1,2-Dimethyl-3-(β-cyano-β-phenyl)vinyl-5-nitroindole (VI). A mixture of aldehyde V (1.08 g, 0.005 mole), sodium hydroxide (8 g, 0.2 mole), and benzyl cyanide (0.59 g, 0.005 mole) was refluxed in methanol (80 ml) for 3 h. The solvent was evaporated in vacuo, the residue treated with water, and the solid filtered, washed with water to neutrality, and dried.

LITERATURE CITED

1. J. M. Makosza, *IUPAC Congress*, Moscow (1987), p. 118.
2. R. B. Davis, *J. Org. Chem.* **25**, 1884 (1960).
3. J. M. Makosza, *Tetrahedron* **30**, 3723 (1974).
4. A. R. Katritzky and K. S. Laurenzo, *J. Org. Chem.* **51**, 5039 (1986).
5. V. M. Pechenina, N. G. Mukhina, V. G. Klimenko, and V. G. Granik, *Khim. Geterotsikl.. Soedin.*, No. 8, 1082 (1986).
6. K. Schuendehuette, in: Houben-Weyl, *Methoden der Organischen Chemie*, Vol. 10 (1965), No. 3, p. 758.
7. W. E. Noland, L. R. Smith, and D. C. Johnson, *J. Org. Chem.* **28**, 2262 (1963).
8. A. N. Grinev, É. S. Krichevskii, O. B. Romanova, T. Ya. Filipenko, and L. I. Polezhaeva, *Khim.-farm. Zh.*, No. 9, 1066 (1983).
9. A. D. Settimo and M. F. Soettone, *Tetrahedron* **21**, 1923 (1965).

REACTION OF 2,3,3-TRIMETHYL-3H-INDOLE HYDROCHLORIDE WITH METHACRYLIC AND CROTONIC AMIDES

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Reaction of 2,3,3-trimethyl- and 2,3,3,5-tetramethyl-3H-indole hydrochlorides with methacrylic and crotonic amides gives 3- and 4-methyl-1,2,3,4,10,10a-hexahydropyrimido[1,2-a]indol-2-ones. With perchloric acid these are converted to 1-carbamoylpropyl-3H-indolium perchlorates. The syntheses of 10a-(4-dimethylaminostyryl)- and 10a-[(4-dimethylaminophenyl)butadienyl]-3,10,10-trimethylpyrimido[1,2-a]indol-2-ones have been studied.

Reaction of 2,3,3-trimethyl-3H-indole salts with acrylamide in proton containing solvents and workup of the mixture with bases leads to formation of 1,2,3,4,10,10*a*-hexahydropyrimido[1,2-*a*]indol-2-one [1]. Their styryl derivatives have been proposed as color-forming materials in data recording [2, 3].

In our work, we have studied the products of the reaction of 2,3,3-trimethyl- and 2,3,3,5-tetramethyl-3H-indole hydrochlorides with methacrylic and crotonic amides.

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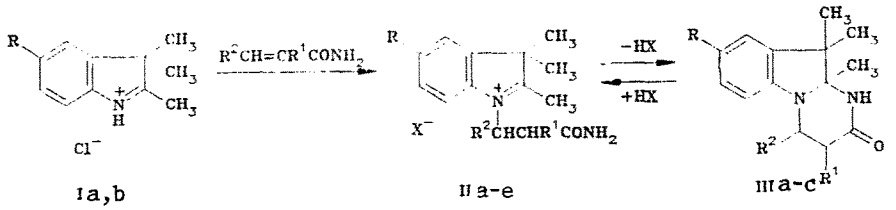
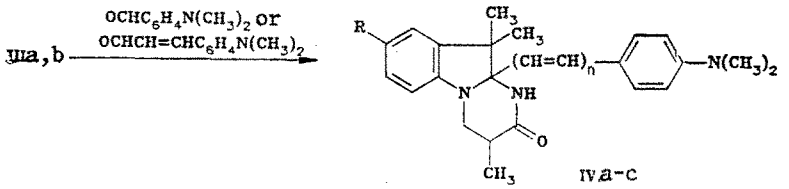


Ia R=H, b R=CH_3; IIa,d IIIa R=R^2=H, R^1=CH_3; IIb, IIIb, R=R^1=CH_3, R^2=H; IIc,e, IIIc R=R^1=H, R^2=CH_3; IIa–c X=CH_3COO, d,e X=ClO_4

