*Russian Journal of Organic Chemistry, Vol. 37, No. 2, 2001, pp. 210–213. Translated from Zhurnal Organicheskoi Khimii, Vol. 37, No. 2, 2001, pp. 223–226.*
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# Synthesis of Nitriles of δ-Oxocarboxylic and γ-Nitrocarboxylic Acids

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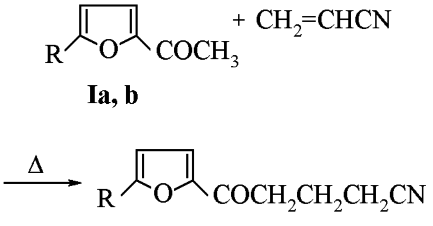
Received February 8, 1999

**Abstract**—A cyanoethylation of 2-acetyl-5-R-furans, 1-nitro-2(5-R-2-furyl)ethanes, and 2-nitro-1-(2-furyl)-propane was investigated. The optimum conditions were determined for preparation of monocyanoethylated products: nitriles of 5-oxo-5-(5-R-2-furyl)pentanoic and 4-nitro-5-(5-R-2-furyl)pentanoic acids. The cyanoethylation of furyl-containing nitroethanes with excess acrylonitrile provided bisadducts, dinitriles of 4-nitro-4-(5-R-furfuryl)heptanedionic acids.

In extension of our investigations on the chemical transformations that undergo furan derivatives containing a functional group in the side chain [1–4] we report here on cyanoethylation of β-nitroalkyl and acetyl derivatives from furan series. The nitriles of γ-nitro and δ-oxocarboxylic acids thus obtained are promising semiproducts for preparation of polyfunctional compounds of furan series and of various heterocyclic systems containing furan moieties.

A limited information was published on cyanoethylation of acetylfurans to obtain products of exhaustive cyanoethylation, tris(β-cyanoethyl) derivatives [5, 6]. Yet no data appeared in the literature on preparation of monocyanoethylation products, nitriles of 5-oxo-5-(5-R-2-furyl)pentanoic acids.

Monocyanoethyl derivatives of alkylaromatic ketones were known [7–9] to arise on heating the appropriate ketone with acrylonitrile in the presence of catalytic quantities of primary amines and organic acids. We planned to extend this method in the present study to the synthesis of monocyanoethylation products of 2-acetyl-5-R-furans **Ia, b**. We established that the most favorable conditions of ketones **Ia, b** cyanoethylation are as follows: heating to 160–180°C at molar ratio ketone Ia, b to acrylonitrile equal to 4 : 1–5 : 1 for 24–25 h in the presence of 5 wt% of 2-aminoethanol and acetic acid. The cyanoethylation under the said compounds afforded the target 5-oxo-5-(5-R-2-furyl)pentanonitriles **IIa, b** in 60–64% yield.



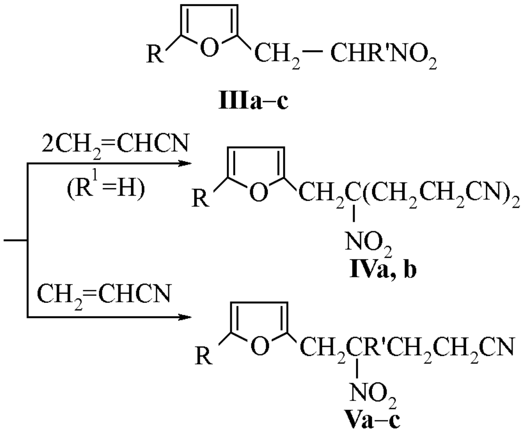
**Ia, b**

**IIa, b**

**I, II,** R = H (**a**), Me (**b**).

Before we started this study only one communication [10] reported on the Michael reaction with participation of 1-nitro-2-(2-furyl)ethane. The investigation of 1-nitro-2-(5-R-2-furyl)ethanes **IIIa, b** cyanoethylation provided a possibility to obtain the corresponding bisadducts, dinitriles of 4-nitro-4-(5-R-furfuryl)heptanedionic acids **IVa, b**, in 65–70% yield when the reaction was carried out in dioxane at 80–85°C for 10–12 h in the presence of catalytic amounts of 25% NaOH and at molar ratio of nitroalkane **IIIa, b** to acrylonitrile equal to 1 : 4.

