Chemistry of Heterocyclic Compounds, Vol. 43, No. 8, 2007

SYNTHESIS OF PYRROLO[2,3-*h*]QUINOLINES FROM 4-AMINO-2,3-DIMETHYL- AND 4-AMINO-1,2,3-TRIMETHYLINDOLES

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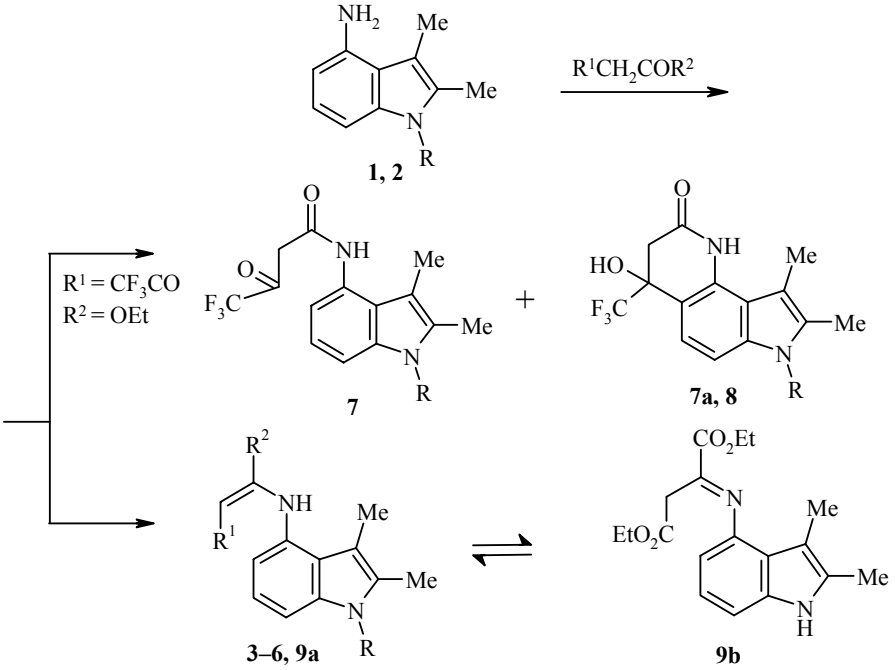
A study was carried out on the reactions of 4-amino-2,3-dimethyl- and 4-amino-1,2,3-trimethylindoles with acetylacetone, dibenzoylmethane, ethyl acetoacetate, ethyl trifluoroacetoacetate, and ethyl oxaloacetate. Methods were developed for the synthesis of a series of substituted pyrrolo-[2,3-h]quinolines.

Keywords: acetylacetone, ethyl acetoacetate, dibenzoylmethane, 4-amino-2,3-dimethyl- and 4-amino-1,2,3-trimethylindoles, substituted pyrrolo[2,3-*h*]quinolines, ethyl trifluoroacetoacetate, ethyl oxaloacetate.

In work on the development of methods for the synthesis of pyrroloquinolines with potential biological activity, reactions of 4-amino-2,3-dimethyl- (**1**) and 4-amino-1,2,3-trimethylindoles (**2**) with β-dicarbonyl compounds have not yet been studied.



1 R = H; **2** R = Me; **3** R = H, R^1 = MeCO, R^2 = Me; **4** R = R^2 = Me, R^1 = MeCO; **5** R = H, R^1 = PhCO, R^2 = Ph; **6** R = Me, R^1 = PhCO, R^2 = Ph; **7**, **7a** (mixture) R = H; **8** R = Me; **9** R = H, R^1 = R^2 = CO_2Et

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TABLE 1. ^{1}H NMR Spectra of Compounds **3-16**

