Chemistry of Heterocyclic Compounds, Vol. 44, No. 2, 2008

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

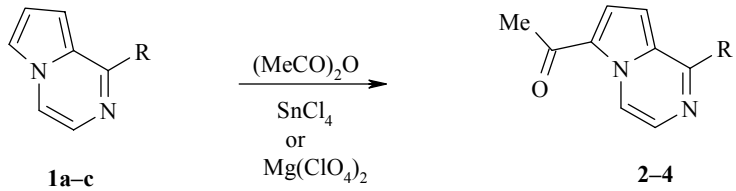
V. I. Terenin, M. A. Butkevich, A. S. Ivanov, and E. V. Kabanova

The acylation of pyrrolo[1,2-a]pyrazines with acetic anhydride and the acid chlorides of various carboxylic acids has been studied. It has been shown that pyrrole[1,2-a]pyrazines are selectively acylated at the α-position of the pyrrole ring when it is free. Products of the condensation of 1-methyl-substituted pyrrolo[1,2-a]pyrazines have been obtained for the first time in the process of acetylation.

Keywords: pyrrolo[1,2-*a*]pyrazines, acylation, electrophilic substitution.

In a continuation of a study of the behavior of the pyrrolo[1,2-*a*]pyrazine system under electrophilic substitution conditions, we have investigated the acylation of alkyl-, aryl-, and hetaryl-substituted pyrrolo-[1,2-*a*]pyrazines. It was established previously that acetylation of 3,4-dihydropyrrolo[1,2-*a*]pyrazines with acetic anhydride (in the presence of magnesium perchlorate as a Lewis acid) proceeded selectively at the pyrazine atom $N_{(2)}$ and formed N-acyl-substituted derivatives in 25-87% yield [1].

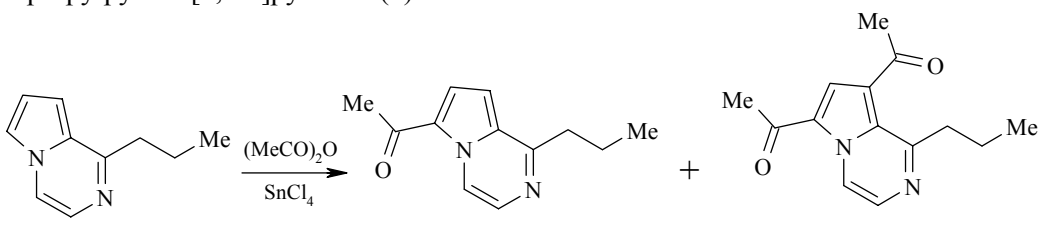
In contrast to the hydrogenated system, acylation of aromatic pyrrolo[1,2-*a*]pyrazines occurs at the free α-position of the pyrrole ring. For example boiling the pyrrolo[1,2-*a*]pyrazines **1a-c** with acetic anhydride in the presence of tin(IV) chloride or magnesium perchlorate proceeded selectively to give the monosubstituted products **2-4**, but the yields of the acyl derivatives did not exceed 14%.



1a–c **2–4**

1a, 2 R = Me; **1b, 3** R = Et; **1c, 4** R = Ph

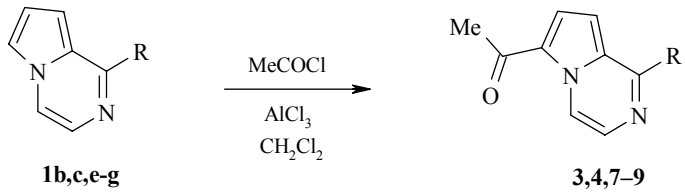
Under analogous conditions 1-propylpyrrolo[1,2-*a*]pyrazine (**1d)** reacted with the formation of a mixture of two products of acylation in low overall yield (10%) – 6-acetyl-1-propylpyrrolo[1,2-*a*]pyrazine (**5**) and 6,8-diacetyl-1-propylpyrrolo[1,2-*a*]pyrazine (**6**).



1d **5** **6**

M. V. Lomonosov Moscow State University, Moscow 119992; e-mail: vter@org.chem.msu.ru. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 2, 263-272, February, 2008. Original article submitted April 16, 2007.

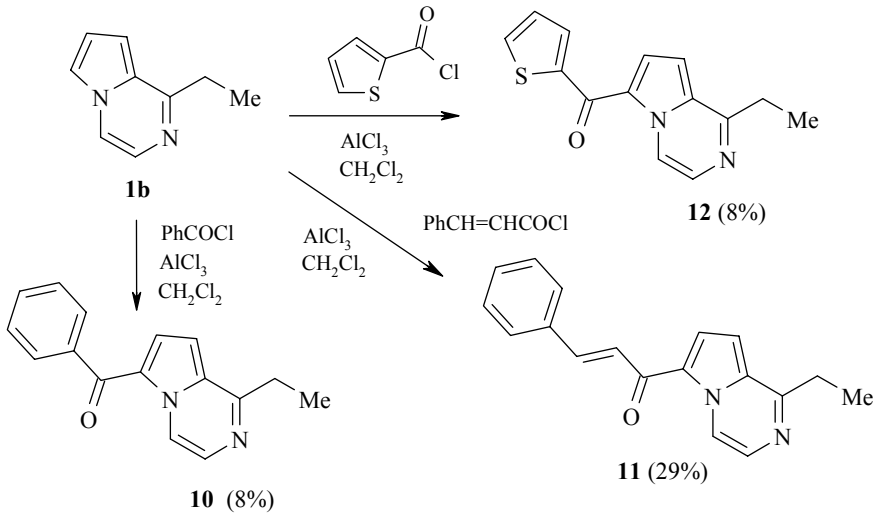
Acetyl chloride in the presence of aluminum chloride was used as acylation reagent in an attempt to increase the yields of products. The expected products of acetylation at the α-position of pyrrole ringwere obtained in 33-74% yield on acetylation of 1-ethyl- (**1b**), 1-phenyl- (**1c**), 1-isopropyl- (**1e**), 1-benzyl- (**1f**), and 1-(2-thienyl)pyrrolo[1,2-*a*]pyrazines.



