Russian Journal of Organic Chemistry, Vol. 40, No. 2, 2004, pp. 219–220. Translated from Zhurnal Organicheskoi Khimii, Vol. 40, No. 2, 2004, pp. 247–248.

2-Acylamino-3-chloroacrylonitriles, Promising Reagents for Heterocyclization

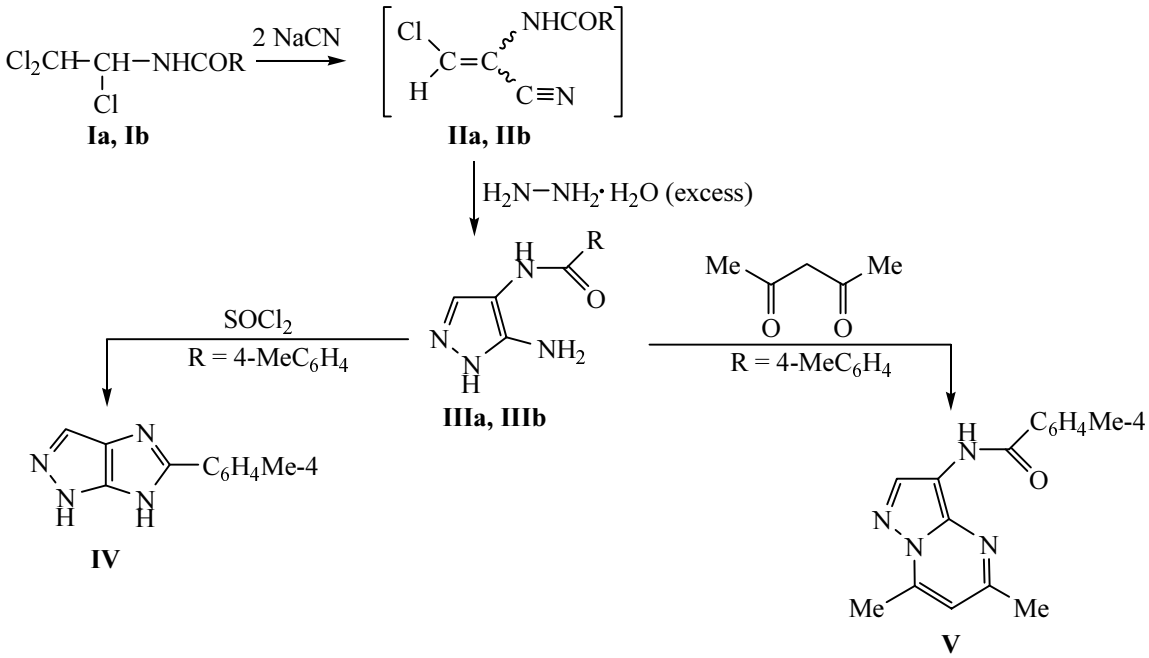
S. V. Popil'nichenko, B. S. Brovarets, and B. S. Drach

Institute of Bioorganic Chemistry and Petrochemistry, National Academy of Sciences of Ukraine, Kiev, 02094 Ukraine

Received July 24, 2003

Abstract—2-Acylamino-3-chloroacrylonitriles prepared by treating available N-(1,2,2-trichloroethyl)amides of carboxylic acids with sodium cyanide readily undergo cyclization in the presence of excess hydrazine hydrate. The cyclization products, 5-amino-4-acylaminopyrazoles, were applied to the synthesis of new imidazo[4,5-c]pyrazole and pyrazolo[1,5 ◊]pyrimidine derivatives.

Substituted acrylonitriles of a general formula $Cl_2C{=}C(NHCOR)C{\equiv}N$ are important reagents for various cyclocondensations [1–4]. Yet heterocyclizations of their analogs with a single chlorine atom in the β-position with respect to the cyano group were not studied. We established that a reaction of *N*-(1,2,2- trichloroethyl)amides of aromatic acids **Ia** and **Ib** with sodium cyanide afforded a mixture of *Z*- and *E* isomers of 2 acylamino-3-chloroacrylonitriles **IIa** and **IIb** that without isolation could be used for cyclization at treatment with hydrazine hydrate along the following scheme.



R = Ph (**a**), 4-MeC_6H_4 (**b**).

The structure of cyclization products **IIIa, b** is consistent with the data of ^1H NMR and IR spectra. It was also confirmed by conversions **IIIb** → **IV** and **IIIb** → **V**. The prospects of application of the promising reagents **IIa, b** and their analogs to the synthesis of new derivatives from the series of nitrogen-containing heterocyles will be reported in more detail elsewhere.

***N*-(5-Amino-1*H*-pyrazol-4-yl)benzamide (IIIa).** To a solution of 0.98g (20 mmol) of sodium cyanide in 5 ml of water at cooling to –10°C was added within 30 min

while vigorous stirring a solution of 2.53 g (10 mmol) of *N*-(1,2,2-trichloroethyl)benzamide [1] in 5 ml of dioxane. The mixture was stirred for 2 h more at –10...–5°C, then 25 ml of water was added, the precipitate was filtered off, washed with water, and dissolved in 30 ml of methanol. To the methanol solution was added 1.00 ml (20 mmol) of hydrazine hydrate. The mixture was left standing for 72 h at 20–25°C, the methanol was removed in a vacuum, the residue was treated with water, filtered off, and recrystallized from aqueous ethanol, 1:2. Yield of compound **IIIa** 0.45 g (45%), mp 221–223°C. Found,%: C 59.03; H 4.89; N 27.33. $C_{10}H_{10}N_4O$. Calculated, %: C 59.40; H 4.98; N 27.71.