Compound	Chemical shifts, δ, ppm (*J*, Hz)
3	1.80 (3H, s, =C–CH_3); 2.00 (3H, s, O=C–CH_3); 2.13 (3H, s, 3–CH_3); 2.28 (3H, s, 2–CH_3); 5.22 (1H, s, =CH); 6.71 (1H, d, $J_{5,6}$ = 8, H-5); 6.94 (1H, t, $J_{5,6,7}$ = 8, H-6); 7.15 (1H, d, $J_{7,6}$ = 8, H-7); 10.91 (1H, s, 4-NH); 12.51 (1H, s, H-1)
4	1.80 (3H, s, =C–CH_3); 2.00 (3H, s, O=C-CH_3); 2.18 (3H, s, 3–CH_3); 2.31 (3H, s, 2–CH_3); 3.65 (3H, s, 1–CH_3); 5.23 (1H, s, =CH); 6.76 (1H, d, $J_{5,6}$ = 8, H-5); 7.05 (1H, t, $J_{5,6,7}$ = 8, H-6); 7.30 (1H, d, $J_{7,6}$ = 8, H-7); 12.51 (1H, s, 4-NH)
5	2.34 (3H, s, 3-CH_3); 2.48 (3H, s, 2-CH_3); 6.08 (1H, d, $J_{5,6}$ = 8, H-5); 6.21 (1H, s, =CH); 6.64 (1H, t, $J_{5,6,7}$ = 8, H-6); 6.97 (1H, d, $J_{7,6}$ = 8, H-7); 7.29-7.60 (10H, m, 2C_6H_5); 10.90 (1H, s, H-1); 13.25 (1H, s, 4-NH)
6	2.36 (3H, s, 3-CH_3); 2.50 (3H, s, 2-CH_3); 3.65 (3H, s, 1-CH_3); 6.12 (1H, d, $J_{5,6}$ = 8, H-5); 6.22 (1H, s, =CH); 6.70 (1H, t, $J_{5,6,7}$ = 8, H-6); 7.10 (1H, d, $J_{6,7}$ = 8, H-7); 7.37-7.55 (10H, m, 2C_6H_5); 13.27 (1H, s, 4-NH)
8	2.29 (3H, s, 9-CH_3); 2.42 (3H, s, 8-CH_3); 2.86 (1H, d, $J_{3H,3H'}$ = 15, H-3); 3.03 (1H, d, $J_{3H',3H}$ = 15, H'-3); 3.61 (3H, s, 7-CH_3); 6.80 (1H, s, 4-OH); 7.12 (1H, d, $J_{5,6}$ = 7, H-5); 7.28 (1H, d, $J_{6,5}$ = 7, H-6); 9.05 (1H, s, NH)
9a	0.94 (3H, t, *J* = 7, $COOCH_2\underline{CH_3}$ chelate); 1.24 (3H, t, *J* = 7, $COOCH_2\underline{CH_3}$); 2.30 (3H, s, 3-CH_3); 2.34 (3H, s, 2-CH_3); 4.05 (2H, q, *J* = 7, $COO\underline{CH_2}CH_3$ chelate); 4.15 (2H, q, *J* = 7, $COO\underline{CH_2}CH_3$); 5.14 (1H, s, =CH); 6.30 (1H, d, $J_{5,6}$ = 8, H-5); 6.85 (1H, t, $J_{5,6,7}$ = 8, H-6); 7.04 (1H, d, $J_{7,6}$ = 7, H-7); 10.05 (1H, s, 4-NH); 10.86 (1H, s, H-1)
9b	1.24 (3H, t, *J* = 7, 2-$COOCH_2\underline{CH_3}$); 2.20 (3H, s, 3-CH_3); 2.34 (3H, s, 2-CH_3); 4.15 (2H, q, *J* = 7, 2-$COO\underline{CH_2}CH_3$); 4.71 (2H, s, –CH_2–); 6.09 (1H, d, $J_{5,6}$ = 8, H-5); 6.48 (1H, d, $J_{7,6}$ = 8, H-7); 6.63 (1H, t, $J_{5,6,7}$ = 8, H-6); 10.27 (1H, s, H-1)
