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INTERACTION OF 2-AMINOINDOLES WITH TETRACYANOETHYLENE. 2.* 3-DICYANOMETHYLENE-2-IMINOINDOLINES

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3-Dicyanomethylene-2-iminoindolines are obtained on interacting 2-aminoindoles with tetracyanoethylene in acidic medium.

Keywords: 2-aminoindoles, 3-dicyanomethylene-2-iminoindolines, α-carbolines, malononitrile, tetracyanoethylene.

We reported previously [1], that on interacting 2-aminoindoles **1** with tetracyanoethylene **2** in neutral or weakly alkaline medium 3,4-dicyano-2-imino-1,2-dihydro-α-carbolines **3** or 2-amino-3,4-dicyano-α-carbolines **3'** are formed. However, according to [2] the oxygen analogs of 2-aminoindoles, the oxindoles, react with compound **2** differently, forming 3-dicyanomethylene derivatives. Assuming that in these processes the acidity of the medium is important, we attempted to obtain dicyanomethylene derivatives of 2-aminoindoles under other conditions.

It turned out that on heating 2-aminoindoles **1a-c** with compound **2** in an acidic medium for 10-60 min in reality the expected 3-dicyanomethylene-2-iminoindolines **4a-c** are formed in good yield. They are easily purified, and are well crystallizing compounds, colored an intense red-violet. In their IR spectra (Table 1) bands were present for the stretching vibrations of conjugated C≡N groups and absorption bands for N–H bonds were absent. The ^{1}H and ^{13}C NMR spectra did not contradict the proposed structure, and in the mass spectra (Table 1) there was the expected peak for the molecular ion. The fragmentation confirmed the proposed structures.

The shade of the coloring of solutions of these compounds depends on the solvent used. Solutions in chloroform and dichloromethane have a red-violet color, but in oxygen-containing solvents (alcohol, acetone, dioxane, DMSO) they are red. The positions of the absorption band maxima in the UV spectra of compounds **4a,c** in DMSO and chloroform are practically unchanged, but in DMSO the absorption in the long wave portion of the spectrum is significantly weakened, and on the other hand the trough between the absorption bands at $\lambda \approx 430$ nm (Fig. 1) is reduced, which leads to a weakening of the blue component of the color. The reason for this effect may probably be coordination of one solvent molecule with the carbon atoms of both nitrile groups of the **4** molecule. Such coordination must lead to some disturbance of the planarity of the dicyanomethylene fragment and consequently to a reduction in the conjugation in molecule **4**.

* For Part 1 see [1].

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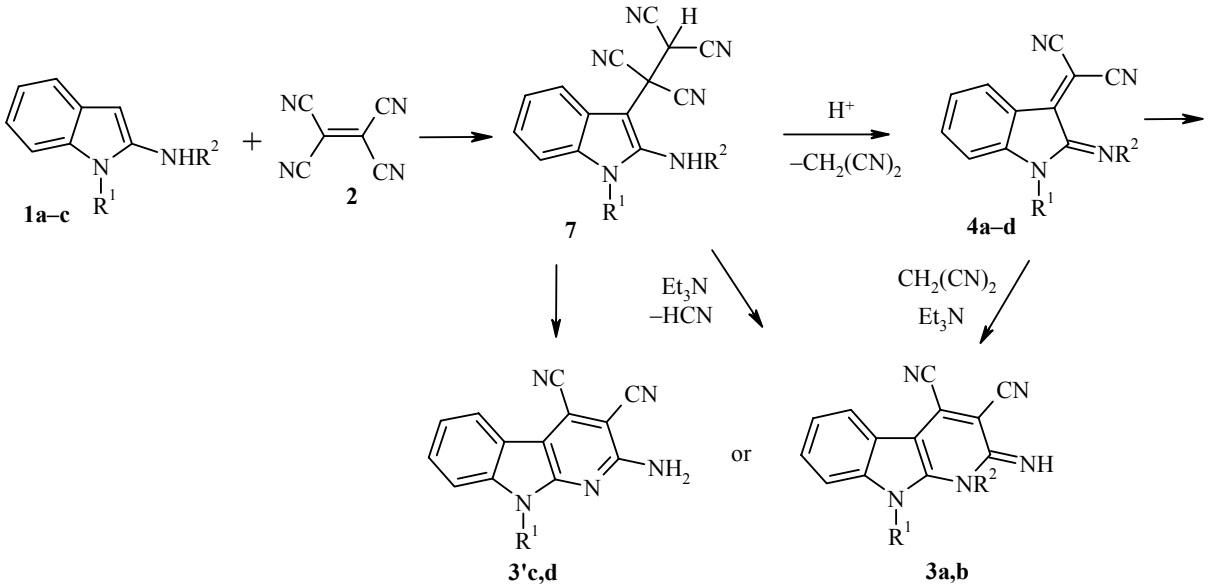
TABLE 1. Spectral Data of Compounds **4a-d** and **5**

