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SHORT COMMUNICATIONS

Synthesis of 2'-Oxo-1',2'-dihydrospiro[cyclopropane-1,3'-indole]-2,2,3,3-tetracarbonitriles

O. V. Kayukova, Ya. S. Kayukov, E. S. Lapteva, I. N. Bardasov, O. V. Ershov, and O. E. Nasakin

I.N. Ul'yanov Chuvash State University, Moskovskii pr. 15, Cheboksary, 428015 Russia
e-mail: kajukov@cbx.ru

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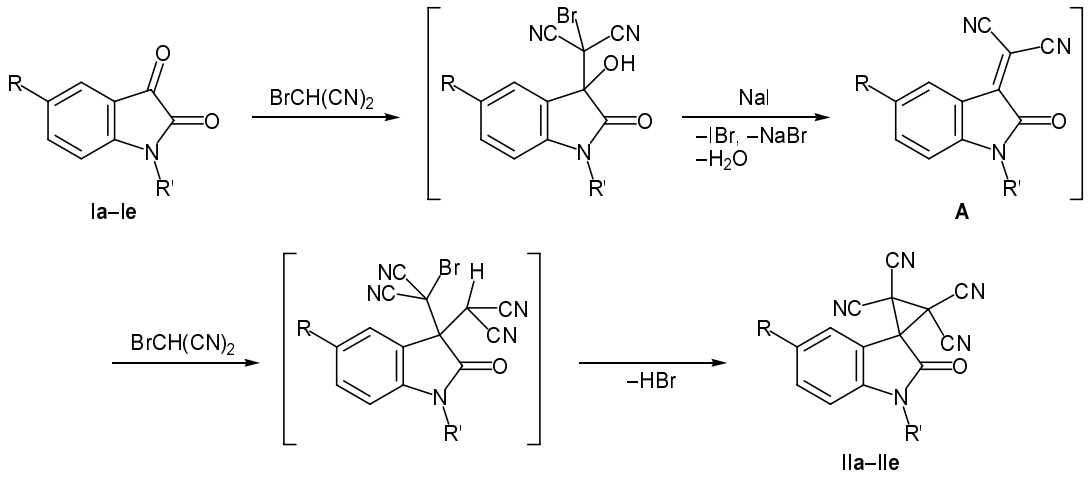
Isatin and numerous derivatives of indole, quinoline, and other heterocycles obtained therefrom have found diverse applications in practice [1, 2]. A considerable part of explored isatin derivatives includes compounds in which the indole ring is spiro-fused to various hetero- and carbocycles at the 3-position. We now propose a new method for isatin modification via Wideqvist reaction to obtain indole derivatives having a tetracyanocyclopropane ring fused at the 3-position. Methods based on this reaction [3, 4] are known to have some limitations related to spatial accessibility and reactivity of the carbonyl group; for example, derivatives of camphor and aromatic ketones cannot be synthesized in such a way. We have found that isatin and 1,5-substituted isatins **Ia**–**Ie** readily react with bromomalononitrile in isopropyl alcohol and that the subsequent treatment with an aqueous solution of sodium iodide leads to the formation of the corresponding spiro-cyclopropane derivatives, 2'-oxo-1',2'-dihydrospiro[cyclopropane-1,3'-indole]-2,2,3,3-tetracarbonitriles **IIa**–**IIe**.

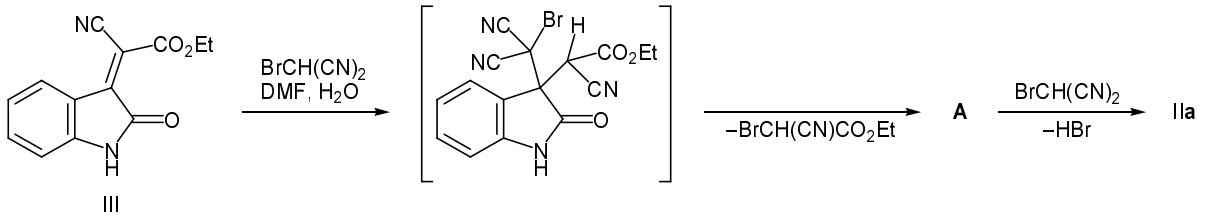
Presumably, the mechanism of this reaction includes formation of intermediate dicyanomethylidene derivatives **A** which are readily accessible compounds (Scheme 1). Their application in the synthesis of tetracyanocyclopropanes should make it possible to avoid the use of relatively expensive iodides and reduce the consumption of bromine. 2-(2-Oxo-2,3-dihydro-1*H*-indol-3-ylidene)malononitriles failed to react with bromomalononitrile in isopropyl alcohol or dioxane, probably because of their insufficient solubility. We succeeded in effecting this transformation in dimethyl-

Scheme 1.