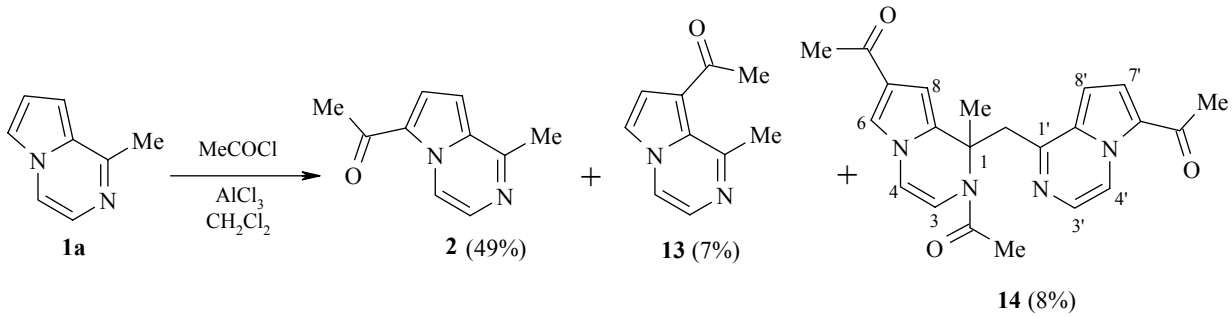
1b,c,e-g **3,4,7–9**

1b, 3 R= Et; **1c, 4** R = Ph; **1e, 7** R = *i*-Pr; **1f, 8** R = CH_2Ph; **1g, 9** R = 2-thienyl

As example the acylation of the most reactive 1-ethylpyrrolo[2,1-*a*]pyrazine (**1b**) with the chlorides of benzoic, cinnamic, and 2-thiophenecarboxylic acids was investigated. The reaction proceeded selectively in all cases with the formation exclusively of 6-acyl-1-ethylpyrrolo[1,2-*a*]pyrazines **10-12**, but the yields of the acylation products decreased to 8-29%.



On acylation of 1-methylpyrrolo[1,2-*a*]pyrazine (**1a**) with acetyl chloride, apart from the products of substitution of the pyrrole ring at position α and β' **2** and **13**, the unexpected heterocycle **14,** the product of condensation of two molecules, was obtained in 8% yield.



The ^{1}H NMR spectrum of compound **14** contained double sets of signals of the pyrrole and pyrazine rings, four singlets of the methyl group protons, and two doublets at 3.60 and 4.32 ppm with J = 13.20 Hz, corresponding to the two protons of the bridging carbon atom. The peak at *m/z* 390 in the mass spectrum corresponds to the molecular mass of compound **14**. The ^{13}C NMR spectrum showed the presence of a signal for the carbon atom in position 1' at 152.77 ppm (J = 4.13, J =10.98 Hz), appearing as a doublet of triplets, on the basis of which it was concluded that the molecules are bonded through the methyl substituent in position 1 of the heterocycle molecule. The structure of the compound obtained was confirmed by X-ray crystallography.

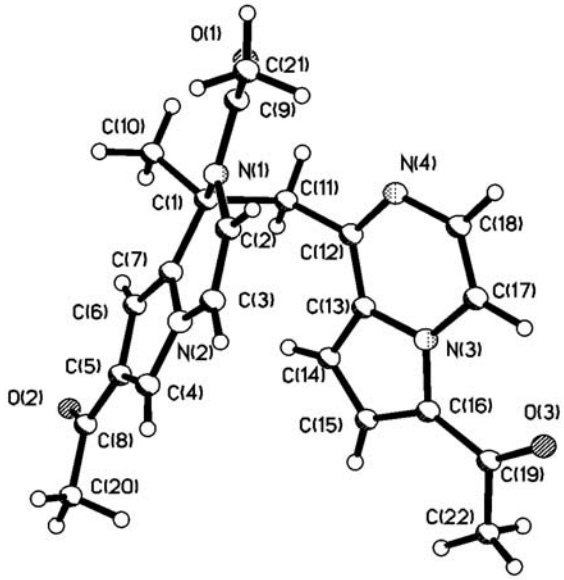


Fig. 1. Structural model of the molecule of compound **14** with numbering of the atoms.

Table 1. Crystallographic Characteristics of Compound **14**

Characteristic	
Molecular formula	$C_{22}H_{22}N_4O_3$
Molecular mass	390.44
Crystal color	Colorless
Size, mm	0.26×0.16×0.14
Crystal system	Monoclinic
Unit cell parameters	
a, Å	9.744(2)
b, Å	21.301(4)
c, Å	9.601(2)
β, deg	95.86(3)
Volume of unit cell, V, Å^3	1982.3(7)
Space group	$P2(1)/c$
Molecules per unit cell, Z	4
Density, d, g/cm^3	1.308
Absorption coefficient, μ, mm^{-1}	0.089
Final R factors [I>2σ(I)]	$R1$ = 0.0297, w$R2$ = 0.0703
R factors (all data)	$R1$ = 0.1270, $wR2$ = 0.0800

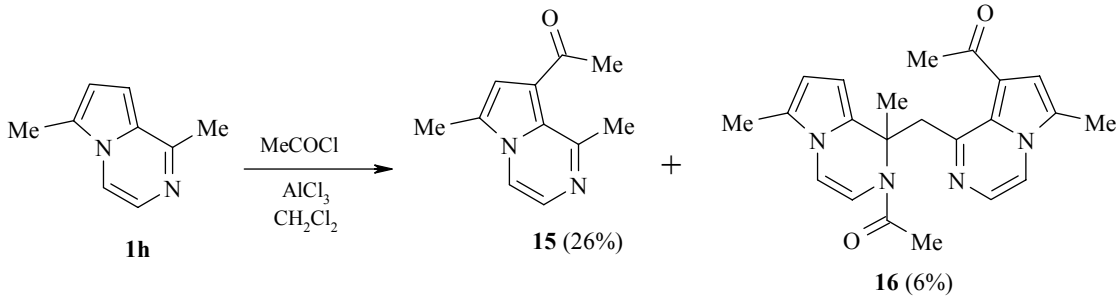
Table 2 Bond Lengths (*l*) in the Structure of Compound **14**

