SUBSTITUTED 2-METHYL-AND 2-METHYLENEINDOLINES

4*. HETARYL-CONDENSED 2-METHYL- AND 2-METHYLENEINDOLINES WITH A LINEAR STRUCTURE

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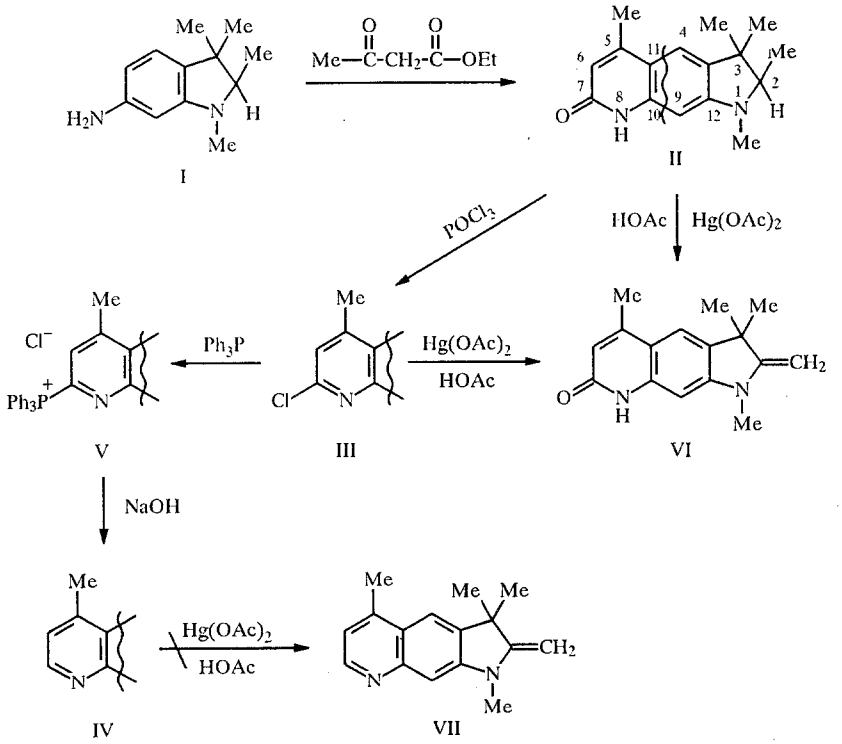
Methods have been developed for the synthesis from amino-substituted indolines of first linear trinuclear hetaryl-condensed 2-methyleneindolines having quinolone, quinoline, quinoxaline, and benzmidazole fragments. The structure of the obtained compounds was confirmed by ^1H and ^{13}C NMR spectra.

It is known that the Fischer cyclization of hydrazones, derived from hydrazines of binuclear aromatic systems, makes it possible to synthesize indoles having an angular structure only [2]. Therefore the linear trinuclear compounds of this type are difficultly available and little investigated [3, 4]. Information on the linear trinuclear heterocyclic systems containing a 2-methyleneindoline fragment is not available in the literature at all [5]. The synthesis of 2-methyleneindolines of this type is of undoubted interest due to the wide use of 2-methyleneidolines for the preparation of dyes, including those used in quantum electronics [6].



*For communication 3, see [1].

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0009-3122/92/2810-1130$12.50 ©1993 Plenum Publishing Corporation

