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SYNTHESIS OF SUBSTITUTED PYRROLO[3,2-*f*]-QUINOLINES FROM 5-AMINOINDOLES AND DIETHYL OXALOACETATE

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The reactions of a series of substituted 5-aminoindoles with diethyl oxaloacetate were studied. A synthesis was developed for 5-indolylamino derivatives of diethyl fumarate as well as 7-ethoxycarbonyl-6,9-dihydro-3H-pyrrolo[3,2-f]quinolin-9-ones.

Keywords: 5-indolylamino derivatives of diethyl fumarate, substituted 5-aminoindoles, diethyl oxaloacetate, 7-ethoxycarbonyl-6,9-dihydro-3H-pyrrolo[3,2-*f*]quinolin-9-ones.

Substituted aminoindoles with the amino group in the benzene part of the molecule have served as synthones in the preparation of pyrroloquinolines [1], which are compounds with potential biological activity. Thus, a natural compound was discovered, namely, a B-group vitamin (methoxatin) with pyrroloquinoline structure (PQQ = 2,7,9-tricarboxy-1H-pyrrolo[2,3-*f*]quinoline-4,5-dione), which acts as a coenzyme in oxidation–reduction reactions in living systems [2].

In the present work, we continued to search for convenient methods for the preparation of pyrroloquinolines, structural analogs of PQQ with a γ-quinolone fragment containing an ethoxycarbonyl group. For this purpose, we studied the reaction of substituted 5-aminoindoles with diethyl oxaloacetate. In the initial step in the condensation of the amines with the keto ester, we might have expected the formation of two different amides and an enamine in light of the three reaction sites in the ester. In the case of aminoindoles with a free position at $C_{(3)}$, we also could not exclude the possibility of attack at the β-position of the indole system. However, we found that aminoindoles **1-11** and diethyl oxaloacetate upon heating at reflux in benzene give the corresponding enamines **12-22** (derivatives of the diethyl ester of 5-aminoindolylfumarate also hold interest for possible physiological activity), i.e., under these conditions, the reaction of the amines with the keto ester proceeds at the carbonyl group.

The ^{1}H NMR spectra of **12-22** (Table 1) show signals for the protons of two nonequivalent ethoxycarbonyl groups. The difference in the chemical shifts of these protons (~0.2 ppm) is probably related to the *Z*-configuration of the enamine such that one of the ethoxycarbonyl groups is chelated with the amino group hydrogen atom.

The enamine structure of **12-22** is supported by the signals for vinyl protons at 5.03-5.10 ppm and for the amine NH proton at 9.50-9.70 ppm.

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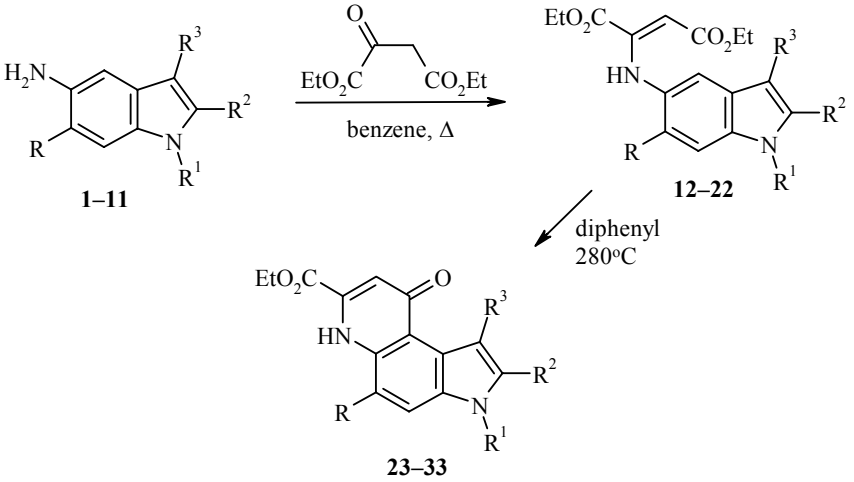

1–11 **12–22** **23–33**

1, **12**, **23** R = R^2 = R^3 = Me, R^1 = H; **2**, **13**, **24** R = R^1 = R^2 = R^3 = Me;
3, **14**, **25** R = Me, R^1 = R^3 = H, R^2 = Ph; **4**, **15**, **26** R = R^1 = Me, R^2 = Ph, R^3 = H;
5, **16**, **27** R = OMe, R^1 = H, R^2 = R^3 = Me; **6**, **17**, **28** R = R^1 = R^3 = H, R^2 = Me; **7**, **18**, **29** R = R^3 = H, R^1 = R^2 = Me;
8, **19**, **30** R = R^1 = Me, R^2 = Ph, R^3 = H; **9**, **20**, **31** R = R^3 = H, R^1 = Me, R^2 = Ph;
10, **21**, **32** R = R^1 = H, R^2 = R^3 = Me; **11**, **22**, **33** R = H, R^1 = R^2 = R^3 = Me

The IR spectra of all enamines **12-22** (Table 2) are virtually identical and contain strong stretching bands at 1600-1605, 1644-1668, and 1712-1725 cm^{-1}. These findings also support *Z*-configuration for the enamine chain. The band at 1712-1725 cm^{-1} should probably be assigned to the stretching vibrations of the free