10	2.35 (3H, s, 8-CH_3); 2.60 (6H, s, 2-, 4-CH_3); 2.65 (3H, s, 9-CH_3); 7.08 (1H, s, H-3); 7.45 (1H, d, $J_{6,5}$ = 8, H-6); 7.51 (1H, d, $J_{5,6}$ = 8, H-5); 11.15 (1H, s, H-7)
11	2.38 (3H, s, 8-CH_3); 2.62 (3H, s, 4-CH_3); 2.64 (3H, s, 2-CH_3); 2.72 (3H, s, 9-CH_3); 3.76 (3H, s, 7-CH_3); 7.10 (1H, s, H-3); 7.57 (1H, d, $J_{6,5}$ = 8, H-6); 7.64 (1H, d, $J_{5,6}$ = 8, H-5)
12	2.44 (3H, s, 8-CH_3); 2.84 (3H, s, 9-CH_3); 7.36 (1H, d, $J_{5,6}$ = 8, H-5); 7.48 (1H, t, *J* = 7, 4-$H_{p\text{-Ph}}$); 7.52 (1H, d, $J_{6,5}$ = 8, H-6); 7.55-7.65 (7H, m, 4-$H_{o\text{-, }m\text{-Ph}}$, 6-$H_{m\text{-, }p\text{-Ph}}$); 7.88 (1H, s, H-3); 8.40 (1H, d, *J* = 7, 2-$H_{o\text{-Ph}}$); 11.38 (1H, s, H-7)
13	2.45 (3H, s, 8-CH_3); 2.85 (3H, s, 9-CH_3); 3.80 (3H, s, 7-CH_3); 7.42 (1H, d, $J_{5,6}$ = 8, H-5); 7.48 (1H, t, *J* = 7, 4$H_{p\text{-Ph}}$); 7.50-7.53 (7H, m, 4-$H_{o\text{-, }m\text{-Ph}}$, 2-$H_{m\text{-, }p\text{-Ph}}$); 7.70 (1H, d, $J_{6,5}$ = 8, H-6); 7.87 (1H, s, H-3); 8.40 (2H, d, *J* = 7, 2-$H_{o\text{-Ph}}$)
14	2.35 (3H, s, 8-CH_3); 2.58 (3H, s, 9-CH_3); 3.75 (3H, s, 7-CH_3); 6.80 (1H, s, H-3); 7.38 (1H, d, $J_{5,6}$ = 8, H-5); 7.45 (1H, d, $J_{6,5}$ = 8, H-6); 10.10 (1H, s, H-1)
15	2.33 (3H, s, 8-CH_3); 2.52 (3H, s, 9-CH_3); 6.80 (1H, s, H-3); 7.30 (2H, br. s, $J_{5,6}$ = 8, H-5,6); 10.11 (1H, s, H-1); 11.44 (1H, s, H-7)
16A	1.29 (3H, t, *J* = 7, 2-$COOCH_2\underline{CH_3}$); 2.19 (3H, s, 8-CH_3); 2.70 (3H, s, 9-CH_3); 4.38 (2H, q, *J* = 7, 2-$COO\underline{CH_2}CH_3$); 7.44 (1H, s, H-3); 7.55 (1H, d, $J_{5,6}$ = 8, H-5); 7.70 (1H, d, $J_{6,5}$ = 8, H-6); 11.24 (1H, s, H-7); 11.34 (1H, s, 4-OH)
16B	1.29 (3H, t, *J* = 7, 2-$COOCH_2\underline{CH_3}$); 2.16 (3H, s, 8-CH_3); 2.58 (3H, s, 9-CH_3); 4.94 (2H, q, *J* = 7, 2-$COO\underline{CH_2}CH_3$); 6.64 (1H, s, H-3); 7.32 (1H, d, $J_{5,6}$ = 8, H-5); 7.72 (1H, d, $J_{6,5}$ = 8, H-6); 9.73 (1H, s, H-1); 11.50 (1H, s, H-7)