Bond	*l*, Å	Bond	*l*, Å
$O_{(1)}$–$C_{(9)}$	1.205(2)	$C_{(1)}$–$C_{(11)}$	1.563(2)
$O_{(2)}$–$C_{(8)}$	1.228(2)	$C_{(2)}$–$C_{(3)}$	1.316(2)
$O_{(2)}$–$C_{(8)}$	1.228(2)	$C_{(4)}$–$C_{(5)}$	1.373(2)
$N_{(1)}$–$C_{(9)}$	1.387(2)	$C_{(5)}$–$C_{(6)}$	1.420(2)
$N_{(1)}$–$C_{(2)}$	1.400(2)	$C_{(5)}$–$C_{(8)}$	1.449(2)
$N_{(1)}$–$C_{(1)}$	1.5033(19)	$C_{(6)}$–$C_{(7)}$	1.354(2)
$N_{(2)}$–$C_{(4)}$	1.358(2)	$C_{(8)}$–$C_{(20)}$	1.489(3)
$N_{(2)}$–$C_{(7)}$	1.3785(18)	$C_{(9)}$–$C_{(21)}$	1.502(3)
$N_{(2)}$–$C_{(3)}$	1.395(2)	$C_{(11)}$–$C_{(12)}$	1.499(2)
$N_{(3)}$–$C_{(17)}$	1.380(2)	$C_{(12)}$–$C_{(13)}$	1.408(2)
$N_{(3)}$–$C_{(16)}$	1.386(2)	$C_{(13)}$–$C_{(14)}$	1.391(2)
$N_{(3)}$–$C_{(16)}$	1.386(2)	$C_{(14)}$–$C_{(15)}$	1.375(2)
$N_{(4)}$–$C_{(12)}$	1.317(2)	$C_{(15)}$–$C_{(16)}$	1.397(2)
$N_{(4)}$–$C_{(18)}$	1.369(2)	$C_{(16)}$–$C_{(19)}$	1.435(2)
$C_{(1)}$–$C_{(7)}$	1.507(2)	$C_{(17)}$–$C_{(18)}$	1.338(2)
$C_{(1)}$–$C_{(10)}$	1.526(2)	$C_{(19)}$–$C_{(22)}$	1.495(3)

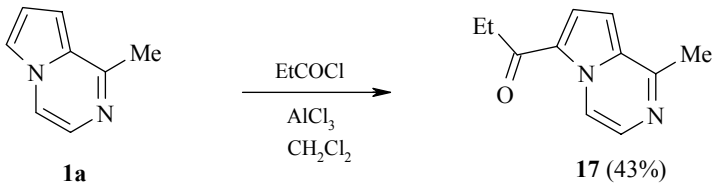
Table 3. Bond Valence (ω) in the Structure of Compound **14**

Angle	ω, deg.	Angle	ω,deg.
$C_{(9)}$–$N_{(1)}$–$C_{(2)}$	119.37(14)	$N_{(2)}$–$C_{(7)}$–$C_{(1)}$	21.30(13)
$C_{(9)}$–$N_{(1)}$–$C_{(1)}$	119.44(13)	$O_{(2)}$–$C_{(8)}$–$C_{(5)}$	120.84(15)
$C_{(2)}$–$N_{(1)}$–$C_{(1)}$	118.64(13)	$O_{(2)}$–$C_{(8)}$–$C_{(20)}$	120.76(16)
$C_{(4)}$–$N_{(2)}$–$C_{(7)}$	109.51(12)	$C_{(5)}$–$C_{(8)}$–$C_{(20)}$	118.40(16)
$C_{(4)}$–$N_{(2)}$–$C_{(3)}$	129.19(13)	$O_{(1)}$–$C_{(9)}$–$N_{(1)}$	121.62(17)
$C_{(7)}$–$N_{(2)}$–$C_{(3)}$	120.97(13)	$O_{(1)}$–$C_{(9)}$–$C_{(21)}$	120.58(17)
$C_{(17)}$–$N_{(3)}$–$C_{(16)}$	131.25(14)	$N_{(1)}$–$C_{(9)}$–$C_{(21)}$	117.79(17)
$C_{(17)}$–$N_{(3)}$–$C_{(13)}$	119.60(14)	$C_{(12)}$–$C_{(11)}$–$C_{(1)}$	114.48(12)
$C_{(16)}$–$N_{(3)}$–$C_{(13)}$	109.15(13)	$N_{(4)}$–$C_{(12)}$–$C_{(13)}$	122.65(15)
$C_{(12)}$–$N_{(4)}$–$C_{(18)}$	116.81(15)	$N_{(4)}$–$C_{(12)}$–$C_{(11)}$	116.84(15)
$N_{(1)}$–$C_{(1)}$–$C_{(7)}$	108.80(12)	$C_{(13)}$–$C_{(12)}$–$C_{(11)}$	120.47(14)
$N_{(1)}$–$C_{(1)}$–$C_{(10)}$	112.50(13)	$C_{(14)}$–$C_{(13)}$–$N_{(3)}$	107.37(14)
$C_{(7)}$–$C_{(1)}$–$C_{(10)}$	106.35(13)	$C_{(14)}$–$C_{(13)}$–$C_{(12)}$	134.76(15)
$N_{(1)}$–$C_{(1)}$–$C_{(11)}$	109.09(12)	$N_{(3)}$–$C_{(13)}$–$C_{(12)}$	117.86(14)
$C_{(7)}$–$C_{(1)}$–$C_{(11)}$	110.61(13)	$C_{(15)}$–$C_{(14)}$–$C_{(13)}$	107.69(14)
$C_{(10)}$–$C_{(1)}$–$C_{(11)}$	109.46(12)	$C_{(14)}$–$C_{(15)}$–$C_{(16)}$	109.60(15)
$C_{(3)}$–$C_{(2)}$–$N_{(1)}$	124.24(15)	$N_{(3)}$–$C_{(16)}$–$C_{(15)}$	106.19(14)
$C_{(2)}$–$C_{(3)}$–$N_{(2)}$	119.14(14)	$N_{(3)}$–$C_{(16)}$–$C_{(19)}$	122.96(15)
$N_{(2)}$–$C_{(4)}$–$C_{(5)}$	108.47(13)	$C_{(15)}$–$C_{(16)}$–$C_{(19)}$	130.82(16)
$C_{(4)}$–$C_{(5)}$–$C_{(6)}$	106.14(14)	$C_{(18)}$–$C_{(17)}$–$N_{(3)}$	117.84(15)
$C_{(4)}$–$C_{(5)}$–$C_{(8)}$	127.59(15)	$C_{(17)}$–$C_{(18)}$–$N_{(4)}$	125.23(15)
$C_{(6)}$–$C_{(5)}$–$C_{(8)}$	126.26(15)	$O_{(3)}$–$C_{(19)}$–$C_{(16)}$	122.99(17)
$C_{(7)}$–$C_{(6)}$–$C_{(5)}$	108.66(13)	$O_{(3)}$–$C_{(19)}$–$C_{(22)}$	119.42(17)
$C_{(6)}$–$C_{(7)}$–$N_{(2)}$	107.21(13)	$C_{(16)}$–$C_{(19)}$–$C_{(22)}$	117.58(16)
$C_{(6)}$–$C_{(7)}$–$C_{(1)}$	131.22(13)		

