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SHORT COMMUNICATIONS

Three-Component “Domino” Synthesis of 1,8-Dialkyl-3-halo-8-methyl-6-oxo-2,7-diazabicyclo[3.2.1]oct-3-ene-4,5-dicarbonitriles

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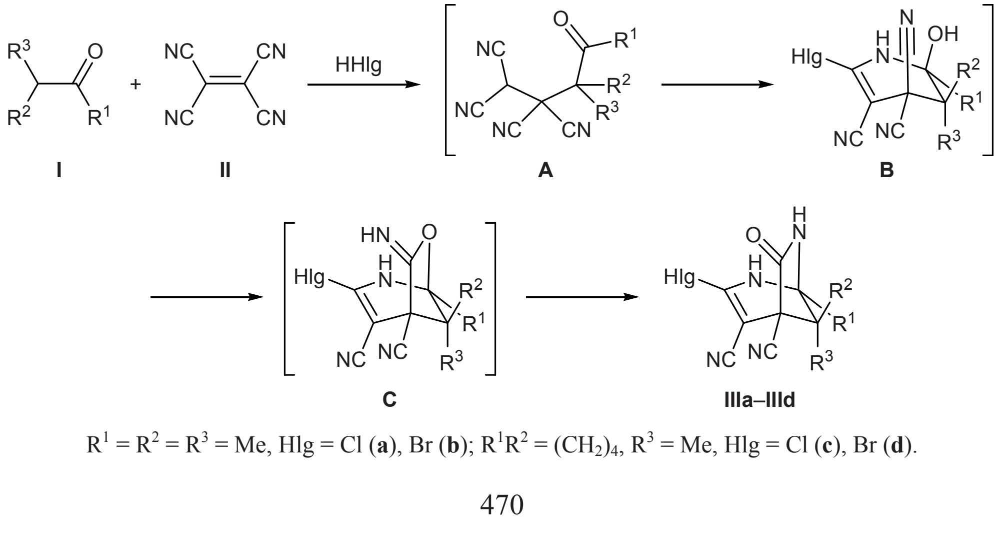
Reactions of tetracyanoethylene with carbonyl compounds [1, 2] underlie one-pot syntheses of polyfunctional heterocycles due to high reactivity of primary adducts, the corresponding oxoalkanetetracarbonitriles [2]. Examples of such reactions are transformations of unstable tetracyanoalkanals [3–5].

We previously reported on reactions of tetracyanoalkanones with hydrohalic acids, which could lead to formation of two types of compounds, depending on the substrate structure: α-unbranched ketones give rise to alkyl-substituted 2-halopyridine-3,4-dicarbonitriles [6], whereas alkyl-substituted 2-halo-6-hydroxy-1,4,5,6-tetrahydropyridine-3,4,4-tricarbonitriles were obtained from ketones branched at the α-position [7].

One-pot syntheses involving reactions of ketones with tetracyanoethylene in the presence of a large amount of hydrogen halide were poorly studied. Therefore, we examined reactions of α-branched ketones **I**, namely 2-methylcyclohexanone and 3-methylbutan-2-one with tetracyanoethylene in excess hydrohalic acid. These reactions resulted in the formation of 67–79% of the corresponding 1,8-dialkyl-3-halo-8-methyl-6-oxo-2,7-diazabicyclo[3.2.1]oct-3-ene-4,5-dicarbonitriles **IIIa**–**IIId**.

Presumably, the primary adduct is tetracyanoalkanone **A** which undergoes intramolecular cyclization to tetrahydropyridine **B** in excess hydrohalic acid. Analogous reactions with tetracyanoalkanals stop at the stage of formation of 2-halo-6-hydroxy-1,4,5,6-tetrahydropyridine-3,4,4-tricarbonitrile [4]. The presence of an alkyl radical in position *6* of tetrahydropyridine **B** is likely to favor axial orientation of the 6-hydroxy group, so that intramolecular heterocyclization with participation of the axial cyano group on C^4 becomes possible. The subsequent rearrangement of the cyclic imidate fragment into lactam yields final diazabicyclooctenes **IIIa**–**IIId**.



$R^1 = R^2 = R^3 = Me$, Hlg = Cl (**a**), Br (**b**); $R^1R^2 = (CH_2)_4$, $R^3 = Me$, Hlg = Cl (**c**), Br (**d**).

