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SYNTHESIS OF PYRROLOQUINOLINES FROM SUBSTITUTED 6-AMINOINDOLES AND OXALOACETIC ESTER

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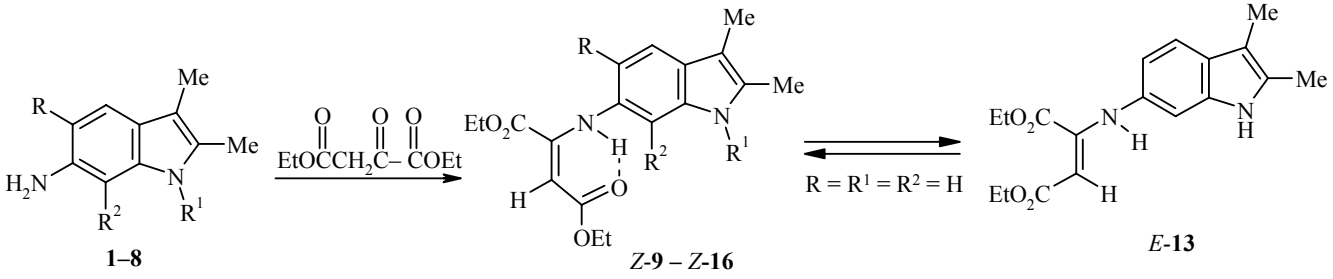
It was established that the initial condensation of substituted 6-aminoindoles and oxaloacetic ester in boiling benzene with the addition of catalytic amounts of acetic acid takes place exclusively through the carboxyl group of the keto ester with the formation of the corresponding enamines, which successfully undergo thermal cyclization (biphenyl, 280°C) to pyrroloquinolines. Here, irrespective of the nature of substituents at the N-1 and C-5 atoms enamines with a free position 7 are transformed into pyrrolo-[2,3-f]quinolines (structural analogs of vitamin PQQ) while 7-OMe-substituted enamines give pyrrolo[3,2-g]quinolines with linear fusion of the rings.

Keywords: substituted 6-aminoindoles, pyrrolo[2,3-*f*]quinolines, pyrrolo[3,2-*g*]quinolines, oxaloacetic ester.

Pyrroloquinolinequinone (PQQ), which has the structure of pyrrolo[2,3-*f*]quinoline is familiar as a vitamin entering as coenzyme into the molecules of certain oxidoreductases [1]. We studied a series of substituted 6-aminoindoles **1-8** in reaction with oxaloacetic ester in order to develop methods for the synthesis of pyrroloquinolines that are structural analogs of PQQ. Here it was established that the initial reaction of amines with the keto ester in boiling absolute benzene takes place similarly to 4- and 5-aminoindoles [2, 3] with the formation of the corresponding enamines **9-16** (Table 1).



1–8 *Z*-**9** – *Z*-**16** *E*-**13**

1-6, **9-14** R^2 = H; **1, 9** R = Me, R^1 = H; **2, 10** R = R1 = Me; **3, 11** R = OMe, R^1 = H; **4, 12** R = OMe, R^1 = Me; 5, **13** R = R^1 = H; **6, 14** R = H, R^1 = Me; **7, 15** R = R^1 = H, R^2 = OMe; **8, 16** R = H, R^1 = Me, R^2 = OMe

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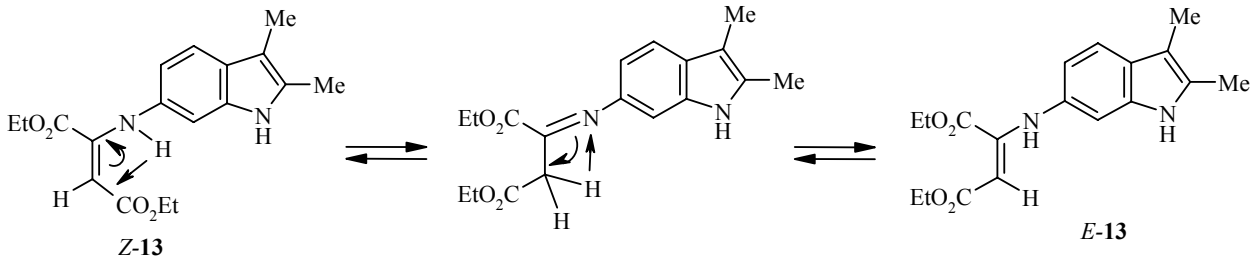
The Physicochemical Characteristics of Compounds **9-13** and **15-24**

