ISSN 1070-4280, Russian Journal of Organic Chemistry, 2014, Vol. 50, No. 5, pp. 749–751. © Pleiades Publishing, Ltd., 2014.
Original Russian Text © M.Yu. Ievlev, K.V. Lipin, O.V. Ershov, V.A. Tafeenko, O.E. Nasakin, 2014, published in Zhurnal Organicheskoi Khimii, 2014, Vol. 50, No. 5, pp. 759–761.

SHORT COMMUNICATIONS

Targeted Synthesis of 2,3-Dicyano-2-(2-oxoalkyl)succinates

M. Yu. Ievlev[a], K. V. Lipin[a], O. V. Ershov[a], V. A. Tafeenko[b], and O. E. Nasakin[a]

[a] *I.N. Ul'yanov Chuvash State University, Moscovskii pr. 15, Cheboksary, 428015 Russia*
e-mail: hiliam@bk.ru

[b] *Lomonosov Moscow State University, Moscow, Russia*

Received November 15, 2013

DOI: 10.1134/S1070428014050224

Electron-deficient alkenes are known to form with ketones reactive adducts. For instance, the application of tetracyanoethylene affords 4-oxoalkane-1,1,2,2-tetracarbonitriles [1, 2] that may be used for the directed synthesis of a number of difficultly available hetero- and carbocyclic structures [3–8]. With the goal to synthesize new polycyano derivatives of carbonyl compounds we performed reactions with ketones of the other olefins activated with electron-withdrawing substituents: esters of dicyano-substituted fumaric acid. Similar conversions were described only for individual methylene-active β-dicarbonyl compounds [9].

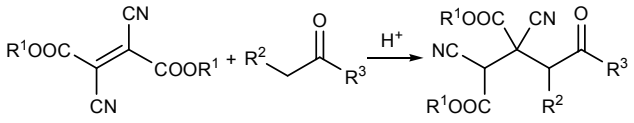
2,3-Dicyanofumarates **I** [10] in reactions with ketones under the action of catalytic quantities of hydrochloric acid formed 2,3-dicyano-2-(2-oxoalkyl)-succinates **II** in 68–76% yields (Scheme 1).

The fundamental distinction of this process from the ketones reaction with tetracyanoethylene consists in the longer duration at the normal conditions. This fact is apparently due to the lesser electron-withdrawing effect of ester subsituents compared to cyano groups, and also to steric hindrances. We applied to the reaction intensification either ultrasound irradiation that reduced the reaction time to 24 h, or performance of the process in a pressure reactor which shortened the reaction time to 1–2 h but led to significantly lower yield of products. Finally we considered as optimum with respect to the quality–reaction rate ratio the boiling of the reaction mixture at reflux: The reaction thus proceeded within 4–5 h with 68–76% yields. The variation of catalysts did not essentially affect the results, and we selected finally conc. hydrochloric acid.

Structures of compounds **IIa–IIe** were established from IR and ^{1}H NMR spectra and from elemental analyses. The obtained spectral data show also that the final products have formed as a mixture of two diastereomers in the ~3 : 1 ratio (melting points and yields are given in Experimental for the diastereomeric mixture, the figures belonging to the minor diastereomer are marked with an asterisk). The structure of one of the steric isomers of compound **IIe** was established by X-ray diffraction (XRD) analysis (CCDC 965232) (see the figure).

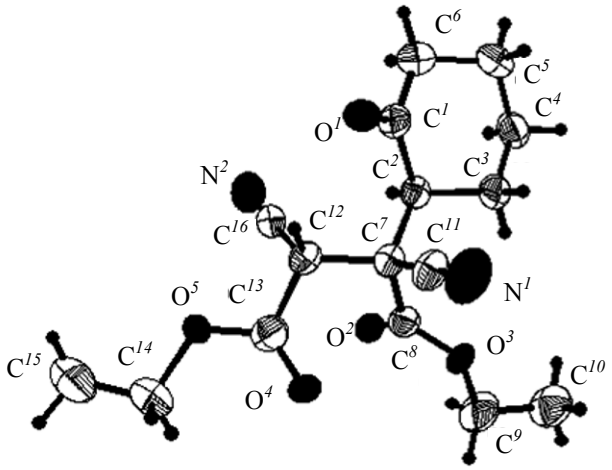
Dimethyl 2,3-dicyano-2-(3-oxobutyl-2)succinate (IIa). To a slurry of 0.97 g (0.5 mmol) dimethyl 2,3-dicyanofumarate (**Ia**) in 15 mL of ethanol was added 0.36 g (0.5 mmol) of 2-butanone and 1–2 drops of conc. HCl. The reaction mixture was boiled at reflux for 4–5 h (monitoring by the negative test on colored π-complex with hydroquinone). The reaction mixture was cooled and poured in 75 mL of ice water. The separated precipitate was filtered off, washed with ice water and cooled 2-propanol. Yield 0.9 g (68%), mp 117–120°C (decomp.). IR spectrum, ν, cm^{-1}: 2258 (C≡N), 1753 (C=O). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.30–1.31 d (3H, CH_3, J 7.3 Hz),* 1.34–1.37 d (3H, CH_3, J 7.3 Hz), 2.30 s (3H, CH_3), 2.30 s (3H, CH_3),* 3.49–3.53 d.d (1H, CH, J 7.3, 17.3 Hz), 3.52–3.56 d.d (1H, CH, J 7.3, 17.3 Hz),* 3.78 s (3H, OCH_3),

