **b** R = Et; **c** R = Pr; **d** R = *i*-Pr

[1] M. V. Lomonosov Moscow State University, Moscow 119899, Russia; e-mail: vter@org.chem.msu.ru.
[2] A. N. Nesmeyanov Institute of Organoelement Compounds, Russian Academy of Sciences, Moscow 119991.
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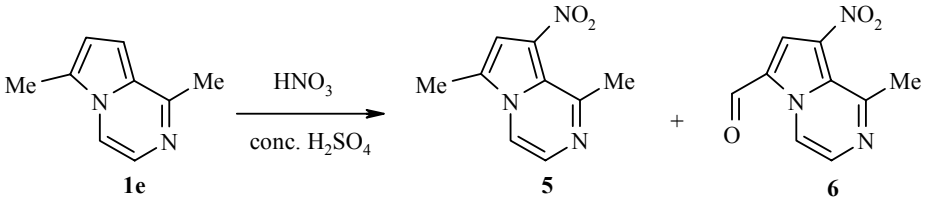
In the molecules of 1-methyl- (**1a**), 1-ethyl- (**1b**), 1-propyl- (**1c**), and 1-isopropyl- (**1d**) pyrrolo[1,2-*a*]-pyrazines, the α-position of the pyrrole ring is free and we might expect that the reaction will occur with formation of 6-nitro-substituted pyrrolo[1,2-*a*]pyrazines. It also seemed likely that 8-nitro derivatives would form analogously to the bromination and formylation products [1].

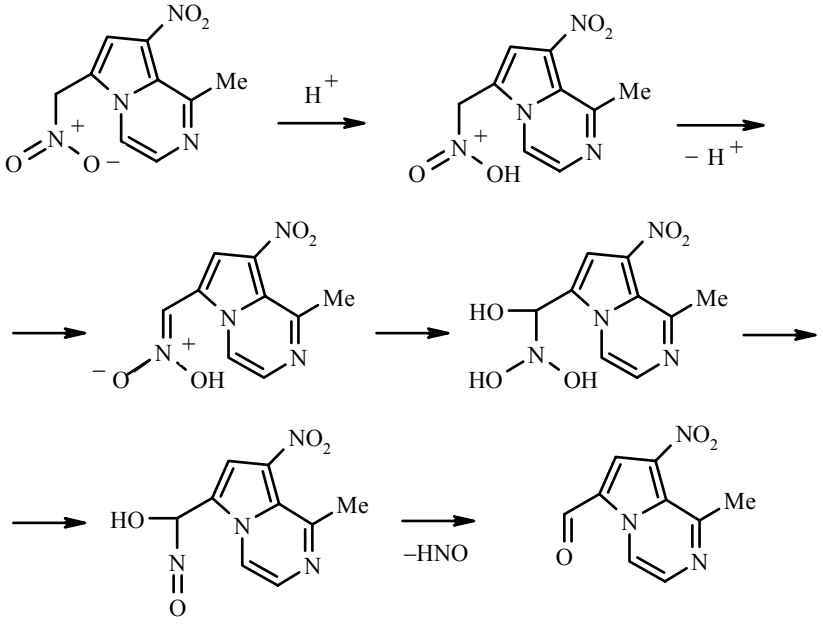
As a result of the reactions carried out using a nitrating mixture (HNO_3, d = 1.35 g/ml), three compounds were isolated in each case: the 6-nitro derivatives (**2a-d**), the 8-nitro derivatives (**3a-d**), and the 6,8-dinitro derivatives **4a-d**.

In nitration of 1,6-dimethylpyrrolo[1,2-*a*]pyrazine (**1e**) by a nitrating mixture with nitric acid of any concentration, two nitration products are formed: 1,6-dimethyl-8-nitropyrrolo[1,2-*a*]pyrazine (**5**) and 1-methyl-8-nitropyrrolo[1,2-*a*]pyrazine-6-carbaldehyde (**6**).