Compound	Empirical formula	Found / Calculated			R_f (system)	mp, °C (solvent for crystallization)	Yield, %
		C, %	H, %	M			
9	$C_{19}H_{24}N_2O_4$	66.14 / 66.26	7.13 / 7.02	344 / 344	0.58 (benzene)	96-97 (benzene–petroleum ether)	40
10	$C_{20}H_{26}N_2O_4$	66.97 / 67.02	7.36 / 7.31	358 / 358	0.44 (benzene)	92-93 (petroleum ether)	65
11	$C_{19}H_{24}N_2O_5$	63.29 / 63.32	6.74 / 6.71	360 / 360	0.55 (benzene)	119-120 (petroleum ether)	43
12	$C_{20}H_{26}N_2O_5$	64.15 / 64.15	6.99 / 7.00	374 / 374	0.55 (benzene–ethyl acetate, 7:1)	104-105 (petroleum ether)	68
13	$C_{18}H_{22}N_2O_4$	64.92 / 65.44	7.48 / 6.71	330 / 330	0.51 (benzene–ethyl acetate, 3:1)	102-103 (petroleum ether)	35
15	$C_{19}H_{24}N_2O_5$	62.99 / 63.32	7.20 / 6.71	360 / 360	0.51 (benzene–ethyl acetate, 10:1)	102-103 (hexane)	37
16	$C_{20}H_{26}N_2O_5$	63.99 / 64.15	7.23 / 7.00	374 / 374	0.52 (benzene–ethyl acetate, 5:1)	88-89 (hexane)	43
17	$C_{17}H_{18}N_2O_3$	68.42 / 68.44	6.09 / 6.08	298 / 298	0.49 (ethyl acetate)	233-234 (ethanol)	58
18	$C_{18}H_{20}N_2O_3$	69.20 / 69.21	6.44 / 6.45	312 / 312	0.45 (benzene–ethyl acetate, 1:1)	143-144 (ethanol)	57
19	$C_{17}H_{18}N_2O_4$	64.89 / 64.96	5.85 / 5.77	314 / 314	0.51 (benzene-ethyl acetate, 1:1)	234-235 (ethanol)	96
20	$C_{18}H_{20}N_2O_4$	65.80 / 65.84	6.13 / 6.14	328 / 328	0.50 (benzene-ethyl acetate, 1:1)	136-137 (ethanol)	67
21	$C_{16}H_{16}N_2O_3$	67.31 / 67.59	5.74 / 5.67	284 / 284	0.52 (benzene–ethyl acetate, 1:4)	287-288 (ethanol)	80
22	$C_{17}H_{18}N_2O_3$	68.25 / 68.44	6.34 / 6.08	298 / 298	0.50 (benzene–ethyl acetate, 1:4)	211-212 (petroleum ether)	64
23	$C_{17}H_{18}N_2O_4$	64.89 / 64.96	5.85 / 5.77	314 / 314	0.56 (ethyl acetate – traces of methanol)	200-202 (ethanol)	61
24	$C_{18}H_{20}N_2O_4$	65.71 / 65.84	6.32 / 6.14	328 / 328	0.56 (ethyl acetate – methanol)	170-172 (ethanol)	76

According to the data from the ^{1}H NMR spectra (Table 2), the 5- and 7-substituted enamines **9-12**, **15**, and **16** have the *Z*-configuration in relation to the double bond, i.e., they can be assigned to indolylamino derivatives of diethyl fumarate. This is demonstrated by the presence in the spectra of these compounds of a singlet for the chelated N–H_{amine} proton (9.51-9.75) and a singlet for H_{vin} (5.01-5.13 ppm) and also two triplets and two quadruplets for the different ethoxycarbonyl groups. In the analogous spectrum of the enamine obtained from 6-amino-2,3-dimethylindole and oxaloacetic ester there are signals for the protons of two

compounds in a ratio of 1.3:1 (according to data from the ^{1}H NMR spectra). The obtained data indicate that the enamine **13** exists in solution in DMSO-d_6 in two forms (*Z*- and *E*-, 1.3:1), and mutual transformations from one to the other through the imine structure are evidently possible for these two geometric isomers.



The presence of the enamine of *Z*-form compound **13** is demonstrated in the ^{1}H NMR spectrum by signals for the vinyl and chelated amine protons (5.07, 9.70 ppm) in the same region as for the other enamines **9-12**, **15**, and **16**. The signals of the analogous protons for the *E*-isomer are shifted upfield by 0.55 (9.15) for N–H_{amine} and by 0.11 (4.96 ppm) for H_{vin}. The chemical shifts of the pairs of four triplets and quadruplets of the ethoxycarbonyl groups differ within 0.1 ppm. The singlet signals of the 2-, 3-CH_3, and H-1 protons appear in practically the same regions both for the *Z*- and for the *E*-isomer (difference 0.01-0.02 ppm). A fairly large difference for the isomers is observed in the chemical shifts of the protons of the benzene ring, which are represented by two doublets and a singlet, and particularly between the signals of the H-4 and H-5 protons (~0.5 ppm). The downfield shift of the aromatic protons is evidently favored by the accepting effect of the ethoxycarbonyl group chelated with the N-H_{amine} group.

The existence of the 5- and 7-substituted indolylenamines **9-12**, **15**, and **16** exclusively in the *Z*-form is probably due to the steric demands of the substituents in the benzene ring. Unfortunately we were unable to confirm this suggestion for the case of the enamine obtained from 6-amino-1,2,3-trimethylindole and oxaloacetic ester. We could not isolate compound **14** on account of the difficulty of purification and used it for the subsequent investigations without identification.

The main pathway in the dissociative ionization of the obtained enamines **9-16** under electron impact (Table 2) is elimination of the ethyl formate molecule from the molecular ion ([M^+−HCOOEt]) with the formation of the molecular ion of ethoxycarbonylpyrroloindole (*m*/*z* [M−74]), which then eliminates the C_2H_5O radical to form the $[M-74-45]^+$ ion. Such behavior of compounds **9-16** under electron impact confirms the presence of the two ethoxycarbonyl groups in their molecules.