The cyanoethylation of primary nitroalkanes in the presence of base catalysts and equimolar reagents



**IIIa–c**

**IVa, b**

**Va–c**

**III**–**V**, R = R' = H (**a**); R = Me, R' = H (**b**); R = H, R' = Me (**c**).

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**Table 1.** Yields, physical constants, and $^1$H NMR spectra of compounds synthesized

| Compd. no. | Yield, % | bp, °C (*p*, mm Hg) or mp, °C | $n_D^{20}$ | $^1$H NMR spectrum, δ, ppm[a] |
|---|---|---|---|---|
| **IIa** | 64 | 168–170 (1) | 1.4968 | 1.56–1.72 m (2H, CH$_2$), 2.30 t (2H, CH$_2$CO), 2.42 t (2H, CH$_2$CN), 6.26 d.d (1H, C$^4$H, $J_{3,4}$ 3.5 Hz), 6.68 d.d (1H, C$^3$H, $J_{3,5}$ 0.8 Hz), 7.50 d.d (1H, C$^5$H, $J_{4,5}$ 1.8 Hz) |
| **IIb** | 60 | 178–180 (1.5) | 1.5004 | 1.50–1.74 m (2H, CH$_2$), 2.20 s (3H, 5-CH$_3$), 2.35 t (2H, CH$_2$CO), 2.50 t (2H, CH$_2$CN), 6.42 d (1H, C$^4$H, $J_{3,4}$ 3.2 Hz), 6.57 d (1H, C$^3$H) |
| **IVa** | 70 | 69–71[b] | – | 2.12 t (4H, CH$_2$), 2.54 t (4H, CH$_2$CN), 3.57 s (2H, HtCH$_2$), 6.30 d.d (1H, C$^4$H, $J_{3,4}$ 3.3 Hz), 6.80 d.d (1H, C$^3$H, $J_{3,5}$ 0.9 Hz), 7.35 d.d (1H, C$^5$H, $J_{4,5}$ 1.9 Hz) |
| **IVb** | 65 | 135–137 (3) | 1.4995 | 2.18 t (4H, CH$_2$), 2.25 s (3H, 5-CH$_3$), 2.40 t (2H, CH$_2$CN), 3.62 s (2H, HtCH$_2$), 6.35 d (1H, C$^3$H, $J_{3,4}$ 3.4 Hz), 6.74 d (1H, C$^4$H) |
| **Va** | 46 | 101–103 (3) | 1.4941 | 2.15 m (2H, CH$_2$), 2.48 t (2H, CH$_2$CN), 3.50 d (2H, HtCH$_2$, *J* 1.5 Hz), 4.10 m (1H, CHNO$_2$), 6.42 d.d (1H, C$^3$H, $J_{3,5}$ 0.8 Hz), 6.68 d.d (1H, C$^4$H, $J_{3,4}$ 3.4 Hz), 7.54 d.d (1H, C$^5$H, $J_{4,5}$ 1.9 Hz) |
| **Vb** | 48 | 110–111 (5) | 1.4760 | 2.08 s (2H, CH$_2$), 2.32 s (3H, 5-CH$_3$), 2.58 t (2H, CH$_2$CN), 3.54 d (2H, HtCH$_2$, *J* 1.2 Hz), 4.05 s (1H, CHNO$_2$), 6.40 d (1H, C$^3$H, $J_{3,4}$ 3.3 Hz), 6.86 d (1H, C$^4$H) |
| **Vc** | 66 | 112–115 (3) | 1.5012 | 1.65 br.s (3H, CH$_3$), 2.15 t (2H, CH$_2$), 2.58 t (2H, CH$_2$CN), 3.46 s (2H, HtCH$_2$), 6.34 d.d (1H, C$^3$H, $J_{3,5}$ 0.9 Hz), 6.67 d.d (1H, C$^4$H, $J_{3,4}$ 3.5 Hz), 7.42 d.d (1H, C$^5$H, $J_{4,5}$ 1.8 Hz) |

