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SYNTHESIS OF FUNCTIONALLY SUBSTITUTED PYRROLO[3,2-*h*]QUINOLINES FROM 2,3-DIMETHYL- AND 1,2,3-TRIMETHYL-7-AMINOINDOLES

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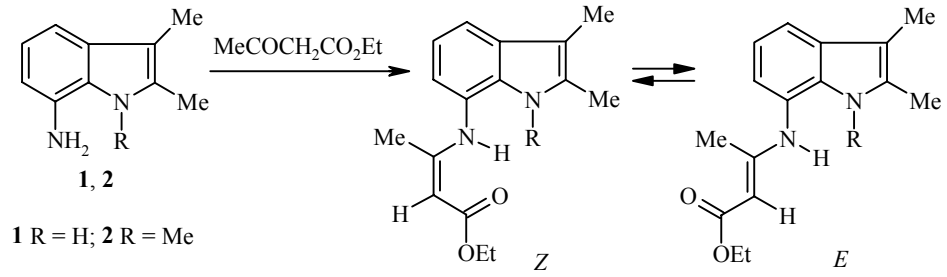
Methods have been developed for the preparation of several functionally substituted pyrrolo[3,2-h]-quinolines via the reaction of 2,3-dimethyl- and 1,2,3-trimethyl-7-aminoindoles with acetoacetic, trifluoroacetoacetic, and ethoxymethylenemalonic esters.

Keywords: 7-amino-2,3-dimethylindole, 7-amino-1,2,3-trimethylindole, acetoacetic ester, trifluoroacetoacetic ester, ethoxymethylenemalonic ester, functionally substituted pyrrolo[3,2-*h*]-quinolines.

It has previously been reported that the enaminoketones obtained from 7-aminoindoles and β-diketones readily undergo conversion to the corresponding pyrrolo[3,2-*h*]quinolines under conditions of acid cyclization [1, 2]. Moreover, the alternative ring closure to the pyrrole fragment to form 1,7-diazepinoindole tricyclic structures with a node nitrogen atom was not observed. In a continuation of our work in this field we have studied the behavior of 7-amino-2,3-dimethyl- (**1**) and 7-amino-1,2,3-trimethylindoles (**2**) in their reactions with acetoacetic, trifluoroacetoacetic, and ethoxymethylenemalonic esters with the aim of synthesizing functionally substituted pyrrolo[3,2-*h*]quinolines as potentially biologically active compounds.

Refluxing of the amines **1** and **2** with acetoacetic ester in absolute benzene in the presence of a catalytic amount of glacial acetic acid led to the formation of a mixture of the *Z*- and *E*-isomers of the corresponding indolylaminocrotonates **3** and **4**.



According to ^{1}H NMR spectroscopic data the ratio of the *Z*- to *E*-forms of the aminocrotonates **3** and **4** in DMSO-d_6 solution is 1.5:1. In the spectra of the *Z*-isomers the protons of the ethoxy group, the vinyl proton, the N–H group proton, and the methyl group in the enamine fragment are shifted to low field by 0.2, 0.3, 2.0,

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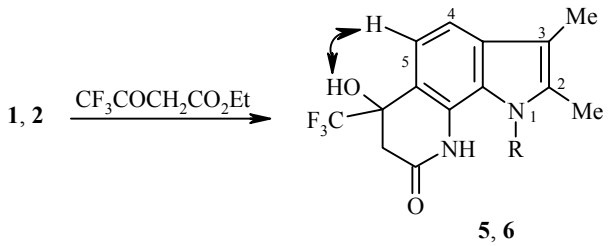
and 0.4 ppm respectively when compared with those for the analogous proton signals in the *E*-isomers (Table 1). The difference in position in space of the enamino carbonyl chain has an effect on the chemical shift of the protons of the benzene ring. Hence the signals for the 5-H protons in the mixture of isomers appear as two triplets and the 4- and 6-H protons are also non equivalent for the isomeric pair and give two doublets in the aromatic part of the spectrum.

In a less polar solvent ($CDCl_3$) compound **4** exists solely in the *Z*-form. Due to the low solubility in deuterochloroform the behavior of the enamine **3** was not studied.

The mass spectra of the enamines **3, 4** showed a strong peak for the $[M-46]^+$ ion which corresponds to a loss of C_2H_5OH with cyclization to a pyrroloquinolone structure. The subsequent fragmentation of the $[M-46]^+$ is typical for dissociation of pyrroloquinolones. The spectroscopic data for the indolyl-7-aminocrotonates **3** and **4** (also including their UV spectra) agree with those of other enamino carbonyl compounds of the indole series [3] and complements them.