The IR spectra (Table 2) of the enamines **9-12**, **15**, and **16** are practically identical: They contain strong bands for the stretching vibrations at 1597-1608, 1644-1668, and 1713-1745 cm^{-1}, confirming their *Z*-configuration. In contrast to this four strong bands appear in the IR spectrum of the enamine **13** in the region of 1645-1730 cm^{-1}, confirming the data from the ^{1}H NMR spectra about the presence of four different ethoxycarbonyl groups, i.e., that this enamine exists as a mixture of *Z*- and *E*-isomers.

The UV spectra of compounds **9-16** (Table 2) are characterized by three absorption bands, i.e., a short-wave band (205-240 nm) and two long-wave bands (280-320, 360 nm), which are split for certain structures depending of the nature of the substituents.

All the spectral data for the enamines that we obtained agree well with published data for similar structures based on 4- and 5-aminoindoles and oxaloacetic ester [2, 3].

We used the synthesized enamines **9-16** for thermal cyclization with a view to preparing pyrroloquinolines with an α-ethoxycarbonyl-containing *p*-quinolone fragments – structural analogs of vitamin PQQ, 2,7,9-tricarboxy-1H-pyrrolo[2,3-*f*]quinoline-4,5-dione.

TABLE 2. The Spectral Characteristics of Compounds **9-16**

Compound	IR spectrum, ν, cm^{-1}	UV, λ_{max}, nm (log ε)	^{1}H MNR spectrum, δ, ppm (*J*, Hz)	Mass-spectrum, *m/z* (I_{rel}, %)
9	1605, 1657, 1736	204 (4.38), 230 sh. (4.23), 295 (4.04), 340 sh. (3.90)	0.93 (3H, t, *J* = 7, COO–CH_2–$CH_{3(chelate)}$); 1.22 (3H, t, *J* = 7, COO–CH_2–CH_3); 2.12 (3H, s, 3-CH_3); 2.27 (3H, s, 2-CH_3); 2.31 (3H, s, 5-CH_3); 4.01 (2H, q, *J* = 7, COO–CH_2–$CH_{3(chelate)}$); 4.15 (2H, q, *J* = 7, COO–CH_2–CH_3); 5.07 (1H, s, H_{vin}); 6.68 (1H, s, H-4); 7.18 (1H, s, H-7); 9.57 (1H, s, N–H_{amine}); 10.53 (1H, s, H-1)	345 (20), 344 $[M]^+$ (100), 299 (910), 298 (35), 272 (5), 271 (35), 270 (67), 255 (14), 242 (17), 226 (16), 225 (40), 224 (27), 197 (90), 196 (38), 184 (30), 173 (25), 156 (20), 115 (20)
10	1605, 1663, 1732	225 (4.19), 300 (4.06), 350 sh. (3.88)	0.93 (3H, t, *J* = 7, COO–CH_2–$CH_{3(chelate)}$); 1.22 (3H, t, *J* = 7, COO–CH_2–CH_3); 2.13 (3H, s, 3-CH_3); 2.29 (3H, s, 2-CH_3); 2.32 (3H, s, 5-CH_3); 3.50 (3H, s, 1-CH_3); 4.01 (2H, q, *J* = 7, COO–CH_2–$CH_{3(chelate)}$); 4.14 (2H, q, *J* = 7, COO–CH_2–CH_3); 5.09 (1H, s, H_{vin}); 6.74 (1H, s, H-7); 7.21 (1H, s, H-4); 9.51 (1H, s, 6-NH)	359 (12), 358 $[M]^+$ (72), 345 (8), 312 (36), 285 (25), 284 (100), 256 (10), 255 (7), 239 (25), 238 (26), 212 (26), 211 (88), 196 (26), 195 (37), 187 (25), 156 (30)
11	1605, 1663, 1732	208 (4.44), 220 sh. (4.35), 295 (4.10), 360 (4.12)	1.06 (3H, t, *J* = 7, COO–CH_2–$CH_{3(chelate)}$); 1.21 (3H, t, *J* = 7, COO–CH_2–CH_3); 2.11 (3H, s, 3-CH_3); 2.26 (3H, s, 2-CH_3); 3.80 (3H, s, 5-OCH_3); 4.10-4.16 (4H, m, 2COO–CH_2–CH_3); 5.07 (1H, s, H_{vin}); 6.68 (1H, s, H-4); 6.91 (1H, s, H-7); 9.72 (1H, s, 6-NH); 10.44 (1H, s, N–H_{amine})	361 (20), 360 $[M]^+$ (100), 315 (5), 314 (12), 287 (20), 286 (70), 271 (8), 258 (10), 242 (8), 241 (35), 214 (15), 213 (15), 199 (20), 190 (10), 175 (10), 143 (20), 77 (10)