R = R' = H (**a**); R = Me, R' = H (**b**); R = H, R' = $EtOCOCH_2$ (**c**), $PhCH_2$ (**d**), MeCO (**e**).

Scheme 2.



formamide with subsequent addition of water. We also found that substituted cyclopropanes **IIa**–**IIe** can be obtained in high yield by reaction of isatins **Ia**–**Ie** with excess bromomalononitrile in aqueous dimethylformamide without addition of sodium iodide. Here, bromomalononitrile is likely to act as reducing agent, being converted into dibromomalononitrile.

We also made an attempt to synthesize an analog of **IIa** in which one cyano group is replaced by ester moiety. For this puprose, ethyl cyano(2-oxo-2,3-dihydro-1*H*-indol-3-ylidene)acetate (**III**) was brought into reaction with bromomalononitrile in aqueous dimethylformamide. However, the isolated product was compound **IIa**. Presumably, the cyano(ethoxycarbonyl)methylidene fragment is replaced by dicyanomethylidene during the process (Scheme 2).

The structure of spiro-fused cyclopropanes **IIa**–**IIe** was confirmed by their IR, ^{1}H NMR, and mass spectra and analytical data.

2'-Oxo-1',2'-dihydrospiro[cyclopropane-1,3'-indole]-2,2,3,3-tetracarbonitrile (IIa). *a*. Isatin (**Ia**), 1.33 g (0.01 mol), was dispersed in 10 ml of propan-2-ol, 2.9 g (0.02 mol) of bromomalononitrile was added, the mixture was stirred until it became homogeneous, and a solution of 4.5 g (0.03 mol) of sodium iodide in 20 ml of water was added. The mixture was stirred and was left to stand for 2 h. The precipitate was filtered off, washed with cold propan-2-ol, recrystallized, and dried in a vacuum desiccator. Yield 1.83 g (75%), mp 143–144°C (decomp., from propan-2-ol). IR spectrum, ν, cm^{-1}: 2260 (C≡N), 1695 (C=O). ^{1}H NMR spectrum, δ, ppm: 11.48 s (1H, NH), 7.52 t (1H, C_6H_4), 7.28–7.18 m (2H, C_6H_4), 7.08 d (1H, C_6H_4). Mass spectrum, *m*/*z* (I_{rel}, %): 259 (95) $[M]^+$, 232 (30) $[M - 27]^+$, 216 (60), 204 (25), 195 (100), 189 (30), 168 (50), 140 (55). Found, %: C 65.06; H 2.07; N 26.82. $C_{14}H_5N_5O$. Calculated, %: C 64.87; H 1.94; N 27.02.

b. 2-(2-Oxo-2,3-dihydro-1*H*-indol-3-ylidene)malononitrile, 1.71 g (0.01 mol), was dissolved in 2 ml of dimethylformamide, 2.9 g (0.02 mol) of bromomalononitrile was added, the mixture was stirred until it became homogeneous, and 0.5 ml of water was added. The mixture was stirred until it became almost colorless, diluted with 50 ml of water, and left to stand for about 2 h until the separated oily material crystallized. The pink precipitate was filtered off, washed with cold propan-2-ol, recrystallized, and dried in a vacuum desiccator. Yield 2.38 g (92%).

c. Isatin (**Ia**), 1.33 g (0.01 mol), and bromomalononitrile, 4.35 g (0.03 mol), were mixed in 3 ml of cold dimethylformamide, the mixture was stirred until it became homogeneous, 0.5 ml of water was added, the mixture was stirred for 15 min, and 50 ml of water and 5 ml of propan-2-ol were added. A red oily material separated; after 2–3 h, it turned colorless and crystallized. The product was filtered off, washed with propan-2-ol, and dried in a vacuum desiccator until constant weight. Yield 2.33 g (90%).

d. The procedure was the same as described above in *b*, but ethyl 2-cyano-2-(2-oxo-2,3-dihydro-1*H*-indol-3-ylidene)acetate was used instead of dicyanomethylidene isatin derivative. The oily material crystallized over a period of 24 h. Yield 1.63 g (63%).

Compounds **IIb**–**IIe** were synthesized as described for **IIa**, method *a*.