In contrast to acetoacetic, the trifluoroacetoacetic ester reacts with the aminoindoles **1** and **2** under the same conditions with the participation of the carbethoxy group.

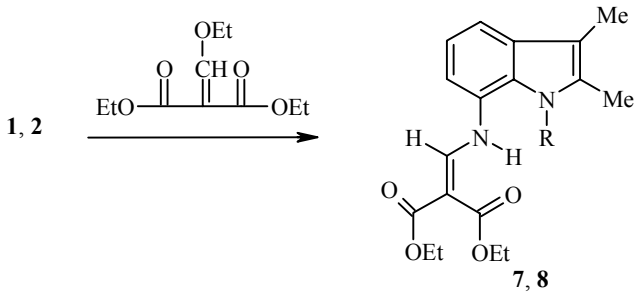


5, **6**

5 R = H, **6** R = Me

Hence in the case of the amine **1** there was separated a compound which could be assigned the structure **5** on the basis of the spectroscopic data. The IR spectrum of this compound showed two stretching bands for the amide carbonyl group at 1682 and 1666 cm^{-1} which can be related to the two conformers with different positioning of the trifluoromethyl and hydroxyl groups. The ^1H NMR spectrum showed signals for protons of methylene, hydroxyl, and for two NH groups. The formation of a cyclic structure is supported by the presence in the spectrum of an AB system for the benzene 4- and 5-H protons (two doublets with $J = 8$ Hz). The conclusive evidence for the proposed structure of compound **5** followed from a 2D ^1H–^1H NMR experiment (NOESY). In fact, the 2D spectrum shows a cross peak due to the approach through space of the 5-H and OH protons. The mass spectrum is characterized by a molecular ion peak as well as the presence of the $[M-18]^+$ and $[M-69]^+$ fragment ions, the latter of which is more intense. Formation of the $[M-18]^+$ ion evidently suggests that the molecule is aromatized *via* the loss of a molecule of water and the formation of a pyrroloquinolone structure. The $[M-69]^+$ peak corresponds to loss of a CF_3 radical which is typical of such compounds. Compound **5** evidently precedes formation of a noncyclic amide which, because of the high reactivity of the trifluorocarbonyl group, is readily electrophilically cyclized at position 6 of the indole. The reaction temperature (~78°C) and the traces of acetic acid are likely insufficient for aromatization through loss of water. According to the TLC and ^1H NMR spectroscopic data the reaction of the aminoindole **2** with the trifluoroacetoacetic ester gives in the reaction product a mixture of the cyclic and non cyclic amides **6**. These compounds could not be separated in the free state.

For the ethoxymethylenemalonic ester the heating of the aminoindoles **1** and **2** in alcohol gives the corresponding indolylaminomethylenemalonic esters **7** and **8**.

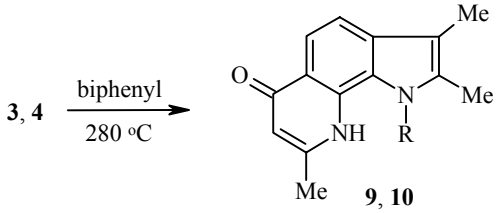


7 R = H, **8** R = Me

The ^{1}H NMR spectra of the enamines **7, 8** showed signals for non-equivalent carbethoxy groups but one of these interacts with the N–H group proton so that the methylene group hydrogen signals are shifted to low field by 0.11 and the methyl by 0.07 ppm.

In all of the reported reactions the amine **1** is more reactive than amine **2**, the reaction with compound **2** requiring a longer reaction than for compound **1**. Evidently, the N–CH_3 group in the aminoindole **2** sterically hinders the approach of the reagent to the 7-amino group. This fact has been reported before in the reactions of amines with β-diketones [1].

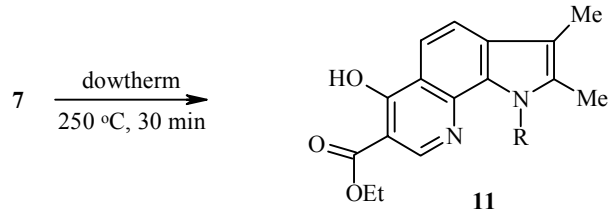
Under high temperature cyclization conditions (refluxing in biphenyl) the enaminocrotonates **3** and **4** are converted to the corresponding pyrrolo[3,2-*h*]quinolones **9, 10**.