[a] Spectra of compounds **IIa, b** were recorded in CD$_3$OD, that of the other compounds in CDCl$_3$.

[b] Crystallized from ethanol.

ratio is known to afford as a rule a small amount of monocyanoethylated products alongside a notable quantity of the corresponding bisadducts. However in [12, 13] the monoadduct yield was considerably increased at the use of potassium fluoride as catalyst.

We found that monocyanoethylation products, nitriles of 4-nitro-5-(5-R-2-furyl)pentanoic acids **Va, b** formed in 46–48% yield at cyanoethylation of nitroalkanes **IIIa, b** with equimolar amount of acrylonitrile in dioxane or ethanol at 75–80°C in 10–12 h in the presence of catalytic quantity of KF-2H$_2$O. Under these conditions in the reaction arise in small amounts (10–12%) as side products also dintriles **IVa, b**.

The cyanoethylation of 2-nitro-1-(2-furyl)propane (**IIIc**) in the presence of aqueous alkali afforded in 66% yield 4-methyl-4-nitro-5-(2-furyl)pentanonitrile (**Vc**).

In the IR spectra of the compounds obtained the stretching vibrations of the cyano group appear as strong bands with absorption maxima in the 2250–2240 cm$^{-1}$ region characteristic of aliphatic nitriles [14]. In the spectra of δ-oxonitriles **IIa, b** are present absorption bands of the stretching vibrations of carbonyl groups at 1700–1690 cm$^{-1}$. In the spectra of dinitriles **IVa, b** and nitriles **Va–c** are observed also strong absorption bands at 1555–1540 and 1360–1345 cm$^{-1}$ corresponding to asymmetrical and symmetrical stretching vibrations of nitro groups [14].

Alongside the above vibrations in the spectra of the compounds synthesized appear also absorption bands of alternating intensity characteristic of 2-substituted or 2,5-disubstituted furan fragments [15]: 3170–3155 [ν(CH)], 1590–1575, 1515–1505, 1395–1375 (ν of the cycle), 1140–1045 [β(CH)], 1010–995 (bending vibrations of the cycle), 965–950 [γ(CH)], 885–870 and 770–755 cm$^{-1}$ (β of the cycle).

$^1$H NMR spectra of compounds obtained (Table 1) also confirm the assumed structures. To the protons of furan cycles in nitriles **IIa, IVa, Va, b** belong three groups of resonances in the form of doublet of doublets at 6.30–6.68 ppm (H$^3$ of furan, $J_{3,5}$ 0.8–0.9 Hz), 6.26–6.80 ppm (H$^4$ of furan, $J_{3,4}$ 3.4–3.5 Hz) and 7.35–7.54 ppm (H$^5$ of furan, $J_{4,5}$ 1.8–1.9 Hz), characteristic of 2-substituted furans [15, 16]. In the spectra of compounds **IIa, IVb, Vb** containing methylfuryl fragments the signals of protons H$^3$ and H$^4$ appear as doublets in the region 6.35–6.57 and 6.42–6.86 ppm with a coupling constant $J_{3,4}$ 3.2–3.4 Hz. Note that in the spectra of