5'-Methyl-2'-oxo-1',2'-dihydrospiro[cyclopropane-1,3'-indole]-2,2,3,3-tetracarbonitrile (IIb). Yield 84%, mp 202–203°C (decomp.). IR spectrum, ν, cm^{-1}: 2270 (C≡N), 1690 (C=O). ^{1}H NMR spectrum, δ, ppm: 11.4 s (1H, NH), 7.3 t (1H, C_6H_3), 7.05–6.95 m (2H, C_6H_3), 2.3 s (3H, CH_3). Mass spectrum, *m*/*z* (I_{rel}, %): 273 (95) $[M]^+$, 258 (100) $[M - 15]^+$, 245 (25), 229 (20), 209 (60), 182 (25), 165 (15), 153 (20). Found, %: C 65.35; H 2.61; N 25.55. $C_{15}H_7N_5O$. Calculated, %: C 65.33; H 2.58; N 25.63.

Ethyl 2-(2,2,3,3-tetracyano-2'-oxo-1',2'-dihydrospiro[cyclopropane-1,3'-indol]-1'-yl)acetate (IIc). Yield 78%, mp 168–169°C (decomp.). IR spectrum, ν, cm^{-1}: 2270 (C≡N); 1725, 1690 (C=O). ^{1}H NMR spectrum, δ, ppm: 7.6 t (1H, C_6H_4), 7.32–7.28 m (3H, C_6H_4), 4.7 s (2H, 1'-CH_2), 4.2 m (2H, OCH_2), 1.25 t (3H, $CH_2C\mathbf{H}_3$). Mass spectrum, *m*/*z* (I_{rel}, %): 345 (35) $[M]^+$, 281 (10), 272 (90), 245 (30), 218 (30), 208

(100), 190 (20), 180 (40), 153 (30). Found, %: C 62.68; H 3.17; N 20.33. $C_{18}H_{11}N_5O_3$. Calculated, %: C 62.61; H 3.21; N 20.28.

1'-Benzyl-2'-oxo-1',2'-dihydrospiro[cyclopropane-1,3'-indole]-2,2,3,3-tetracarbonitrile (IId). Yield 72%, mp 171–172°C (decomp.). IR spectrum, ν, cm^{-1}: 2260 (C≡N), 1685 (C=O). ^{1}H NMR spectrum, δ, ppm: 7.54–7.50 m (3H), 7.42–7.38 t (2H), 7.32–7.30 (2H), 7.26–7.24 t (1H), and 7.14–7.10 d (1H) (C_6H_4, C_6H_5), 5.05 s (2H, C**H**$_2$C$_6$H$_5$). Mass spectrum, *m*/*z* (I_{rel}, %): 349 (15) $[M]^+$, 91 (100). Found, %: C 72.52; H 3.09; N 20.11. $C_{21}H_{11}N_5O$. Calculated, %: C 72.20; H 3.17; N 20.05.

1'-Acetyl-2'-oxo-1',2'-dihydrospiro[cyclopropane-1,3'-indole]-2,2,3,3-tetracarbonitrile (IIe). Yield 72%, mp 142–143°C (decomp.). IR spectrum, ν, cm^{-1}: 2260 (C≡N); 1690, 1680 (C=O). ^{1}H NMR spectrum, δ, ppm: 8.30 d (1H, C_6H_4), 7.72–7.68 t (1H, C_6H_4), 7.52–7.48 t (1H, C_6H_4), 7.42–7.38 d (1H, C_6H_4), 2.71 s (3H, CH_3). Mass spectrum, *m*/*z* (I_{rel}, %): 301 (3) $[M]^+$, 259 (30), 216 (3), 195 (10), 168 (3), 140 (30), 113 (4), 87 (2), 77 (3), 64 (2), 43 (100). Found, %: C 63.87; H 2.42; N 23.34. $C_{16}H_7N_5O_2$. Calculated, %: C 63.79; H 2.34; N 23.25.

The purity of the products was checked by TLC on Silufol UV-254 plates; spots were visualized by UV irradiation, treatment with iodine vapor, or heating. The IR spectra were recorded on a UR-20 spectrometer from samples dispersed in mineral oil. The ^{1}H NMR spectra were measured on a Bruker DRX-500 instrument at 500.13 MHz using DMSO-d_6 as solvent and TMS as internal reference. The mass spectra (electron impact, 70 eV) were obtained on a Finnigan MAT INCOS-50 spectrometer.

REFERENCES

1. Sumpter, W.C., *Chem. Rev*., 1944, vol. 34, p. 407.
2. Popp, F.D., *Adv. Heterocycl. Chem*., 1975, vol. 18, p. 1.
3. Hart, H. and Freeman, F., *J. Org. Chem*., 1963, vol. 28, p. 1220.
4. Freeman, F., *Synthesis*, 1981, p. 925.