Compound	IR spectrum, ν, cm^{-1}	Masspectrum, *m/z* (I_{rel}, %)
4a	2225, 2215, 1645, 1610	235 $[M+1]^+$ (13), 234 $[M]^+$ (95), 233 $[M–H]^+$ (60), 232 $[M–H_2]$ (30), 231 $[M–H–H_2]^+$ (20), 208 [M–CN] (25), 207 $[M–HCN]^+$ (45), 206 $[M–H–HCN]^+$ (55), 179 $[M–H–2HCN]^+$ (100), 151 $[179–H_2CN]^+$ (100)
4b	2225, 2220, 1650, 1610	249 $[M+1]^+$ (15), 248 $[M]^+$ (100), 247 $[M–H]^+$ (16), 233 $[M–CH_3]^+$ (38), 220 $[M–H–HCN]^+$ (14.5), 218* [247 → 233], 208 $[M–HC{\equiv}CCH_3]^+$ (14.5), 207 $[M–H–HC{\equiv}CCH_3]^+$ (14.5), 206 [M–$CH_3CH{=}CH_2$ and 207–$H]^+$ (62), 179 $[206–HCN]^+$ (43.5), 175* [248 → 208], 171* [248 → 206], 156* [206 → 179], 153 $[179–CN]^+$ (17), 152 $[179–HCN]^+$ (52), 129* [248 → 179]
4c	2240, 1640, 1610, 1330, 1160	363 $[M+1]^+$ (10), 362 $[M]^+$ (55), 298 $[M–C_3N_2]^+$ (97), 283 $[M–C_3N_2–CH_3]^+$ (100), 272 $[M+H–C_7H_7]^+$ (19), 192 $[M–TsNH]^+$ (14), 181 $[TsNC]^+$ (23), 105 (19)
4d	3320, 3270, 2250, 2230, 1630, 1340, 1190	348 $[M]^+$ (13), 285 $[M+H–C_3N_2]^+$ (13), 284 $[M–C_3N_2]^+$ (66), 283 $[M–HC(CN)_2]^+$ (55), 269 (32), 258 $[M+H–C_6H_6N]^+$ (15), 194 $[M+H–Ts]^+$ (33), 168 $[TsN–H]^+$ (17), 167 $[TsN–2H]^+$ (26), 155 $[Ts]^+$ (10), 154 $[Ts–H]^+$ (63), 92 $[C_6H_6N]^+$ (48), 91 $[C_6H_5N]^+$ (100), 65 $[HC(CN)_2]^+$ (60), 64 $[C_3N_2]^+$ (14)
5	3400, 3360, 3290, 3240, 2220, 1600, 1380, 1320, 1150	416 $[M]^+$ (8), 415 $[M–H]^+$ (35), 261 $[M–Ts]^+$ (20), 260 $[M–TsH]^+$ (100), 247 $[M–TsN]^+$ (11), 233 $[260–HCN]^+$ (27), 231 (12), 205 (14), 156 (10), 130 $[260/2]^+$ (25), 129 (14), 123 (11), 111 (13), 110 (15), 103 (11), 99 (11), 98 (21), 97 (10), 96 (27), 93 (14), 92 (42), 86 (17), 85 (14), 84 (28), 83 (14), 82 (27), 79 (13), 78 (25), 77 (27), 76 (15), 72 (19), 70 (34), 69 (13), 68 (38), 66 (20), 63 (16), 62 (26), 57 (22), 53 (57), 52 (21), 51 (56)