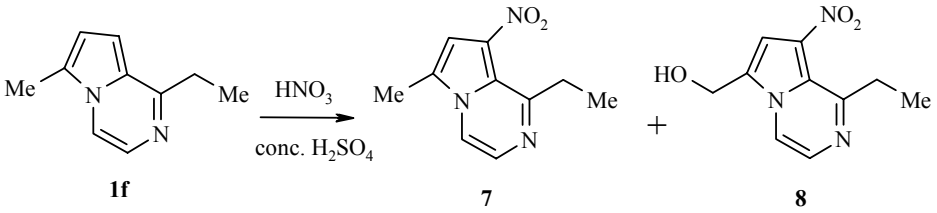


1e **5** **6**

It is likely that the product of nitration of the methyl group in the 6 position is formed as an intermediate, which then is converted to the aldehyde according to the Nef reaction when treated with concentrated sulfuric acid [4].

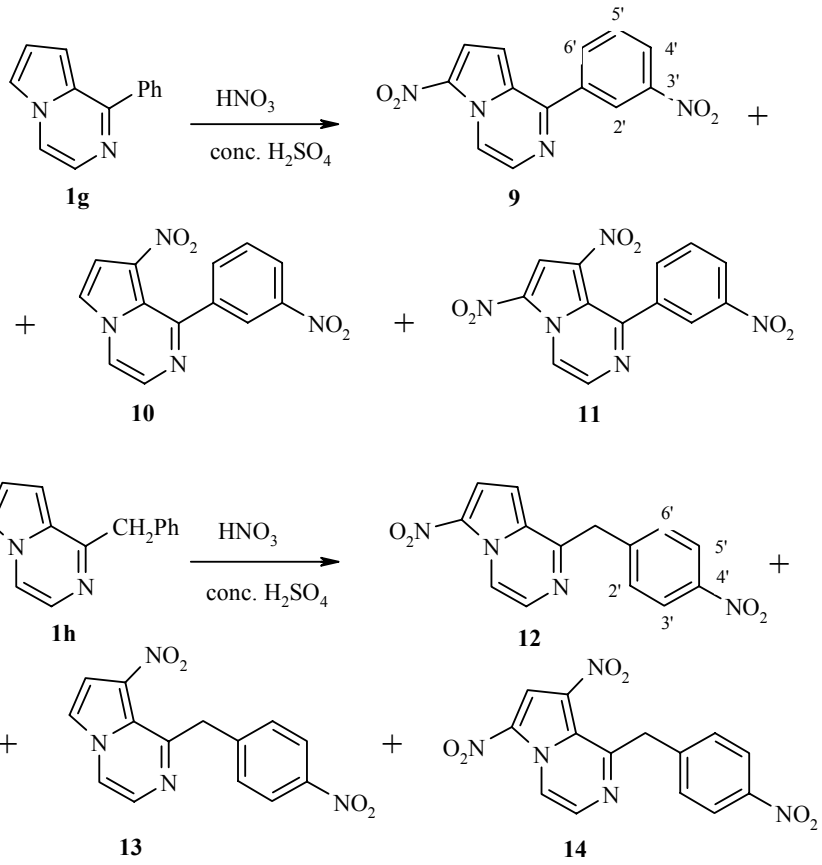


When the methyl group in the 1 position of the heterocyclic system is replaced by an ethyl group (compound **1f**), the 8-nitro derivative **7** is also formed (HNO_3, d = 1.35 g/ml). If we carry out the reaction with concentrated nitric acid (d = 1.42), the yield of compound **7** is decreased by almost a factor of five. In addition, the product of transformation of the methyl group at the α-position is formed: (1-ethyl-8-nitropyrrolo[1,2-*a*]-pyrazin-6-yl)methanol (**8**).