Scheme 1.



Ia, **Ib** **IIa-IIe**

I, R^1 = CH_3 (**a**), C_2H_5 (**b**); **II**, R^1 = R^2 = R^3 = CH_3 (**a**); R^1 = CH_3, R^2+R^3 = $(CH_2)_4$ (**b**); R^1 = CH_3, R^2+R^3 = $(CH_2)_5$ (**c**); R^1 = C_2H_5, R^2+R^3 = $(CH_2)_3$ (**d**); R^1 = C_2H_5, R^2+R^3 = $(CH_2)_4$ (**e**).



Molecular structure of diethyl 2,3-dicyano-2-(2-oxocyclohexyl)succinate (**IIe**) according to XRD data.

3.81 s (3H, OCH_3),* 3.82 s (3H, OCH_3),* 3.83 s (3H, OCH_3), 5.27 s (1H, CH),* 5.46 s (1H, CH). Found, %: C 54.21; H 5.25; N 10.59. $C_{12}H_{14}N_2O_5$. Calculated, %: C 54.13; H 5.30; N 10.52. *M* 266.09.

Compounds **IIb–IIe** were obtained similarly.

Dimethyl 2,3-dicyano-2-(2-oxocyclohexyl)succinate (IIb). Yield 1.11 g (76%), mp 165–168°C (decomp.). IR spectrum, ν, cm^{-1}: 2257 (C≡N), 1745 (C=O). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 1.21–2.63 m (8H, $4CH_2$),* 1.21–2.63 m (8H, $4CH_2$), 3.39–3.41 d.d (1H, CH, *J* 7.3, 17.2 Hz), 3.54–3.50 d.d (1H, CH, *J* 7.3, 17.3 Hz),* 3.78 s (3H, OCH_3), 3.79 s (3H, OCH_3),* 3.81 s (3H, OCH_3), 3.82 s (3H, OCH_3),* 5.23 s (1H, CH),* 5.64 s (1H, CH). Found, %: C 57.59; H 5.48; N 9.65. $C_{14}H_{16}N_2O_5$. Calculated, %: C 57.53; H 5.52; N 9.58. *M* 292.11.

Dimethyl 2,3-dicyano-2-(2-oxocycloheptyl)succinate (IIc). Yield 1.07 g (70%), mp 139–141°C (decomp.). IR spectrum, ν, cm^{-1}: 2257 (C≡N), 1748 (C=O). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 1.21–2.63 m (10H, $5CH_2$),* 1.23–2.63 m (10H, $5CH_2$), 3.52–3.56 m (1H, CH), 3.52–3.56 m (1H, CH),* 3.78 s (3H, OCH_3), 3.79 s (3H, OCH_3),* 3.83 s (3H, OCH_3), 3,85 s (3H, OCH_3),* 5.24 s (1H, CH),* 5.43 s (1H, CH). Found, %: C 58.72; H 5.99; N 9.21. $C_{15}H_{18}N_2O_5$. Calculated, %: C 58.82; H 5.92; N 9.15. *M* 306.12.

Diethyl 2,3-dicyano-2-(2-oxocyclopentyl)succinate (IId). Yield 1.09 g (71%), mp 115–117°C (decomp.). IR spectrum, ν, cm^{-1}: 2256 (C≡N), 1736 (C=O). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 1.23–1.25 t (3H, $2CH_3$, *J* 7.1 Hz),* 1.29–1.33 t (3H, $2CH_3$, *J* 7.1 Hz), 1.81–2.49 m (8H, $4CH_2$),* 1.81–2.49 m (8H, $4CH_2$), 3.14–3.18 d.d (1H, CH, *J* 7.2, 17.5 Hz), 3.21–3.27 d.d (1H, CH, *J* 7.3, 17.1 Hz),* 4.23–4.27 q (4H, $2OCH_2$, *J* 7.12 Hz),* 4.35–4.40 q (4H, $2OCH_2$, *J* 7.1 Hz), 5.38 s (1H, CH),* 5.70 s (1H, CH). Found, %: C 58.74; H 5.97; N 9.25. $C_{15}H_{18}N_2O_5$. Calculated, %: C 58.82; H 5.92; N 9.15. *M* 306.12.