9 R = H, **10** R = Me

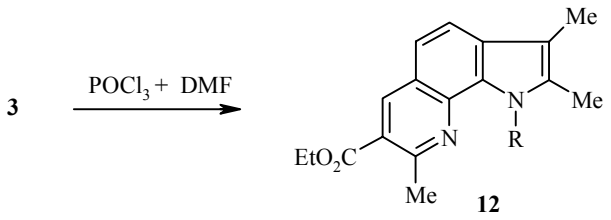
Formation of a possible 1,7-diazepinoindole structure does not occur, even in the case of compound **3**, i.e. the alternative closure of the ring to the pyrrole nitrogen under thermal conditions is not achieved. The ^{1}H NMR spectra of the pyrrolo[3,2-*h*]quinolones **9, 10** show signals for the protons of three methyl groups and for compound **10** a further signal for the N–CH_3 group protons, a 7-H proton singlet, doublet signals for the benzene ring protons with J = 8 Hz, and a 9-H proton singlet as well as a low field proton signal for the 1-H proton in the pyrroloquinolone **9**. In the mass spectra of the pyrroloquinolones **9, 10** the strongest peak is that for the $[M-1]^+$ ion and there are also peaks for the fragment ions $[M-15]^+$ and $[M-H-28]^+$ which are typical of the mass spectroscopic decomposition of similar γ-quinolone structure. The UV spectra of compounds **9** and **10** are virtually identical and show three absorption maxima, which also agrees with literature data for these types of pyrroloquinolones.

Heteroaromatization of enaminomethylenemalonates usually occurs upon heating in dowtherm (250°C), i.e. under milder conditions than the enaminocrotonates. In fact, under these conditions, enamine **7** is converted in good yield to the corresponding pyrroloquinoline **11** in 30 min.



The ^{1}H NMR spectrum of compound **11** shows singlet signals for the methyl group protons, signals for the ethoxy group protons, two doublets for 4- and 5-H with J = 8 Hz, and singlets for the 8-H and 1-H protons. The mass spectrum of compound **11** shows an ion peak for $[M-46]^+$ (elimination of a molecule of ethanol) which is the strongest and this is characteristic of aromatic structures having *ortho*-placed hydroxyl and carbethoxy groups.

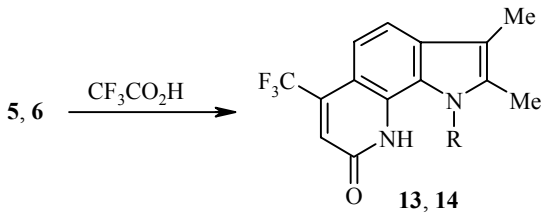
It was unexpectedly found that the N-methylated analog of compound **7** (the enaminoindole **8**) is not converted to the corresponding pyrroloquinoline either in dowtherm or upon prolonged heating in biphenyl. It was found only in trace amounts in the oily reaction product by chromatography. Similarly it was not possible to obtain the cyclization product from the N-methyl aminocrotonate **4** under Vilsmeier reaction conditions even though compound **3** gives the corresponding pyrroloquinoline **12**.



12

The ^{1}H NMR spectrum of the pyrroloquinoline **12** contains three singlets for the methyl group protons, signals for the ethoxy group protons, two doublets with J = 8 Hz for the 4- and 5-H aromatic protons, and singlet signals for the 6- and 1-H protons. The most intense peak in the mass spectrum of the pyrrolo[3,2-h]quinoline **12** is the molecular ion and this indicates the stability of the molecule towards electron impact. The $[M-73]^+$ ion is due to fission of the C_2H_5OCO radical and confirms the presence of the carbethoxy group in the molecule. The UV spectrum of compound **12** contains three absorption maxima and is typical for pyrroloquinolines.

Hence in the case of the N-methylation at the pyrrole nitrogen of the enaminocarbonyl compounds the formation of the pyrrolo[3,2-*h*]quinoline system is hindered. This is in contrast to a pyrroloquinolone. Evidently the pyridone ring contrasts with a pyridine and is able partially to move out of the plane of the tricyclic system. This is also confirmed by the ready formation of the corresponding cyclic trifluoroacetoacetic acid amides **5** and **6** prepared from both the 2,3-dimethyl- and the 7-amino-1,2,3-trimethylindoles which are then aromatized to the trifluoromethylpyrrolo[3,2-*h*]quinolones **13** and **14** when heated above 100°C in the presence of trifluoroacetic acid.