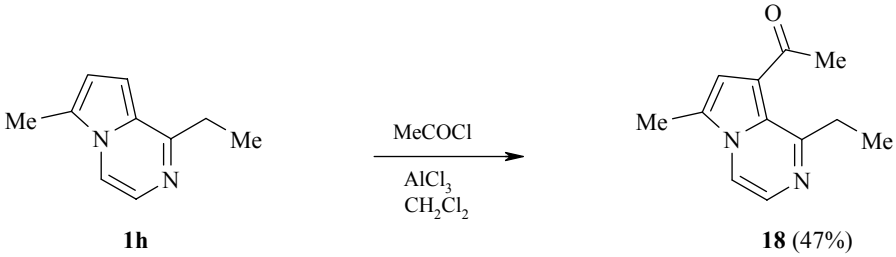
A similar picture was observed on acetylation of 1,6-dimethylpyrrolo[1,2-*a*]pyrazine (**1h**) with acetyl chloride: a mixture of two compounds was formed – 8-acetyl-1,6-dimethylpyrrolo[1,2-*a*]pyrazine (**15**) (yield 26%) and the pyrrolopyrazine **16** (yield 6%). The low overall yield of the reaction may be explained by the lower reactivity of the β'-position in the acylation reaction, while the α-position is occupied by the methyl substituent.



Formation of condensed compounds was observed only when a methyl group is found in position 1 of pyrrolo[1,2-*a*]pyrazine and acetyl chloride is used as the acylation reagent. When compound **1a** was acylated with propionyl chloride under analogous conditions compound **17 (**43% yield**),** product of the substitution in the α-position of the pyrrole ring was the only product.



Acetylation of 1-ethyl-6-methylpyrrolo[1,2-*a*]pyrazine (**1i**) with acetyl chloride, in contrast to 1,6-dimethylpyrrolo[1,2-*a*]pyrazine (**1h**), gave only the 8-acetyl derivative **18**.



EXPERIMENTAL

^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance-400 machine (400 and 100 MHz respectively) in $CDCl_3$ (compounds **2-13**, **17**, and **18**), acetone-d_6, DMSO-d_6, and CD_3OD with TMS as internal standard. Mass spectra were recorded on a Kratos MS-30 with an ionization energy of 70 eV (T = 210°C). Reactions were monitored by TLC on Silufol UV-254 plates in 1:1 benzene–ethyl acetate.

Acetylation with Acetic Anhydride. A. To a stirred solution of pyrrolo[1,2-*a*]pyrazine (2 mmol) in acetic anhydride (20 ml), magnesium perchlorate (2 mmol) was added at 20°C or tin(IV) chloride (2 mmol) at 0°C. The reaction mixture was boiled for 12 h, cooled to room temperature, and poured into cold water. The aqueous solution was neutralized with sodium carbonate, extracted with benzene, dried over 3Å molecular sieves, and the solvent was evaporated. The residue was chromatographed on a Silpearl silica gel column with 3:1 benzene-ethyl acetate.

Acylation with Acid Chlorides. B. The corresponding acid chloride (20 mmol) was added dropwise with stirring at 20°C to a solution of pyrrolo[1,2-*a*]pyrazine (2 mmol) in methylene chloride (20 ml) , and then

aluminum chloride (20 mmol) was added over 30 min. The reaction mixture was stirred for 24 h at 20°C and then poured onto crushed ice. The aqueous solution was neutralized with sodium carbonate, the precipitate was filtered off and washed with methylene chloride. The mother liquor was extracted with methylene chloride, dried over 3Å molecular sieves, the solvent was evaporated, and the residue recrystallized from hexane.

In the case of 1-methylpyrrolo[1,2-*a*]pyrazine (**1a**) the oil remaining after evaporation of the solvent was recrystallized from hexane to give 6-acetyl-1-methylpyrrolo[1,2-*a*]pyrazine (**2**) and 8-acetyl-1-methyl-pyrrolo[1,2-*a*]pyrazine (**13**). On addition of acetone to the residue after recrystallization precipitation of **14** occurred.