Diethyl 2,3-dicyano-2-(2-oxocyclohexyl)succinate (IIe). Yield 1.17 g (73%), mp 120–121°C (decomp.). IR spectrum, ν, cm^{-1}: 2257 (C≡N), 1737 (C=O). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 1.21–1.25 t (3H, $2CH_3$, *J* 7.1 Hz), 1.24–1.27 t (3H, $2CH_3$, *J* 7.1 Hz),* 1.60–2.63 m (8H, $4CH_2$),* 1.60–2.63 m (8H, $4CH_2$), 3.37–3.40 d.d (1H, CH, *J* 7.3, 17.8 Hz), 3.52–3.49 d.d (1H, CH, *J* 7.2, 17.4 Hz),* 4.21–4.25 q (4H, $2OCH_2$, *J* 7.11 Hz), 4.22–4.27 m (4H, $2OCH_2$),* 5.21 s (1H, CH),* 5.64 s (1H, CH). Found, %: C 60.07; H 6.19; N 8.81. $C_{16}H_{20}N_2O_5$. Calculated, %: C 59.99; H 6.29; N 8.74. *M* 320.14.

The purity of compounds obtained was checked by TLC on Silufol-UV-254 plates, eluent ethyl acetate, development under UV irradiation, in iodine vapor, or by thermal decomposition. IR spectra were recorded on a Fourier IR spectrophotometer FSM-1202 from thin film (mull in mineral oil). ^1H NMR spectra were registered on a spectrometer Bruker DRX-500, operating frequency 500.13 MHz, solvent DMSO-d_6, internal reference TMS. Elemental analysis was carried out on an analyzer Laboratorni Pristroje. XRD study of a single crystal of compound **IIe** was carried out on a diffractometer StadiVari Pilatus 100K (STOE Co), MoK_α radiation. Data collection, determination and refining of the unit cell parameters, and the processing of the diffraction data were carried out applying the program package STOE X-Area. The structure was solved by the direct method using SHELXS-97 software [11]. The XRD study was carried out using the equipment purchased from the funds of the Program of development of Moscow University and within the framework of the Agreement on collaboration between the Chemical Department of the Lomonsov Moscow State University and the Chemical-Pharmaceutical Department of the I.N. Ul'yanov Chuvash State University.

The study was performed in the framework of the basic part of the State contract with the Ministry of Education and Science of the Russian Federation.

REFERENCES

1. Middleton, W.I., Heckert, R.E., Little, E.L., and Krespas, C.G., *J. Am. Chem. Soc.*, 1958, vol. 80, p. 2783.
2. Nikolaev, E.G., Nasakin, Terent'ev, P.B., Khaskin, B.A., and Petrov, V.G., *Zh. Org. Khim.*, 1984, vol. 20, p. 205.
3. Sheverdov, V.P., Ershov, O.V., Nasakin, O.E., Slyunina, E.V., Tikhonova, I.G., Chernushkin, A.N., and Khrustalev, V.N., *Zh. Org. Khim.*, 2000, vol. 70, p. 1334.
4. Sheverdov, V.P., Ershov, O.V., Nasakin, O.E., Chernushkin, A.N., Tafeenko, V.A., and Firgang, S.I., *Tetrahedron*, 2001, vol. 57, p. 5815.
5. Ershov, O.V., Lipin, K.V., Maksimova, V.N., Eremkin, A.V., Kayukov, Ya.S., and Nasakin, O.E., *Russ. J. Org. Chem.*, 2009, vol. 45, p. 475.
6. Belikov, M.Yu., Ershov, O.V., Eremkin, A.V., Nasakin, O.E., Tafeenko, V.A., and Nurieva, E.V., *Tetrahedron Lett.*, 2011, vol. 52, p. 6407.
7. Belikov, M.Yu., Ershov, O.V., Lipovskaya, I.V., Fedoseev, S.V., and Nasakin, O.E., *Russ. J. Org. Chem.*, 2013, vol. 49, p. 864.
8. Fedoseev, S.V., Ershov, O.V., Belikov, M.Yu., Lipin, K.V., Bardasov, I.N., Nasakin, O.E., and Tafeenko, V.A., *Tetrahedron Lett.*, 2013, vol. 54, p. 2143.
9. Rappoport, Z. and Ladkani, D., *J. Chem. Soc., Perkin Trans. 1*, 1974, vol. 22, p. 2595.
10. Ireland, C.J. and Pizey, J.S., *J. Chem. Soc., Chem. Commun.*, 1972, p. 4.
11. Sheldrick, G.M., *Acta Cryst.*, 2008, vol. A64, p. 112.