13, **14**

13 R = H, **14** R = Me

The ^{1}H NMR spectra of the trifluoromethylpyrroloquinolones obtained have two singlets (compound **13**) or three singlets (compound **14**) for the methyl groups, a singlet signal for the 7-H proton, two doublets for the 4- and 5-H protons with J = 8 Hz, and singlets for the 9- and 1-H protons (compound **13**). The most intense peaks in the mass spectra are the molecular ions, $[M-H]^+$, $[M-Me]^+$, and $[M-CO]^+$ which are typical of all α- and γ-pyrroloquinolone structures. The UV spectra of compounds **13** and **14** are virtually identical and are characterized by three absorption bands.

TABLE 1. Spectroscopic Characteristics of Compounds **3-15**

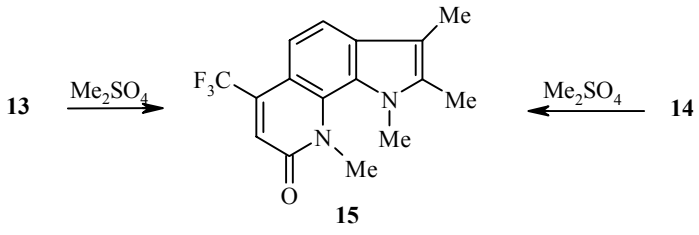
Compound	^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz)	Mass spectrum, *m/z* (I_{rel}, %)	UV spectrum	
			λ_{max}	log ε
1	2	3	4	5
3-*E*	1.04 (3H, t, *J* = 7, $OCH_2\underline{CH_3}$); 2.16 (3H, s, 3-CH_3); 2.18 (3H, s, C=C–CH_3); 2.42 (3H, s, 2-CH_3); 3.85 (2H, q, *J* = 7, $O\underline{CH_2}CH_3$); 4.38 (1H, s, H vin.); 6.78 (1H, d, *J* = 8, 4-H); 6.94 (1H, t, *J* = 8, 5-H); 7.25 (1H, d, *J* = 8, 6-H); 8.18 (1H, s, N–H amin.); 10.35 (1H, s, N–H ind.)	272 (M^+) (100) 238 (20) 226 (80) 211 (10) 198 (65) 183 (35)	231 286 298	4.18 4.36 4.34
3-*Z*	1.22 (3H, t, *J* = 7, $OCH_2\underline{CH_3}$); 1.79 (3H, s, C=C–CH_3); 2.16 (3H, s, 3-CH_3); 2.31 (3H, s, 2-CH_3); 4.07 (2H, q, *J* = 7, $O\underline{CH_2}CH_3$); 4.72 (1H, s, H vin.); 6.78 (1H, d, *J* = 8, 4-H); 6.93 (1H, t, *J* = 8, 5-H); 7.26 (1H, d, *J* = 8, 6-H); 10.02 (1H, s, N–H amin.); 10.62 (3H, s, N–H ind.)	144 (15)		
4-*E*	1.03 (3H, t, *J* = 7, $OCH_2\underline{CH_3}$); 2.18 (3H, s, 3-CH_3); 2.28 (3H, s, C=CCH_3); 2.40 (3H, s, 2-CH_3); 3.69 (3H, s, N–CH_3); 3.83 (2H, q, *J* = 7, $O\underline{CH_2}CH_3$); 4.35 (1H, s, H vin); 6.82 (1H, d, *J* = 8, 4-H); 6.98 (1H, t, *J* = 8, 5-H); 7.35 (1H, d, *J* = 8, 6-H); 8.51 (1H, s, N–H amin.)	286 (M^+) (87) 240 (75) 225 (70) 212 (100) 197 (60) 184 (36)	235 286 299	3.99 4.20 4.34
4-*Z*	1.20 (3H, t, *J* = 7, $OCH_2\underline{CH_3}$); 1.62 (3H, s, C=C–CH_3); 2.18 (3H, s, 3-CH_3); 2.28 (3H, s, 2-CH_3); 3.69 (3H, s, N–CH_3); 4.06 (2H, q, *J* = 7, $O\underline{CH_2}CH_3$); 4.71 (1H, s, H vin.); 6.74 (1H, d, *J* = 8, 4-H); 6.96 (1H, t, *J* = 8, 5-H); 7.35 (1H, d, *J* = 8, 6-H); 10.4 (1H, s, N–H amin.)	158 (26) 115 (25) 92 (20)		