12	1608, 1655, 1742	205 (4.38), 220 sh. (4.30), 295 (4.05), 360 (4.05)	1.08 (3H, t, *J* = 7, COO–CH_2–$CH_{3(chelate)}$); 1.22 (3H, t, *J* = 7, COO–CH_2–CH_3); 2.15 (3H, s, 3-CH_3); 2.29 (3H, s, 2-CH_3); 3.54 (3H, s, 1-CH_3); 3.80 (3H, s, 5-OCH_3); 4.10–4.16 (4H, m, 2COO–CH_2–CH_3); 5.13 (1H, s, H_{vin}); 6.85 (1H, s, H-4); 6.97 (1H, s, H-7); 9.73 (1H, s, N–H_{amine})	375 (10), 374 $[M]^+$ (50), 328 (5), 301 (25), 300 (100), 272 (15), 256 (12), 255 (35), 241 (18), 240 (25), 239 (20), 228 (22), 227 (22), 189 (20), 161 (25), 160 (25), 115 (30), 77 (30)
Z-**13**	1607, 1645, 1659, 1711, 1730	220 (4.33), 236 sh. (4.26), 295 (3.99), 340 (4.01)	0.98 (3H, t, *J* = 7, COO–CH_2–$CH_{3(chelate)}$); 1.23 (3H, t, *J* = 7, COO–CH_2–CH_3); 2.12 (3H, s, 3-CH_3); 2.26 (3H, s, 2-CH_3); 4.05 (2H, q, *J* = 7, COO–CH_2–$CH_{3(chelate)}$); 4.13 (2H, q, *J* = 7, COO–CH_2–CH_3); 5.07 (1H, s, H_{vin}); 6.83 (1H, s, H-7); 7.26 (1H, d, $J_{4,5}$ = 8, H-4); 7.34 (1H, d, $J_{5,4}$ = 8, H-5); 9.70 (1H, s, N–H_{amine}), 10.67 (1H, s, H-1)	331 (7), 330 $[M]^+$ (55), 285 (5), 284 (15), 256 (80), 255 (25), 241 (10), 227 (5), 228 (25), 212 (26), 211 (55), 184 (45), 183 (100), 169 (20), 160 (45), 159 (55), 143 (47), 128 (30), 115 (60), 77 (30)
E-**13**			1.12 (3H, t, *J* = 7, COO–CH_2–CH_3); 1.28 (3H, t, *J* = 7, COO–CH_2–CH_3); 2.13 (3H, s, 3-CH_3); 2.27 (3H, s, 2-CH_3); 3.95 (2H, q, *J* = 7, COO–CH_2–CH_3); 4.24 (2H, q, *J* = 7, COO–CH_2–CH_3); 4.96 (1H, s, H_{vin}); 6.61 (1H, d, $J_{4,5}$ = 8, H-4); 6.76 (1H, d, $J_{5,4}$ = 8, H-5); 7.01 (1H, s, H-7); 9.15 (1H, s, N–H_{amine}), 10.65 (1H, s, H-1)	
15	1605, 1655, 1717	224 (4.50), 280 (4.14), 360 sh. (3.88)	0.89 (3H, t, *J* = 7, COO–CH_2–$CH_{3(chelate)}$); 1.22 (3H, t, *J* = 7, COO–CH_2–CH_3); 2.25 (6H, s, 2-, 3-CH_3); 3.84 (3H, s, 7-OCH_3); 3.98 (2H, q, *J* = 7, COO–CH_2–$CH_{3(chelate)}$); 4.13 (2H, q, *J* = 7, COO–CH_2–CH_3); 5.01 (1H, s, H_{vin}); 6.30 (1H, d, $J_{5,4}$ = 8, H-5); 6.43 (1H, d, $J_{4,5}$ = 8, H-4); 9.76 (1H, s, N–H_{amine}); 10.72 (1H, s, H-1)	361 (16), 360 $[M]^+$ (100), 315 (11), 314 (41), 287 (42), 286 (100), 271 (40), 258 (10), 257 (16), 241 (53), 240 (53), 225 (39), 213 (62), 198 (60), 197 (75), 175 (75), 130 (41), 77 (32)
16	1605, 1659, 1732	225 (4.27), 295 (3.87), 360 (3.78)	0.90 (3H, t, *J* = 7, COO–CH_2–$CH_{3(chelate)}$); 1.21 (3H, t, *J* = 7, COO–CH_2–CH_3); 2.24 (3H, s, 3-CH_3); 2.28 (3H, s, 2-CH_3); 3.82 (3H, s, 1-CH_3); 3.86 (3H, s, 7-OCH_3); 3.98 (2H, q, *J* = 7, COO–CH_2–$CH_{3(chelate)}$); 4.13 (2H, q, *J* = 7, COO–CH_2–CH_3); 5.02 (1H, s, H_{vin}); 6.30 (1H, d, J_{54} = 8, H-5); 6.46 (1H, d, J_{45} = 7, H-4); 9.75 (1H, s, N–H_{amine})	375 (19), 374 $[M]^+$ (100), 359 (6), 327 (11), 328 (43), 300 (85), 299 (31), 285 (43), 272 (6), 271 (15), 255 (41), 254 (34), 239 (27), 227 (43), 197 (35), 189 (58)