1f **7** **8**

1-Phenylpyrrolo[1,2-*a*]pyrazine (**1g**) and 1-benzylpyrrolo[1,2-*a*]pyrazine (**1h**) react to form the 6-nitro and 8-nitro derivatives (HNO_3, d = 1.35). Furthermore, the benzene rings of the substituents also undergo attack simultaneously. In 1-phenylpyrrolo[1,2-*a*]pyrazine, the benzene ring reacts at the *meta* position to form compounds **9-11**, while in the case of 1-benzylpyrrolo[1,2-*a*]pyrazine this leads to dinitro- and trinitro-1-(4-nitrobenzyl)pyrrolo[1,2-*a*]pyrazines **12-14**:



1g **9**

10 **11**

1h **12**

13 **14**

With concentrated nitric acid, only compounds **11** and **14** are formed.

When we go to acetyl nitrate as the nitrating agent for pyrrolo[1,2-*a*]pyrazines that do not have substituents at the 6 position of the heterocycle, the overall product yield decreases and pyrrolo[1,2-*a*]pyrazines are formed containing only one nitro group on the pyrrole ring, and in addition acetylation products are formed in trace amounts.

However, when there is a methyl substituent at the α-position of the pyrrole ring, nitropyrrolo[1,2-*a*]-pyrazines **5** and **7** are formed in 44% and 65% yields respectively.

In the case of compounds **1g** and **1h**, we did not achieve satisfactory results for nitration by acetyl nitrate. Mixtures of a large number of nitration and acetylation products are formed which could not be separated.