TABLE 1. Spectral Characteristics of Compounds II-IV, VI, VII, X-XII

Compound	^{1}H and ^{13}C NMR spectra ($CDCl_3$), δ, ppm (J, Hz)
II	2,78 (3H, s, N–CH_3), 1,16 (3H, d, 2-CH_3, J = 7,6), 3,08 (1H, q., 2-H), 1,06 (3H, s, 3-CH_3), 1,31 (3H, s, 3-CH_3), 2,43 (3H, s, 5-CH_3), 6,29 (1H, s.br, 6-H), 6,31 (1H, s, 9-H), 7,17 (1H, s, 4-H), 12,17 (1H, s, br. nonloc). NH) 30,52 (N–CH_3), 10,49 (2-CH_3), 17,47 (3-CH_3), 21,40 (3-CH_3), 24,40 (5-CH_3), 40,35 C(3), 69,47 C(2), 90,72 C(3), 111,19 C(11), 112,95 C(6), 114,82 C(4), 134,51 C(5), 138,79 C(13), 147,43 C(12), 152,12 C(10), 163,40 (C=O)
III	2,83 (3H, s, N–CH_3), 1,22 (3H, d, 2-CH_3, J = 7,2), 3,19 (1H, q, 2-H), 1,14 (3H, s, 3-CH_3), 1,38 (3H, s, 3-CH_3), 2,58 (3H, s, 5-CH_3), 6,92 (1H, s.br., 6-H), 6,79 (1H, s, 9-H), 7,42 (1H, s, 4-H)
IV	2,84 (3H, s, N–CH_3), 1,22 (3H, d, 2-CH_3, J = 7,0), 3,13 (1H, q, 2-H), 1,15 (3H, s., 3-CH_3), 1,38 (3H, s, 3-CH_3), 2,61 (3H, s, 5-CH_3), 8,51 (1H, d, 7-H, J = 5,3), 6,91 (1H, d, 6-H), 6,90 (1H, s, 9-H), 7,48 (1H, s, 4-H)
VI	3,08 (3H, s, N–CH_3), 3,96 (2H, s, =CH_2), 1,37 (6H, s, 3,3-CH_3), 2,46 (3H, s, 5-CH_3), 6,34 (1H, s.br, 6-H), 6,50 (1H, s, 9-H), 7,30 (1H, s, 4-H), 12,77 (1H, s, br. nonloc., NH), 28,40 (N–CH_3), 28,30 (3,3-CH_3), 27,20 (5-CH_3), 74,02 (=CH_2), 41,48 C(3), 160,36 C(2), 89,69 C(9), 112,82 C(11), 113,60 C(6), 115,15 C(4), 132,86 C(5), 138,73 C(13), 147,69 C(12), 152,20 C(10), 163,48 (C=O)
VII	2,83 (3H, s, N–CH_3), 1,44 (6H, s, 3,3-CH_3), 3,96 (2H, s.br, =CH_2), 2,59 (3H, s, 5-CH_3), 8,52 (1H, d, 7-H, J = 5,3), 6,95 (1H, d, 6-H), 6,90 (1H, s, 9-H), 7,47 (1H, s, 4-H)
X	*4,02 (3H, s, N–CH_3), 3,35 (3H, s, 2-CH_3), 1,57 (6H, s, 3,3-CH_3), 7,33 (1H, s, 7-H), 7,51 (1H, s, 4-H) **34,55 (N–CH_3), 13,78 (2-CH_3), 22,00 (3,3-CH_3), 53,38 C(3), 107,56 C(7), 113,53 C(4)
XI	2,98 (3H, s, N–CH_3), 3,75 (2H, s, =CH_2), 1,25 (6H, s, 7,7-CH_3), 6,47 (1H, s, 4-H), 7,20 (1H, s, 8-H), 7,27...7,30 (3H, m, t-, p-Th, 8,01...8,05 (2H, m, *o*-Ph)
XII	3,17 (3H, s, N–CH_3), 4,03, 4,06 (2H, AB system, J_{AB} = 2,1, C=CH_2), 1,48 (6H, s., 8,8-CH_3), 7,02 (1H, s, 5-H), 7,78 (1H, s, 9-H), 7,29...7,32 (6H, m., t-, *n*-Ph), 7,47...7,49 (4H, m, *o*-Ph), 28,78 (N–CH_3), 29,62 (8,8-CH_3), 43,30 C(8), 161,03 C(7), 76,59 (=CH_2), 98,70 C(5), 121,41 C(9), 143,61 C(2), 145,41 C(3), 138,13 C(13), 139,62 C(11), 148,59 C(12), 152,19 C(10). 128,02...129,83 (C_6H_5 signals)

*In the ^{1}H spectrum in CD_3OD, the =CH_2 group protons do not appear because of deutero exchange.

**The ^{13}C NMR spectrum was taken in CD_3SOCD_3.

For the synthesis of hetaryl-condensed 2-methyleneindolines we used amino-substituted indolines, convenient paths of preparation of which have been described in the preceding articles of this series [1, 7].

Heating of 1,2,3,4-tetramethyl-6-aminoindoline (I) with acetoacetic ester enabled the separation in a good yield of only one of the possible isomers – quinolone II, which by the action of phosphorus oxychloride [8] readily converts into the chloroquinoline III. For its reduction into quinoline IV, advantage was taken of the ability of phosphonium salts with heteroaromatic groupings to relatively readily undergo selective hydrolysis [9]. The phosphonium salt V was obtained by fusing chloroquinoline III with triphenylphosphine.

The structure of compounds II-IV was verified by ^1H and ^{13}C NMR spectra (Table 1). The signal of the second quinoline proton appearing in the form of a doublet in the region of 8.51 ppm, J = 5.3 Hz, indicates the formation of a 4-methyl-substituted quinoline IV. The proton signals of the central benzene ring in the PMR spectra of all the synthesized compounds II-IV appear in the form of narrow singles in the region of 7.17-7.48 ppm (the fourth proton) and 6.31-6.90 ppm (the ninth proton), which confirms the linear structure of these compounds.

We should note that repeated attempts to synthesize compounds of the quinolone series starting from 5- and 6-amino-substituted 1,3,3-trimethyl-2-methyleneindolines did not bring the desired results because of side reactions proceeding at the methylene group (according to the PMR spectral data).