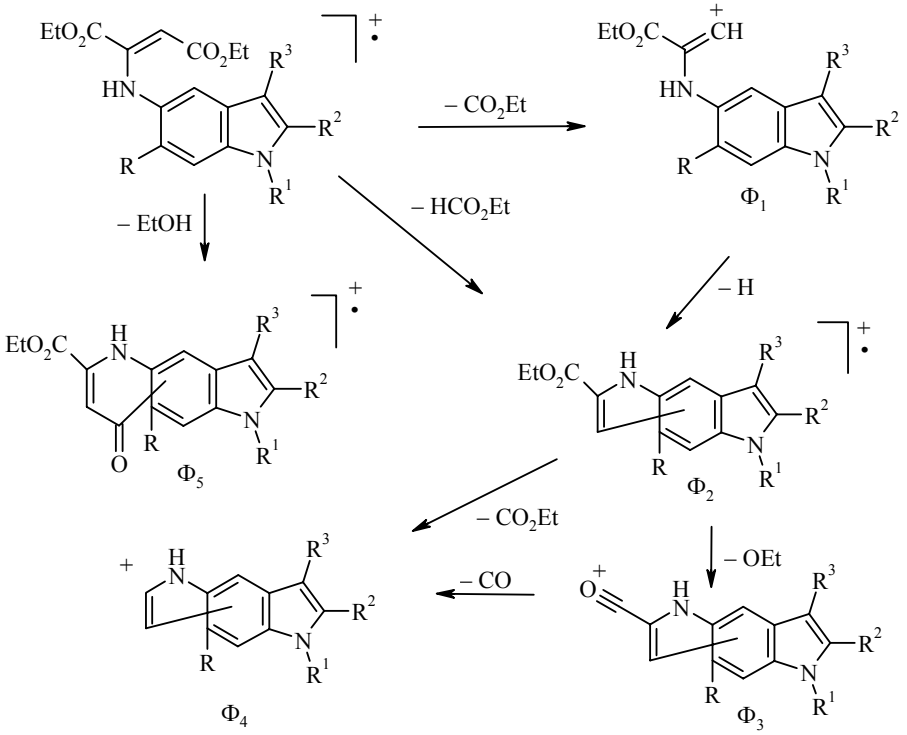

TABLE 1. ^{1}H NMR Spectra of **12-33**

Compound	Chemical shifts, δ, ppm (*J*, Hz)
1	2
12	0.90 (3H, t, *J* = 7, $CO_2CH_2\underline{CH_3}$); 1.22 (3H, t, *J* = 7, $CO_2CH_2\underline{CH_3}$); 2.04 (3H, s, 3-CH_3); 2.27 (3H, s, 2-CH_3); 2.30 (3H, s, 6-CH_3); 3.98 (2H, q, *J* = 7, $CO_2\underline{CH_2}CH_3$ chelate); 4.14 (2H, q, *J* = 7, $CO_2\underline{CH_2}CH_3$); 5.03 (1H, s, H vin); 6.78 (1H, s, H-4); 7.08 (1H, s, H-7); 9.50 (1H, s, NH amine); 10.56 (1H, s, H-1)
13	0.91 (3H, t, *J* = 7, $CO_2CH_2\underline{CH_3}$ chelate); 1.22 (3H, t, *J* = 7, $COO_2CH_2\underline{CH_3}$); 2.09 (3H, s, 3-$CH_3$); 2.28 (3H, s, 2-$CH_3$); 2.35 (3H, s, 6-$CH_3$); 3.60 (3H, s, 1-$CH_3$); 3.98 (2H, q, *J* = 7, $CO_2\underline{CH_2}CH_3$ chelate); 4.14 (2H, q, *J* = 7, $CO_2\underline{CH_2}CH_3$); 5.05 (1H, s, H vin); 6.82 (1H, s, H-4); 7.21 (1H, s, H-7); 9.53 (1H, s, NH amine)
14	0.89 (3H, t, *J* = 7, $CO_2CH_2\underline{CH_3}$); 1.24 (3H, t, *J* = 7, $CO_2CH_2\underline{CH_3}$); 2.35 (3H, s, 6-CH_3); 3.98 (2H, q, *J* = 7, $CO_2\underline{CH_2}CH_3$ chelate); 4.15 (2H, q, *J* = 7, $CO_2\underline{CH_2}CH_3$); 5.08 (1H, s, H vin); 6.82 (1H, s, H-3); 6.98 (1H, s, H-4); 7.26 (1H, s, H-7); 7.31 (1H, t, *J* = 7, H–*p*-C_6H_5); 7.45 (2H, t, *J* = 7, H–*m*-C_6H_5); 7.83 (2H, d, *J* = 7, H-*o*-C_6H_5); 9.52 (1H, s, NH amine); 11.45 (1H, s, H-1)
15	0.92 (3H, t, *J* = 7, $CO_2CH_2\underline{CH_3}$ chelate); 1.23 (3H, t, *J* = 7, $CO_2CH_2\underline{CH_3}$); 2.40 (3H, s, 6-CH_3); 3.72 (3H, s, 1-CH_3); 4.00 (2H, q, *J* = 7, $CO_2\underline{CH_2}CH_3$ chelate); 4.14 (2H, q, *J* = 7, $CO_2\underline{CH_2}CH_3$); 5.10 (1H, s, H vin); 6.47 (1H, s, H-3); 7.00 (1H, s, H-4); 40 (1H, s, H-7); 7.44 (1H, t, *J* = 7, H–*p*-C_6H_5); 7.50 (2H, t, *J* = 7, H–*m*-C_6H_5); 7.57 (2H, d, *J* = 7, H–*o*-C_6H_5); 9.53 (1H, s, NH amine)
16	1.04 (3H, t, *J* = 7, $CO_2CH_2\underline{CH_3}$ chelate); 1.22 (3H, t, *J* = 7, $CO_2CH_2\underline{CH_3}$); 2.04 (3H, s, 3-CH_3); 2.25 (3H, s, 2-CH_3); 3.78 (3H, s, 6-OCH_3); 4.11 (2H, q, *J* = 7, $CO_2\underline{CH_2}CH_3$ chelate); 4.14 (2H, q, *J* = 7, $CO_2\underline{CH_2}CH_3$); 5.05 (1H, s, H vin); 6.79 (1H, s, H-4); 6.81 (1H, s, H-7); 9.67 (1H, s, NH amine); 10.50 (1H, s, H-1)
17	0.97 (3H, t, *J* = 7, $CO_2CH_2\underline{CH_3}$ chelate); 1.22 (3H, t, *J* = 7, $CO_2CH_2\underline{CH_3}$); 2.35 (3H, s, 2-CH_3); 4.02 (2H, q, *J* = 7, $CO_2\underline{CH_2}CH_3$ chelate); 4.14 (2H, q, *J* = 7, $CO_2\underline{CH_2}CH_3$); 5.03 (1H, s, H vin); 6.07 (1H, s, H-3); 6.69 (1H, d, *J* = 8, H-6); 7.00 (1H, s, H-4); 7.20 (1H, d, *J* = 8, H-7); 9.68 (1H, s, NH amine); 10.94 (1H, s, H-1)
