ISSN 1070-4280, Russian Journal of Organic Chemistry, 2017, Vol. 53, No. 2, pp. 296–298. © Pleiades Publishing, Ltd., 2017. Original Russian Text © G.M. Talybov, 2017, published in Zhurnal Organicheskoi Khimii, 2017, Vol. 53, No. 2, pp. 295–296.

> SHORT COMMUNICATIONS

## **Condensation of Chloromethyl Propargyl Ether with Nitriles**

G. M. Talybov

Mamedaliev Institute of Petrochemical Processes, National Academy of Sciences of Azerbaijan, pr. Khodzhaly 30, Baku, AZ 1025 Azerbaijan e-mail: ahmed adna@rambler.ru

Received July 29, 2016

**Abstract**—Reactions of aromatic and aliphatic nitriles with chloromethyl propargyl ether in the presence of activated zinc followed by treatment with water in the presence of  $H_3PMo_{12}O_{40}$  afforded  $\beta$ -oxoethers.

DOI: 10.1134/S1070428017020269

One of important methods of building up a C–C bond is Blaise reaction [1] that up till now is widely used in the synthesis of various organic compounds [2–9]. The reaction consists in the interaction of nitriles with esters of haloorganic acids in the presence of zinc to obtain the corresponding  $\beta$ -ketoesters.

We studied for the first time the reaction of organic nitriles with  $\alpha$ -haloether (chloromethyl propargyl ether) on activated zinc with subsequent treatment with water in the presence of phosphomolybdic heteropolyacid H<sub>3</sub>PMo<sub>12</sub>O<sub>40</sub> of Keggin structure resulting in the formation of ketoethers **1–6**. Applying the asymmetric reduction they can be used in the synthesis of chiral  $\beta$ -oxyethers.

The reaction proceeding in a nitrogen atmosphere excludes the hydrolysis of  $\alpha$ -haloether, which easily suffers decomposition by moist air, and the high yields (up to 68%) of target compounds **1–6** are attained at elevated temperature, in particular, by using diglyme as solvent.

As known, the first stage of Blaise reaction is the formation on the zinc surface of Reformatsky reagent in the form of a solvate complex, same as in the case of  $\alpha$ -halosubstituted esters [10, 11]. This complex is surrounded with a dense solvate shell thus impeding

the formation of side products [2, 4]. In the course of the reaction chloromethyl propargyl ether adds to the cyano group forming an intermediate organozinc compound [6–9]. Both aliphatic and aromatic nitriles enter this reaction.

The structure of synthesized ketoethers 1-6 was confirmed by spectral methods.

2-[(Prop-2-yn-1-yl)oxy]-1-phenylethan-1-one(1). Under inert atmosphere (nitrogen) to 0.1 g of copper bromide and 9.7 g (0.15 g-atom) of freshly cleaned zinc foil was charged in a three-neck flask and 300 mL of dry diglyme was added. Then quickly 10.3 g (0.1 mol) of benzonitrile and 20.8 g (0.2 mol) of chloromethyl propargyl ether were charged in the flask. The reaction mixture was boiled for 45 min, then cooled for 15 min with an ice bath, 0.018 g (0.01 mol) of  $H_3PMo_{12}O_{40}$ was added, and the mixture was stirred for 45 min at room temperature. After separating the layers the water layer was diluted with water and extracted with diglyme. The combined organic solutions were washed with water, with saturated solution of sodium hydrogen carbonate, and again with water. The extract was dried with sodium sulfate, the solvent was removed, the residue was distilled in a vacuum. Yield 10.5 g (61%), bp 86–88°C (2 mmHg),  $d_4^{20}$  1.007,  $n_D^{20}$ 1.5141,  $MR_D$  52.04, calc. 51.36. IR spectrum, v, cm<sup>-1</sup>:



3289, 2110 (C=CH), 3083, 3064, 3029, 1601, 1488, 985, 700, 770 (Ph), 1725 (C=O), 1100 (C–O–C). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 2.65 t (1H, =CH, <sup>4</sup>J 2 Hz), 4.14 s (2H, COCH<sub>2</sub>O), 4.25 d (2H, OCH<sub>2</sub>C=, <sup>4</sup>J 2 Hz), 7.25–7.45 m (5H, Ph). <sup>13</sup>C NMR spectrum,  $\delta$ , ppm: 56.0 (=C<u>C</u>H<sub>2</sub>O), 69.0 (=CH), 75.0 (=<u>C</u>CH<sub>2</sub>O), 88.0 (O<u>C</u>H<sub>2</sub>CO), 126.0 (CH<sub>arom</sub>), 126.8 (2CH<sub>arom</sub>), 126.9 (2CH<sub>arom</sub>), 129.9 (CH<sub>arom</sub>), 206.13 (C=O). Found, %: C 76.02; H 5.82. C<sub>11</sub>H<sub>10</sub>O<sub>2</sub>. Calculated, %: C 75.84; H 5.79.

Compounds 2–6 were obtained similarly.