Reaction of salts Ia,b with these amides in acetic acid occurs with more difficulty than for acrylamide. Even heating the reaction mixture at 100°C for 10 h leaves a significant part of the starting material unreacted. This is explained by the decreased electrophilic character of the β-carbon atom in the methacrylic and crotonic amides due to the effect of the methyl group [4]. Treatment of adducts IIa-c with bases gives 3- and 4-methyl-1,2,3,4,10,10*a*-hexahydropyrimido[1,2-*a*]indol-2-ones (IIIa–c) in 25–30% yields. They have two asymmetric carbons (C_{10a} and C_3 or C_4) but the PMR spectrum shows only one set of proton signals, thus pointing to the formation of IIIa–c as a single pair of enantiomers [5].

Study of a Dreiding model of IIIa–c shows that the hexahydropyrimidine ring is in a half-chair conformation with the atoms C_2, N_1, C_{10a}, and N_5 approximately planar. The spin-spin coupling for the 3-H and 4-H protons (^3J = 11.0–11.5 Hz, PMR spectrum, $CDCl_3$ solvent) point to predominance of a conformation in which the 3- or 4-methyl groups are equatorial [6].

Workup of IIIa,c with perchloric acid gives 3H-indolium perchlorates IId,e. In their PMR spectra (CF_3COOH solvent) the methylene group appears as the AB part of an ABX spin system. Their diastereotopy is due to the hindered rotation about the single bonds in the carbon chain containing the chiral center.



IVa R=H, n=1, b R=CH_3, *n*=1, c R=H, *n*=2

A method of obtaining 10*a*-styryl-3,10,10-trimethylpyrimido[1,2-*a*]indol-2-ones by reaction of a 2-styryl-3H-indolium salt with methacrylamide has been described in the patent literature [2], but yields and physical constants were not given. By condensing IIIa,b with p-dimethylaminobenzaldehyde and p-dimethylaminocinnamaldehyde in acetic acid and acetic anhydride we obtained 10*a*-(4-dimethylaminostyryl)- and 10*a*-[(4-dimethylaminophenyl)butadienyl]pyrimido[1,2-*a*]indol-2-ones (IVa–c) in 40–65% yields.

EXPERIMENTAL

IR spectra were recorded on a UR-20 spectrometer as KBr tablets and PMR spectra on a Tesla BS-487C (80 MHz) instrument using HMDS as internal standard. Mass spectra were taken on a Riber-1010 machine with direct introduction of the sample into the ion source at 180–190°C and ionization energy of 100 eV. Reaction monitoring and compound purity were carried out using TLC on aluminum oxide plates (grade II) using acetone–hexane (3:5) and iodine vapor visualization.

Elemental analytical data for C, H, and N (Cl) agreed with those calculated.

3,10,10,10*a*-Tetramethyl-1,2,3,4,10,10*a*-hexahydropyrimido[1,2-*a*]indol-2-one (IIIa, $C_{15}H_{20}N_2O$). A solution of hydrochloride Ia (5.87 g, 30 mmoles) and methacrylamide (3.87 g, 45 mmoles) in acetic acid (12 ml) was heated for 10 h at 100°C. The mixture was poured into water (120 ml), basified with a 5% solution of potassium hydroxide, and extracted with ether (2 × 20 ml). The extract was washed with water (2 × 20 ml), dried with calcium chloride, the solvent removed, and the residue crystallized from ether (5 ml) at –5°C to give 2.20 g (30%) with mp 144–145°C (from acetone). IR spectrum: 3190 (N–H), 1660 cm^{-1} (C=O). PMR spectrum ($CDCl_3$): 1.13 (3H, s, 10-CH_3); 1.21 (3H, d, J = 7.2 Hz, 3-CH_3); 1.36 (3H, s, 10-CH_3); 1.53 (3H, s, 10*a*-CH_3); 2.21–2.78 (1H, m, CH); 3.18, 3.76 (2H, AB part of ABX system, $^2J_{AB}$ = 15.0, $^3J_{AX}$ = 6.6, $^3J_{BX}$ = 11.5 Hz, CH_2); 6.70 (1H, br.s, NH); 6.57–7.31 ppm (4H, m, Ar). M^+ 244.