18	0.96 (3H, t, *J* = 7, $CO_2CH_2\underline{CH_3}$ chelate); 1.23 (3H, t, *J* = 7, $CO_2CH_2\underline{CH_3}$); 2.47 (3H, s, 2-CH_3); 3.64 (3H, s, 1-CH_3); 4.04 (2H, q, *J* = 7, $CO_2\underline{CH_2}CH_3$ chelate); 4.13 (2H, q, *J* = 7, $CO_2\underline{CH_2}CH_3$); 5.05 (1H, s, H vin); 6.15 (1H, s, H-3); 6.76 (1H, d, *J* = 8, H-6); 7.00 (1H, s, H-4); 7.31 (1H, d, *J* = 8, H-7); 9.68 (1H, s, NH amine)
19	0.96 (3H, t, *J* = 7, $CO_2CH_2\underline{CH_3}$ chelate); 1.24 (3H, t, *J* = 7, $CO_2CH_2\underline{CH_3}$); 4.06 (2H, q, *J* = 7, $CO_2\underline{CH_2}CH_3$ chelate); 4.14 (2H, q, *J* = 7, $CO_2\underline{CH_2}CH_3$); 5.09 (1H, s, H vin); 6.82 (1H, d, *J* = 8, H-6); 6.85 (1H, s, H-3); 7.12 (1H, s, H-4); 7.32 (1H, t, *J* = 8, H-*p*-C_6H_5); 7.34 (1H, d, *J* = 8, H-7); 7.47 (2H, t, *J* = 8, H–*m*-C_6H_5); 7.86 (2H, d, *J* = 8, H–*o*-C_6H_5); 9.70 (1H, s, NH amine); 11.59 (1H, s, H-1)
20	1.00 (3H, t, *J* = 7, $CO_2CH_2\underline{CH_3}$ chelate); 1.22 (3H, t, *J* = 7, $CO_2CH_2\underline{CH_3}$); 3.72 (3H, s, 1-CH_3); 4.07 (2H, q, *J* = 7, $CO_2\underline{CH_2}CH_3$ chelate); 4.14 (2H, q, *J* = 7, $CO_2\underline{CH_2}CH_3$); 5.10 (1H, s, H vin); 6.52 (1H, s, H-4); 6.89 (1H, d, *J* = 7, H-6); 7.15 (1H, s, H-3); 7.44 (1H, t, *J* = 7, H–*p*-C_6H_5); 7.45 (1H, d, *J* = 7, H-7); 7.52 (2H, t, *J* = 7, H–*m*-C_6H_5); 7.59 (2H, d, *J* = 7, H–*o*-C_6H_5); 9.72 (1H, s, NH amine)
21	0.96 (3H, t, *J* = 7, $CO_2CH_2\underline{CH_3}$ chelate); 1.24 (3H, t, *J* = 7, $CO_2CH_2\underline{CH_3}$); 2.09 (3H, s, 3-CH_3); 2.29 (3H, s, 2-CH_3); 4.04 (2H, q, *J* = 7, $CO_2\underline{CH_2}CH_3$ chelate); 4.12 (2H, q, *J* = 7, $CO_2\underline{CH_2}CH_3$); 5.04 (1H, s, H vin); 6.69 (1H, d, *J* = 8, H-6); 6.93 (1H, s, H-4); 7.15 (1H, d, *J* = 8, H-7); 9.70 (1H, s, NH amine); 10.70 (1H, s, H-1)
22	0.98 (3H, t, *J* = 7, $CO_2CH_2\underline{CH_3}$ chelate); 1.23 (3H, t, *J* = 7, $CO_2CH_2\underline{CH_3}$); 2.13 (3H, s, 3-CH_3); 2.30 (3H, s, 2-CH_3); 3.62 (3H, s, 1-CH_3); 4.05 (2H, q, *J* = 7, $CO_2\underline{CH_2}CH_3$ chelate); 4.14 (2H, q, *J* = 7, $CO_2\underline{CH_2}CH_3$); 5.05 (1H, s, H vin); 6.75 (1H, d, *J* = 8.5, H-6); 6.98 (1H, s, H-4); 7.29 (1H, d, *J* = 8.5, H-7); 9.72 (1H, s, NH amine)
23	1.35 (3H, t, *J* = 7, 7-$CO_2CH_2\underline{CH_3}$); 2.35 (3H, s, 2-CH_3); 2.59 (3H, s, 5-CH_3); 2.68 (3H, s, 1-CH_3); 4.36 (2H, q, *J* = 7, 7-$CO_2\underline{CH_2}CH_3$); 7.53 (1H, s, H-8); 7.60 (1H, s, H-4); 11.19 (1H, s, H-6); 11.30 (1H, s, H-3)
24	1.37 (3H, t, *J* = 7, 7-$CO_2CH_2\underline{CH_3}$); 2.36 (3H, s, 2-CH_3); 2.55 (3H, s, 5-CH_3) 2.74 (3H, s, 1-CH_3); 3.75 (3H, s, 3-CH_3); 4.46 (2H, q, *J* = 7, 7-$CO_2\underline{CH_2}CH_3$); 7.55 (1H, s, H-8); 7.80 (1H, s, H-4); 11.22 (1H, s, H-6)
25	1.39 (3H, t, *J* = 7, 7-$CO_2CH_2\underline{CH_3}$); 2.77 (3H, s, 5-CH_3); 4.39 (2H, q, *J* = 7, 7-$CO_2\underline{CH_2}CH_3$); 7.32 (1H, t, *J* = 8, H-p-C_6H_5); 7.48 (2H, t, *J* = 8, H–m-C_6H_5); 7.65 (1H, s, H-8); 7.67 (1H, s, H-1); 7.75 (1H, s, H-4); 7.90 (2H, d, *J* = 8, H–*o*-C_6H_5); 11.52 (1H, s, H-6); 12.05 (1H, s, H-3)