**1-(4-Methylphenyl)-2-[(prop-2-yn-1-yl)oxy]ethan-1-one(2)** was obtained from *p*-tolunitrile. Yield 63%, bp 92–93°C (2 mmHg),  $d_4^{20}$  1.095,  $n_D^{20}$  1.5191,  $MR_D$ 52.14, calc. 51.36. IR spectrum, v, cm<sup>-1</sup>: 3300, 2110 (C=CH), 3043, 3074, 3034, 1611, 1498, 975, 710, 760 (Ph), 1715 (C=O), 1160 (C–O–C). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 2.31 s (3H, Me), 2.55 t (1H, =CH, <sup>4</sup>J 2 Hz), 4.14 s (2H, COCH<sub>2</sub>O), 4.08 d (2H, OCH<sub>2</sub>C=, <sup>4</sup>J 2 Hz), 7.25–7.45 m (4H, Ph). <sup>13</sup>C NMR spectrum,  $\delta$ , ppm: 21.0 (Me), 57.0 (=CCH<sub>2</sub>O), 70.0 (=CH), 74.0 (=CCH<sub>2</sub>O), 89.0 (OCH<sub>2</sub>), 126.0 (CH<sub>arom</sub>), 126.8 (2CH<sub>arom</sub>), 127.9 (2CH<sub>arom</sub>), 129.9 (CH<sub>arom</sub>), 206.13 (C=O). Found, %: C 76.52; H 5.42. C<sub>12</sub>H<sub>12</sub>O<sub>2</sub>. Calculated, %: C 76.57; H 6.43.

**1-(2-Methylphenyl)-2-[(prop-2-yn-1-yl)oxy]ethan-1-one(3)** was obtained from *o*-tolunitrile. Yield 68%, bp 86–88°C (2 mmHg),  $d_4^{20}$  1.0978,  $n_D^{20}$  1.5201,  $MR_D$ 52.08, calc. 51.36. IR spectrum, v, cm<sup>-1</sup>: 3310, 2100 (C=CH), 3023, 3064, 3044, 1611, 1498, 975, 710, 758 (Ph), 1713 (C=O), 1140 (C–O–C). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 2.30 s (3H, Me), 2.53 t (1H, =CH, <sup>4</sup>J 2 Hz), 4.12 s (2H, COCH<sub>2</sub>O), 4.11 d (2H, OCH<sub>2</sub>C=, <sup>4</sup>J 2 Hz), 7.21–7.43 m (4H, Ph). <sup>13</sup>C NMR spectrum,  $\delta$ , ppm: 21.0 (Me), 56.0 (=C<u>C</u>H<sub>2</sub>O), 69.0 (=CH), 73.0 (=<u>C</u>CH<sub>2</sub>O), 87.0 (OCH<sub>2</sub>), 125.0 (CH<sub>arom</sub>), 126.8 (2CH<sub>arom</sub>), 128.9 (2CH<sub>arom</sub>), 129.9 (CH<sub>arom</sub>), 210.13 (C=O). Found, %: C 76.72; H 5.92. C<sub>12</sub>H<sub>12</sub>O<sub>2</sub>. Calculated, %: C 76.57; H 6.43.

**1-(3-Methylphenyl)-2-[(prop-2-yn-1-yl)oxy]ethan-1-one(4)** was obtained from *m*-tolunitrile. Yield 67%, bp 97–99°C (2 mmHg),  $d_4^{20}$  1.1001,  $n_D^{20}$  1.5211,  $MR_D$  52.04, calc. 51.36. IR spectrum, v, cm<sup>-1</sup>: 3300, 2110 (C=CH), 3033, 3054, 3034, 1621, 1498, 975, 710, 760 (Ph), 1717 (C=O), 1150 (C–O–C). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 2.29 s (3H, Me), 2.55 t (1H, =CH, <sup>4</sup>J 2 Hz), 4.18 s (2H, COCH<sub>2</sub>O), 4.10 d (2H, OCH<sub>2</sub>C=, <sup>4</sup>J 2 Hz), 7.25–7.45 m (4H, Ph). <sup>13</sup>C NMR spectrum,  $\delta$ , ppm: 18.0 (Me), 56.0 (=CH<sub>2</sub>O), 72.0 (=CH), 74.0 **1-[(Prop-2-yn-1-yl)oxy]heptan-1-one** (5) was obtained from hexanenitrile. Yield 68%, bp 65–66°C (2 mmHg),  $d_4^{20}$  0.6608,  $n_D^{20}$  1.4089,  $MR_D$  62.88, calc. 62.10. IR spectrum, v, cm<sup>-1</sup>: 3310, 2100 (C≡CH), 3085, 3065, 3068, 1682, 1441, 985, 776, 719 (Ph), 1727 (C=O), 1110 (C–O–C). <sup>1</sup>H NMR spectrum,  $\delta$ , ppm: 0.91 t (3H, Me, <sup>3</sup>J 7.5 Hz), 0.98–1.12 m [6H, (CH<sub>2</sub>)<sub>3</sub>], 2.50 t (1H, ≡CH, <sup>4</sup>J 2 Hz), 3.99 t (2H, CH<sub>2</sub>O, <sup>3</sup>J 6.1 Hz), 4.14 s (2H, COCH<sub>2</sub>O), 4.16 d (2H, OCH<sub>2</sub>C≡, <sup>4</sup>J 2 Hz). <sup>13</sup>C NMR spectrum,  $\delta$ , ppm: 25.0 (CH<sub>3</sub>), 34.0 (CH<sub>2</sub>), 36.0 (CH<sub>2</sub>), 38.0 (CH<sub>2</sub>), 39.0 (CH<sub>2</sub>), 53.0 (CH<sub>2</sub>), 66.0 (CH<sub>2</sub>), 73.0 (≡C), 79.0 (CO<u>C</u>H<sub>2</sub>O), 81.0 (C≡), 204.0 (C=O), 210.0 (OCH<sub>2</sub>O). Found, %: C 74.19; H 10.42. C<sub>10</sub>H<sub>16</sub>O<sub>2</sub>. Calculated, %: C 71.39; H 9.59.

