

SHORT  
COMMUNICATIONSSynthesis of 5-Amino-3*H*-pyrrole-3,4-dicarbonitriles  
from 4-Aryl-4-oxobutane-1,1,2,2-tetracarbonitriles

M. Yu. Belikov, O. V. Ershov, I. V. Lipovskaya, A. V. Eremkin, and O. E. Nasakin

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

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It is known that 4-oxoalkane-1,1,2,2-tetracarbonitriles react with nitrogen-centered nucleophiles, such as ammonia and amines, to give 3-amino-7-oxo-4,6-diazabicyclo[3.2.1]oct-2-ene-1,2-dicarbonitriles [1], 3-amidinio-2-aminopyridine-4-carboxylates [2], diethylammonium 3,4-dicyano-5,6,7,8-tetrahydroquinolin-2-olates [3], and ammonium 4-aryl-4-oxo-1,1,2-tricyanobut-2-en-1-ides [4]. However, these results do not allow us to draw a definite conclusion on the direction of attack by N-nucleophiles on the reaction centers in polyelectrophilic 4-oxoalkane-1,1,2,2-tetracarbonitriles.

While continuing studies on reactions of tetracyanoethylated ketones with N-nucleophiles, we found that 4-aryl-4-oxobutane-1,1,2,2-tetracarbonitriles **Ia–Ic** react with morpholine to produce 80–93% of previously unknown 5-amino-3-(2-aryl-2-oxoethyl)-2-morpholino-3*H*-pyrrole-3,4-dicarbonitriles **IIa–IIc**.

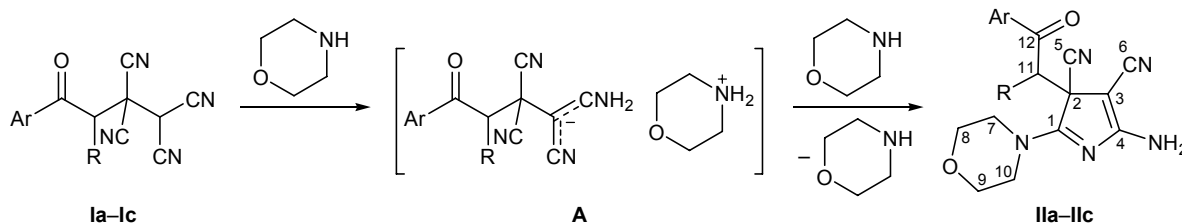
Presumably, the initial step in this reaction is formation of morpholinium salt **A** with CH acid **Ia–Ic**. Analogous salts containing metal and ammonium ions as cationic species have been reported [4–6]. Salts **A** undergo further transformations by the action of excess morpholine. These transformations involve primarily the β-cyano group, as follows from the presence of morpholine fragment in position 2 of the 3*H*-pyrrole

ring in **IIa–IIc**. Attack on the β-cyano group is determined by reduced electrophilicity of the terminal cyano groups due to delocalization of the negative charge in the anion of salt **A**. 3*H*-Pyrrole **IIc** possesses two asymmetric carbon atoms (C<sup>2</sup>, C<sup>11</sup>), but this compound was isolated as a single diastereoisomer.

The structure of pyrroles **IIa–IIc** was confirmed by their IR, <sup>1</sup>H and <sup>13</sup>C NMR, and mass spectra and elemental analyses. The structure of compound **IIa** was unambiguously proved by the X-ray diffraction data.

**General procedure for the synthesis of compounds IIa–IIc.** A solution of 0.5 mmol of 4-aryl-4-oxobutane-1,1,2,2-tetracarbonitrile **Ia–Ic** in 3 ml of anhydrous ethyl acetate was cooled to –10 to –15°C, 0.087 g (1 mmol) of morpholine was added under vigorous stirring, and the resulting yellow–orange solution was left to stand at –10 to –15°C in a closed vessel. After 2–3 days, the yellowish precipitate was filtered off, washed on a filter with cold ethyl acetate and diethyl ether, and dried in air.

**5-Amino-2-morpholino-3-(2-oxo-2-phenylethyl)-3*H*-pyrrole-3,4-dicarbonitrile (IIa).** Yield 0.156 g (93%), mp 208–209°C (decomp.). IR spectrum, ν, cm<sup>–1</sup>: 3184–3311 (NH<sub>2</sub>); 2232, 2182 (C≡N); 1691 (C=O). <sup>1</sup>H NMR spectrum, δ, ppm (*J*, Hz): 3.62–3.80 m (8H, NCH<sub>2</sub>CH<sub>2</sub>O), 3.92 d (1H, CH<sub>2</sub>, *J* = 17.8),



Ar = Ph, R = H (**a**); Ar = 4-ClC<sub>6</sub>H<sub>4</sub>, R = H (**b**); Ar = 4-MeOC<sub>6</sub>H<sub>4</sub>, R = Me (**c**).