TABLE 1 (continued)

1	2
26	1.38 (3H, t, J = 7, 7-$CO_2CH_2\underline{CH_3}$); 2.80 (3H, s, 5-CH_3); 3.89 (3H, s, 3-CH_3); 4.39 (2H, q, J = 7, 7-$CO_2\underline{CH_2}CH_3$); 7.37 (1H, s, H-8); 7.44 (1H, t, J = 7, H-p-C_6H_5); 7.54 (2H, t, H–m-C_6H_5); 7.63 (1H, s, H-1); 7.64 (2H, d, J = 8, H–o-C_6H_5); 7.94 (1H, s, H-4); 11.51 (1H, s, H-6)
27	1.30 (3H, t, J = 7, 7-$CO_2CH_2\underline{CH_3}$); 2.37 (3H, s, 2-CH_3); 2.55 (3H, s, 1-CH_3); 4.08 (3H, s, 5-OCH_3); 4.46 (2H, q, J = 7, 7-$CO_2\underline{CH_2}CH_3$); 7.04 (1H, s, H-8); 7.40 (1H, s, H-4); 11.41 (1H, s, H-3)
28	1.38 (3H, t, J = 7, 7-$CO_2CH_2\underline{CH_3}$); 2.46 (3H, s, 2-CH_3); 4.41 (2H, q, J = 7, 7-$CO_2\underline{CH_2}CH_3$); 6.66 (1H, s, H-8); 7.25 (1H, s, H-1); 7.60 (1H, d, J = 8, H-5); 7.68 (1H, d, J = 8, H-4); 11.44 (1H, s, H-6); 11.90 (1H, s, H-3)
29	1.39 (3H, t, J = 7, 7-$CO_2CH_2\underline{CH_3}$); 2.46 (3H, s, 2-CH_3); 3.76 (3H, s, 3-CH_3); 4.40 (2H, q, J = 7, 7-$CO_2\underline{CH_2}CH_3$); 6.67 (1H, s, H-8); 7.35 (1H, s, H-1); 7.67 (1H, d, J = 8, H-5); 7.85 (1H, d, J = 8, H-4); 11.90 (1H, s, H-6)
30	1.39 (3H, t, J = 7, 7-$CO_2CH_2\underline{CH_3}$); 4.42 (2H, q, J = 7, 7-$CO_2\underline{CH_2}CH_3$); 6.72 (1H, s, H-8); 7.34 (1H, t, J = 7.5, H–p-C_6H_5); 7.50 (2H, t, J = 7.5, H–m-C_6H_5); 7.75 (1H, d, J = 8, H-5); 7.82 (1H, d, J = 8, H-4); 7.90 (2H, d, J = 7.5, H–o-C_6H_5); 7.98 (1H, s, H-1); 12.04 (1H, s, H-6); 12.10 (1H, s, H-3)
31	1.39 (3H, t, J = 7, 7-$CO_2CH_2\underline{CH_3}$); 3.87 (3H, s, 1-CH_3); 4.45 (2H, q, J = 7, 7-$CO_2\underline{CH_2}CH_3$); 6.72 (1H, s, H-8); 7.46 (1H, t, J = 7.5, H–p-C_6H_5); 7.56 (2H, t, J = 7.5, H–m-C_6H_5); 7.65 (2H, d, J = 7.5, H–o-C_6H_5); 7.70 (1H, s, H-1); 7.80 (1H, d, J = 8, H-5); 8.00 (1H, d, J = 8, H-4); 12.05 (1H, s, H-6)
32	1.37 (3H, t, J = 7, 7-$CO_2CH_2\underline{CH_3}$); 2.32 (3H, s, 2-CH_3); 2.61 (3H, s, 1-CH_3); 4.40 (2H, q, J = 7, 7-$CO_2\underline{CH_2}CH_3$); 6.59 (1H, s, H-8); 7.58 (1H, d, J = 8, H-5); 7.60 (1H, d, J = 8, H-4); 11.28 (1H, s, H-4); 11.68 (1H, s, H-6)
33	1.38 (3H, t, J = 7, 7-$CO_2CH_2\underline{CH_3}$); 2.39 (3H, s, 2-CH_3); 2.68 (3H, s, 1-CH_3); 3.73 (3H, s, 3-CH_3); 4.42 (2H, q, J = 7, $CO_2\underline{CH_2}CH_3$); 6.60 (1H, s, H-8); 7.61 (1H, d, J = 8, H-5); 7.69 (1H, d, J = 8, H-4); 11.55 (1H, s, H-6)