**Table 2.** Elemental analyses of compounds synthesized

| Compd. no. | Found, % | | | Formula | Calculated, % | | |
|---|---|---|---|---|---|---|---|
| | C | H | N | | C | H | N |
| **IIa** | 66.41 | 5.42 | 8.82 | $C_9H_9NO_2$ | 66.26 | 5.52 | 8.59 |
| **IIb** | 67.64 | 6.10 | 8.09 | $C_{10}H_{11}NO_2$ | 67.80 | 6.21 | 7.91 |
| **IVa** | 58.13 | 5.38 | 16.81 | $C_{12}H_{13}N_3O_3$ | 58.30 | 5.26 | 17.00 |
| **IVb** | 59.93 | 5.61 | 16.22 | $C_{13}H_{15}N_3O_3$ | 59.77 | 5.75 | 16.09 |
| **Va** | 55.80 | 5.03 | 14.65 | $C_9H_{10}N_2O_3$ | 55.67 | 5.15 | 14.43 |
| **Vb** | 57.51 | 5.90 | 13.54 | $C_{10}H_{12}N_2O_3$ | 57.69 | 5.77 | 13.46 |
| **Vc** | 57.82 | 5.86 | 13.37 | $C_{10}H_{12}N_2O_3$ | 57.69 | 5.77 | 13.46 |

δ-oxonitriles **IIa, b** the signal of the proton $H^3$ is displaced downfield compared to the resonance of the $H^4$ proton apparently due to the deshielding effect of the carbonyl group [14, 16].

## EXPERIMENTAL

IR spectra were recorded on spectrometer Bruker IFS-48 from thin film or KBr pellets (compound **IVa**). $^1$H NMR spectra were registered on Bruker WP-250 SY instrument (250 MHz), internal standard TMS. The reaction progress and purity of compounds obtained were monitored by GLC on chromatograph Chrom-5 equipped with a flame-ionization detector, column 1200 × 2 mm, stationary phase 15% of Apiezon-L on Chromaton N-AW, carrier gas helium, flow rate 3.6 l/h, evaporator temperature 120–299°C, column temperature 70–200°C.

The initial 2-acetylfuran (**Ia**) [17], 2-acetyl-5-methylfuran (**Ib**) [17], 2-nitro-1-(furyl)ethane (**IIIa**) [1], (1-methyl-2-furyl)-2-nitroethane (**IIIb**) [1], and 2-nitro-1-(2-furyl)propane (**IIIc**) [1] were obtained along known procedures.

**Nitriles of 5-oxo-5-(5-R-2-furyl)pentanoic acids IIa, b.** A mixture of 2 mol of 2-acetyl-5-R-furan **Ia, b**, 26.5 g of acrylonitrile, 15 g of 2-aminoethanol, 3 g of acetic acid, and 0.3 g of hydroquinone was stirred for 24–25 h at 160–180°C. The excess initial ketone was distilled off from the reaction mixture under reduced pressure, and the residue was distilled in vacuo to obtain nitriles **IIa, b**.

**Dinitriles of 4-nitro-4-(5-R-furfuryl)pentanoic acids IVa, b.** To a solution of 0.04 mol of 1-nitro-2-(5-R-2-furyl)ethane **IIIa, b** in 30 ml of dioxane was added while stirring 1.5 ml of 25% aqueous NaOH, and then dropwise 8.48 g of acetonitrile. The reaction mixture was stirred for 10–12 h at 80–85°C, cooled to 20°C, neutralized with 5% HCl, and poured into 100 ml of water. The separated oily substance was extracted into ether (3×20 ml), the extract was washed with water and dried with $Na_2SO_4$. The solvent was removed under reduced pressure, and the residue either was crystallized from ethanol (in preparation of dinitrile **IVa**) or was distilled in vacuo in the stream of inert gas (in preparation of dinitrile **IVb**).

**Nitrile of 4-methyl-4-nitro-5-(2-furyl)pentanoic acid (Vc)** was obtained similarly from 2-nitropropane **IIIc** and equimolar amount of acrylonitrile.