3,8,10,10,10*a*-Pentamethyl-1,2,3,4,10,10*a*-hexahydropyrimido[1,2-*a*]indol-2-one (IIIb, $C_{16}H_{22}N_2O$) was extracted similarly to IIIa from hydrochloride Ib (6.29 g, 30 mmoles) and methacrylamide (3.87 g, 45 mmoles) in a yield of 2.10 g (27%) with mp 157–158°C (from acetone). PMR spectrum ($CDCl_3$): 1.09 (3H, s, 10-CH_3); 1.15 (3H, d, J = 7.2 Hz, 3-CH_3); 1.34 (3H, s, 10-CH_3); 1.50 (3H, s, 10*a*-CH_3); 2.22–2.79 (1H, m, CH); 2.29 (3H, s, 8-CH_3); 3.18, 3.77 (2H, AB part of ABX system, $^2J_{AB}$ = 15.0, $^3J_{AX}$ = 6.6, $^3J_{BX}$ = 11.5 Hz, CH_2); 5.90 (1H, br.s, NH); 6.50-7.05 ppm (3H, m, Ar). M^+ 258.

4,10,10,10*a*-Tetramethyl-1,2,3,4,10,10*a*-hexahydropyrimido[1,2-*a*]indol-2-one (IIIc, $C_{15}H_{20}N_2O$) was obtained similarly to IIIa from hydrochloride Ia (5.87 g, 30 mmoles) and crotonamide (5.11 g, 60 mmoles) in 1.83 g (25%) yield with mp 176–177°C (from alcohol). IR spectrum: 3195 (N–H); 1670 cm^{-1} (C=O). PMR spectrum ($CDCl_3$): 1.08 (3H, s, 10-CH_3); 1.22 (3H, s, 10-CH_3); 1.44 (3H, s, 10*a*-CH_3); 1.62 (3H, d, J = 7.2 Hz, 4-CH_3); 2.29, 2.59 (2H, AB part of ABX system, $^2J_{AB}$ = 17.0, $^3J_{AX}$ = 5.0, $^3J_{BX}$ = 11.0 Hz, CH_2); 3.56–4.08 (1H, m, CH); 6.61–7.43 ppm (4H, m, Ar, NH). M^+ 244.

1-(2-Carbamoylpropyl)-2,3,3-trimethyl-3H-indolium Perchlorate (IId, $C_{15}H_{21}ClN_2O_5$). A solution of IIIa (0.49 g, 2 mmoles) in alcohol (5 ml) was treated with perchloric acid (30%) to pH 2. The mixture was held at –5°C for 18 h and the precipitated solid filtered off and recrystallized from alcohol to give 0.42 g (61%) with mp 164–165°C. IR spectrum: 3455, 3345 (N–H), 1700 (C=O), 1095, 650 cm^{-1} (ClO_4^-). PMR spectrum (CF_3COOH): 1.15 (3H, d, J = 7.3 Hz, $CHCH_3$); 1.23 (6H, s, 3,3-CH_3); 2.54 (3H, s, 2-CH_3); 2.88–3.43 (1H, m, CH); 4.23, 4.55 (2H, AB part of ABX system, $^2J_{AB}$ = 13.5, $^3J_{AX}$ = 5.5, $^3J_{BX}$ = 10.5 Hz, CH_2); 6.75–7.18 (1H, br.s, NH); 7.26–7.51 ppm (4H, m, Ar).

1-(1-Carbamoylprop-2-yl)-2,3,3-trimethyl-3H-indolium perchlorate (IIe, $C_{15}H_{21}ClN_2O_5$) was obtained from IIIc (0.49 g, 2 mmoles) similarly to perchlorate IId in 0.45 g (64%) yield with mp 217–218°C (from alcohol). IR spectrum: 3440, 3340 (N–H), 1695 (C=O), 1095, 650 cm^{-1} (ClO_4^-). PMR spectrum (CF_3COOH): 1.21 (3H, s, 3-CH_3); 1.24 (3H, s, 3-CH_3); 1.53 (3H, d, J = 7.3 Hz, $CHCH_3$); 2.99, 3.34 (2H, AB part of ABX system, $^2J_{AB}$ = 16.0, $^3J_{AX}$ = 5.0, $^3J_{BX}$ = 11.0 Hz, CH_2); 4.93–5.47 (1H, m, CH); 7.18–7.63 ppm (5H, m, Ar, NH).