4.06 d (1H, CH<sub>2</sub>,  $J = 17.8$ ), 7.27 s (2H, NH<sub>2</sub>), 7.53–7.57 m (2H, H<sub>arom</sub>), 7.60–7.70 m (1H, H<sub>arom</sub>), 7.98–8.01 m (2H, H<sub>arom</sub>). <sup>13</sup>C NMR spectrum,  $\delta_C$ , ppm: 42.73 (C<sup>11</sup>), 47.45 (C<sup>2</sup>, C<sup>7</sup>, C<sup>10</sup>), 57.54 (C<sup>3</sup>), 65.98 (C<sup>8</sup>, C<sup>9</sup>), 117.56, 118.54 (C<sup>5</sup>, C<sup>6</sup>), 128.66, 129.17, 134.24, 136.17 (C<sub>6</sub>H<sub>5</sub>); 170.66, 170.94 (C<sup>1</sup>, C<sup>4</sup>); 194.10 (C<sup>12</sup>). Mass spectrum,  $m/z$  ( $I_{rel}$ , %): 335 (43) [ $M$ ]<sup>+</sup>, 216 (100). Found, %: C 64.57; H 5.02; N 20.97. C<sub>18</sub>H<sub>17</sub>N<sub>5</sub>O<sub>2</sub>. Calculated, %: C 64.47; H 5.11; N 20.88.  $M$  335.36.

**5-Amino-3-[2-(4-chlorophenyl)-2-oxoethyl]-2-morpholino-3H-pyrrole-3,4-dicarbonitrile (IIb).** Yield 0.157 g (85%), mp 220–221°C (decomp.). IR spectrum,  $\nu$ , cm<sup>-1</sup>: 3157–3403 (NH<sub>2</sub>); 2233, 2172 (C≡N); 1667 (C=O). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm ( $J$ , Hz): 3.66–3.78 m (8H, NCH<sub>2</sub>CH<sub>2</sub>O), 3.90 d and 4.06 d (1H each, CH<sub>2</sub>CO,  $J = 17.7$ ), 7.26 s (2H, NH<sub>2</sub>), 7.61–7.64 m (2H, H<sub>arom</sub>), 7.99–8.03 m (2H, H<sub>arom</sub>). Mass spectrum,  $m/z$  ( $I_{rel}$ , %): 369 (3) [ $M$ ]<sup>+</sup>, 216 (100). Found, %: C 58.53; H 4.31; N 19.02. C<sub>18</sub>H<sub>16</sub>ClN<sub>5</sub>O<sub>2</sub>. Calculated, %: C 58.46; H 4.36; N 18.94.  $M$  369.80.

**5-Amino-3-[2-(4-methoxyphenyl)-1-methyl-2-oxoethyl]-2-morpholino-3H-pyrrole-3,4-dicarbonitrile (IIc).** Yield 0.152 g (80%), mp 211–212°C (decomp.). IR spectrum,  $\nu$ , cm<sup>-1</sup>: 3149–3347 (NH<sub>2</sub>); 2233, 2169 (C≡N); 1672 (C=O). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm ( $J$ , Hz): 0.98 d (3H, CH<sub>3</sub>,  $J = 6.9$ ), 3.68–3.76 m (8H, NCH<sub>2</sub>CH<sub>2</sub>O), 3.86 s (3H, OCH<sub>3</sub>), 4.26 q (1H, CHCH<sub>3</sub>,  $J = 6.9$ ), 7.08 d (2H, H<sub>arom</sub>,  $J = 8.9$ ), 7.28 s (2H, NH<sub>2</sub>), 8.00 d (2H, H<sub>arom</sub>,  $J = 8.9$ ). Mass spectrum,  $m/z$  ( $I_{rel}$ , %): 379 (3) [ $M$ ]<sup>+</sup>, 216 (100). Found, %: C 63.33; H 5.51; N 18.52. C<sub>20</sub>H<sub>21</sub>N<sub>5</sub>O<sub>3</sub>. Calculated, %: C 63.31; H 5.58; N 18.46.  $M$  379.41.

The progress of reactions and the purity of products were monitored by TLC on Silufol UV-254 plates

(spots were visualized by UV irradiation, treatment with iodine vapor, or thermal decomposition). The IR spectra were recorded on an FSM-1202 spectrometer with Fourier transform from samples dispersed in mineral oil. The <sup>1</sup>H and <sup>13</sup>C NMR spectra were measured on a Bruker DRX-500 spectrometer at 500.13 and 125.76 MHz, respectively, using DMSO-*d*<sub>6</sub> as solvent and tetramethylsilane as internal reference. The elemental compositions were determined on a Laboratori Pŕistroje instrument. The mass spectra (electron impact, 70 eV) were obtained on a Finnigan MAT INCOS-50 spectrometer.

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