TABLE 3. The ^{1}H NMR Spectra of the Pyrroloquinolines

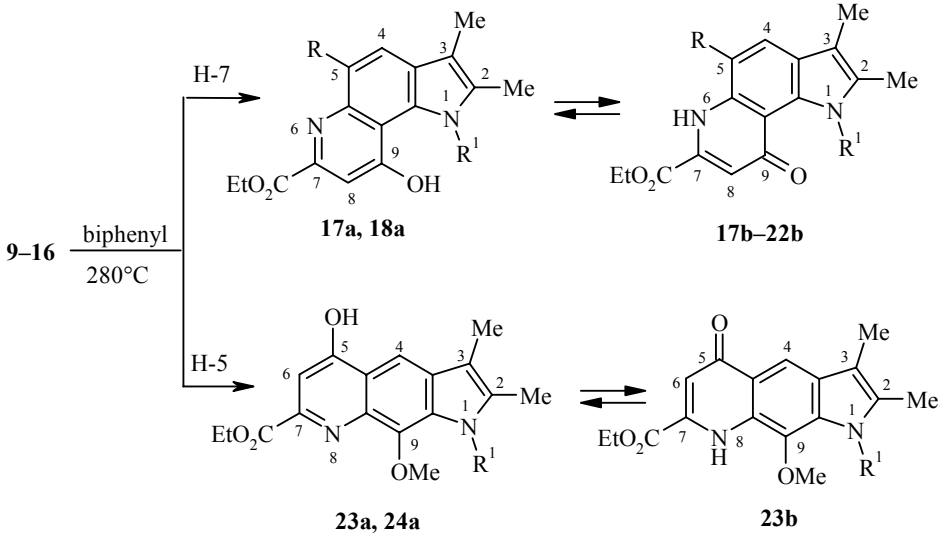
Compound	Spectrum*	Chemical shifts, δ, ppm (*J*, Hz)								
		1-R[1]	H-2 (s, CH_3)	3-CH_3 (s)	H-4	5-R	H-6 (s)	7-$CO_2CH_2CH_3$ (*J* = 7.0)	H-8 (s)	9-R[2]
17a	E	10.87	2.42	2.25	7.60 (s)	2.70 (s, CH_3)	—	1.37 (t), 4.39 (q)	7.72	11.76 (s, OH)
	C	10.75	2.33	2.29	7.47 (s)	2.84 (s, CH_3)	—	1.39 (t), 4.39 (q)	8.05	10.75 (s, OH)
17b	E	11.25	2.40	2.24	7.72 (s)	2.63 (s, CH_3)	9.81	1.37 (t), 4.44 (q)	6.75	—
	C	7.31	2.43	2.11	7.08 (s)	2.39 (s, CH_3)	7.31	1.36 (t), 4.42 (q)	7.20	—
18a	E	3.94 (sH_3)	2.35	2.23	7.57 (s)	2.71 (s, CH_3)	—	1.37 (t), 4.39 (q)	7.71	11.61 (s, OH)
	C	3.61 (sH_3)	2.20	2.20	7.31 (s)	2.84 (s, CH_3)	—	1.39 (t), 4.39 (q)	8.02	10.08 (s, OH)
18b	E	3.91 (sH_3)	2.33	2.25	7.71 (s)	2.63 (s, CH_3)	9.49	1.37 (t), 4.40 (q)	6.68	—
	C	3.49 (sH_3)	2.20	2.20	6.88 (s)	2.39 (s, CH_3)	9.56	1.36 (t), 4.42 (q)	7.20	—
19b	E	11.14	2.40	2.22	7.47 (s)	4.06 (s, OCH_3)	9.85	1.38 (t), 4.44 (q)	6.73	—
19a	C	10.75	2.33	2.26	7.09 (s)	3.93 (s, OCH_3)	—	1.39 (t), 4.39 (q)	8.15	10.75 (s, OH)
19b	C	7.45	2.43	2.27	6.79 (s)	3.70 (s, OCH_3)	7.45	1.36 (t), 4.42 (q)	7.20	—
20b	E	3.99 (sH_3)	2.33	2.23	7.42 (s)	4.05 (s, OCH_3)	9.66	1.37 (t), 4.43 (q)	6.65	
20a	C	3.61 (sH_3)	2.20	2.20	6.88 (s)	3.93 (s, OCH_3)	—	1.39 (t), 4.39 (q)	8.11	10.08 (s, OH)
20b	C	3.49 (sH_3)	2.20	2.20	6.54 (s)	3.70 (s, OCH_3)	9.84	1.36 (t), 4.42 (q)	7.20	
21b	E	12.15	2.41	2.23	7.80 (d, *J* = 8)	7.58 (d, *J* = 8)	11.33	1.38 (t), 4.44 (q)	6.75	
21a	C	10.75	2.33	2.22	7.13 (d, *J* = 8)	8.07 (d, *J* = 8)	—	1.39 (t), 4.39 (q)	8.09	10.75 (s, OH)
21b	C	7.45	2.43	2.11	7.21 (d, *J* = 8)	6.65 (d, *J* = 8)	7.45	1.36 (t), 4.42 (q)	7.20	
22b	E	4.00 (sH_3)	2.35	2.24	7.78 (d, *J* = 8)	7.61 (d, *J* = 8)	11.90	1.38 (t), 4.44 (q)	6.67	
22a	C	3.61 (sH_3)	2.20	2.20	7.57 (d, *J* = 8)	8.03 (d, *J* = 8)	—	1.39 (t), 4.39 (q)	8.05	10.08 (s, OH)
22b	C	3.49 (sH_3)	2.20	2.20	6.96 (d, *J* = 8)	6.61 (d, *J* = 8)	9.85	1.36 (t), 4.42 (q)	7.20	
23a	E	11.44	2.65	2.35	7.06 (s)	11.10 (s, OH)	7.46	1.38 (t), 4.37 (q)	—	4.04 (s, OCH_3)
	C	10.93	2.78	2.26	7.28 (s)	10.93 (s, OH)	8.03	1.39 (t), 4.39 (q)	—	4.13 (s, OCH_3)
23b	E	11.65	2.53	2.35	7.16 (s)	—	6.64	1.38 (t), 4.42 (q)	9.78	4.02 (s, OCH_3)
	C	10.66	2.78	2.27	7.72 (s)	—	6.75	1.36 (t), 4.42 (q)	10.66	3.74 (s, OCH_3)
24a	E	3.94 (sH_3)	2.64	2.29	7.04 (s)	11.13 (s, OH)	7.45	1.36 (t), 4.36 (q)	—	3.98 (s, OCH_3)
	C	3.49 (sH_3)	2.20	2.20	6.98 (s)	10.36 (s, OH)	8.03	1.39 (t), 4.39 (q)	—	4.14 (s, OCH_3)
24b	C	3.49 (sH_3)	2.20	2.20	7.70 (s)	—	6.75	1.36 (t), 4.42 (q)	9.84	3.74 (s, OCH_3)

* E = experimental spectra; C = calculated spectra.