In the case of 1,6-dimethylpyrrolo[1,2-*a*]pyrazine (**1h**) the residue after evaporation of the solvent was chromatographed on a column of Silpearl silica gel with 1:1 benzene–ethyl acetate.

6-Acetyl-1-methylpyrrolo[1,2-*a*]pyrazine (2). Yield by method A 7%, by method B 49%; mp 96-97 °C (dec.). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.61 (3H, s, $COCH_3$); 2.76 (3H, s, 1-CH_3); 6.79 (1H, d, $J_{8,7}$ = 4.51, H-8); 7.50 (1H, d, $J_{7,8}$ = 4.51, H-7); 7.80 (1H, d, $J_{3,4}$ = 4.79, H-3); 9.43 (1H, d, $J_{4,3}$ = 4.79, H-4). Mass spectrum, *m/z* (I_{rel}, %): 174 [M^+] (85.09), 159 (100), 131 (37.44), 117 (2.30), 104 (28.93), 90 (10.01), 77 (64.06). Found, %: C 68.82; H 5.75; N 15.88. $C_{10}H_{10}N_2O$. Calculated, %: C 68.97; H 5.75; N 16.09.

6-Acetyl-1-ethylpyrrolo[2,1-*a*]pyrazine (3). Yield by method A 14%, by method B 74 %; mp 92-95°C. ^{1}H NMR spectrum, δ, ppm, (*J*, Hz): 1.43 (3H, t, *J* =7.58, $CH_2C\underline{H}_3$); 2.61 (3H, s, $COCH_3$); 3.08 (2H, q, *J* = 7.58, $C\underline{H}_2CH_3$); 6.82 (1H, d, $J_{8,7}$ = 4.60, H-8); 7.50 (1H, d, $J_{7,8}$ = 4.60, H-7); 7.84 (1H, d, $J_{3,4}$ = 4.89, H-3); 9.44 (1H, d, $J_{4,3}$ = 4.89, H-4). ^{13}C NMR spectrum, δ, ppm: 12.02 ($CH_2\underline{C}H_3$); 26.38 ($\underline{C}H_2CH_3$); 28.93 ($CO\underline{C}H_3$); 103.39, 118.42, 122.16, 124.22, 130.37, 157.65, 188.45 ($\underline{C}OCH_3$). Mass spectrum, *m/z*,(I_{rel}, %): [188 M^+] (100), 173 (34.78), 145 (17.32), 131 (3.00), 118 (14.50), 104 (6.89), 90 (9.57), 69 (5.41). Found, %: C 70.63; H 5.90; N 14.31. $C_{11}H_{12}N_2O$. Calculated, %: C 70.21; H 5.38; N 14.89.

6-Acetyl-1-phenylpyrrolo[2,1-*a*]-pyrazine (4). Yield by method A 5%, by method B 45%; mp 81-82°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.62 (3H, s, $COC\underline{H}_3$); 6.97 (1H, dd, $J_{8,7}$ = 4.79, $J_{8,4}$ = 0.74, H-8); 7.52-7.54 (4H, m, H-3, *m*-, *p*-C_6H_5); 7.90-7.93 (1H, m, H-*o*-C_6H_5); 8.01 (1H, d, $J_{7,8}$ = 4.79, H-7); 9.57 (1H, dd, $J_{4,3}$ = 4.91, $J_{4,8}$ =0.74, H-4). Mass spectrum, *m/z* (I_{rel}, %): 236 [M^+] (100), 221 (75.26), 193 (30.90), 168 (34.27), 152 (3.65), 140 (15.99), 115 (8.93), 103 (7.61), 89 (4.53), 76 (7.26). Found, %: C 76.35; H 4.91; N 12.03. $C_{15}H_{12}N_2O$. Calculated, %: C 76.27; H 5.08; N 11.86.

6-Acetyl-1-propylpyrrolo[1,2-*a*]pyrazine (5). Yield by method A 7% (accordind to ^{1}H NMR spectrum data). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.01 (3H, t, *J* = 7.43, $CH_2CH_2\underline{C}H_3$)); 1.88 (2H, sext. *J* = 7.43, $CH_2C\underline{H}_2CH_3$); 2.59 (3H, s, $COCH_3$); 3.01 (2H, t, *J* = 7.43, $C\underline{H}_2CH_2CH_3$); 6.80 (1H, d, $J_{8,7}$ = 4.66, H-8); 7.48 (1H, d, $J_{7,8}$ = 4.88, H-7); 7.82 (1H, d, $J_{3,4}$ = 4.88, H-3); 9.41 (1H, d, $J_{4,3}$ = 4.46, H-4).

6,8-Diacetyl-1-pyrrolo[1,2-*a*]pyrazine (6). Yield by method A 3% (accordind to ^{1}H NMR spectrum data). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 0.99 (3H, t, *J* = 7.50, $CH_2CH_2C\underline{H}_3$); 1.73 (2H, sext, *J* = 7.50, $CH_2C\underline{H}_2CH_3$); 2.65 (3H, s, 6-$COC\underline{H}_3$); 2.69 (3H, s, 8-$COC\underline{H}_3$) , 3.39 (2H, t, *J* = 7.50, $C\underline{H}_2CH_2CH_3$); 7.90 (1H, s, H-7); 8.06 (1H, d, $J_{3,4}$ = 4.46, H-3); 9.62 (1H, d, $J_{4,3}$ = 4.46, H-4).

6-Acetyl-1-isopropylpyrrolo[1,2-*a*]pyrazine (7). Yield by method B 51%; mp 61-62°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.40 (6H, d, *J* = 6.87, $CH(C\underline{H}_3)_2$); 2.59 (3H, s $COC\underline{H}_3$); 3.94 (1H, sept, *J* = 6.87, $C\underline{H}(CH_3)_2$); 6.82 (1H, d, $J_{8,7}$ = 4.37, H-8); 7.48 (1H, d, $J_{7,8}$ = 4.37, H-7); 7.86 (1H, d, $J_{3,4}$ = 4.75, H-3); 9.42 (1H, d, $J_{4,3}$ = 4.75, H-4). Mass spectrum, *m/z* (I_{rel}, %): 202 [M^+] (100), 187 (61.05), 174 (86.62), 159 (21.08), 144 (45.93), 131 (17.70), 117 (29.54), 104 (14.97), 89 (21.58), 77 (16.47), 64 (26.97). Found, %: C 71.22; H 7.31; N 13.98. $C_{12}H_{14}N_2O$. Calculated, %: C 71.29; H 6.93; N 13.86.