We have found that amines **1** and **2** react upon heating with acetylacetone (at ~139°C) and dibenzoylmethane (at ~180°C) to give enamino ketones **3-6**.

The ^{1}H NMR spectra of enamino ketones **3-6** given in Table 1 show singlets for two methyl groups (**3** and **5**) or three methyl groups (**4** and **6**) of the indole fragment, vinyl proton (=CH), 4-NH, H-1 (**3** and **5**), two doublets for H-5, H-7, and a triplet for H-6 with *J* = 8 Hz. The spectra of **3** and **4** also show singlets for the $COCH_3$ and $=CCH_3$ methyl groups. The spectra of **5** and **6** also show multiplets for two phenyl substituents. The UV spectra of **3-6** are typical for indolylenamino ketones [1].

TABLE 2. UV and Mass Spectra of Compounds **3-16**

Compound	UV spectrum		Mass spectrum, *m/z* (I_{rel}, %)
	λ_{max}, nm	log ε	
3	227 314	4.45 4.21	242 $[M]^+$ (100), 227 (31), 225 (55), 212 (11), 211 (11), 200 (13), 199 (72), 197 (11), 186 (13), 185 (99), 184 (79), 183 (33), 182 (13), 170 (48), 169 (13), 159 (20), 158 (19), 144 (23), 143 (20), 115 (14), 114 (14)
4	229 318	4.46 4.23	256 $[M]^+$ (61), 241 (11), 213 (40), 199 (60), 198 (62), 184 (48), 183 (18), 173 (19), 158 (22), 157 (12), 143 (12), 128 (14), 120 (24), 116 (13), 115 (26), 99 (27), 98 (25), 84 (31), 43 (100)
5	224 344	4.54 4.18	366 $[M]^+$ (25), 261 (39), 247 (34), 246 (23), 159 (11), 158 (11), 145 (11), 144 (11), 115 (14), 105 (77), 77 (100), 51 (16)
6	226 345	4.45 4.09	380 $[M]^+$ (9), 275 (27), 261 (34), 260 (30), 173 (11), 158 (11), 105 (57), 77 (100)
7, **7a**			298 $[M]^+$ (33), 279 (13), 257 (13), 229 (100), 187 (67), 160 (82), 159 (93), 69 (82)
8	232 305	4.53 3.93	312 $[M]^+$ (27), 244 (15), 243 (100), 225 (10), 173 (30)
9a	223 280 345	4.47 4.08 3.90	330 $[M]^+$ (48), 284 (9), 257 (63), 256 (20). 211 (54), 210 (41), 209 (26), 183 (100), 170 (57), 143 (33), 115 (33), 77 (20), 57 (20), 43 (30)
10	227 265 339	4.45 4.35 3.90	224 $[M]^+$ (100), 223 (70), 209 (24), 112 (21)
11	236 266 342	4.45 4.36 3.96	238 $[M]^+$ (89), 237 (49), 223 (100), 224 (17), 181 (13), 119 (44)
12	224 245 295 360	4.45 4.56 4.33 3.97	348 $[M]^+$ (100), 347 (35), 174 (37), 77 (33)
13	225 248 270 365	4.55 4.68 4.54 4.11	362 $[M]^+$ (100), 361 (26), 348 (11), 347 (48), 181 (87), 180 (26), 173 (39), 77 (54)
14	218 240 281 345	4.52 4.42 4.33 3.83	294 $[M]^+$ (100), 293 (87), 279 (48), 147 (26), 69 (25)
15	215 234 281 340	4.48 4.31 4.27 3.78	280 $[M]^+$ (100), 279 (83), 265 (37), 69 (45)
16	240 284 380	4.72 4.17 3.85	284 $[M]^+$ (50), 211 (22), 210 (100), 182 (70), 181 (48), 167 (12), 154 (28), 127 (20), 115 (14), 77 (27), 63 (20), 45 (28)

The decomposition of the molecular ions of enamines **3-6** upon electron impact proceeds through two major pathways: elimination of $Me(Ph)CO^{\cdot}$ or $Me(Ph)COCH_2$ to give fragment ions $[M–Me(Ph)CO]^+$ and $[M–Me(Ph)COCH_2]^+$ respectively. These results indicate that in the gas phase, the compounds studied are found in at least two forms: imino and enamino ketone (Table 2).

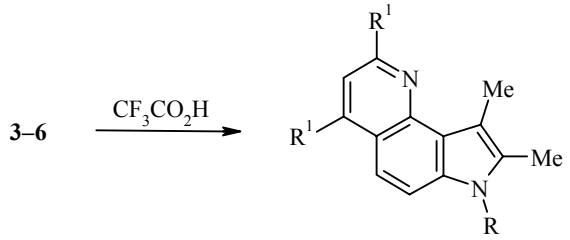
A mixture of products is formed in the reaction of aminoindole **1** and ethyl 4,4,4-trifluoroacetoacetate upon heating in benzene at reflux with catalytic amounts of acetic acid. Acording to the ^{1}H NMR spectrum this mixture contains acyclic amide **7** (probably in different tautomeric forms) and a cyclic amide **7a**. Amides **7** and **7a** were not isolated as pure compounds. The formation of a mixture of **7** and **7a** was supported by the mass spectrum. The $[M–69]^+$ peak (100%), corresponding to the loss of the CF_3 radical from the molecular ion, was the strongest peak in the spectrum. This is the major decomposition pathway, as noted previously for cyclic amides obtained from 6-aminoindoles [1]. The strong $[M–138]^+$ peak (82%) corresponds to the loss of trifluorodiketene from the amide molecular ion to give the corresponding aminoindole. This decomposition pathway was observed for the described acyclic amides.