N-(5-Amino-1*H*-pyrazol-4-yl)methylbenzamide (IIIb) was synthesized in the same way as compound **IIIa** from 2.66 g (20 mmol) of *p*-toluic acid N-(1,2,2-trichloroethyl)amide [1]. After the reaction with sodium cyanide the precipitate was filtered off, washed with water, and dried in a vacuum desiccator over phosphorus pentoxide to obtain 1.15 g of a mixture of geometrical isomers of substituted acrylonitrile **IIb** in a ratio ~3:1 according to relative intensity of signals in the ^{1}H NMR spectrum at 7.49 and 7.40 ppm (C^3H) and also at 10.56 and 10.12 ppm (N–H). Inasmuch as this isomer mixture under common conditions suffered fast tarring it was immediately dissolved in 30 ml of methanol and treated with hydrazine hydrate as described above. Yield of compound **IIIb** 0.56 g (50%), mp 252–254°C after recrystallization from aqueous ethanol, 1:2. IR spectrum, ν, cm^{-1}: 1640 (C=O), 3200–3440 (NH, NH_2 associated} ^{1}H NMR spectrum, δ, ppm: 2.36 s (3H, CH_3), 4.69 s (2H, NH_2), 7.32 d (2H, H arom), 7.66 s (1H, C^3H), 7.82 d (2H, H arom), 9.52 s (N^1H), 11.42 br.s (1H, NHCO). Found,%: C 61.05; H 5.46; N 25.73. $C_{11}H_{12}N_4O$. Calculated, %: C61.11; H 5.59; N 25.91.

5-*p*-Tolyl-1,4(6)-dihydroimidazo[4,5-*c*]pyrazole (IV). A mixture of 0.43 g (2 mmol) of compound **IIIb**, 5 ml of anhydrous benzene, and 0.5 ml of thionyl chloride was heated at 40–50°C for 20 h. The volatile substances were removed in a vacuum, the residue was treated with 5 ml of ethanol, the precipitate was filtered off and recrystallized from aqueous ethanol, 1:1. Yield of compound **IV** 0.22 g (55%), mp 209–210°C. ^{1}H NMR spectrum, δ, ppm: 2.40 s (3H, CH_3), 7.30 d (2H, H arom), 7.98 d (2H, H arom), 8.15s (1H,C^3H), 10.23 s (1H, N–H). The proton signal of another N–H bond was not observed. Found, %: C 66.49; H 4.93; N 28.14. $C_{11}H_{10}N_4$. Calculated, %: C 66.65; H 5.09; N.26.

N-(5,7-Dimethylpyrazolo[1,5-α]pyrimidin-3-yl)-4-methylbenzamide (V). To a solution of 0.43 g (2 mmol) of compound **IIIb** in 30 ml of toluene was added 0.21 ml (2 mmol) of acetylacetone, the mixture was refluxed for 10 h, the most of solvent was removed in a vacuum, the precipitate was filtered off, and recrystallized from toluene. Yield of compound **V** 0.40 g (72%), mp 160–162°C. IR spectrum, ν, cm^{-1}: 1660 (C=O), 3440 (NH associated). ^{1}H NMR spectrum, δ, ppm: 2.39 s (3H, $\underline{CH_3}C_6H_4$), 2.52 s (3H, CH_3), 2.68 s (3H, CH_3), 6.88 s (1H, C^6H), 7.33 d (2H, H arom), 7.96 d (2H, H arom), 8.42 s (1H, C^2H), 10.07 s (1H, NHCO). Found, %: C 68.38; H 5.65; N 19.83. $C_{16}H_{16}N_4O$. Calculated, %: C 68.55; H 5.75; N.99.

IR spectra were registered on spectrometer Specord M-80 from samples pelletized with KBr. ^{1}H NMR spectra were registered on Varian VXR-300 instrument from solutions of compounds in DMSO d_6, internal reference TMS.

REFERENCES

1. Drach, B.S., Brovarets, V.S., and Smolii, O.B., *Sintezy azotsoderzhashchikh geterotsiklicheskikh soedinenii na osnove amidoalkiliruyushchikh agentov* (Syntheses of Nitrogen-Containing Heterocyclic Compounds on the base of Amidoalkilating Reagents), Kiev: Naukova Dumka, 1992, p. 81.
2. Brovarets, V.S., Pil'o, S.G., Chernega, A.N., Romanenko, E.A., and Drach, B.S., *Zh. Obshch. Khim.*,1999, vol. 69, p. 1946.
3. Pil'o, S.G., Brovarets, V.S., Vinogradova, T.K., Golovchenko, A.V., and Drach, B.S., *Zh. Obshch. Khim.*, 2002, vol. 72, p. 1818.
4. Pil'o, S.G., Brovarets, V.S., Romanenko, E.A., and Drach, B.S., *Zh. Obshch. Khim.*, 2002, vol. 72, p. 1828.