6-Acetyl-1-benzylpyrrolo[1,2-*a*]pyrazine (8). Yield by method B 33%; mp 98-99°C. ^{1}H NMR spectrum, ppm (*J*, Hz): 2.59 (3H, s, $COCH_3$); 4.40 (2H, s, CH_2Ph); 6.77 (1H, d, $J_{8,7}$ = 4.80, H-8); 7.21-7.39 (5H, m, H-C_6H_5); 7.46 (1H, d, $J_{7,8}$ = 4.80, H-7); 7.87 (1H, d, $J_{3,4}$ = 4.50, H-3); 9.47 (1H, d, $J_{4,3}$ = 4.50, H-4). Mass spectrum, *m/z* (I_{rel}, %): 250 [M^+] (53.75), 249 (100), 235 (4.00), 219 (2.50), 206 (88.39), 178 (13.11), 151 (13.01), 133 (3.20), 118 (3.30), 104 (6.81), 99 (11.81), 78 (15.32). Found, %: C 77.22; H 5.69; N 10.98. $C_{16}H_{14}N_2O$. Calculated, %: C 76.80, 5.60; N 11.20.

6-Acetyl-1-(2-thienyl)pyrrolo[1,2-*a*]pyrazine (9). Yield by method B 51%; mp 112-114°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.63 (3H, s, $COCH_3$); 7.19 (1H, dd, $J_{8,7}$ = 4.72, $J_{8,4}$ = 0.72, H-8); 7,23 (1H, dd, $J_{\beta'\alpha'}$ = 5.05, $J_{\beta'\beta}$ = 3.76, H-β'-Th); 7.56 (1H, dd, $J_{\alpha'\beta'}$ = 5.05, $J_{\alpha'\beta}$ = 1.05, H-α'-Th); 7.57 (1H, d, $J_{7,8}$ = 4.72, H-7); 7.88 (1H, dd, $J_{\beta\beta'}$ = 3.76, $J_{\beta\alpha'}$ = 1.05, H-β-Th); 7.93 (1H, d, $J_{3,4}$ = 4.77, H-3); 9.54 (1H, dd, $J_{4,3}$ = 4.77, $J_{4,8}$ = 0.72, H-4). Mass spectrum, *m/z* (I_{rel}, %): 242 [M^+] (91.66), 227 (100), 199 (68.75), 172 (24.31), 155 (31.94), 145 (18.06), 128 (21.53), 101 (14.58), 77 (11.81). Found, %: C 64.86; H 4.29; N 11.12. $C_{13}H_{10}N_2OS$. Calculated, %: C 64.46; H 4.13; N 11.34.

6-Benzoyl-1-ethylpyrrolo[1,2-*a*]pyrazine (10). Yield by method B 8%; mp 137-140°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.45 (3H, t, *J* = 7.55**,** $CH_2\underline{C}H_3$); 3.13 (2H, q, *J* = 7.55, $C\underline{H}_2CH_3$); 6.84 (1H, d, $J_{8,7}$ = 4.60, H-8); 7.37 (1H, d, $J_{7,8}$ = 4.60, H-7); 7.52 (2H, m, H-*m*-C_6H_5); 7.59 (2H, m, H-*p*-C_6H_5); 7.84 (1H, dd, $J_{o,m}$ = 8.41, $J_{o,p}$ = 1.36, *J*-*o*-C_6H_5); 7.92 (1H, d, $J_{3,4}$ = 4.69, H-3); 9.51 (1H, d, $J_{4,3}$ = 4.69, H-4). Mass spectrum, *m/z* (I_{rel}, %): 250 [M^+] (84.58), 249 (100), 222 (8.51), 173 (19.42), 145 (21.02), 117 (26.13), 105 (29.13), 85 (9.81), 77 (38.94). Found, %: C 77.02; H 5.55; N 11.34. $C_{16}H_{14}N_2O$. Calculated, %: C 76.80; H 5.55; N 11.34.

(2*E*)-1-(1-Ethylpyrrolo[1,2-*a*]pyrazin-6-yl)-3-phenyl-2-propen-1-one (11). Yield by method B 29%; mp 131-133°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.43 (3H, t, *J* = 7.55, $CH_2C\underline{H}_3$); 3.10 (2H, q, *J* = 7.55, $C\underline{H}_2CH_3$); 6.87 (1H, d, $J_{8,7}$ = 4.70, H-8); 7.41-7.43 (3H, m, H-*m,p*-C_6H_5); 7.50 (1H, d, *J* = 15.46, $C\underline{H}$=CHC_6H_5); 7.65-7.67 (3H, m, H-*o*-C_6H_5 and H-7); 7.86 (1H, d, *J* =15.46, CH=$C\underline{H}C_6H_5$); 7.89 (1H, d, $J_{3,4}$ = 4.70, H-3); 9.61 (1H, d, $J_{4,3}$ = 4.70, H-4). Mass spectrum, *m/z* (I_{rel}, %): 276 [M^+] (100), 248 (24.52), 173 (4.80), 146 (27.33), 131 (16.72), 117 (11.91), 102 (21.62), 77 (24.62). Found, %: C 78.09; H 5.69; N 10.27. $C_{18}H_{16}N_2O$. Calculated, %: C 78.26; H 5.80; N 10.14.