In contrast to the case of amide **1**, cyclic amide **8** is the product of the reaction of amine **2** with ethyl trifluoroacetate. The ^{1}H NMR spectrum of amide **8** has signals for the methyl groups at positions 7, 8, and 9, signal for 4-OH, and two AB doublets for H-5 and H-6. The protons of the methylene group also appear as two doublets (at 2.86 and 3.03 ppm) with coupling constant 15 Hz. The nonequivalence of the H-3 protons is attributed to the effect of differently positioned CF_3 and OH groups at the asymmetric $C_{(4)}$ atom. The strongest

peak in the mass spectrum of **8** is found for the fragmentation ion with *m/z* 243 corresponding to the loss of the CF_3 radical from the molecular ion, leading to the stable protonated pyrrolo[2,3-*h*]quinolinedione system. This finding also supports the assigned cyclic structure for **8**. The formation of cyclic amides was also observed for other 1-methylaminoindoles upon reaction with ethyl trifluoroacetate [1] and attributed to enhanced reactivity of the benzene ring carbon atoms in the indole system due to the effect of the N–Me group.

The analogous reaction of aminoindole **1** with ethyl oxaloacetate under the same conditions, in contrast to the reaction with ethyl trifluoroacetate, gives the diethyl ester of (4-amino-2,3-dimethylindolyl)fumaric acid (**9**). ^{1}H NMR spectroscopy in DMSO-d_6 indicated that ~20% imine form of **9** (lack of signals for vinyl and amine protons and presence of a signal for methylene group protons) exists along with ~80% enamine form (presence of singlets for =CH and 4-NH protons). The two triplets and two quartets for the protons of the ethoxycarbonyl groups in the spectrum also indicate the condensation of 4-amino-2,3-dimethylindole due to the ketone group of ethyl oxaloacetate to give enamine **9**. The structure and composition of **9** were supported by the mass spectrum, in which the strongest peak with *m/z* 183 (100%) corresponds to the consecutive elimination of the ethoxycarbonyl radical, EtOH molecule, and CO molecule from the molecular ion.

Products **3-8** were then studied under conditions of acid cyclization. Enamino ketones **3-6** in trifluoroacetic acid give the expected pyrroloquinolines **10-13**.

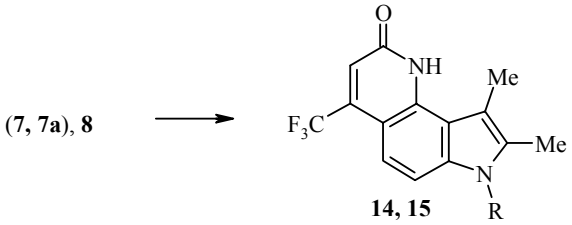


10–13

10 R = H, R^1 = Me; **11** R = R^1 = Me; **12** R = H, R^1 = Ph; **13** R = Me, R^1 = Ph

The ^{1}H NMR spectra of **10** and **11** showed singlets for 2-CH_3, 4-CH_3, 8-CH_3, 9-CH_3, H-3, and H-7 (**10**) and 7-CH_3 (**11**) as well as doublets for H-5 and H-6. The spectra of **12** and **13** lack signals for 2-CH_3 and 4-CH_3 characteristic for pyrroloquinolines **10** and **11** but display multiplets for phenyl group protons.

Amides (**7, 7a)** and **8** differ in their behavior under acid cyclization conditions. Thus, while methylated amide **8** is converted over 3.5 h into the corresponding pyrroloquinoline **14**, heating the mixture of **7** and **7a** in trifluoroacetic acid at reflux for 30 h does not lead to complete cyclization. Only the use of more vigorous conditions ($ZnCl_2$, 140°C) gives pure pyrroloquinoline **15**.

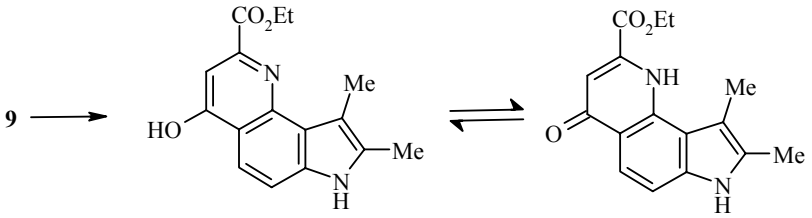


14, 15

14 R = Me; **15** R = H

The ^{1}H NMR spectra of **14** and **15** show two (**15**) or three (**14**) methyl group signals, signal for aromatic proton H-3, as well as singlets for H-7 (for **15**) and H-1 and two doublets for H-5 and H-6. The mass spectra of pyrroloquinolines **14** and **15** display molecular ion peaks at *m/z* 294 (100%) and 280 (100%), respectively, and fragment peaks only for $[M–H]^+$ (83 and 87%) and $[M–CH_3]^+$ (37 and 48%), which indicates stability of the molecule toward electron impact.