a $R^1+R^2 = –(CH_2)_3–$; **b** $R^1+R^2 = –CH_2CH(Me)CH_2–$; **c** R^1 = Me, R^2 = Ts; **d** R^1 = H, R^2 = Ts

In the case of derivative **1d** the reaction requires far more extended boiling (2-3 days) with periodical addition of tetracyanoethylene **2**, probably as a result of the lower solubility of the starting material. Nonetheless the characteristic color of the reaction mixture appears in the first minutes of the reaction, as in the cases of

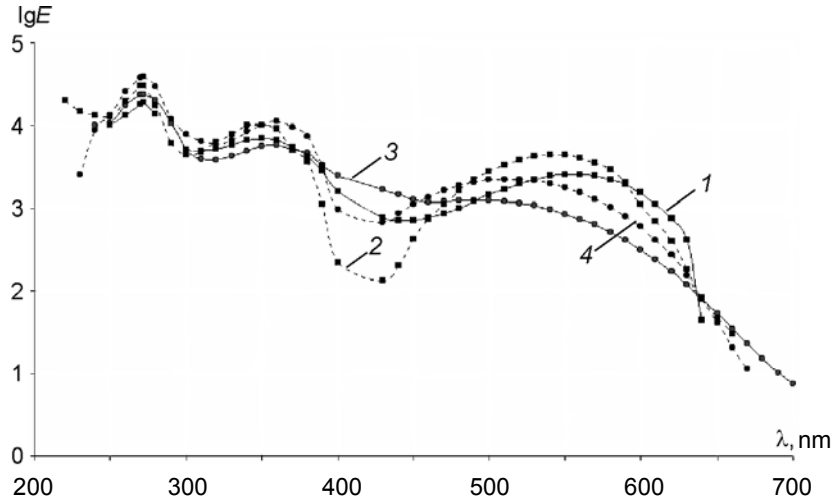
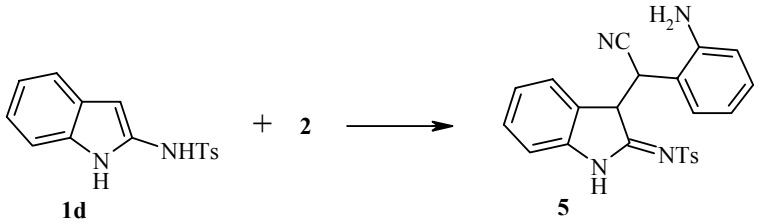


Fig. 1. UV spectra of compounds **4a,c** in DMSO (*1* - **4a**, *3* - **4c**) and $CHCl_3$ (*2* - **4a**, *4* – **4c**).