4-*Z**	1.31 (3H, t, *J* = 7, $OCH_2\underline{CH_3}$); 1.78 (3H, s, C=C–CH_3); 2.25 (3H, s, 3-CH_3); 2.34 (3H, s, 2-CH_3); 3.75 (3H, s, N–CH_3); 4.18 (2H, q, *J* = 7, $O\underline{CH_2}CH_3$); 4.75 (1H, s, H vin.); 6.85 (1H, d, *J* = 8, 4-H); 7.01 (1H, t, *J* = 8, 5-H); 7.40 (3H, d, *J* = 8, 6-H); 10.18 (1H, s, N–H amin.)			
5	2.16 (3H, s, 3-CH_3); 2.35 (3H, s, 2-CH_3); 2.90 (2H, s, CH_2); 6.32 (1H, s, O–H); 7.02 (1H, d, *J* = 8, 4-H); 7.20 (1H, d, *J* = 8, 5-H); 9.81 (1H, s, N–H amid.); 10.11 (1H, s, N–H ind.)	298 (M^+) (47) 280 (11) 229 (100) 187 (16)	213 240 308	4.32 4.47 3.86
7	1.23 (3H, t, *J* = 7, $OCH_2\underline{CH_3}$); 1.30 (3H, t, *J* = 7, $OCH_2\underline{CH_3}$); 2.16 (3H, s, 3-CH_3); 2.34 (3H, s, 2-CH_3); 4.14 (2H, q, *J* = 7, $O\underline{CH_2}CH_3$); 4.25 (2H, q, *J* = 7, $O\underline{CH_2}CH_3$); 6.91 (1H, d, *J* = 8, 4-H); 7.00 (1H, t, *J* = 8, 5-H); 7.26 (1H, d, *J* = 8, 6-H); 8.35 (1H, d, *J* = 15, H vin.); 10.36 (1H, d, *J* = 15, N–H amin.); 11.03 (1H, s, N–H ind.)	330 (M^+) (30) 284 (35) 238 (100) 210 (65) 182 (31) 169 (20) 143 (20) 115 (20)	249 286 339	3.88 4.06 4.24
8	1.23 (3H, t, *J* = 7, $OCH_2\underline{CH_3}$); 1.27 (3H, t, *J* = 7, $OCH_2\underline{CH_3}$); 2.18 (3H, s, 3-CH_3); 2.31 (3H, s, 2-CH_3); 3.83 (3H, s, N–CH_3); 4.10 (2H, dd, *J* = 7, $O\underline{CH_2}CH_3$); 4.21 (2H, q, *J* = 7, $O\underline{CH_2}CH_3$); 6.91 (1H, d, *J* = 8, 4-H); 7.00 (1H, t, *J* = 8, 5-H); 7.34 (1H, d, *J* = 8, 6-H); 8.21 (1H, d, *J* = 15, H vin.); 11.05 (1H, d, *J* = 15, N–H amin.)	344 (M^+) (30) 298 (100) 270 (10) 252 (15) 237 (15) 226 (20) 197 (42) 184 (50) 115 (30)	233 290 338	4.16 4.13 4.21
9	2.22 (3H, s, 3-CH_3); 2.40 (3H, s, 2-CH_3); 2.43 (3H, s, 8-CH_3); 5.85 (1H, s, 7-H); 7.25 (1H, d, *J* = 8, 4-H); 7.64 (1H, d, *J* = 8, 5-H); 10.68 (1H, s, 9-H); 10.74 (1H, s, 1-H)	226 (M^+) (82) 225 (100) 211 (12) 183 (10)	217 272 323	4.34 4.75 3.88
10	2.27 (3H, s, 3-CH_3); 2.38 (3H, s, 2-CH_3); 2.55 (3H, s, 8-CH_3); 4.42 (3H, s, 1-CH_3); 6.65 (1H, s, 7-H); 7.45 (1H, d, *J* = 8, 4-H); 7.64 (1H, d, 5-H); 10.74 (1H, s, 9-H)	240 (M^+) (59) 239 (100) 225 (30) 211 (10) 195 (10)	230 274 345	3.89 4.80 4.24

TABLE 1 (continued)