The product of the condensation of 4-amino-2,3-dimethylindole with ethyl oxaloacetate **9** is converted to pyrroloquinoline **16** upon heating in diphenyl at reflux.



The ^{1}H NMR spectrum of **16** in DMSO-d_6 indicates that this compound exists as a 3:1 mixture of two tautomeric forms: hydroxyquinoline form **A** and quinolone form **B** (according to the proton integral intensities). The spectra of both forms have a triplet and quartet for the 2-CO_2Et group, signals for 8-CH_3, 9-CH_3, H-3, and H-7, two doublets for H-5 and H-6, as well as singlets for the 4-OH proton (for form **A**) and H-1 (for form **B**). In

TABLE 3. Physicochemical Characteristics of **3-6** and **8-16**

Compound	Empirical formula	Found, % / Calculated, %			R_f*	mp, °C *[2]	Yield, %
		C	H	M			
3	$C_{15}H_{18}N_2O$	74.23 / 74.35	7.65 / 7.49	242 / 242	0.48	96-97	53
4	$C_{16}H_{20}N_2O$	74.88 / 74.97	7.98 / 7.86	256 / 256	0.61	100-101	39
5	$C_{25}H_{22}N_2O$	81.72 / 81.94	6.29 / 6.05	366 / 366	0.61	152-153	45
6	$C_{26}H_{24}N_2O$	81.71 / 82.07	6.80 / 6.36	380 / 380	0.68	150-51	41
8	$C_{15}H_{15}F_3N_2O_2$	57.51 / 57.69	4.96 / 4.84	312 / 312	0.76	206-207	50
9	$C_{18}H_{22}N_2O_4$	65.21 / 65.44	6.92 / 6.71	330 / 330	0.48	113	27
10	$C_{15}H_{16}N_2$	80.20 / 80.32	7.34 / 7.19	224 / 224	0.56	158	67
11	$C_{16}H_{18}N_2$	80.44 / 80.63	7.72 / 7.61	238 / 238	0.42	196-197	77
12	$C_{25}H_{22}N_2$	86.00 / 86.17	5.91 / 5.79	348 / 348	0.77	274-275	79
13	$C_{26}H_{22}N_2$	—	—	362 / 362	0.83	204-205	91
14	$C_{15}H_{13}F_3N_2O$	61.03 / 61.22	4.67 / 4.45	294 / 294	0.54	237-238	95
15	$C_{14}H_{11}F_3N_2O$	59.54 / 60.00	4.46 / 3.96	280 / 280	0.47	266-267	76
16	$C_{16}H_{16}N_2O_3$	67.49 / 67.59	5.69 / 5.67	284 / 284	0.43	273	47

* Elution systems: 3:1 benzene-ethyl acetate for **3, 4, 10, 11**, 1:1 benzene-ethyl acetate for **8** and **15**, 10:1 benzene-ethyl acetate for **9**, and 1:2 benzene-ethyl acetate for **14**, chloroform with traces of methanol for **5, 6, 12, 13,** and **16.**

***[2]** Crystallization solvents: petroleum ether for **3, 4, 9**, chloroform for **5, 6**, benzene-petroleum ether for **8, 10, 14, 15**, ethanol for **11, 12**, hexane for **13**, and ethanol for **16.**

addition, the differences in the spectra of tautomers **A** and **B** entail different chemical shifts for the signals of monotypic protons. Thus, the signal for H-3 for form **A** appears at lower field than the analogous signal for form **B** ($\Delta\delta$ = 1 ppm). The assignment of the proton signals to a specific form was accomplished by a comparative analysis of the calculated ^{1}H NMR spectra of tautomers **A** and **B** as well as the experimental spectral characteristics of **10-15**.

The mass spectrum of pyrroloquinoline **16** shows a molecular ion peak $[M]^+$ (55%). The two strongest peaks in this spectrum are found for ions with *m/z* 210 (100%) and 182 (70%), corresponding to the consecutive elimination of HCO_2Et and CO from the molecular ion.