TABLE 1. ^{1}H NMR Spectra of Synthesized Compounds

Com-pound	Chemical shifts, δ, ppm, *J*, Hz
2a	2.81 (3H, s, 1-CH_3); 6.87 (1H, d, J_{87} = 5.06, H-8); 7.78 (1H, d, J_{78} = 5.06, H-7); 8.01 (1H, d, J_{34} = 4.75, H-3); 9.18 (1H, d, J_{43} = 4.75, H-4)
3a	3.04 (3H, s, 1-CH_3); 7.29 (1H, d, J_{67} = 2.34, H-6); 7.52 (1H, d, J_{76} = 2.34, H-7); 7.81 (2H, s, H-3,4)
4a	3.08 (3H, s, 1-CH_3); 8.31 (1H, d, J_{34} = 4.68, H-3); 8.39 (1H, s, H-7); 9.38 (1H, d, J_{43} = 4.68, H -4)
2b	1.44 (3H, t, *J* = 7.49, $CH_2\underline{CH_3}$); 3.12 (2H, q, *J* = 7.49, $\underline{CH_2}CH_3$); 6.88 (1H, d, J_{87} = 4.97, H-8); 7.77 (1H, d, J_{78} = 4.97, H-7); 8.05 (1H, d, J_{34} = 4.26, H-3); 9.18 (1H, d, J_{43} = 4.26, H-4)
3b	1.35 (3H, t, *J* = 7.27, $CH_2\underline{CH_3}$); 3.42 (2H, q, *J* = 7.27, $\underline{CH_2}CH_3$); 7.32 (1H, d, J_{67} = 3.46, H-6); 7.53 (1H, d, J_{76} = 3.46, H-7); 7.82 (1H, d, J_{34} = 4.26, H-3); 7.86 (1H, d, J_{43} = 4.26, H-4)
4b	1.39 (3H, t, *J* = 7.36, $CH_2\underline{CH_3}$); 3.42 (2H, q, *J* = 7.36, $\underline{CH_2}CH_3$); 8.36 (1H, d, J_{34} = 4.27, H-3); 8.38 (1H, s, H-7); 9.38 (1H, d, J_{43} = 4.27, H-4)
2c	1.05 (3H, t, *J* = 7.57, $CH_2CH_2\underline{CH_3}$); 1.91 (2H, sext, *J* = 7.57, $CH_2\underline{CH_2}CH_3$); 3.06 (2H, t, *J* = 7.57, $\underline{CH_2}CH_2CH_3$); 6.89 (1H, d, J_{87} = 5.19, H-8); 7.77 (1H, d, J_{78} = 5.19, H-7); 8.05 (1H, d, J_{34} = 4.89, H-3); 9.17 (1H, d, J_{43} = 4.89, H-4)
3c	1.04 (3H, t, *J* = 7.52, $CH_2CH_2\underline{CH_3}$); 1.78 (2H, sext, *J* = 7.52, $CH_2\underline{CH_2}CH_3$); 3.36 (2H, t, *J* = 7.52, $\underline{CH_2}CH_2CH_3$); 7.31 (1H, d, J_{67} = 3.27, H-6); 7.54 (1H, d, J_{76} = 3.27, H-7); 7.81 (1H, d, J_{34} = 4.58, H-3); 7.85 (1H, d, J_{43} = 4.58, H-4)
4c	1.05 (3H, t, *J* = 7.63, $CH_2CH_2\underline{CH_3}$); 1.81 (2H, sext, *J* = 7.63, $CH_2\underline{CH_2}CH_3$); 3.35 (2H, t, *J* = 7.63, $\underline{CH_2}CH_2CH_3$); 8.35 (1H, d, J_{34} = 4.76, H-3); 8.40 (1H, s, H-7); 9.40 (1H, d, J_{43} = 4.76, H-4)
2d	1.42 (6H, d, *J* = 6.78, $CH(\underline{CH_3})_2$); 3.52 (1H, sept, *J* = 6.78, $\underline{CH}(CH_3)_2$); 6.91 (1H, dd, J_{87} = 5.16, J_{84} = 0.74, H-8); 7.77 (1H, d, J_{78} = 5.16, H-7); 8.08 (1H, d, J_{34} = 4.67, H-3); 9.16 (1H, dd, J_{43} = 4.67, J_{48} = 0.74, H-4)
3d	1.34 (6H, d, *J* = 6.66, $CH(\underline{CH_3})_2$); 4.19 (1H, sept, *J* = 6.66, $\underline{CH}(CH_3)_2$); 7.30 (1H, d, J_{67} = 3.02, H-6); 7.54 (1H, d, J_{76} = 3.02, H-7); 7.79 (1H, d, J_{34} = 4.46, H-3); 7.90 (1H, d, J_{43} = 4.46, H-4)
4d	1.38 (6H, d, *J* = 6.50, $CH(\underline{CH_3})_2$); 3.99 (1H, sept, *J* = 6.50, $\underline{CH}(CH_3)_2$); 8.38 (1H, s, 7-H); 8.39 (1H, d, J_{34} = 4.89, H-3); 9.38 (1H, d, J_{43} = 4.89, H-4)