**Nitriles of 4-nitro-5-(5-R-2-furyl)pentanoic acids Va, b.** To a mixture of 0.04 mol of nitroethane **IIIa, b** and 0.5 g of KF–$2H_2O$ in 30 ml of ethanol was added dropwise 2.12 g of acrylonitrile. The reaction mixture was stirred for 10–12 h at 75–80°C, cooled to 20°C, the catalyst was filtered off, and the filtrate was evaporated at reduced pressure. The residue was distilled in vacuo in a stream of inert gas to obtain nitriles **Va, b**. The characteristics of compounds obtained are given in Tables 1, 2.

## REFERENCES

1. Karakhanov, R.A., Bogacheva, E.S., Romero, I., and Kelarev V.I., *Khim. Geterotsikl. Soed.*, 1991, no. 4, pp. 449–452.
2. Karakhanov, R.A., Kelarev, V.I., Remizov A.S., Polivin, Yu.N., and Oietaio, D., *Khim. Geterotsikl. Soed.*, 1992, no. 10, pp. 1312–1315.
3. Karakhanov, R.A., Kelarev, V.I., Kokosova, A.S., Malyshev, V.A., and Zav'yalov, V.I., *Zh. Org. Khim.*, 1992, vol. 28, no. 8, pp. 1750–1755.
4. Polivin, Yu.N., Karakhanov, R.A., Kelarev, V.I., Ugrak, V.I., and Panina, M.A., *Izv. Russian Akad. Nauk, Ser. Khim.*, 1993, no. 5, pp. 921–923.
5. Terent'ev, A.P. and Kost, A.N., *Reaktsii i metody*

*issledovaniya organicheskikh soedinenii* (Reactions and Methods of Investigations of Organic Compounds), Moscow: Goskhimizdat, 1952, vol. 2, pp. 47–208.

6. Acara, N.A. and Levine, R., *J. Am. Chem. Soc.*, 1950, vol. 72, no. 7, pp. 2864–2866.
7. German Patent 1002342, 1957; *Ref. Zh. Khim.*, 1958, 44217.
8. US Patent 2850519, 1958; *Chem. Abstr.*, 1959, vol. 53, 14026.
9. Van De Moes, V., *Chem. Ind.*, 1986, no. 4, pp. 129–135.
10. Karakhanov, V.A., Kelarev, V.I., Remizov, A.S., and Polivin, Yu.N., *Izv. Vuzov, Ser. Khim. i Khim. Tekhnol.*, 1992, vol. 35, no. 10, pp. 3–22.
11. Novikov, S.S., Shveigeimer, G.A., Sevast'yanov, V.V., and Shlyapochnikov, V.A., *Khimiya alifaticheskikh i alitsiklicheskikh nitrosoedinenii* (Chemistry Alifatic and Acyclic Nitro Compounds), Moscow: Khimiya, 1974.
12. Kambe, S. and Yasuda, H., *Sci. Papers Inst. Phys. Chem. Rec. (Tokyo)*, 1964, vol. 58, no. 4, pp. 148–149.
13. Oda, R., *Chemistry (Japan)*, 1982, vol. 37, no. 6, pp. 450–457.
14. Silverstein, R., Bassler, G., and Morril, T., *Spectrometric Identification of Organic Compounds*, New York: Wiley, 1963. Translated under the title *Spektrometricheskaya identifikatsiya organicheskikh soedinenii*, Moscow: Mir, 1977.
15. *Fizicheskie metody v khimii geterotsiklicheskikh soedinenii* (Physical Methods in Chemistry of Heterocyclic Compounds), Katritskii, A.R., Ed., Moscow: Khimiya, 1966, pp. 430–433, 504–511.
16. *Uspekhi khimii furana* (Achievements in Furan Chemistry), Lukevitsa, E.Ya., Ed., Riga: Zinatne, 1978, pp. 19–54.
17. Ponomarev, A.A., *Sintez i reaktsii furanovykh veshchestv* (Synthesis and Reactions of Furanic Substances), Saratov: Izd. Saratov. Gos. Univ., 1960.