During thermolysis of the enamines in boiling biphenyl pyrrolo[2,3-*f*]quinoline **17** was obtained from compound **9**. Its ^{1}H NMR spectrum in DMSO-d_6 solution showed two tautomeric forms (**a**,**b**) in approximately equal proportions. The difference between the tautomers **17a** and **17b** lies in the different chemical shifts of the signals for protons of the same type. As the main test we used the substantial difference (0.8 ppm) in the chemical shifts of the signal for the H-8 proton. On the basis of the fact that this hydrogen atom does not undergo exchange processes either in form **a** or in form **b** it is right to assign its signal for the various tautomers on the basis of their calculated ^{1}H NMR spectra. (The experimental and calculated spectra are presented in Table 3.)

In the ^{1}H NMR spectrum of compound **17** there are signals for all the protons both of form **a** and of form **b**, differing in chemical shifts. Thus, the signal for the H-8 proton of the hydroxyquinoline structure appears in the region of 7.72 while that for the *p*-quinolone structure appears at 6.75 ppm, which agrees with the data of the calculated spectra.

The N-methyl-substituted enamine **10** also readily undergoes thermal cyclization irrespective of some steric hindrance of position 7. As also for the unmethylated analog, the ^{1}H NMR spectrum of the isolated pyrroloquinoline **18** indicates that it exists in the form of a mixture of the tautomeric forms **a** and **b** in approximately equal proportions.



17 R = Me, R^1 = H; **18** R = R^1 = Me; **19** R = OMe, R^1 = H; **20** R = OMe, R^1 = Me;
21 R = R^1 = H; **22** R = H, R^1 = Me; **23** R^1 = H; **24** R^1 = Me

The pyrroloquinolines **19** and **20** are formed from the 5-methoxy-substituted enamines **11** and **12** with somewhat greater difficulty, as seen in the increased reaction time.

According to the data from the ^{1}H NMR spectra, the obtained compounds **19** and **20** are exclusively in form **b**. (The chemical shifts of the signal for the H-8 proton amount to 6.73 for the pyrroloquinoline **19** and 6.65 ppm for the N-methylated analog **20)**.

The formation of a mixture of pyrroloquinolines of linear and angular structure is not ruled out during the thermolysis of enamines **13** and **14** with two positions (5, 7) free for the amino group. However, as in the case of the enamines obtained from acetoacetic ester and ethoxymethylenemalonic ester [4], compound **13** undergoes cyclization exclusively to the angular pyrroloquinoline **21**.

The introduction of a methyl substituent at the pyrrole nitrogen atom in order to create steric hindrances for attack at position 7 does not change the direction of ring formation. The enamine **14** is also transformed into the corresponding pyrrolo[2,3-*f*]quinoline **22**.

TABLE 4. The Spectral Characteristics of Compounds **17-24**

Compound	IR spectrum, ν, cm^{-1}	UV spectrum, λ_{max}, nm (log ε)	Mass-spectrum, *m/z* (I_{rel}, %)
17	1519, 1558, 1614, 1721	205 (4.23), 235 (4.13), 285 (3.94), 315 (4.04)	299 (15), 298 [M^+] (70), 297 (5), 270 (5), 225 (20), 224 (100), 223 (20), 209 (5), 197 (8), 196 (16), 195 (24), 181 (12), 154 (10), 77 (5)
18	1559, 1585, 1635, 1717	205 (4.35), 240 (4.29), 285 (4.12), 320 (4.24)	313 (12), 312 $[M]^+$ (65), 311 (60), 283 (12), 239 (31), 238 (55), 237 (100), 223 (60), 209 (34), 208 (12), 195 (27), 119 (29), 77 (20)
19	1560, 1593, 1614, 1718,	204 (4.34), 235 (4.32), 280 (4.16), 325 (4.31)	315 (15), 314 $[M]^+$ (100), 299 (50), 286(10), 271 (13), 241 (23), 240 (95), 226 (15), 225 (100), 197 (15), 143 (20), 120 (22), 77 (12)
20	1577, 1600, 1614, 1716	205 (4.41), 235 (4.29), 285 (4.09), 330 (4.26)	329 (22), 328 $[M]^+$ (100), 327 (70), 313 (35), 299 (20), 254 (40), 253 (80), 241 (80), 239 (80), 225 (15), 224 (20), 211 (21), 197 (20), 183 (30), 168 (28), 156 (30), 141 (30), 127 (75), 115 (48), 77 (65)
21	1515, 1551, 1602, 1718	205 (4.44), 227 (4.46), 280 (4.34), 310 (4.36)	285 (10), 284 $[M]^+$ (41), 283 (5), 256 (5), 211 (25), 210 (100), 209 (14), 182 (15), 181 (20), 157 (15), 156 (15), 140 (15), 115 (10), 77 (15)
22	1525, 1554, 1607, 1730	205 (4.33), 227 (4.29), 280 (4.09), 310 (4.19)	299 (15), 298 $[M]^+$ (75), 297 (40), 269 (10), 225 (30), 224 (70), 223 (100), 210 (12), 209 (60), 197 (20), 196 (20), 195 (35), 182 (20), 181 (30), 154 (30), 115 (25), 77 (45)
23	1543, 1558, 1605, 1628, 1716, 1740	235 (4.57), 285 (4.05), 350 sh. (3.64), 390 (3.79)	314 $[M]^+$ (93), 313 (13), 299 (8), 285 (7), 241 (21), 240 (100), 239 (44), 225 (48), 212 (30), 211 (6), 197 (38), 169 (28), 113 (19), 86 (16)
24	1593, 1620, 1709, 1717, 1732	240 (4.68), 280 (4.15), 350 sh. (3.78), 390 (3.88)	329 (14), 328 $[M]^+$ (70), 313 (20), 255 (19), 254 (65), 253 (29), 239 (45), 226 (15), 69 (30), 55 (60), 43 (100)