ethoxycarbonyl group conjugated with the double bond, while the band at 1644-1668 cm^{-1} should be assigned to the chelated ethoxycarbonyl group. The band at 1600-1605 cm^{-1} corresponds to stretching vibrations of the enamine double bond conjugated with the aromatic system. The UV spectra also indicate an identical structure for **12-22**. The mass spectral decomposition of enamines **12-22** follows a single pathway: $[M-73]^+$ (Φ_1) results from the elimination of CO_2Et, $[M-74]^{+\cdot}$ (Φ_2) results from the elimination of a hydrogen atom from Φ_1 or HCO_2Et from the molecular ion, $[M-119]^+$ results from the elimination of OEt from Φ_2, and $[M-147]^+$ (Φ_4) results from the elimination of CO from Φ_3, which confirms the existence of two ethoxycarbonyl groups in these compounds. Ion Φ_5 is probably formed due to cyclization of the enamine under the mass spectral conditions.

We then studied the behavior of these derivatives of the diethyl ester of 5-aminoindolylfumarate **12-22** under thermal conditions. Heating **12** for 20 min in diphenyl at 280°C gave a compound, which was assigned structure **23** on the basis of its spectral data. The ^1H NMR spectrum of **23** (Table 1) shows signals for the ethoxycarbonyl group protons, singlets for the 1-Me, 2-Me, and 5-Me groups, and for H-3, H-4, H-6, and H-8. Similarly, thermolysis of **13-16** gave ethoxycarbonylpyrroloquinolines **24-28**. We should note that **28** is formed only after more prolonged heating (30 min) and with lower yield due to tar formation. In the case of this enamine, obviously the 6-methoxy group has a deactivating effect on the cyclization reaction. This effect was previously noted in the reactions of 5-amino-6-methoxyindoles with other dicarbonyl compounds [3].

The possibility of forming pyrroloquinolines both with angular and linear ring fusion depending on the presence of a methyl substituent at $C_{(3)}$ of the pyrrole ring is not excluded in the cyclization of enamines **17-22**

TABLE 2. Spectral Data for **12-33**

Compound	IR spectrum, cm^{-1}	UV spectrum		Mass spectrum, *m/z* ($I_{отн}$, %)
		λ_{max}, nm	log ε	
1	2	3	4	5
12	1605, 1661, 1713	205 235 305 340 sh.	4.38 4.36 4.27 4.07	344 $[M]^+$ (85), 298 (15), 272 (15), 271 (73), 270 (31), 242 (10), 225 (62), 224 (50), 198 (38), 197 (100), 196 (25), 195 (26), 182 (25), 158 (30), 115 (18)
13	1605, 1664, 1734	205 235 300 330 sh.	4.30 4.29 4.19 4.07	358 $[M]^+$ (50), 312 (11), 285 (50), 284 (22), 239 (60), 238 (46), 212 (44), 211 (100), 210 (25), 196 (35), 195 (40), 172 (50), 156 (30), 128 (30), 115 (30)
14	1603, 1668, 1718	210 230 327	4.39 4.27 4.46	392 $[M]^+$ (70), 346 (15), 320 (15), 319 (63), 318 (25), 290 (10), 273 (60), 272 (40), 246 (39), 245 (100), 244 (30), 206 (29)
15	1603, 1666, 1732	205 225 310	4.47 4.46 4.49	406 $[M]^+$ (100), 360 (13), 333 (95), 332 (25), 288 (20), 287 (74), 286 (42), 260 (40), 259 (100), 244 (24), 220 (45), 144 (47)
16	1605, 1654, 1713	210 235 305 340 sh.	4.19 4.18 3.92 3.94	360 $[M]^+$ (100), 314 (24), 287 (39), 286 (83), 271 (25), 258 (14), 241 (86), 226 (30), 224 (30), 214 (37), 199 (60) 160 (24), 143 (43), 130 (50), 113 (40), 77 (40)
17	1605, 1667, 1717	202 290 330	4.47 4.13 4.12	316 $[M]^+$ (24), 270 (5), 243 (14), 242 (28), 197 (100), 170 (50), 169 (60), 145 (17), 131 (32), 130 (53), 103 (35), 77 (28)
18	1597, 1655, 1744	215 295 330	4.29 4.11 4.10	330 $[M]^+$ (58), 284 (5), 257 (25), 256 (53), 228 (20), 212 (25), 211 (100), 200 (20), 182 (45), 183 (63), 144 (40), 115 (40), 105 (15), 91 (15), 77 (15)
19	1601, 1644, 1725	210 235 327	4.39 4.33 4.47	378 $[M]^+$ (95), 332 (10), 305 (50), 304 (56), 276 (21), 260 (26), 259 (100), 258 (22), 248 (18), 232 (57), 231 (57), 192 (38), 165 (30), 129 (15)
20	1607, 1661, 1732	205 230 310	4.42 4.45 4.44	392 $[M]^+$ (86), 346 (5), 319 (50), 318 (49), 290 (20), 274 (32), 273 (100), 262 (20), 246 (52), 245 (62), 206 (45), 204 (40), 136 (50), 77 (15)
21	1605, 1663, 1713	205 235 295 340 sh.	4.31 4.30 4.15 4.09	330 $[M]^+$ (100), 284 (10), 257 (42), 256 (60), 228 (20), 211 (85), 210 (20), 200 (20), 144 (30), 143 (29), 115 (20)
22	1601, 1655, 1745	205 240 305 340 sh.	4.30 4.27 4.15 4.06	344 $[M]^+$ (34), 298 (5), 271 (25), 270 (48), 255 (10), 242 (18), 226 (25), 225 (100), 224 (20), 214 (25), 158 (70), 115 (55), 91 (30), 77 (25)
23	1552, 1587, 1628, 1726	225 270 325 375	4.35 4.11 4.07 3.71	298 $[M]^+$ (70), 225 (25), 224 (100), 223 (35), 209 (14), 194 (22), 195 (25)
24	1526, 1610, 1624, 1718	230 275 325 370	4.58 4.29 4.25 4.01	312 $[M]^+$ (70), 268 (25), 239 (48), 238 (100), 223 (32), 209 (15)
25	1544, 1610, 1621, 1718	205 230 275 335	4.38 4.29 4.17 4.31	346 $[M]^+$ (70), 273 (30), 272 (100), 271 (31), 245 (31), 244 (82), 243 (45), 242 (30), 154 (40)
26	1583, 1620, 1722	225 275 325 360	4.52 4.36 4.40 4.13	360 $[M]^+$ (100), 287 (25), 286 (96), 258 (30)
27	1592, 1627, 1729	215 260 335 380 sh.	4.36 4.14 4.06 3.67	314 [M]+ (90), 299 (76), 239 (25), 225 (30), 64 (95), 48 (100)