**1-[(Prop-2-yn-1-yl)oxy]decan-1-one** (6) was obtained from nonanenitrile. Yield 59%, bp 76–78°C (3 mmHg),  $d_4^{20}$  0.8720,  $n_D^{20}$  1.4282,  $MR_D$  62.08, calc. 62.10. IR spectrum, v, cm<sup>-1</sup>: 3310, 2110 (C≡CH), 3085, 3065, 3061, 1682, 1441, 985, 776, 719 (Ph), 1715 (C=O), 1120 (C–O–C). <sup>1</sup>H NMR spectrum, δ, ppm: 0.90 t (3H, Me, <sup>3</sup>J 7.5 Hz), 0.91–1.16 m [12H, (CH<sub>2</sub>)<sub>6</sub>], 2.41 t (1H, ≡CH, <sup>4</sup>J 2 Hz), 3.89 t (2H, CH<sub>2</sub>O, <sup>3</sup>J 6.1 Hz), 4.14 s (2H, COCH<sub>2</sub>O), 4.16 d (2H, OCH<sub>2</sub>C≡, <sup>4</sup>J 2 Hz). <sup>13</sup>C NMR spectrum, δ, ppm: 25.0 (CH<sub>3</sub>), 34.0 (CH<sub>2</sub>), 36.0 (CH<sub>2</sub>), 38.0 (CH<sub>2</sub>), 39.0 (CH<sub>2</sub>), 80.0 (C≡), 206.0 (C=O), 211.0 (OCH<sub>2</sub>O). Found, %: C 74.09; H 10.52. C<sub>13</sub>H<sub>22</sub>O<sub>2</sub>. Calculated, %: C 74.24; H 10.54.

IR spectra of compounds **1–6** in tetrachloromethane were recorded on a spectrophotometer Specord 75 IR. NMR spectra were registered on a spectrometer Bruker SF-300 [300.13 (<sup>1</sup>H), 75 (<sup>13</sup>C) MHz] in CDCl<sub>3</sub>, internal reference HMDS.

## REFERENCES

- 1. Blaise, E.E., C. R. Hebd. Seances Acad. Sci., 1901, vol. 132, p. 478.
- Lee, J.H., Choi, B.S., Chang, J.H., Lee, H.B., Yoon, J.-Y., Lee, J., and Shin, H., *J. Org. Chem.*, 2007, vol. 72, p. 10261. doi 10.1021/jo701743m
- Rao, H.S.P., Rafi, S., and Padmavathy, K., *Tetrahedron*, 2008, vol. 64, p. 8037. doi 10.1016/ j.tet.2008.05.109

- Chun, Y.S., Ryu, K.Y., Ko, Y.O., Hong, J.Y., Hong, J., Shin, H., and Lee, S.-g., *J. Org. Chem.*, 2009, vol. 74, p. 7556. doi 10.1021/jo901642t
- Hoang, C.T., Bouillère, F., Johannesen, S., Zulauf, A., Panel, C., Pouilhès, A., Gori, D., Alezra, V., and Kouklovsky, C., *J. Org. Chem.*, 2009, vol. 74, p. 4177. doi 10.1021/jo900324d
- Kim, J.H., Shin, H., and Lee, S.-g., J. Org. Chem., 2012, vol. 77, p. 1560. doi 10.1021/jo201964a
- Kim, J.H., Chun, Y.S., and Lee, S.-g., J. Org. Chem., 2013, vol. 78, p. 11483. doi 10.1021/jo402015n

- Sakthivel, K. and Srinivasan, K., J. Org. Chem., 2014, vol. 79, p. 3244. doi 10.1021/jo500137m
- Kim, J.H., Choi, S.Y., Bouffard, J., and Lee, S.-g., J. Org. Chem., 2014, vol. 79, p. 9253. doi 10.1021/ jo501672c
- 10. Zil'berman, E.N., *Reaktsii nitrilov* (Reactions of Nitriles), Moscow: Khimiya, 1972.
- 11. *Metody elementoorganicheskoi khimii* (Methods of Organoelemental Chemistry), Nesmeyanov, A.N. and Kocheshkov, K.A., Eds., Moscow: Nauka, 1964.