1	2	3	4	5
11	1.34 (3H, br. s, $OCH_2\underline{CH_3}$); 2.23 (3H, s, 3-CH_3); 2.43 (3H, s, 2-CH_3); 4.30 (2H, br. s, $O\underline{CH_2}CH_3$); 7.43 (1H, d, *J* = 8, 4-H); 7.77 (1H, d, *J* = 8, 5-H); 8.64 (1H, s, 8-H); 11.07 (1H, br. s, 1-H)	284 (M^+) (34) 238 (100) 223 (11) 209 (10) 181 (10)	215 289 330	3.80 4.15 3.50
12	1.42 (3H, t, *J* = 7, $OCH_2\underline{CH_3}$); 2.28 (3H, s, 3-H); 2.43 (3H, s, 2-CH_3); 2.94 (3H, s, 8-CH_3); 4.38 (2H, q, *J* = 7, $O\underline{CH_2}CH_3$); 7.45 (1H, d, *J* = 8, 4-H); 7.63 (1H, d, *J* = 8, 5-H); 8.74 (1H, s, 6-H); 11.76 (1H, s, 1-H)	282 (M^+) (100) 281 (30) 254 (20) 253 (50) 237 (15) 209 (12)	238 254 294 382	4.08 4.20 4.54 4.18
13	2.20 (3H, s, 3-CH_3); 2.40 (3H, s, 2-CH_3); 6.74 (1H, s, 7-H); 7.28 (1H, d, *J* = 8, 4-H); 7.37 (1H, d, *J* = 8, 5-H); 11.00 (1H, s, 9-H); 11.94 (1H, s, 1-H)	280 (M^+) (100) 279 (96) 265 (34) 252 (10) 231 (12) 140 (13) 69 (10)	235 278 385	4.23 4.20 3.75
14	2.26 (3H, s, 3-CH_3); 2.39 (3H, s, 2-CH_3); 4.38 (3H, s, 1-CH_3); 7.08 (1H, s, 7-H); 7.44 (1H, d, *J* = 8, 4-H); 7.59 (1H, d, *J* = 8, 5-H); 11.40 (1H, s, 9-H)	294 (M^+) (100) 293 (90) 279 (50) 69 (10)	237 282 385	4.42 4.48 4.15
15	2.27 (3H, s, 3-CH_3); 2.40 (3H, s, 2-CH_3); 4.10 (3H, s, 9-CH_3); 4.35 (3H, s, 1-CH_3); 7.21 (1H, s, 7-H); 7.48 (1H, d, *J* = 8, 4-H); 7.66 (1H, d, *J* = 8, 5-H)	308 (M^+) (55) 307 (54) 293(40) 280 (100) 279 (100) 265 (35) 250 (10) 231 (10)	236 282 377	4.30 4.46 4.14

* Recorded in $CDCl_3$.

A confirmation of the advantage of structures of type **13, 14** is the fact that from these angular structures, although with greater difficulty than for those which are linear, it is possible to prepare the pyrrolo[3,2-*h*]quinolone **15** with *peri*-methyl groups on both nitrogen atoms. This is carried out by the methylation of compounds **13** or **14** with dimethyl sulfate.



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Formation of the pyrroloquinolone structure proves possible although it appears strained by the close positioning of the N–CH_3 group. This is confirmed by the ^{1}H NMR spectrum in which the signals of the 1- and 9-CH_3 group protons appear 0.5 to 0.6 ppm to low field of the position of the same group proton signals which do not have the *peri* positioning. The remaining ^{1}H NMR spectrum for compound **15** is little different to the spectra of compounds **13, 14**. Additional confirmation that compounds **13, 14** have undergone N- rather than O-methylation comes from the mass spectrum of the obtained pyrroloquinolone **15** which has a strong $[M-28]^+$ peak, as for all of the studied pyrroloquinolones. The UV spectra of compounds **13-15** are similar and this also confirms the similarity of their structures.