TABLE 2 (continued)

1	2	3	4	5
28	1616, 1639, 1716	220 270 315 360	4.45 4.26 4.20 3.89	270 $[M]^+$ (35), 197 (20), 196 (100), 169 (15), 168 (30), 142 (40), 141 (45), 115 (10), 44(20)
29	1608, 1707, 1726	225 270 315 355	4.39 4.17 4.08 3.88	284 $[M]^+$ (58), 211 (20), 210 (100), 182 (15), 181 (20), 156 (20), 155 (22)
30	1542, 1615, 1718	210 240 275 330	4.30 4.26 4.12 4.28	332 $[M]^+$ (60), 259 (20), 258 (100), 230 (20), 229 (25), 205 (20), 204 (20)
31	1520, 1606, 1728	225 275 320 360 sh.	4.33 4.14 4.17 3.92	346 $[M]^+$ (100), 273 (20), 272 (80), 243 (20), 217 (20)
32	1589, 1614, 1715	228 270 320 370	4.12 3.91 3.83 3.63	284 $[M]^+$ (85), 256 (5), 211 (24), 210 (100), 194 (17), 193 (20), 181 (15), 156 (22)
33	1567, 1617, 1706	230 275 320 365	4.36 4.13 4.09 3.87	298 $[M]^+$ (100), 283 (13), 225 (25), 224 (85), 223 (39), 209 (33), 207 (30), 170 (15)

with two free *ortho* positions ($C_{(4)}$ and $C_{(6)}$) in the indole benzene ring. However, the ^1H NMR spectra of all products **29-33** show two doublets for H-4 and H-5 characteristic for a benzene ring AB system, which confirms their angular structure. Furthermore, the same UV spectral behavior is found for **24-28** and **29-33**, namely, three maxima at ~240, ~270, and ~330 nm. The short-wavelength maximum for all the pyrroloquinolines is stronger than the band at ~270 nm, which is characteristic for this type of angular pyrroloquinolines [4].

The strongest peak in the mass spectra of all the pyrroloquinoline products **23-33** is $[M-74]^{+\cdot}$ (100%), which is formed either due to elimination of the ethoxycarbonyl group and then hydrogen or of ethyl formate. The presence of the OMe group has an effect on the direction of the mass spectral decomposition for only pyrroloquinoline **27**.

The IR spectra of cyclization products **23-33** differ somewhat from the spectra of the starting compounds, **12-22**. While the band for the free ethoxycarbonyl group in the pyrroloquinolines remains virtually unchanged (1705-1728 cm^{-1}), the following bands are shifted by about 30 cm^{-1} toward shorter wavelengths relative to the enamines. Stretching bands for the γ-quinoline carbonyl group appear at 1614-1627 cm^{-1}, while bands for the aromatic double bonds in the pyridine and benzene parts of the pyrroloquinoline molecule are seen at 1566-1592 cm^{-1}.

Thus, a series of new compounds was obtained in the reactions of substituted 5-aminoindoles with diethyl oxaloacetate. These compounds, namely, derivatives of the diethyl ester of 5-aminoindolylfumarate, hold pharmacological interest. These compounds undergo thermal cyclization at $C_{(4)}$ of the indole molecule, regardless of the presence of two alternative *ortho* positions for cyclization and absence of a substituent at $C_{(3)}$. These reactions were used to develop a synthesis for 7-ethoxycarbonyl-6,9-dihydro-3H-pyrrolo[3,2-*f*]quinolin-9-ones, which are previously unreported analogs of vitamin PQQ.