5	2.94 (3H, s, 6-CH_3); 3.04 (3H, c, 1-CH_3); 7.32 (1H, s, H-7); 7.62 (1H, d, J_{34} = 4.27, H-3); 7.86 (1H, d, J_{43} = 4.27, H-4)
6	3.09 (3H, s, 1-CH_3); 8.14 (1H, s, H-7); 8.18 (1H, d, J_{34} = 4.37, H-3); 9.51 (1H, d, J_{43} = 4.37, H-4); 9.92 (1H, s, CHO); [^{13}C NMR: 26.64 (CH_3); 117.97 ($C_{(7)}$); 122.09 ($C_{(6)}$); 123.82 ($C_{(4)}$); 125.26 ($C_{(8)}$); 128.49 ($C_{(9)}$); 133.79 ($C_{(3)}$); 154.09 ($C_{(1)}$); 179.89 (CHO)]
7	1.35 (3H, t, *J* = 7.39, $CH_2\underline{CH_3}$); 2.49 (3H, s, 6-CH_3); 3.43 (2H, q, *J* = 7.39, $\underline{CH_2}CH_3$); 7.34 (1H, s, H-7); 7.63 (1H, d, J_{34} = 4.78, H-3); 7.92 (1H, d, J_{43} = 4.78, H-4)
8	1.34 (3H, t, *J* = 7.28, $CH_2\underline{CH_3}$); 3.42 (2H, q, *J* = 7.28, $\underline{CH_2}CH_3$); 4.95 (2H, s, $\underline{CH_2}$OH); 7.47 (1H, s, H-7); 7.94 (1H, d, J_{34} = 4.25, H-3); 8.08 (1H, d, J_{43} = 4.25, H-4); [^{13}C NMR: 13.26 ($CH_2\underline{CH_3}$); 31.66 ($\underline{CH_2}CH_3$); 56.18 (CH_2OH); 114.07 ($C_{(7)}$); 115.45 ($C_{(4)}$); 115.55 ($C_{(6)}$); 123.11 ($C_{(8)}$); 124.86 ($C_{(9)}$); 126.78 ($C_{(1)}$); 130.53 ($C_{(3)}$)]
9	7.05 (1H, d, J_{87} = 5.09, H-8); 7.75-7.79 (1H , m, H-5'); 7.88 (1H, d, J_{78} = 5.09, H-7); 8.26-8.29 (3H, m, H-3,4',6'); 8.81 (1H, t, $J_{2'4'} = J_{2'6'}$ = 1.67, H-2'); 9.38 (1H, d, J_{43} = 4.89, H-4)
10	7.53 (2H, d, J_{67} = 3.22, H-6); 7.63 (1H, d, J_{76} = 3.22, H-7); 7.64 (1H, m, H-5'); 7.83 (1H, dt, $J_{6'5'}$ = 7.62, $J_{6'2'} = J_{6'4'}$ = 1.49, H-6'); 8.04 (1H, d, J_{34} = 4.59, H-3); 8.12 (1H, d, J_{43} = 4.59, H-4); 8.35 (1H, ddd, $J_{4'5'}$ = 8.15, $J_{4'2'} = J_{4'6'}$ = 1.49, H-4'); 8.45 (1H, t, $J_{2'4'} = J_{2'6'}$ = 1.49, H-2')
11	7.68-7.83 (2H, m, H-5',6'); 8.36-8.48 (3H, m, H-7,2',4'); 8.58 (1H, d, J_{34} = 4.49, H-3); 9.57 (1H, d, J_{43} = 4.49, H-4)
12	4.54 (2H, s, CH_2); 6.89 (1H, dd, J_{87} = 4.88, J_{84} = 0.77, H-8); 7.51 (2H, d, $J_{2'3'} = J_{6'5'}$ = 8.67, H-2',6'); 7.77 (1H, d, J_{78} = 4.88, H-7); 8.08 (1H, d, J_{34} = 4.82, H-3); 8.15 (2H, d, $J_{3'2'} = J_{5'6'}$ = 8.67, H-3',5'); 9.22 (1H, d.d, J_{43} = 4.82, J_{48} = 0.77, H-4)
13	4.93 (2H, s, CH_2); 7.38 (1H, d, J_{67} = 3.29, H-6); 7.40 (2H, d, $J_{2'3'} = J_{6'5'}$ = 8.92, H-2',6'); 7.55 (1H, d, J_{76} = 3.29, H-7); 7.90 (1H, d, J_{34} = 4.50, H-3); 7.92 (1H, d, J_{43} = 4.50, H-4); 8.12 (2H, d, $J_{3'2'} = J_{5'6'}$ = 8.92, H-3',5)
14	4.93 (2H, s, CH_2); 7.37 (2H, d, $J_{2'3'} = J_{6'5'}$ = 8.75, H-2',6'); 8.11 (2H, d, $J_{3'2'} = J_{5'6'}$ = 8.75, H-3',5'); 8.38 (1H, s, H-7); 8.40 (1H, d, J_{34} = 4.82, H-3); 9.47 (1H, d, J_{43} = 4.82, H-4)