TABLE 2. Physicochemical Characteristics of the Compounds Prepared

Compound	Empirical formula	Found, % / Calculated, %			R_f (system)*	mp, °C (crystallization solvent)	Yield, %
		C	H	M^+			
3	$C_{16}H_{20}N_2O_2$	70.33 / 70.56	7.51 / 7.40	272 / 272	0.65 (A)	113 (benzene-petroleum ether)	86
4	$C_{17}H_{22}N_2O_2$	71.19 / 71.30	7.52 / 7.74	286 / 286	0.74 (B)	90-91 (hexane)	78
5	$C_{14}H_{13}F_3N_2O_2$	56.32 / 56.38	4.41 / 4.39	298 / 298	0.29 (C)	>300 (toluene)	79
7	$C_{18}H_{22}N_2O_4$	65.39 / 65.44	6.63 / 6.71	330 / 330	0.34 (B)	175-177 (alcohol)	80
8	$C_{19}H_{24}N_2O_4$	66.31 / 66.26	7.12 / 7.02	344 / 344	0.53 (B)	105-106 (aqueous alcohol)	63
9	$C_{14}H_{14}N_2O$	74.20 / 74.31	6.35 / 6.24	226 / 226	0.25 (D)	293-295 (DMF)	76
10	$C_{15}H_{16}N_2O$	74.15 / 74.97	6.45 / 6.71	240 / 240	0.63 (D)	244-245 (benzene)	75
11	$C_{16}H_{16}N_2O_3$	67.40 / 67.59	5.81 / 5.67	284 / 284	0.83 (D)	>300 (DMF)	85
12	$C_{17}H_{18}N_2O_2$	72.42 / 72.32	6.30 / 6.43	282 / 282	0.78 (C)	152-153 (aqueous alcohol)	38
13	$C_{14}H_{11}F_3N_2O$	59.73 / 60.00	4.12 / 3.96	280 / 280	0.26 (C) 0.76 (D)	>300 (DMF)	79
14	$C_{15}H_{13}F_3N_2O$	61.03 / 61.22	4.68 / 4.45	294 / 294	0.40 (C)	234-235 (alcohol)	88
15	$C_{16}H_{15}F_3N_2O$	62.10 / 62.33	4.96 / 4.90	308 / 308	0.61 (E)	152-153 (benzene)	85

* Systems were benzene–ethyl acetate, 10:1 (A), 8:1 (B), 3:2 (C) or ethyl acetate–methanol, 5:1 (D), or benzene–hexane, 1:2 (E).

Hence we have developed a method for the preparation of functionally substituted pyrrolo[3,2-*h*]-quinolines from the 2,3-dimethyl- and 1,2,3-trimethyl-7-aminoindoles.

EXPERIMENTAL

^{1}H NMR spectra were recorded on a Bruker DRX 500 (500 MsHz) instrument using TMS as internal standard. IR spectra were recorded on an "Untitled Spectrum" instrument for KBr tablets. Mass spectra were taken on a Finnigan MAT INCOS-50 mass spectrometer with direct introduction of the sample into the ion source and an ionization energy of 70 eV. Electronic spectra were measured on a Specord spectrophotometer using ethanol. Purification of the reaction products was carried out on an Al_2O_3 chromatography column (Neutral I and II Brockmann activity grade). Monitoring of the course of the reaction and the purity of the obtained compounds was performed using TLC on Silufol UV-254 plates.

The physicochemical and spectroscopic parameters for the compounds obtained are given in Tables 1 and 2. The preparation of the starting aminoindoles **1, 2** has been reported in [1].

(*E*,*Z*)-3-(2,3-Dimethyl-1H-indol-7-yl)aminobutenoic Acid Ethyl Ester (3). A solution of the aminoindole **1** (0.92 g, 5.75 mmol) and acetoacetic ester (0.615 g, 4.73 mmol) in absolute benzene (200 ml) in the presence of traces of glacial acetic acid was heated for 34 h (chromatographic monitoring) using a

Dean–Stark apparatus. The benzene was distilled off at the end of the reaction. The aminocrotonate obtained was purified by passing a solution in benzene heated to reflux with petroleum ether through a layer of aluminium oxide (1.5-2 cm). Yield 1.25 g.

(*E*,*Z*)-3-(1,2,3-Trimethyl-1H-indol-7-yl)aminobutenoic Acid Ethyl Ester (4) was prepared similarly from the aminoindole **2** (0.5 g, 2.87 mmol) and acetoacetic ester (0.4 g, 8 mmol) with the heating prolonged to 38 h. Purification by passage of a solution in petroleum ether through an aluminium oxide layer (1.5-2 cm) gave a yield of 0.64 g.

6-Hydroxy-2,3-dimethyl-6-trifluoromethyl-6,7,8,9-tetrahydro-1H-pyrrolo[3,2-*h*]quinolin-8-one (5) was prepared similarly by heating the aminoindole **1** (0.4 g, 2.5 mmol) and trifluoroacetoacetic ester (0.5 g, 2.72 mmol) for 15 h. Yield 0.585 g. When carrying out the melting point determination the substance obtained was converted to the pyrroloquinolone **13**.