TABLE 3. Physicochemical Characteristics for **12-33**

Compound	Empirical formula	Found, % / Calculated, %			R_f*	mp, C**	Yield, %
		C, %	H, %	M			
12	$C_{19}H_{24}N_2O_4$	66.17 / 66.26	7.09 / 7.02	344 / 344	0.61	147	62
13	$C_{20}H_{26}N_2O_4$	66.90 / 67.02	7.42 / 7.31	358 / 358	0.60	112	16
14	$C_{23}H_{24}N_2O_4$	70.23 / 70.39	6.23 / 6.16	392 / 392	0.55	144	23
15	$C_{24}H_{26}N_2O_4$	70.84 / 70.92	6.42 / 6.40	406 / 406	0.75	95	20
16	$C_{19}H_{24}N_2O_5$	63.23 / 63.32	6.78 / 6.71	360 / 360	0.42	154	27
17	$C_{17}H_{20}N_2O_4$	64.42 / 64.54	6.43 / 6.37	316 / 316	0.56	72	19
18	$C_{18}H_{22}N_2O_4$	65.29 / 65.44	6.76 / 6.71	330 / 330	0.60	78	55
19	$C_{22}H_{22}N_2O_4$	69.75 / 69.83	5.84 / 5.86	378 / 378	0.58	143.5	40
20	$C_{23}H_{24}N_2O_4$	70.30 / 70.39	6.20 / 6.16	392 / 392	0.63	76	21
21	$C_{18}H_{22}N_2O_4$	65.36 / 65.44	6.80 / 6.71	330 / 330	0.68	70	34
22	$C_{19}H_{24}N_2O_4$	66.14 / 66.26	7.09 / 7.02	344 / 344	0.45	87	40
23	$C_{17}H_{18}N_2O_3$	68.09 / 68.44	6.42 / 6.08	298 / 298	0.45	245	81
24	$C_{18}H_{20}N_2O_3$	68.70 / 69.21	6.93 / 6.45	312 / 312	0.62	172	66
25	$C_{21}H_{18}N_2O_3$	72.56 / 72.82	5.48 / 5.24	346 / 346	0.63	258	57
26	$C_{22}H_{20}N_2O_3$	73.14 / 73.32	5.71 / 5.59	360 / 360	0.43	121	40
27	$C_{17}H_{18}N_2O_4$	64.48 / 64.96	6.28 / 5.77	314 / 314	0.54	260	69
28	$C_{15}H_{14}N_2O_3$	66.35 / 66.66	5.41 / 5.22	270 / 270	0.60	282	23
29	$C_{16}H_{16}N_2O_3$	67.13 / 67.59	5.95 / 5.67	284 / 284	0.53	232	41
30	$C_{20}H_{16}N_2O_3$	72.03 / 72.28	5.09 / 4.85	332 / 332	0.37	257.5	76
31	$C_{21}H_{18}N_2O_3$	72.45 / 72.82	5.51 / 5.24	346 / 346	0.52	176	95
32	$C_{16}H_{16}N_2O_3$	67.41 / 67.59	5.79 / 5.67	284 / 284	0.54	290	84
33	$C_{17}H_{18}N_2O_3$	67.95 / 68.44	6.48 / 6.08	298 / 298	0.43	219	54

* Eluent systems: benzene (**12-15, 19, 20, 22**), 5:1 benzene–ethyl acetate (**16, 21**), 3:1 benzene–ethyl acetate (**17, 18**), ethyl acetate (**23, 23, 30, 31**), ethyl acetate with traces of methanol (**25, 27, 29, 32, 33**), 1:1 benzene–ethyl acetate (**26**), 10:1 ethyl acetate–methanol (**28**).

*[2] Solvents: benzene–petroleum ether (**12, 14-16, 19, 21**), petroleum ether (**13, 17, 18, 20, 22**), benzene–ethyl acetate (**23**), and ethanol (**24-33**).

EXPERIMENTAL

The ^{1}H NMR spectra were taken on a Bruker DRX-500 spectrometer at 500 MHz in DMSO-d_6 relative to TMS. The IR spectra were taken on a Unititled Spektrum instrument for KBr pellets. The mass spectra were taken on a Finnigan MAT Incos-50 mass spectrometer with direct sample inlet into the ion source at 70 eV.

The UV spectra were taken on a Specord spectrophotometer for ethanol solutions. The reaction products were purified by chromatography on a neutral alumina column (grade-I and grade-II Brockmann activity). The reaction course, purity of the products, and determination of the R_f values were carried out by thin-layer chromatography on Silufol UV-254 plates. The yields, physical constants, and elemental analysis data of the products are given in Table 3.

Diethyl (5-Amino-2,3,6-trimethyl-1H-indolyl)fumarate (12). A mixture of 5-amino-2,3,6-trimethylindole (**1**) (0.4 g, 2.30 mmol) and diethyl oxaloacetate (0.8 g, 4.26 mmol) in absolute benzene (400 ml) was heated at reflux for 25 h in the presence of catalytic amounts of glacial acetic acid using a Dean–Stark trap. After all the aminoindole had reacted as indicated by thin-layer chromatography, benzene was distilled off. The enamine was dissolved in 3:1 benzene–petroleum ether heated to reflux and passed through an alumina column. The solvent was distilled off to give **12**. Yield 0.49 g.

Diethyl (5-Amino-1,2,3,6-tetramethyl-1H-indolyl)fumarate (13) was prepared analogously from 5-amino-1,2,3,6-tetramethylindole (**2**) (0.8 g, 4.26 mmol) and diethyl oxaloacetate (0.8 g, 4.26 mmol). The mixture was heated at reflux in benzene for 64 h. Yield 0.25 g.

Diethyl (5-Amino-2-phenyl-1H-indolyl)fumarate (14) was prepared analogously from 5-amino-2-phenylindole (**3**) (0.5 g, 2.25 mmol) and diethyl oxaloacetate (1 g, 5.32 mmol). The mixture was heated in benzene at reflux for 33 h. Yield 0.20 g.

Diethyl (5-Amino-1,6-dimethyl-2-phenyl-1H-indolyl)fumarate (15) was prepared analogously from 5-amino-1,6-dimethyl-2-phenylindole (**4**) (0.6 g, 2.54 mmol) and diethyl oxaloacetate (0.8 g, 4.26 mmol). The mixture was heated in benzene at reflux for 40 h. Yield 0.21 g.