In nitration of pyrrolo[1,2-*a*]pyrazines **1e** and **1f** by concentrated nitric acid, compounds **5** and **7** are formed in good yields. In the case of pyrrolo[1,2-*a*]pyrazines that do not contain a methyl group in the α-position, a mixture of dinitro and trinitro derivatives is formed.

TABLE 2. Mass Spectra of Synthesized Compounds

Com-pound	*m/z* (I_{rel}, %)
2a	177 $[M]^+$ (100), 147 (29.43), 131 (12.22), 119 (10.69), 104 (15.33), 77 (25.63), 63 (7.84), 51 (11.79)
3a	177 $[M]^+$ (100), 160 (89.58), 147 (26.75), 132 (19.21), 118 (11.60), 117 (17.10), 104 (30.46), 93 (51.32), 77 (24.46), 63 (18.37), 51 (22.09)
4a	222 $[M]^+$ (100) 205 (61.23), 177 (15.06), 146 (23.65), 130 (17.03), 118 (49.90), 103 (19.10), 91 (16.93), 76 (33.43), 52 (17.52)
2b	191 $[M]^+$ (100), 163 (5.17), 145 (10.06), 132 (6.64), 117 (18.94), 104 (7.27), 91 (15.91), 77 (10.85), 63 (12.47), 52 (13.77)
3b	191 $[M]^+$ (94.54), 176 (100), 174 (89.67), 157 (47.60), 143 (50.41), 131 (42.92), 118 (88.27), 106 (34.37), 90 (36.59), 79 (19.93), 63 (33.01), 52 (20.48)
4b	236 $[M]^+$ (15.60), 221 (100), 206 (48.26), 173 (68.66), 144 (29.79), 131 (72.22), 117 (65.02), 104 (33.93), 89 (57.84), 77 (48.45), 63 (73.59), 52 (87.32)
2c	205 $[M]^+$ (22.40), 190 (30.63), 177 (100), 158 (23.37), 144 (46.74), 131 (29.19), 118 (26.39), 104 (15.72), 91 (9.67), 77 (18.54), 59 (20.13)
3c	205 $[M]^+$ (51.77), 190 (19.11), 176 (48.99), 157 (73.72), 132 (100), 118 (84.26), 106 (38.75), 76 (23.60), 62 (47.67), 53 (38.51)]
4c	250 $[M]^+$ (17.77), 235 (14.22), 222 (38.50), 206 (82.44), 172 (58.98), 156 (59.12), 143 (25.77), 132 (93.92), 117 (100), 103 (51.59), 90 (48.67), 78 (51.81), 64 (57.96)
2d	205 $[M]^+$ (59.46), 190 (37.29), 177 (70.19), 158 (21.63), 144 (100), 131 (29.56), 117 (42.19), 90 (16.68), 78 (18.43), 53 (26.72)
3d	205 $[M]^+$ (34.98), 190 (45.33), 172 (26.12), 157 (40.17), 143 (31.03), 118 (52.61), 105 (10.80), 90 (41.61), 77 (24.63), 63 (37.33), 51 (38.02), 43 (100)
4d	250 $[M]^+$ (45.32), 235 (100), 217 (53.54), 187 (27.02), 156 (61.85), 143 (47.81), 132 (71.29), 117 (71.88), 105 (39.98), 89 (58.61), 77 (80.88), 64 (57.91), 52 (82.03)
5	191 $[M]^+$ (100), 174 (50.88), 161 (16.77), 144 (18.01), 131 (19.19), 106 (15.70), 93 (56. 88), 77 (80.50), 63 (24.45), 51 (15.76)
6	205 $[M]^+$ (86.00), 188 (100), 175 (16.14), 159 (6.60), 146 (9.07), 104 (26.72), 93 (38.21), 77 (26.63), 63 (23.11), 51 (24.64)
7	205 $[M]^+$ (92.83), 188 (100), 175 (20.31), 160 (13.45), 145 (17.48), 132 (9.01), 117 (6.77), 105 (27.17), 93 (45.71), 77 (21.04), 63 (18.11), 51 (17.31)
8	221 $[M]^+$ (90.71), 206 (100), 191 (31.30), 177 (29.64), 161 (17.37), 157 (62.33), 148 (43.07), 131 (32.14), 119 (34.99), 107 (30.42), 90 (20.02), 77 (25.47), 63 (36.82), 52 (41.98)
9	284 $[M]^+$ (100), 268 (12.61), 253 (20.64), 239 (68.96), 222 (67.00), 205 (72.90), 192 (80.92), 180 (47.27), 166 (17.29), 140 (40.71), 127 (31.04), 92 (29.00), 76 (53.70)
10	284 $[M]^+$ (100), 268 (8.93), 254 (28.95), 237 (12.25), 221 (12.60), 208 (66.88), 191 (43.53), 179 (21.15), 166 (22.50), 154 (15.73), 138 (12.14), 126 (6.15), 114 (4.48), 91 (2.72), 76 (3.68)
11	329 $[M]^+$ (100), 313 (3.01), 299 (5.83), 282 (2.82), 253 (10.36), 237 (4.10), 207 (12.42), 191 (14.00), 179 (22.34), 164 (13.82), 152 (11.35), 125 (7.28), 102 (7.61), 75 (9.24)
12	298 $[M]^+$ (62.50), 297 (100), 281 (13.46), 251 (44.52), 205 (60.23), 193 (18.81), 177 (11.70), 164 (5.18), 151 (15.42), 126 (4.91), 89 (14.77)
13	298 $[M]^+$ (21.41), 281 (100), 252 (26.73), 235 (87.53), 221 (19.41), 205 (96.70), 178 (46.08), 147 (90.52), 132 (74.77), 89 (52.10)
14	343 $[M]^+$ (5.40), 326 (84.61), 297 (21.66), 280 (62.72), 250 (31.93), 221 (28.01), 205 (73.12), 192 (100), 177 (92.34), 164 (23.55), 150 (75.50), 104 (33.21), 89 (45.84)