1-Ethylpyrrolo[1,2-*a*]pyrazin-6-yl 2-Thienyl Ketone (12). Yield by method B 8%; mp 230-232°C (dec.). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.66 (3H, t, *J* = 7.67, $CH_2C\underline{H}_3$); 3.56 (2H, q, *J* = 7.67, $C\underline{H}_2CH_3$); 7.30 (1H, m, H-β'-Th); 7.51 (1H, d, $J_{8,7}$ = 4.21, H-8); 7.81 (1H, d, $J_{3,4}$ = 4.38, H-3); 7.86 (1H, d, $J_{7,8}$ = 4.21, H-7); 7.92 (1H, d, $J_{\beta,\beta'}$ =3.13, 1-H-β-Th); 7.94 (1H, d, $J_{\alpha',\beta'}$ = 4.69, 1-H-α'-Th); 9.57 (1H, d, $J_{4,3}$ = 4.38, H-4). Mass spectrum, *m/z,* (I_{rel}, %): 256 [M^+] (100), 228 (19.52), 199 (5.71), 173 (17.92), 145 (54.55), 128 (11.31), 118 (13.11), 111 (72.17), 90 (10.71), 77 (8.51), 65 (12.02). Found, %: C 65.10; H 4.82; N 10.77. $C_{14}H_{12}N_2OS$. Calculated, %: C 65.63; H 4.69; N 10.94.

8-Acetyl-1-methylpyrrolo[1,2-*a*]pyrazine (13). Yield by method B 7% (according to ^{1}H NMR spectrum data). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 2.63 (3H, s, $COCH_3$); 3.04 (3H, s, 1-CH_3); 7.25 (1H, d, $J_{6,7}$ = 2.83, H-6); 7.36 (1H, d, $J_{7,6}$ = 2.83, H-7); 7.69 (1H, d, $J_{3,4}$ = 4.52, H-3); 7.77 (1H, d, $J_{4,3}$ = 4.52, H-4).

2,7-Diacetyl-1-[(6-acetylpyrrolo[1,2-*a*]pyrazin-1-yl)methyl]-1-methyl-1,2-dihydropyrrolo[1,2-*a*]-pyrazine (14). Yield by method B 8%; mp 215-216°C (dec., ethanol). ^{1}H NMR spectrum (acetone-d_6)), δ, ppm (*J*, Hz): 2.29 (3H, s, 1-CH_3); 2.36 (3H, s; $NCOCH_3$); 2.63 (3H, s, 6′-$COCH_3$); 2.93 (3H, s, 7-$COCH_3$); 3.60 (1H, d, $J_{9,10}$ = 13.20, H-9(10)); 4.32 (1H, d, $J_{9,10}$ =13.20, H9(10)); 6.13 (1H, dd, $J_{4,3}$ = 6.58, $J_{4,8}$ = 0.82, H-4); 6.33 (1H, d, $J_{3,4}$ = 6.58, H-3); 6.64 (1H, dd, $J_{8,7'}$ = 4.69, $J_{8',4'}$ =0.78, H-8′); 6.70 (1H, dd, $J_{8,6}$ = 1.76, $J_{8,4}$ = 0.82, H-8); 7.26 (1H, d, $J_{6,8}$ =1.76, H-6); 7.68 (1H, d, $J_{7',8'}$ = 4.69, H-7'); 7.83 (1H, d, $J_{3',4'}$ = 4.89, H-3'); 9.47 (1H, dd, $J_{4',3'}$ = 4.89, $J_{4',8'}$ = 0.78, H-4′). ^{13}C NMR spectrum (DMSO-d_6); δ, ppm (*J*, Hz): 25.12 (CH_3); 27.29 (CH_3); 27.54 (CH_3); 27.88 (CH_3); 44.22 (CH_2); 60.99 ($C_{(1)}$); 104.05, 105.71, 106.80, 116.96, 118.09, 122.16, 123.39, 123.74, 125.95, 130.74, 132.06, 132,11, 153.77 (1C, dt, J_{CH} =4.13, J_{CH} =10.98, $C_{(1')}$); 170.73 ($N\underline{C}OCH_3$); 188.83 ($\underline{C}OCH_3$-7); 192.29 ($\underline{C}OCH_3$-6'). Mass spectrum, *m/z* (I_{rel}, %): 390 [M^+] (32.61), 375 (4.35), 347 (10.87), 333 (8.69), 305 (4.31), 289 (8.72), 263 (2.71), 175 (100), 146 (4.29), 132 (11.00), 104 (6.52). Found, %: C 67.77; H 5.75; N 14.48. $C_{22}H_{22}N_4O_3$. Calculated, %: C 67.69; H 5.64; N 14.36.

8-Acetyl-1,6-dimethylpyrrolo[1,2-*a*]pyrazine (15). Yield by method B 47%; mp 104-105°C. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 2.49 (3H, s, 6-CH_3); 2.61 (3H, s, $COCH_3$); 2.98 (3H, s, 1-CH_3); 7.04 (1H, s, H-7); 7.56 (1H, d, $J_{3,4}$ = 4.60, H-3); 7.75 (1H, d, $J_{4,3}$ = 4.60, H-4). ^{1}H NMR spectrum (acetone-d_6), δ, ppm (*J* (Hz): 2.53 (3H, s, 6-CH_3); 2.56 (3H, s, $COCH_3$); 2.86 (3H, s, 1-CH_3); 7.22 (1H, s, H-7); 7.71 (1H, d, $J_{3,4}$ = 4.70, H-3); 7.90 (1H, d, $J_{4,3}$ = 4.70, H-4). Mass spectrum, *m/z* (I_{rel}, %): 188 [M^+] (75.87), 173 (100), 143

(5.91), 117 (4.50), 104 (17.12), 91 (6.11), 77 (15.92). Found, %: C 70.06; H 6.26; N 14.84. $C_{11}H_{12}N_2O$. Calculated, %: C 70.21; H 6.38; N 14.89.