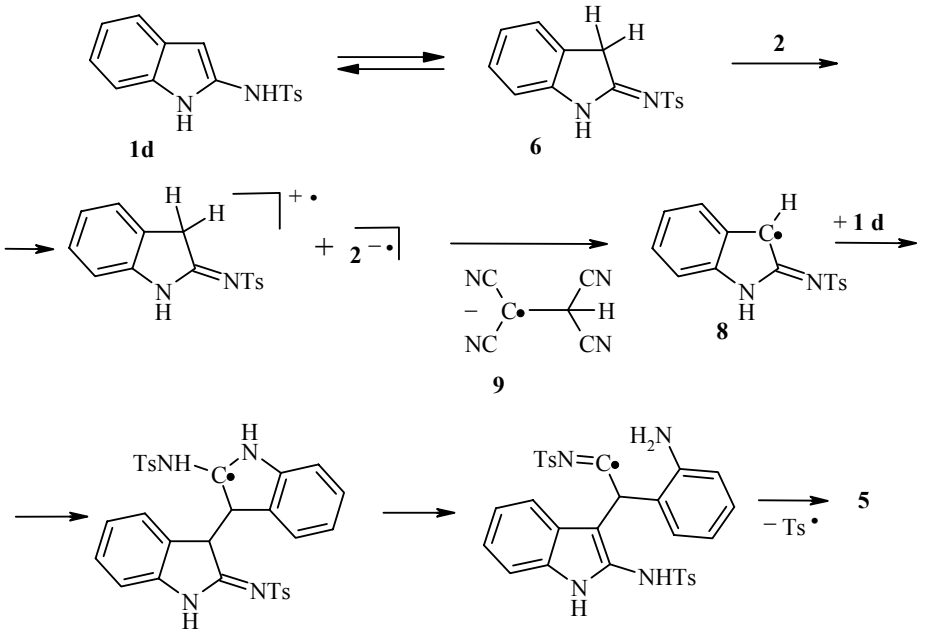
compounds **1a-c**. Attempts to isolate compound **4d** by column chromatography, undertaken 1 h after the start of the reaction, led to the obtaining of a small quantity (0.016 g) of a colored compound, which in combination with the spectral data has structure **5**.



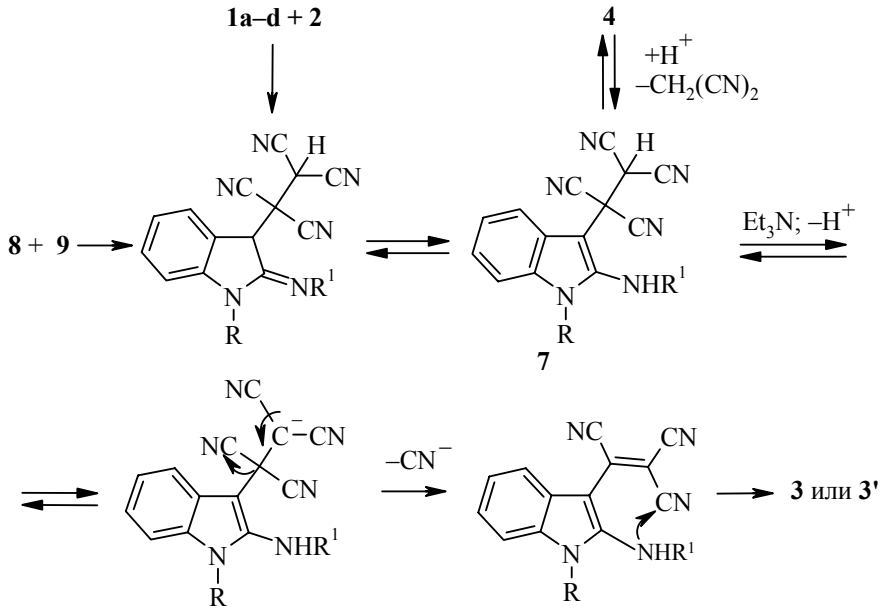
Compound **5** is constructed from two molecules of the initial aminoindole **1d**, one of which has lost a tosyl group and has undergone fission of the pyrrole ring. We note that in the first few seconds after adding compound **2** to the solution of aminoindoles a deep blue coloration develops, characteristic of anion-radicals **2** (see, for example [3]), which then changes to red, characteristic of compounds **4** and **5**. It is known that in solutions of aminoindoles a tautomeric equilibrium exists between the aminoindole and the iminoindoline forms **1** and **6** [4]. Furthermore aminoindoles are capable of radical reactions, for example with oxygen [5]. Consequently it may be suggested that the reaction forming compound **5** begins with a one-electron transfer, after which follows proton exchange, interaction with a second molecule of **1d**, opening of the ring, and stabilization of the reaction product (Scheme 1).