2-Methyleneindoline VI was obtained in a good yield by oxidation of indoline II with mercuric acetate [10]. Oxidation of quinolines III and IV under these conditions could not be carried out on a preparative scale. The oxidation of chloroquinoline III was accompanied by hydrolysis with the formation of quinolone IV. The oxidation of quinoline IV, even using a 100% excess of mercuric acetate, and with increase in the time of reaction leads only to a mixture of products IV and VII, in which compound VII comprises 30% (according to the PMR spectral data). Such a difficult course of oxidation is possibly due to the complexation of mercuric acetate at the nitrogen atom of the quinoline and not the pyrrole ring [11].

Therefore a more promising synthone for the synthesis of linear trinuclear hetaryl-condensed 2-methyleneindolines is 5,6-diamono-2-methyleneindoline VIII. The synthesis of 5-amino-6-nitro-2-melthyleneindoline IX was described by us in the preceding article [1].

The signals of the four sp^3-hybridized carbon atoms in the ^{13}C NMR spectra prove the existence of stannate X in the form of an indoleninium salt. The conversion of hexachlorostannate X into the free base leads to an extremely unstable diaminoindoline VIII (after only 10 min additional signals appear in the PMR spectrum). Therefore hexachlorostannate X was used directly for the synthesis of hetaryl-condensed 2-methyleneindolines XI and XII.

Its condensation with benzoic acid in polyphosphoric acid (PPA) gave pyrrolobenzimidazole XI, while boiling with benzil in pyridine gives pyrroloquinoxaline XII.

The ^{13}C and ^1H NMR spectra of VI and XII indicate a strong electron-acceptor influence of the quinolone and quinoxaline rings on the pyrrole part of the molecule. Thus, in the PMR spectra of compounds VI and XII, the signals of the methylene group protons are shifted relative to the corresponding signal in the PMR spectrum of the Fischer base – 1,3,3,-trimethyl-2-methyleneindoline, to a weak field by 0.11 ppm (VI) and 1.21 ppm (XII). In the ^{13}C NMR spectra the methylene carbon atom undergoes a weak-field shift by 5.27 ppm (VI) and 7.84 ppm (XII).

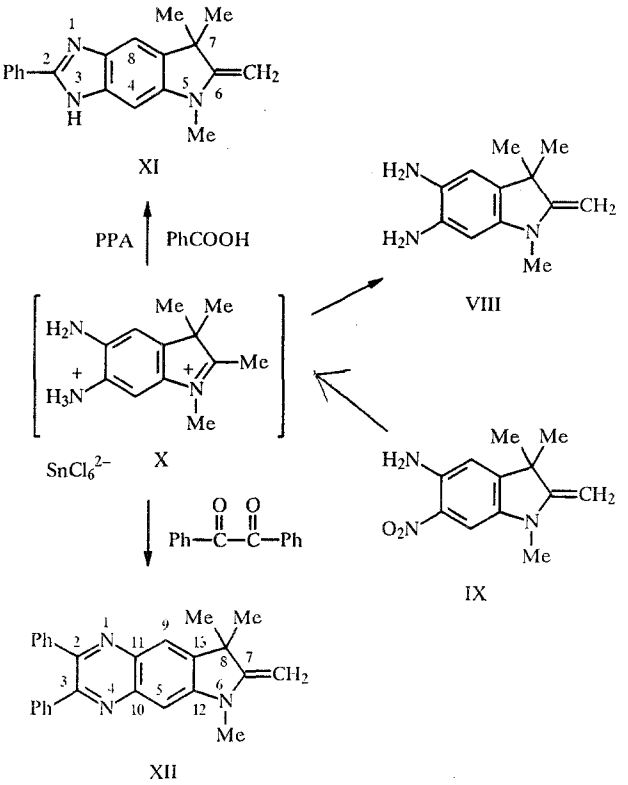
The ^1H and ^{13}C NMR spectra of a series of substituted 2-methyleneindolines are given in [1, 7, 10, 12, 13]. The synthesis and the spectral properties of polymethine dyes obtained from linear trinuclear 2-methyleneindolines will be described in subsequent articles.

EXPERIMENTAL

The ^1H NMR spectra were run on a Bruker WP-100 SV spectrometer in deuterochloroform (internal standard TMS) and the ^{13}C NMR spectra on a Gemini-200 Varian spectrometer (internal standard TMS).

The data of the elemental analysis for C, H, N, Cl correspond to the calculated values.