2-Acetyl-1-[(8-acetyl-6-methylpyrrolo[1,2-*a*]pyrazin-1-yl)methyl]-1,6-dimethyl-1,2-dihydropyrrolo-[1,2-*a*]pyrazine (16). Yield by method B 6%. ^{1}H NMR spectrum ($CDCl_3$), δ ppm (*J*, Hz): 2.11 (3H, s, 1-CH_3); 2.29 (3H, s; $NCOCH_3$); 2.35 (3H, s, 6′-CH_3); 2.36 (3H, s, 6-CH_3); 2.41 (3H, s, 8′-$COCH_3$); 3.25 (1H, d, $J_{9,10}$ = 12.91, H-9(10)); 3.90 (1H, d, $J_{10,9}$ = 12.91, H-10(9)); 5.76 (1H, d, $J_{4,3}$ = 5.76, H-4); 5.80 (1H, d, $J_{3,4}$ = 5.76, H-3); 6.35 (1H, s, H-7′); 6.40 (1H, d, $J_{8,7}$ = 3.91, H-8); 6.50 (1H, d, $J_{7,8}$ = 3.91, H-7); 7.30 (1H, d, $J_{3',4'}$ = 4.89, H-3′); 7.43 (1H, d, $J_{4',3'}$ = 4.89, H-4′). ^{13}C NMR spectrum (CD_3OD); δ, ppm (*J*, Hz): 9.04 (CH_3); 9.65 (CH_3); 23.44 (CH_3); 25.68 (CH_3); 27.17 (CH_3); 44.65 (CH_2); 61.34 ($C_{(1)}$); 102.96, 103.07, 108.35, 113.95, 114.02, 115.98, 120.91, 123.55, 124.89, 128.24, 129.17, 131.06, 151.57 (1C, dt, J_{CH} = 5.86, J_{CH} = 9.51, C-1′); 171.57 ($NCOCH_3$); 196.12 ($COCH_3$-8′). Mass spectrum, *m/z* (I_{rel},%): 376 [M^+] (3.20), 245 (1.70), 231 (47.05), 189 (100), 173 (18.32), 159 (3.10), 145 (53.45), 131 (2.50), 104 (5.91), 91 (11.11). Found, %: C 71.69; H 6.43; N 15.03. $C_{22}H_{24}N_4O_2$. Calculated, %: C 71.21; H 6.38; N 14.89.

1-Methyl-6-propionylpyrrolo[1,2-*a*]pyrazine (17). Yield by method B 43%; mp 119-120°C (dec.). ^{1}H NMR spectrum, δ ppm, (*J*, Hz): 1.29 (3H, t, *J* = 7.43, $COCH_2CH_3$); 2.77 (3H, s, CH_3-1); 2.99 (2H, q, *J* = 7.43, $COCH_2CH_3$); 6.80 (1H, dd, $J_{8,7}$ = 4.63, $J_{8,4}$ = 0.69, H-8); 7.52 (1H, d, $J_{7,8}$ = 4.63, H-7); 7.80 (1H, d, $J_{3,4}$ = 4.89, H-3); 9.46 (1H, d, $J_{4,3}$ = 4.89, H-4). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 8.88 ($COCH_2CH_3$); 21.78 (1-CH_3); 32.87 ($COCH_2CH_3$); 103.78, 118.56, 121.38, 123.97, 130.16, 131.45, 153.14, 192.15 ($COCH_2CH_3$). Mass spectrum, *m/z* (I_{rel},%): 188 [M^+] (58.56), 173 (25.73), 159 (100), 145 (14.01), 131 (35.04), 117 (9.2), 104 (36.24), 91 (10.51), 77 (36.54), 63 (20.22). Found, %: C 69.94; H 6.47; N 14.76. $C_{11}H_{12}N_2O$. Calculated, %: C 70.21; H 6.38; N 14.89.

8-Acetyl-1-ethyl-6-methyl-pyrrolo[1,2-*a*]pyrazine (18). Yield by method B 47%; mp 104-105°C. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 1.31 (3H, t, *J* = 7.43, CH_2CH_3); 2.48 (3H, s, 6-CH_3); 2.62 (3H, s, $COCH_3$); 3.44 (2H, q, *J* = 7.43, CH_2CH_3); 7.06 (1H, s, H-7); 7.56 (1H, d, $J_{3,4}$ = 4.70, H-3); 7.81 (1H, d, $J_{4,3}$ = 4.70, H-4). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 11.28 (CH_2CH_3); 13.26 (6-CH_3); 29.81 (CH_2CH_3); 30.93 ($COCH_3$); 113.22, 117.53, 117.94, 122.36, 129.24, 160.06, 193.84 ($COCH_3$). Mass spectrum, *m/z* (I_{rel}, %): 202 [M^+] (100), 186 (14.41), 174 (24.43), 160 (28.53), 145 (8.71), 132 (6.41), 116 (3.80), 102 (5.1), 86 (4.80). Found, %: C 71.11; H 7.27; N 14.05. $C_{12}H_{14}N_2O$. Calculated, %: 71.29; H 6.93; N 13.86.

X-ray Structural Investigation. Monocrystal of compound **14** was grown from CH_2Cl_2. The diffraction pattern was obtained at 293 K using an Engraft Nonius CAD4 diffractometer (MoKα radiation, θ interval for all data from 1.91 to 25.47°). The structure was solved by direct method with full matrix least squares in the anisotropic approximation. Calculations were carried out with the SHELX97 suite of programs [2]. Complete crystallographic information has been deposited in the Cambridge Structural Database (No. CCDC 644154). Interatomic distances and valence angles are given in Tables 2 and 3.

REFERENCES

1. V. I. Terenin, E. V. Kabanova, N. A. Tselishcheva, M. A. Kovalkina, and A. P. Pleshkova. *Khim. Geterotsikl. Soed.,* 431 (20040. [*Chem. Heterocycl. Comp.,* **40**, 351 (2004)].
2. G. M. Sheldrick, *SHELX97. PC Version. A System of Computer Programs for the Crystal Structure Solution and Refinement.* Rev. 2 (1998).