The structure of compounds **IIIa–IIId** was confirmed by IR and ^{1}H NMR spectroscopy and mass spectrometry.

3-Chloro-1,8,8-trimethyl-6-oxo-2,7-diazabicyclo-[3.2.1]oct-3-ene-4,5-dicarbonitrile (IIIa). A solution of 0.5 g (0.006 mol) of 3-methylbutan-2-one in 10 ml of 1,4-dioxane was heated to 60–70°C, 0.64 g (0.005 mol) of tetracyanoethylene and 5 ml of hydrochloric acid were added in succession under stirring, and the mixture was stirred for 1 h. The precipitate was filtered off, and washed with water and 1,4-dioxane. Yield 0.9 g (72%), mp 260–261°C (decomp.). IR spectrum, ν, cm^{-1}: 1717 (C=O); 2221, 2250 (C≡N); 3110–3227 (NH). ^{1}H NMR spectrum, δ, ppm: 9.80 s and 9.23 s (1H each, NH); 1.30 s, 1.15 s, and 0.90 s (3H each, CH_3). Mass spectrum: m/z 207 (I_{rel} 4%) $[M-43]^+$. Found, %: C 52.75; H 4.45; N 22.42. $C_{11}H_{11}ClN_4O$. Calculated, %: C 52.70; H 4.42; N 22.35.

Compounds **IIIb–IIId** were synthesized in a similar way.

3-Bromo-1,8,8-trimethyl-6-oxo-2,7-diazabicyclo-[3.2.1]oct-3-ene-4,5-dicarbonitrile (IIIb). Yield 0.99 g (67%), mp 265–266°C (decomp.). IR spectrum, ν, cm^{-1}: 1701 (C=O); 2210, 2249 (C≡N); 3110–3278 (NH). ^{1}H NMR spectrum, δ, ppm: 9.62 s and 9.22 s (1H each, NH); 1.31 s, 1.14 s, and 0.93 s (3H each, CH_3). Mass spectrum: m/z 251 (I_{rel} 3%) $[M-43]^+$. Found, %: C 45.01; H 3.89; N 19.43. $C_{11}H_{11}BrN_4O$. Calculated, %: C 44.77; H 3.76; N 18.98.

9-Chloro-2-oxo-10,11-diazatricyclo[5.3.2.0^{1,6}]-dodec-8-ene-7,8-dicarbonitrile (IIIc). Yield 1.1 g (79%), mp 240–241°C (decomp.). IR spectrum, ν, cm^{-1}: 1714 (C=O); 2203, 2244 (C≡N); 3100–3317 (NH). ^{1}H NMR spectrum, δ, ppm: 9.83 s and 9.19 s (1H each, NH), 1.14–1.84 m (8H, CH_2), 0.98 s (3H, CH_3). Mass spectrum: m/z 276 (I_{rel} 2.5%). Found, %: C 54.75; H 4.48; N 20.52. $C_{13}H_{13}ClN_4O$. Calculated, %: C 56.42; H 4.74; N 20.25.

9-Bromo-12-oxo-10,11-diazatricyclo[5.3.2.0^{1,6}]-dodec-8-ene-7,8-dicarbonitrile (IIId). Yield 1.1 g (70%), mp 204–205°C (decomp.). IR spectrum, ν, cm^{-1}: 1705 (C=O); 2195, 2260 (C≡N); 3120–3312 (NH). ^{1}H NMR spectrum, δ, ppm: 9.69 s and 9.13 s (1H each, NH), 1.10–1.85 m (8H, CH_2), 0.97 s (3H, CH_3). Mass spectrum: m/z 277 (I_{rel} 3%) $[M-43]^+$. Found, %: C 49.23; H 4.16; N 18.03. $C_{13}H_{13}BrN_4O$. Calculated, %: C 48.62; H 4.08; N 17.44.

The purity of the products was checked by TLC on Silufol UV-254 plates; spots were visualized under UV light, by treatment with iodine vapor, or by thermal treatment. The IR spectra were recorded from samples dispersed in mineral oil on an FSM-1202 spectrometer with Fourier transform. The ^{1}H NMR spectra were measured on a Bruker DRX-500 instrument at 500.13 MHz using DMSO-d_6 as solvent and tetramethylsilane as internal reference. The mass spectra (electron impact, 70 eV) were obtained on a Finnigan MAT Incos-50 spectrometer.

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