1,2,3,3,5-Pentamethyl-2,3,7,8-tetrahydro-1H,8H-pyrrolo[3,2-g]quinolin-7-one (II, $C_{16}H_{20}N_2O$). A mixture of 1.90 g (0.01 M) of 1,2,3,3-tetramethyl-6-aminoindolines I and 1.95 g (0.15 M) of acetoacetic ester was held for 7 h on an oil bath at 170°C. The colorless precipitate that separated out was filtered off and combined with the precipitate, which was salted out from the mother liquor by diethyl ether, and washed with diethyl ether. mp 229-231°C (from diethyl ether). Yield, 1.95 g (86%).



1,2,3,3,5-Pentamethyl-7-chloro-2,3-dihydro-1H-pyrrolo[3,2-g]-quinoline (III, $C_{16}H_{19}N_2Cl$). A mixture of 5.12 g (0.02 M) of quinolone II and 16.75 g (0.11 M) of a freshly distilled phosphorus oxychloride was heated for 30 min on an oil bath at 110°C to the complete dissolution of the solid substance. After the removal of phosphorus oxychloride in a water pump vacuum, the oily residue was poured into ice water. The yellow precipitate that separated out was dissolved in chloroform and was washed with water (3 × 70 ml), and then with sodium carbonate solution (1 × 70 ml). The chloroformic solution was dried over potassium carbonate, and evaporated. mp 89-91°C (from heptane). Yield, 4.39 (80%).

1,2,3,3,5-Pentamethyl-2,3-dihydro-1H-pyrrolo[3,2-g]-quinoline (IV, $C_{16}H_{20}N_2$). A mixture of 5.50 g (0.02 M) of chloroquinoline III and 6.46 g (0.025 M) of triphenylphosphine was heated for 14 h on an oil bath at 150°C. The glass-like mixture that was formed was ground thoroughly with benzene, the oil that separated out was dissolved in 20 ml of ethanol, boiled with activated carbon for 5 min, and precipitated with diethyl ether. The orange precipitate of the phosphonium salt V (in a ^{31}P NMR spectrum a signal at 15.3 ppm) was filtered off, dissolved in a 10% NaOH solution, and compound IV was extracted with chloroform. The chloroformic solution was dried over $MgSO_4$, evaporated and a 17-18% hydrochloric acid was added to the residue. The aqueous layer was separated, made alkaline with a 10% NaOH solution and extracted with chloroform. The chloroformic solution was dried over $MgSO_4$ and evaporated in a water pump vacuum. The residue was an oil. Yield, 2.60 g (54%).

1,3,3,5-Tetramethyl-2-methylene-2,3,7,8-tetrahydro-1H,8H-pyrrolo[3,2-g]quinolin-7-one (VI, $C_{16}H_{18}N_2O$) was obtained by the method described in [10]. mp 243-244°C (from benzene). Yield 70%.

1,2,3,3-Tetramethyl-5,6-diaminoindoleninium Hexachlorostannate (X, $C_{12}H_{19}N_3SnCl_6$). A mixture of 3.0 g (0.013 M) of 5-amino-6-nitro-2-methyleneindoline IX, 9.43 g (0.042 M) of $SnCl_2 \cdot 2H_2O$, 17 ml of conc. HCl, 8.5 ml of water, and 25 ml of toluene was boiled with stirring for 1.5 h. The aqueous and organic layers were separated. The precipitate of indoleninium hexachlorostannate X that separated out in the aqueous layer was filtered off, washed first with ether, and then with isopropanol. mp 300°C (dec.), (from methanol). Yield, 5.52 g (80%).

5,7,7-Trimethyl-6-methylene-6,7-dihydro-5H-pyrrolo[2,3-f]-benzimidazole (XI, $C_{19}H_{19}N_3$). A 1.5 g portion (0.003 M) of 5,6-diaminoindoleninium hexachlorostannate X, 0.34 g (0.003 M) of benzoic acid, and 0.35 g (0.003 M) of triethylamine were mixed with 10.0 g of polyphosphoric acid and the mixture was heated with stirring to 170-180°C, and then held at this temperature for 3 h. After cooling, the reaction mixture was poured into ice water, made alkaline with a 25% NH_4OH solution to pH 10, and extracted with chloroform. The extract was evaporated, and the residue was boiled for 10-15 min in hexane. mp 194-196°C (dec.) (from n-octane). Yield, 0.55 g (68%).

6,8,8-Trimethyl-7-methylene-2,3,-diphenyl-7,8-dihydro-6H-pyrrolo[2,3-g]quinoxaline (XII, $C_{26}H_{23}N_3$). A mixture of 1.8 g (0.003 M) of indoleninium hexachlorostannate X, 0.7 g (0.003 M) of benzil, and 5 ml of dry freshly distilled pyridine was held at 150°C on an oil bath for 3 h. After cooling, the reaction mixture was poured into ice water and made alkaline with a 25% solution of ammonia to pH 10, and then was extracted with chloroform. The extract was dried over $MgSO_4$ and evaporated, mp 186-188°C (dec.) (from heptane). Yield, 0.78 g (62%).

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