Unlike this anomalous process compounds **3** and **4** have a common precursor, adduct **7**. Together with the usual scheme of its formation by electrophilic addition it is possible to suggest the parallel occurrence of a radical process, causing the characteristic coloration in the intermediate stages. Adduct **7** is a strong acid, in neutral or basic medium it undergoes dissociation, after which cyanide ion is discarded and the molecule is stabilized as a result of intramolecular cyclization with the formation of compound **3** (or **3'**). If also the ionization of acid **7** is suppressed by the addition of a stronger acid, then the stabilization comes as a result of the ejection of a molecule of malononitrile and the formation of compound **4** (Scheme 2).

Scheme 1



Scheme 2



This scheme for the process is confirmed by the following observations.

1) Malononitrile is detected by TLC among the reaction products when obtaining compound **4**.

2) The yield of compounds **4c,d** depends on the acid used. In the presence of dilute acetic acid compound **4** is not formed, and only carbolines **3'c,d** (with loss of the tosyl group) are obtained. In the presence of the stronger chloroacetic and trichloroacetic acids the main reaction products are iminoindolines **4** and the

yield of carbolines **3'** is insignificant. The use of hydrochloric acid causes resinification of the reaction mixture as a result of hydrolytic processes, but on using anhydrous hydrochlorides of **1a,b** the reaction proceeds smoothly, without resinification.

3) On boiling compound **4c** with malononitrile in dioxane in the presence of Et_3N, the very same carboline **3'c** is formed in good yield, as in the case of the direct synthesis from aminoindole **1c** [1] (pathway is **1** → **7** → **3'**).

EXPERIMENTAL

A check on the progress of reactions and the purity of the synthesized products was effected by TLC on Silufol UV 254 plates, visualization was with UV radiation or iodine vapor. The IR spectra were recorded on a UR 20 instrument (nujol). The UV spectra were obtained on a Specord M 40 instrument. The ^{1}H NMR spectra were taken on a Bruker MV 250 (250 MHz) or a Bruker AM 300 (300 MHz) instrument, and ^{13}C NMR spectra on a Varian 400 (80 MHz) instrument, internal standard was TMS. Mass spectra (EC, 70 eV) were obtained on a Varian MAT 111 instrument with insertion of samples into the ion source.

Commercially available tetracyanoethylene was additionally purified before use by recrystallization from dioxane and dried at room temperature and atmospheric pressure to break down any solvate formed.

Compounds **1a,b** were obtained as described in [6], and compounds **1c,d** by the procedure of [7].

3-Dicyanomethylene-2-iminoindolines 4a-d (General Procedure). An excess (1.2 mmol) of crystalline **2** was added in small portions during 10-30 min with stirring to a solution of **1a,b** hydrochloride (1 mmol) in boiling 2-propanol (30 ml), and the whole boiled for 1 h. The mixture was cooled, the solid was filtered off, washed with 2-propanol, with ether, and recrystallized from $CHCl_3$ with a hot filtration or a solution in $CHCl_3$ was passed through silica gel. Compounds **4c,d** were obtained analogously from **1c,d** bases with addition to the reaction mixture of catalytic amounts of chloroacetic or trichloroacetic acids. To obtain compound **4d** the reaction mixture was boiled for 2-3 days, periodically adding crystalline compound **2** until the disappearance of the initial **1d**.

2-(3,4-Dihydro-2H-pyrimido[1,2-*a*]indol-10-ylidene)malononitrile (4a). Yield 52%; mp 223-225°C (decomp., from $CHCl_3$); R_f 0.3 ($CHCl_3$). Found, %: C 71.55; H 4.22; N 24.15. $C_{14}H_{10}N_4$. Calculated, %: C 71.78; H 4.30; N 23.92.