Thus, we studied the behavior of 4-aminoindoles **1** and **2** in reactions with acetylacetone, dibenzoylmethane, ethyl trifluoroacetate, and ethyl oxaloacetate and developed syntheses for the corresponding pyrrolo[2,3-*h*]quinolines. In evaluating the reactivity of these amines in the first step of the reaction with the dicarbonyl component, we should note their relative inertness in comparison with all substituted 5- and 6-aminoindoles and 7-amino-2,3-dimethylindole [2, 3], whose condensation with acetylacetone and dibenzoylmethane proceeds upon heating (139-180°C) over 0.5-1.5 h. Completion of these reactions under the same conditions for 4-aminoindoles requires 2-7 h. The 3-methyl group in **1** and **2** probably shields the amine nitrogen atom, similar to the N–CH_3 group in 7-amino-1,2,3-trimethylindole. Thus, formation of an enamine from this aminoindole is known to be more difficult than from 7-amino-2,3-dimethylindole [3]. Since the charges on the amino group nitrogen atoms in **1** and **2** are similar (0.066 and 0.059, respectively) as indicated by quantum-chemical calculations, the lower activity of 4-amino-1,2,3-trimethylindole (**2**) in comparison with 4-amino-2,3-dimethylindole (**1**) should be attributed to a steric effect of the three methyl groups.

The difficulties in the cyclization of enamines **4** and **6**, in light of their strong basicity, are probably a result of the presence of forms protonated at $C_{(3)}$ in trifluoroacetic acid. This leads to a diminution in the reactivity of indole $C_{(5)}$ for the electrophilic closure of the pyridine ring. Similarly, vigorous conditions are also required for the cyclization of acyclic amide **7**. On the other hand, the aromatization of cyclic amides **7a** and **8** proceeds smoothly upon heating in trifluoroacetic acid at reflux. The thermal cyclization of enamine **9** also proceeds without the participation of acid, which is further support for our hypotheses given above.

EXPERIMENTAL

The ^{1}H NMR spectra were taken on a Bruker DRX 500 spectrometer at 500 MHz in DMSO-d_6 with TMS as the internal standard. The mass spectra were taken on a Finnigan MAT Incos-50 mass spectrometer with direct sample inlet into the ion chamber and 70 eV ionization voltage. The electronic absorption spectra were taken on a Specord spectrophotometer in ethanol. The products were purified by column chromatography and preparative thick-layer chromatography on an unattached layer of neutral, Brockmann grade-I or II activity alumina. The reaction course and purity of the products were monitored by thin-layer chromatography on Silufol UV-254 plates with benzene-ethyl acetate as the eluent.

The physicochemical characteristics of **3-6** and **8-16** are given in Table 3.

PM3 semiempirical quantum-chemical calculations were carried out for **1** and **2** (RHF, algorithm, Polak Ribiere; RMS gradient: 0.01 kcal/Å·mol) using the *HyperChem 7.0* program package.

(*Z*)-4-[(2,3-Dimethyl-1H-indol-4-yl)amino]pent-3-en-2-one (3). A mixture of 4-amino-2,3-dimethylindole (**1**) (0.40 g, 2.50 mmol) and acetylacetone (3 ml) was heated at reflux for 2 h. Excess acetylacetone was then distilled off in vacuum. The residue was dissolved in benzene-petroleum ether and filtered hot through 2 cm alumina. The filtrate was cooled. The precipitate formed of enamine **3** was filtered off. Recrystallization from petroleum ether gave enamine **3** (0.32 g).

(*Z*)-4-[(1,2,3-Trimethyl-1H-indol-4-yl)amino]pent-3-en-2-one (4) was obtained analogously from 4-amino-1,2,3-trimethylindole (**2**) (0.30 g, 1.72 mmol) after heating at reflux for 2.5 h. Recrystallization of the crude product from petroleum ether gave enamine **4** (0.17 g).

(*Z*)-3-[(2,3-Dimethyl-1H-indol-4-yl)amino]-1,3-diphenyl-2-propen-1-one (5). A mixture of aminoindole **1** (0.16 g, 0.99 mmol) and dibenzoylmethane (0.33 g, 1.48 mmol) was maintained for 2.5 h at 180-185°C. At the end of the reaction as indicated by thin-layer chromatography, **5** was isolated by preparative thick-layer chromatography on alumina with chloroform as the eluent. The yield of **5** was 0.16 g.

(*Z*)-3-[(1,2,3-Trimethyl-1H-indol-4-yl)amino]-1,3-diphenyl-2-propen-1-one (6) was obtained analogously from aminoindole **2** (0.45 g, 2.59 mmol) and dibenzoylmethane (1.16 g, 5.17 mmol) after heating for 7 h at 180-185°C. The yield of **6** was 0.35 g.