The angular fusion of the rings in the molecules of the isolated compounds **21** and **22** is indicated by the presence of two doublet signals for the H-4,5 protons with $J = 8$ Hz in their ^{1}H NMR spectra and for form **b** by the chemical shifts of the H-8 proton (6.75, 6.67 ppm).

As starting compounds for the specific production of the linear pyrrolo[3,2-*g*]quinolines we used the enamines **15** and **16**, obtained from 7-methoxy-2,3-dimethyl- and 7-methoxy-1,2,3-trimethyl-6-aminoindoles and oxaloacetic ester. During their thermal cyclization in boiling biphenyl it was possible to obtain the linear pyrrolo[3,2-*g*]quinolines **23** and **24**.

In the ^{1}H NMR spectra in DMSO-d_6 for compound **23**, obtained from the enamine **15**, there are signals for the protons both of form **a** and of form **b** in a ratio of 8:1, according to the integral intensity of the signal of the H-6 proton, which appears at 7.46 for the hydroxyquinoline form **a** and at 6.64 ppm for tautomer **b**, and this agrees with the calculated spectra. According to the data from the ^{1}H NMR spectrum, the pyrroloquinoline **24** obtained from the enamine **16** is only detected in form **a** under the same conditions.

The IR, UV, and mass spectral characteristics (Table 4) confirm the structure of the pyrroloquinolines **17-24** and agree well with the published data [2, 3].

Thus, under the conditions of thermal cyclization the enamines **9-14** obtained both from the 5-substituted and from the unsubstituted 6-aminoindoles and oxaloacetic ester are transformed exclusively into pyrrolo[2,3-*f*]quinolines. Here a new series of compounds – structural analogs of methoxatin (PQQ) – is

obtained. The method developed for the production of pyrrolo[2,3-*f*]quinolines is regiodirected in so far as the nature of the substituent at the pyrrole nitrogen atom does not affect the direction of closure of the pyridine ring. The pyrrolo[3,2-*g*]quinoline system with the participation of oxaloacetic ester is only formed readily from 7-substituted 6-aminoindoles. (The 7-OCH_3 group has a favorable effect on cyclization.)

EXPERIMENTAL

The ^{1}H NMR spectra were recorded in DMSO-d_6 on a Bruker DRX-500 instrument (500 MHz) with reference to TMS. The IR spectra were recorded in tablets with potassium bromide on an Unititled Spektrum instrument. The mass spectra were obtained on a Finnigan MAT Incos-50 mass spectrometer with direct injection of the sample into the ion source at ionization energy 70 eV. The electronic spectra were obtained in ethanol on a Specord spectrophotometer. The enamines were purified by column chromatography with Al_2O_3 (neutral, I and II Brockman activity) as sorbent. The reaction course and the purity of the compounds obtained were monitored by TLC on Silufol UV-254 plates. The calculated ^{1}H NMR spectra were obtained by the ACD/LABS Chemsketch Windows HNMR Spectrum Generator.

Diethyl (2-*Z*)-2-(2,3,5-Trimethyl-1H-indol-6-ylamino)-2-butenedioate (9). A mixture of of 6-amino-2,3,5-trimethylindole (**1**) (0.50 g, 2.87 mmol) and oxaloacetic ester (0.60 g, 3.19 mmol) was boiled in absolute benzene (300 ml) in the presence of a catalytic amount of glacial acetic acid with a Dean–Stark tube for 27 h. At 9 h intervals the benzene was distilled from the reaction mixture, and a new portion was added. After all the aminoindole had reacted (monitored by TLC) the benzene was distilled. The residue was dissolved in a mixture of benzene and petroleum ether, and the hot solution was passed through a layer (2 cm) of Al_2O_3. The enamine was recrystallized from a mixture of petroleum ether and benzene. The yield was 0.40 g.

Diethyl (2-*Z*)-2-(1,2,3,5-Tetramethyl-1H-indol-6-ylamino)-2-butenedioate (10). This compound was obtained similarly from 6-amino-1,2,3,5-tetramethylindole (**2)** (1.30 g, 6.91 mmol) and oxaloacetic ester (1.50 g, 7.98 mmol). The mixture was heated for 30 h. The enamine was recrystallized from petroleum ether. The yield was 1.60 g.