10*a*-(4-Dimethylaminostyryl)-3,10,10-trimethyl-1,2,3,4,10,10*a*-hexahydropyrimido[1,2-*a*]indol-2-one (IVa, $C_{24}H_{29}N_3O$). A solution of IIIa (1.22 g, 5 mmoles) and p-dimethylaminobenzaldehyde (0.75 g, 5 mmoles) in a mixture of acetic acid (6 ml) and acetic anhydride (0.2 ml) was heated for 2 h at 95°C. The mixture was poured into water (100 ml) and potassium hydroxide solution (5%) added until basic. The precipitate was filtered, dried, and recrystallized from acetone to give 1.20 g (64%) of IVa with mp 208–209°C. IR spectrum: 3200 (N–H), 1670 cm^{-1} (C=O). PMR spectrum ($CDCl_3$): 1.13 (3H, d, J = 7.2 Hz, 3-CH_3); 1.19 (3H, s, 10-CH_3); 1.35 (3H, s, 10-CH_3); 2.43–3.88 (3H, m, $CHCH_2$); 3.00 (6H, s, N,N-CH_3); 6.10–7.43 ppm (11H, m, Ar, CH=CH, NH).

10*a*-(4-Dimethylaminostyryl)-3,8,10,10-tetramethyl-1,2,3,4,10,10*a*-hexahydropyrimido[1,2-*a*]indol-2-one (IVb, $C_{25}H_{31}N_3O$) was obtained from IIIb (1.29 g, 5 mmoles) and p-dimethylaminobenzaldehyde (0.75 g, 5 mmoles) similarly to IVa in 1.26 g (65%) yield with mp 216–217°C (from acetone). PMR spectrum ($CDCl_3$): 1.10 (3H, d, J = 7.2 Hz, 3-CH_3); 1.15 (3H, s, 10-CH_3); 1.30 (3H, s, 10-CH_3); 2.30 (3H, s, 8-CH_3); 2.43–3.88 (3H, m, $CHCH_2$); 3.00 (6H, s, N,N-CH_3); 6.08–7.43 ppm (10H, m, Ar, CH=CH, NH).

10*a*-[(4-Dimethylaminophenyl)butadienyl]-3,10,10-trimethyl-1,2,3,4,10,10*a*-hexahydropyrimido-[1,2-*a*]indol-2-one (IVc, $C_{26}H_{31}N_3O$) was obtained from IIIa (0.49 g, 2 mmoles) and p-dimethylaminocinnamaldehyde (0.35 g, 2 mmoles) similarly to IVa in 0.32 g (40%) yield with mp 237–238°C (from acetone). PMR spectrum ($CDCl_3$): 1.11 (3H, d, J = 7.2 Hz, 3-CH_3); 1.12 (3H, s, 10-CH_3); 1.30 (3H, s, 10-CH_3); 2.36-3.88 (3H, m, $CHCH_2$); 2.97 (6H, s, N,N-CH_3); 5.76–7.46 ppm (13H, m, Ar, CH=CH–CH=CH, NH).

LITERATURE CITED

1. A. A. Shachkus and R. Yu. Dyagutite, *Khim. Geterotsikl. Soedin.*, No. 8, 1056 (1986).
2. H. Psaar, German Patent No. 2,510,238; *Russ. Zh. Khim.*, 17N268P (1977).
3. A. A. Shachkus, A. V. Vannikov, A. D. Grishina, A. Yu. Kryukov, R. Yu. Dyagutite, and Yu. I. Kozhenyauskaite, USSR Inventor's Certificate No. 1,101,442; *Byull. Izobret.*, No. 25, 57 (1984).
4. S. I. Suminov and A. N. Kost, *Usp. Khim.* 38, 1933 (1969).
5. K. Blaga, O. Chervinka, and Ya. Kovar, *Basic Stereochemistry and Conformational Analysis* [in Russian], Khimiya, Leningrad (1974), p. 15.
6. A. Gaudemer, "Determination of configuration by NMR spectroscopy," in: *Stereochemistry*, H. Kagan (ed.), Vol. 1, George Thieme, Stuttgart (1977), p. 44.