4-Hydroxy-7,8,9-trimethyl-4-trifluoromethyl-1,2,3,4-tetrahydro-2H-pyrrolo[2,3-*h*]quinolin-2-one (8). A mixture of aminoindole **2** (0.40 g, 2.29 mmol) and ethyl 4,4,4-trifluoroacetoacetate (0.45 g, 2.44 mmol) in absolute benzene (200 ml) in the presence of a catalytic amount of glacial acetic acid was heated at reflux for 21 h with a Dean–Stark trap. After all the aminoindole had been consumed in the reaction as indicated by thin-layer chromatography, the volume of the reaction mixture was reduced to 50 ml by distilling off benzene. The precipitate formed of amide **8** was filtered off, washed with benzene, and recrystallized from petroleum ether to give amide **8** (0.36 g).

Diethyl Ester of [(2,3-Dimethyl-1H-indol-4-yl)amino]fumaric Acid (9) was obtained analogously from aminoindole **1** (0.595 g, 3.72 mmol) and ethyl oxaloacetate (0.7 g, 3.72 mmol) after heating for 44 h. The crude product was recrystallized from 3:1 benzene–petroleum ether to give compound **9** (0.334 g).

2,4,8,9-Tetramethyl-7H-pyrrolo[2,3-*h*]quinoline (10). Enamine **3** (0.14 g, 0.58 mmol) in a 10-fold excess of trifluoroacetic acid was heated for 4 h at reflux. At the end of the reaction as indicated by thin-layer chromatography, the reaction mixture was poured into 12% aqueous ammonia containing ice. The precipitate formed was filtered off, repeatedly washed with water, and dried in the air. The crude product was recrystallized from benzene-petroleum ether to give compound **10** (0.086 g).

2,4,7,8,9-Pentamethyl-7H-pyrrolo[2,3-*h*]quinoline (11) was obtained analogously from enamine **4** (0.16 g, 0.63 mmol) after heating for 6 h. The crude product was recrystallized from aqueous ethanol to give compound **11** (0.114 g).

8,9-Dimethyl-2,4-diphenyl-7H-pyrrolo[2,3-*h*]quinoline (12) was obtained analogously from enamine **5** (0.067 g, 0.18 mmol) after heating for 5 h. The crude product was recrystallized from ethanol to give compound **12** (0.05 g).

7,8,9-Trimethyl-2,4-diphenyl-7H-pyrrolo[2,3-*h*]quinoline (13) was obtained analogously from enamine **6** (0.120 g, 0.32 mmol) after heating for 10 h. The yield of **13** was 0.1 g.

7,8,9-Trimethyl-4-trifluoromethyl-1,7-dihydro-2H-pyrrolo[2,3-*h*]quinolin-2-one (15). A mixture of aminoindole **1** (0.22 g, 1.38 mmol) and ethyl 4,4,4-trifluoroacetoacetate (0.26 g, 1.39 mmol) in absolute benzene (200 ml) in the presence of a catalytic amount of glacial acetic acid was heated at reflux for 17 h with a Dean-Stark trap. After all the aminoindole had been consumed in the reaction as indicated by thin-layer chromatography, the volume of the reaction mixture was reduced to 50 ml by distilling off benzene. The precipitate formed was filtered off and washed with benzene. The mixture of **7** and **7a** and a 10-fold excess of $ZnCl_2$ was heated at 140-145°C for 2 h. At the end of the reaction as indicated by thin-layer chromatography, the reaction mixture was treated with 10-12% aqueous ammonia. The precipitate formed was filtered off, washed repeatedly with warm water, and dried in the air. The crude product was recrystallized from benzene to give compound **15** (0.203 g).

2-Ethoxycarbonyl-4-hydroxy-8,9-dimethyl-7H-pyrrolo[2,3-*h*]quinoline (A) and 2-Ethoxycarbonyl-8,9-dimethyl-4-oxo-4,7-dihydro-7H-pyrrolo[2,3-*h*]quinoline (B) (16). Enamine **9** (0.15 g, 0.45 mmol) was added to diphenyl (5 ml) heated at reflux. The mixture was heated at reflux for 15 min. At the end of the reaction as indicated by thin-layer chromatography, the still warm reaction mixture was poured into petroleum ether. The precipitate formed was filtered off and washed repeatedly with hot petroleum ether to remove diphenyl. The crude product was recrystallized from ethanol to give compound **16** (0.06 g).

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