TABLE 3. Physicochemical Characteristics of Synthesized Compounds

Compound	Empirical formula	Found, % / Calculated, %			mp, °C	Yield, %*			
		C	H	N		A	B	C	D
2a	$C_8H_7N_3O_2$	54.34 / 54.24	3.81 / 3.95	23.32 / 23.73	142-144	17	0	7	
3a	$C_8H_7N_3O_2$	53.92 / 54.24	3.73 / 3.95	23.48 / 23.73	185-186	37	0	6	
4a	$C_8H_6N_4O_4$	43.38 / 43.24	2.77 / 2.70	25.34 / 25.23	158-160	18	50	0	
2b	$C_9H_9N_3O_2$	56.19 / 56.54	4.64 / 4.71	21.59 / 21.99	145-150	6	1	4	
3b	$C_9H_9N_3O_2$	56.16 / 56.54	4.50 / 4.71	21.58 / 21.99	142-144	4	0	14	
4b	$C_9H_8N_4O_4$	45.54 / 45.76	3.28 / 3.39	23.62 / 23.73	129-131	63	59	0	
2c	$C_{10}H_{11}N_3O_2$	58.43 / 58.54	5.13 / 5.36	20.59 / 20.49	60	0	0	4	
3c	$C_{10}H_{11}N_3O_2$	58.85 / 58.54	4.04 / 5.36	20.94 / 20.49	92-94	0	0	13	
4c	$C_{10}H_{10}N_4O_4$	47.95 / 48.00	4.04 / 4.00	22.23 / 22.40	105-106	61	84	0	
2d	$C_{10}H_{11}N_3O_2$	58.36 / 58.54	5.67 / 5.36	20.96 / 20.49	82-84	4	0	0	
3d	$C_{10}H_{11}N_3O_2$	58.87 / 58.54	5.61 / 5.36	20.05 / 20.49	100	12	0	1	
4d	$C_{10}H_{10}N_4O_4$	47.87 / 48.00	4.00 / 4.00	22.16 / 22.40	106-107	55	65	0	
5	$C_9H_9N_3O_2$	56.36 / 56.54	4.57 / 4.71	21.52 / 21.99	164-166	13	17	44	92
6	$C_9H_7N_3O_3$	52.36 / 52.68	3.02 / 3.41	20.37 / 20.49	204 (with dec.)	10	3	0	
7	$C_{10}H_{11}N_3O_2$	58.34 / 58.54	5.55 / 5.37	20.21 / 20.49	128-130	70	15	31	65
8	$C_{10}H_{11}N_3O_3$	54.10 / 54.29	4.77 / 4.98	18.88 / 19.00	144-146	0	9	0	0
9*[2]	$C_{13}H_8N_4O_4$	/ 54.93	/ 2.82	/ 19.71	—	6	0	0	
10	$C_{13}H_8N_4O_4$	54.49 / 54.93	2.70 / 2.82	20.13 / 19.71	185-186	17	0	0	
11	$C_{13}H_7N_5O_6$	47.12 / 47.42	2.53 / 2.13	21.47 / 21.28	218-220	49	31	0	
12	$C_{14}H_{10}N_4O_4$	56.10 / 56.38	3.77 / 3.36	18.48 / 18.79	135-140	0	13	0	
13	$C_{14}H_{10}N_4O_4$	56.63 / 56.38	3.61 / 3.36	18.87 / 18.79	135-138	0	18	0	
14	$C_{14}H_9N_5O_6$	49.04 / 48.98	2.47 / 2.62	20.62 / 20.41	65-70	32	11	0	