6-Hydroxy-1,2,3-trimethyl-6-trifluoromethyl-6,7,8,9-tetrahydro-1H-pyrrolo[3,2-*h*]quinolin-8-one and 4,4,4-Trifluoro-3-oxobutanoic Acid N-(1,2,3-Trimethyl-1H-indol-7-yl)amide (6) was prepared similarly from the aminoindole **2** (0.45 g, 2.59 mmol) and the trifluoroacetoacetic ester (0.5 g, 2.72 mmol) with heating for 20 h. The mixture of substances was purified by passage of a solution in petroleum ether heated to reflux through a layer (1 cm) of aluminium oxide. Yield 0.6 g.

2-[(2,3-Dimethyl-1H-indol-7-yl)aminomethylene]malonic Acid Diethyl Ester (7). A mixture of the aminoindole **1** (0.7 g, 4.38 mmol) and ethoxymethylenemalonic ester (1.0 g, 4.63 mmol) in alcohol (4 ml) was refluxed for 1 h. The precipitate formed after cooling was filtered off. Yield 1.1 g.

2-[(1,2,3-Trimethyl-1H-indol-7-yl)aminomethylene]malonic Acid Diethyl Ester (8) was prepared similarly from the aminoindole **2** (0.6 g, 3.45 mmol) and ethoxymethylenemalonic ester (0.75 g, 3.47 mmol). The product was purified by passage of a solution in petroleum ether heated to reflux through a layer (1.5-2 cm) of aluminium oxide. Yield 0.816 g.

2,3,8-Trimethyl-6,9-dihydro-1H-pyrrolo[3,2-*h*]quinolin-6-one (9). The aminocrotonate **3** (0.44 g, 1.62 mmol) was introduced into refluxing biphenyl and refluxed for 30 min. The cooled mixture was poured into petroleum ether and the precipitate was filtered and repeatedly washed with hot hexane to remove biphenyl. Yield 0.28 g.

1,2,3,8-Tetramethyl-6,9-dihydro-1H-pyrrolo[3,2-*h*]quinolin-6-one (10) was prepared similarly from the aminocrotonate **4** (0.2 g, 0.7 mmol) by cyclization in biphenyl. Yield 0.15 g. The product was purified by passage of a solution in benzene heated to reflux through an aluminium oxide layer (1.5 cm).

6-Hydroxy-2,3-dimethyl-1H-pyrrolo[3,2-*h*]quinoline-7-carboxylic Acid Ethyl Ester (11). Compound **7** (0.45 g, 1.36 mmol) was introduced into refluxing dowtherm and then refluxed for 30 min. The cooled solution was poured into petroleum ether. The precipitated solid was filtered and repeatedly washed with hot hexane to remove dowtherm. Yield 0.33 g.

2,3,8-Trimethyl-1H-pyrrolo[3,2-*h*]quinoline-7-carboxylic Acid Ethyl Ester (12). The Vilsmeier reagent prepared from $POCl_3$ (1 ml) and DMF (1 ml) was added to a solution of the aminocrotonate **3** (1.0 g, 3.68 mmol) in chloroform (50 ml). The reaction mixture was refluxed for 6 h (chromatographic monitoring), cooled, diluted with chloroform (200 ml), and treated with aqueous ammonia (12%, 50 ml). The chloroform layer was separated, washed 3-4 times with water, and dried with sodium sulfate. Chloroform was evaporated off. Yield 0.4 g.

2,3-Dimethyl-6-trifluoromethyl-8,9-dihydro-1H-pyrrolo[3,2-*h*]quinolin-8-one (13) was obtained by refluxing the amine **5** (1.34 g, 4.51 mmol) in CF_3COOH for 1 h. The reaction product was poured into iced aqueous ammonia. The precipitated solid was filtered off and repeatedly washed with water. Yield 1.0 g.

1,2,3-Trimethyl-6-trifluoromethyl-8,9-dihydro-1H-pyrrolo[3,2-*h*]quinolin-8-one (14) was prepared similarly by heating the mixture of amides **6** (1.8 g, 5.79 mmol) in CF_3COOH for 1 h. Yield 1.5 g.

1,2,3,9-Tetramethyl-6-trifluoromethyl-8,9-dihydro-1H-pyrrolo[3,2-*h*]quinolin-8-one (15). A. Prepared by refluxing the pyrroloquinolone **13** (0.168 g, 0.6 mmol) with a 10 fold excess of dimethyl sulfate in the presence of KOH in acetone for 8.5 h. At the end of the reaction (chromatographic monitoring) the reaction mixture was poured into water and the precipitated solid was filtered off. Yield 0.157 g.

B. Prepared similarly from the pyrroloquinolone **14** (0.04 g, 0.14 mmol) with the heating carried out for 10 h. Yield 0.018 g.

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