Diethyl (5-Amino-6-methoxy-2,3-dimethyl-1H-indolyl)fumarate (16) was prepared analogously from 5-amino-2,3-dimethyl-6-methoxyindole (**5**) (0.5 g, 2.63 mmol) and diethyl oxaloacetate (0.9 g, 4.79 mmol). The mixture was heated in benzene at reflux for 29 h. Yield 0.25 g.

Diethyl (5-Amino-2-methyl-1H-indolyl)fumarate (17) was prepared analogously from 5-amino-2-methylindole (**6**) (0.5 g, 3.425 mmol) and diethyl oxaloacetate (0.66 g, 3.51 mmol). The mixture was heated in benzene at reflux for 50 h. The product separated as a precipitate from hexane upon the addition of diethyl ether. Yield 0.21 g.

Diethyl (5-Amino-1,2-dimethyl-1H-indolyl)fumarate (18) was prepared analogously from 5-amino-1,2-dimethylindole (**7**) (0.45 g, 3.425 mmol) and diethyl oxaloacetate (0.55 g, 2.29 mmol). The mixture was heated in benzene at reflux for 53 h. The product separated as a precipitate from hexane upon the addition of diethyl ether. Yield 0.506 g.

Diethyl (5-Amino-2-phenyl-1H-indolyl)fumarate (19) was prepared analogously from 5-amino-2-phenylindole (**8**) (0.5 g, 2.40 mmol) and diethyl oxaloacetate (0.5 g, 2.66 mmol). The mixture was heated in benzene at reflux for 27 h. Yield 0.36 g.

Diethyl (5-Amino-1-methyl-2-phenyl-1H-indolyl)fumarate (20) was prepared analogously from 5-amino-1-methyl-2-phenylindole (**9**) (0.6 g, 2.70 mmol) and diethyl oxaloacetate (1 g, 5.32 mmol). The mixture was heated in benzene at reflux for 61 h. Yield 0.226 g.

Diethyl (5-Amino-2,3-dimethyl-1H-indolyl)fumarate (21) was prepared analogously from 5-amino-2,3-dimethylindole (**10**) (0.5 g, 3.125 mmol) and diethyl oxaloacetate (1 g, 5.32 mmol). The mixture was heated in benzene at reflux for 30 h. Yield 0.35 g.

Diethyl (5-Amino-1,2,3-trimethyl-1H-indolyl)fumarate (22) was prepared analogously from 5-amino-1,2,3-trimethylindole (**11**) (0.45 g, 2.59 mmol) and diethyl oxaloacetate (0.5 g, 2.66 mmol). The mixture was heated in benzene at reflux for 55 h. Yield 0.36 g.

7-Ethoxycarbonyl-1,2,5-trimethyl-6,9-dihydro-3H-pyrrolo[3,2-*f*]quinolin-9-one (23). Enamine **12** (0.3 g, 0.87 mmol) was added to diphenyl (5 ml) and heated at reflux for 15 min. The still hot reaction mixture was poured into petroleum ether. The precipitate formed was filtered off and washed repeatedly with petroleum ether. The product was recrystallized from 1:1 benzene–ethyl acetate. Yield 0.21 g.

7-Ethoxycarbonyl-1,2,3,5-tetramethyl-6,9-dihydro-3H-pyrrolo[3,2-*f*]quinolin-9-one (24) was prepared analogously from enamine **13** (0.14 g, 0.39 mmol). The product was recrystallized from ethanol. Yield 0.08 g.

7-Ethoxycarbonyl-5-methyl-2-phenyl-6,9-dihydro-3H-pyrrolo[3,2-*f*]quinolin-9-one (25) was prepared analogously from enamine **14** (0.06 g, 0.15 mmol). Yield 0.03 g.

7-Ethoxycarbonyl-3,5-dimethyl-2-phenyl-6,9-dihydro-3H-pyrrolo[3,2-*f*]quinolin-9-one (26) was prepared analogously from enamine **15** (0.1 g, 0.25 mmol). Yield 0.036 g.

7-Ethoxycarbonyl-5-methoxy-1,2-dimethyl-6,9-dihydro-3H-pyrrolo[3,2-*f*]quinolin-9-one (27) was prepared analogously from enamine **16** (0.15 g, 0.42 mmol) by heating in diphenyl at reflux for 30 min. Yield 0.09 g.

7-Ethoxycarbonyl-2-methyl-6,9-dihydro-3H-pyrrolo[3,2-*f*]quinolin-9-one (28) was prepared analogously from enamine **17** (0.2 g, 0.63 mmol). Yield 0.04 g.

7-Ethoxycarbonyl-2,3-dimethyl-6,9-dihydro-3H-pyrrolo[3,2-*f*]quinolin-9-one (29) was prepared analogously from enamine **18** (0.4 g, 1.21 mmol). Yield 0.14 g.

7-Ethoxycarbonyl-2-phenyl-6,9-dihydro-3H-pyrrolo[3,2-*f*]quinolin-9-one (30) was prepared analogously from enamine **19** (0.21 g, 0.55 mmol). Yield 0.14 g.

7-Ethoxycarbonyl-3-methyl-2-phenyl-6,9-dihydro-3H-pyrrolo[3,2-*f*]quinolin-9-one (31) was prepared analogously from enamine **20** (0.19 g, 0.48 mmol). Yield 0.16 g.

7-Ethoxycarbonyl-1,2-dimethyl-6,9-dihydro-3H-pyrrolo[3,2-*f*]quinolin-9-one (32) was prepared analogously from enamine **21** (0.29 g, 0.88 mmol). Yield 0.21 g.

7-Ethoxycarbonyl-1,2,3-trimethyl-6,9-dihydro-3H-pyrrolo[3,2-*f*]quinolin-9-one (33) was prepared analogously from enamine **22** (0.26 g, 0.76 mmol). Yield 0.122 g.

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