Diethyl (2-*Z*)-2-(5-Methoxy-2,3-dimethyl-1H-indol-6-ylamino)-2-butenedioate (11). This compound was obtained similarly from 6-amino-5-methoxy-2,3-dimethylindole (**3**) (0.60 g, 3.16 mmol) and oxaloacetic ester (0.80 g, 4.255 mmol). The mixture was boiled for 55 h. The yield was 0.49 g.

Diethyl (2-*Z*)-2-(5-Methoxy-1,2,3-trimethyl-1H-indol-6-ylamino)-2-butenedioate (12). This compound was obtained similarly from 6-amino-5-methoxy-1,2,3-trimethylindole (**4**) (0.60 g. 2.94 mmol) and oxaloacetic ester (0.80 g, 4.255 mmol). The mixture was boiled for 60 h. The yield was 0.75 g.

Diethyl (2-*Z*)- and (2-*E*)-2-(2,3-Dimethyl-1H-indol-6-ylamino)-2-butenedioate (13). This compound was obtained similarly from 6-amino-2,3-dimethylindole (**5**) (0.70 g, 4.375 mmol) and oxaloacetic ester (0.85 g, 4.52 mmol). The mixture was heated for 40 h, and the enamine was recrystallized from hexane. The yield was 0.51 g.

Diethyl (2-*Z*)-2-(7-Methoxy-2,3-dimethyl-1H-indol-6-ylamino)-2-butenedioate (15). This compound was obtained similarly from 6-amino-7-methoxy-2,3-dimethylindole (**7**) (0.50 g, 2.63 mmol) and oxaloacetic ester (0.50 g, 2.66 mmol). The mixture was heated for 36 h. The yield was 0.35 g.

Diethyl (2-*Z*)-2-(7-Methoxy-1,2,3-trimethyl-1H-indol-6-ylamino)-2-butenedioate (16). This compound was obtained similarly from 6-amino-7-methoxy-1,2,3-trimethylindole (**8**) (0.60 g, 2.94 mmol) and oxaloacetic ester (0.60 g, 3.19 mmol). The mixture was heated for 50 h. The yield was 0.47 g.

7-Ethoxycarbonyl--9-hydroxy-2,3,5-trimethyl-1H-pyrrolo[2,3-*f*]quinoline (17a) and 7-Ethoxycarbonyl-2,3,5-trimethyl-6,9-dihydro-1H-pyrrolo[2,3-*f*]quinolin-9-one (17b). Enamine **9** (0.10 g, 0.291 mmol) was heated in boiling biphenyl for 10 min. At the end of the reaction (monitored by TLC) the still hot reaction mixture was poured into petroleum ether. The precipitate was filtered off and washed repeatedly with hot petroleum ether. The product was recrystallized from ethanol. The yield was 0.05 g.

7-Ethoxycarbonyl-9-hydroxy-1,2,3,5-tetramethyl-1H-pyrrolo[2,3-*f*]quinolin-9-one (18a) and 7-Ethoxycarbonyl-1,2,3,5-tetramethyl-6,9-dihydro-1H-pyrrolo[2,3-*f*]quinolin-9-one (18b). These compounds were obtained similarly from the enamine **10** (0.60 g, 1,68 mmol). The yield was 0.30 g.

7-Ethoxycarbonyl-5-methoxy-2,3-dimethyl-6,9-dihydro-1H-pyrrolo[2,3-*f*]quinolin-9-one (19b). This compound was obtained similarly from enamine **11** (0.20 g, 0.556 mmol). The mixture was boiled for 20 min. The yield was 0.167 g.

7-Ethoxycarbonyl-5-methoxy-1,2,3-trimethyl-6,9-dihydro-1H-pyrrolo[2,3-*f*]quinolin-9-one (20b). This compound was obtained similarly from enamine **12** (0.75 g, 2.005 mmol). The yield was 0.44 g.

7-Ethoxycarbonyl-2,3-dimethyl-6,9-dihydro-1H-pyrrolo[2,3-*f*]quinolin-9-one (21b). This compound was obtained similarly from enamine **13** (0.098 g, 0.293 mmol). The mixture was boiled for 10 min. The yield was 0.067 g.

7-Ethoxycarbonyl-1,2,3-trimethyl-6,9-dihydro-1H-pyrrolo[2,3-*f*]quinolin-9-one (22b). This compound was obtained similarly from the enamine **14** (0.205, g 0.596 mmol). The product was recrystallized from petroleum ether. The yield was 0.138 g.

7-Ethoxycarbonyl-5-hydroxy-9-methoxy-2,3-dimethyl-1H-pyrrolo[2,3-*g*]quinoline (23a) and 7-Ethoxycarbonyl-9-methoxy-2,3-dimethyl-5,8-dihydro-1H-pyrrolo[3,2-*g*]quinolin-5-one (23b). These compounds were obtained similarly from enamine **15** (0.17 g, 0.472 mmol). The product was recrystallized from alcohol. The yield was 0.09 g.

7-Ethoxycarbonyl-5-hydroxy-9-methoxy-1,2,3-trimethyl-1H-pyrrolo[3,2-*g*]quinoline (24a). This compound was obtained similarly from enamine **16** (0.09 g, 0.241 mmol). The yield was 0.06 g.

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