* A = reagent H_2SO_4 + HNO_3 (d = 1.35 g/ml); B = reagent H_2SO_4 + HNO_3 (d = 1.42 g/ml); C = reagent $(MeCO)_2O$ + HNO_3 (d = 1.35 g/ml); D = HNO_3 (d = 1.42 g/ml).

*[2] The compound was not isolated in pure form.

EXPERIMENTAL

The ^1H and ^{13}C NMR spectra were recorded on a Varian VXR-400 (400 MHz and 100 MHz respectively) in $CDCl_3$, internal standard TMS. The mass spectra were recorded on an MS Kratos with ionization energy 70 eV. The course of the reaction was monitored by TLC on Silufol UV-254 plates. The

starting pyrrolo[1,2-*a*]pyrazines were synthesized by the procedure in [5]. The physicochemical and spectral characteristics of the compounds obtained are presented in Tables 1-3.

Nitration by the Nitrating Mixture (General Procedure). Nitric acid of the appropriate concentration (6 mmol) were added dropwise with stirring to a solution (cooled down to 0°C) of pyrrolo[1,2-*a*]pyrazine (2 mmol) in conc. H_2SO_4 (3 ml). The mixture was stirred for 72 h at 20°C and then poured over crushed ice. In the case of compounds **4a-d**, the precipitate formed was filtered out and washed with hot water. The mother liquor was extracted with benzene and dried by 3 Å sieves, and then the solvent was evaporated. Compounds **2a-d** and **3a-d** were chromatographed on a column with Silpearl silica gel in the system 1:1 benzene–ethyl acetate. In the case of compounds **5-14**, the aqueous solution was neutralized with sodium carbonate; the precipitate formed was filtered out and washed with hot water. The mother liquor was extracted with benzene and dried. The precipitate and the extracts were combined and chromatographed on a column with Silpearl silica gel in a mixture of a 3:1 solution of benzene–ethyl acetate.

Nitration by Acetyl Nitrate (General Procedure). A solution of pyrrolo[1,2-*a*]pyrazine (2 mmol) in acetic anhydride (16 mmol) was added dropwise with stirring to a solution (cooled down to 5°C-10°C) of nitric acid (d = 1.35 g/ml) (6 mmol) in acetic anhydride (12 mmol). The mixture was stirred for 48 h at 20°C until the starting compound disappeared according to TLC, and then it was poured into cold water. The aqueous solution was neutralized with sodium carbonate; the precipitate formed was filtered out and washed with hot water. The mother liquor was extracted with benzene and dried by 3 Å sieves. The precipitate and evaporated extract were combined and chromatographed on a column with Silpearl silica gel in a 1:1 benzene–ethyl acetate mixture.

Nitration by Nitric Acid (General Procedure). Compounds **1e** and **1f** were dissolved (with cooling down to 0°C) in nitric acid (d = 1.42 g/ml). The solution was stirred for 72 h at 20°C and then poured into cold water. The aqueous solution was neutralized with sodium carbonate; the precipitate formed was filtered out and washed with hot water.

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