2-(3-Methyl-3,4-dihydro-2H-pyrimido[1,2-*a*]indol-10-ylidene)malononitrile (4b). Yield 49%; mp 210-212°C ($CHCl_3$); R_f 0.47 ($CHCl_3$). ^{13}C NMR (CD_2Cl_2), δ, ppm: 152.0, 150.9, 147.95, 137.5, 126.1, 121.2, 113.85, 118.9, 107.4, 53.65, 45.65, 25.4, 16.35. Found, %: C 72.22; H 4.62; N 22.83. $C_{15}H_{12}N_4$. Calculated, %: C 72.56; H 4.87; N 22.57.

2-(1-Methyl-2-tosyliminoindol-3-ylidene)malononitrile (4c). Yield 72%; mp 269-271°C ($CHCl_3$); R_f 0.46 ($CHCl_3$), 0.67 (benzene–methanol, 10:1). ^{1}H NMR spectrum (CD_2Cl_2), δ, ppm (*J*, Hz): 8.2 (1H, d, *J* = 8, H-4); 7.9 and 7.4 (4H, 2d, *J* = 7, $CH_3C_6\underline{H}_4SO_2$); 7.7 (1H, t, *J* = 8, H-6); 7.25 (1H, t, *J* = 8, H-5); 7.05 (1H, d, *J* = 8, H-7); 3.85 (3H, s, NCH_3); 2.45 (3H, s, CH_3). ^{13}C NMR spectrum (CD_2Cl_2), δ, ppm: 153.3, 147.3, 142.9, 137.4, 129.1, 126.9, 126.2, 124.8, 110,6, 110.3, 32.9, 21.3. Found, %: C 63.12, H 4.09; N 15.44. $C_{19}H_{14}N_4O_2S$. Calculated, %: C 62.97; H 3.89; N 15.46.

2-(2-Tosyliminoindol-3-ylidene)malononitrile (4d). Yield 88%; mp >300°C ($CHCl_3$). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm (*J*, Hz): 11.6 (1H, br. s, NH); 8.05 (1H, d, *J* = 7, H-4); 7.9 and 7.4 (4H, 2d, *J* = 7, $CH_3C_6\underline{H}_4SO_2$); 7.6 (1H, t, *J* = 7, H-6); 7.3 (1H, d, *J* = 7, H-7); 7.15 (1H, t, *J* = 7, H-5); 2.5 (3H, s, CH_3). Found, %: C 61.87; H 3.62; N 16.11. $C_{18}H_{12}N_4O_2S$. Calculated, %: C 62.06; H 3.47; N 16.08.

N-{3-[(2-Aminophenyl)cyanomethyl]-1H-indol-2-yl}-4-methylbenzenesulfonamide (5). Tetracyanoethylene **2** (0.16 g, 1.26 mmol) was added in portions with stirring to a suspension of compound **1d** (0.3 g, 1.05 mmol) in hot 2-propanol (30 ml), and the mixture stirred with heating for 1 h. The solvent was distilled in

vacuum, the residue was dissolved in chloroform, and chromatographed on a column of silica gel. A red-violet compound was isolated. Yield 0.016 g (7%); mp 312-314°C ($CHCl_3$). Found, %: C 66.02; H 5.12; N 13.50. $C_{23}H_{20}N_4O_2S$. Calculated, %: C 66.33; H 4.84; N 13.45.

2-Amino-9-methyl-9*H*-pyrido[2,3-*b*]indole-3,4-dicarbonitrile (3'c). A mixture of indole **4c** (0.36 g, 1 mmol) and malononitrile (0.13 g, 2 mmol) in dioxane (30 ml) in the presence of Et_3N (0.26 ml, 2 mmol) was stirred and boiled until disappearance of the starting material (2-3 h). The reaction mixture was cooled, and treated with an excess of glacial acetic acid. The solid was filtered off, washed with dioxane, and recrystallized from glacial acetic acid. Carboline **3'c** (0.18 g, 72%) was obtained, the properties of which conformed with those described previously in [1].

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