ISSN 1070-4280, Russian Journal of Organic Chemistry, 2018, Vol. 54, No. 12, pp. 1831–1834. © Pleiades Publishing, Ltd., 2018.
Original Russian Text © O.A.Tarasova, N.A. Nedolya, A.I. Albanov, 2018, published in Zhurnal Organicheskoi Khimii, 2018, Vol. 54, No. 12, pp. 1817–1820.

SHORT COMMUNICATIONS

One-Pot Synthesis of 1-(1-Alkoxyethoxy)allenes

O. A.Tarasova[a], N. A. Nedolya[a],* and A. I. Albanov[a]

[a] *Favorskii Irkutsk Institute of Chemistry, Siberian Branch, Russian Academy of Sciences, ul. Favorskogo 1, Irkutsk, 664033 Russia*
**e-mail: nina@irioch.irk.ru*

Received October 3, 2018; revised October 15, 2018; accepted October 17, 2018

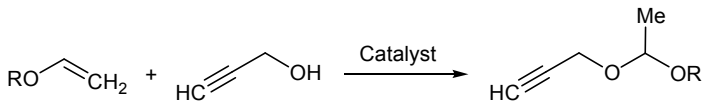
Abstract—A convenient one-pot procedure has been proposed for the preparation of 1-(1-alkoxyethoxy)allenes from alkoxyethenes and prop-2-yn-1-ol with the use of trifluoroacetic acid as highly efficient catalyst for the synthesis of 3-(1-alkoxyethoxy)prop-1-ynes and of the system *t*-BuOK–DMSO for the isomerization of the latter into allenes.

DOI: 10.1134/S1070428018120163

3-(1-Alkoxyethoxy)prop-1-ynes **1** and their allene isomers, 1-(1-alkoxyethoxy)allenes **2**, are promising starting compounds for cascade syntheses and functionalization of most important nitrogen and sulfur heterocycles [1, 2] such as pyrroles [3–6], dihydropyridines [7–10], pyridines [8–10], azepines, dihydroazepines [11], thiophenes [12–15], and dihydrothiazoles [16, 17]. The presence in these heterocycles of highly reactive and pharmacophoric substituents, including acetal groups, not only extends their synthetic potential but also gives hopes to broaden the spectrum of their biological activity. Acetals are valuable synthetic raw materials and technologically important products [18, 19] with wide and diverse scope of application; in particular, their high biological and physiological activity determines their use as repellents, attractants, plant growth and fruiting regulators, herbicides, zoocides, fungicides, bactericides, insecticides and their synergists, pharmacological agents (tranquilizers, anesthetics, analgesics, anticonvulsants, neuroleptics, spasmolytics), components of fragrance compositions (perfumes, lotions, detergents), intermediate compounds in the synthesis of important biologically active compounds of natural origin, etc.

Four 3-(1-alkoxyethoxy)prop-1-ynes like **1** have been reported. They were synthesized by the addition of prop-2-yn-1-ol to the corresponding alkoxyethene in the presence of an acid catalyst such as *p*-toluenesulfonic acid [1, 3, 20, 21], its monohydrate [22] or pyridinium salt [23], trifluoromethanesulfonic acid [24], concentrated aqueous HCl [25–28], and $CoCl_2$ [29] (Scheme 1). The reactions were carried out under solvent-free conditions [1, 3, 21, 25] or in an anhydrous solvent (benzene, diethyl ether, acetonitrile, methylene chloride) on cooling (–20 to –15°C [1, 3], 0°C [22, 23], 5–10°C [21]), at room temperature [20, 24, 26, 29], or on heating (85–90°C [28], 110–130°C under pressure [25]); the reaction time ranged from 4 to 15 h (mostly 10–12 h). The reactions catalyzed by trifluoromethanesulfonic acid were conducted in an inert atmosphere [24]. To avoid alcoholysis of the resulting mixed acetal **1**, excess alkoxyethene (1.1 to 2.0 equiv) was generally used. One of the reactants (prop-2-yn-1-ol or alkoxyethene) was added dropwise to a solution of the catalyst in the other reagent [1, 3, 21] or of the catalyst and the other reagent in an appropriate solvent. When the reaction was complete, the reaction mixture was treated with sodium

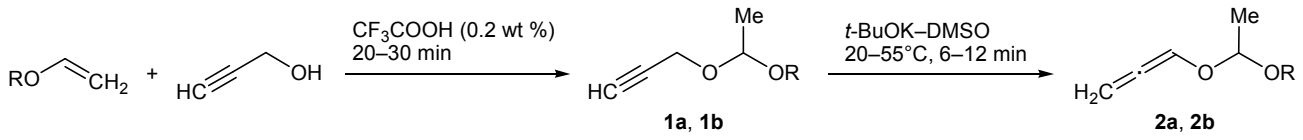
Scheme 1.



1

R = Me, Et, *n*-Bu, *i*-Bu; catalyst: 4-$MeC_6H_4SO_3H$, 4-$MeC_6H_4SO_3H \cdot H_2O$, 4-$MeC_6H_4SO_3H$·pyridine, CF_3SO_3H, HCl, $CoCl_2$.

Scheme 2.



R = Et (**a**), *n*-Bu (**b**).

methoxide [20], concentrated aqueous solution of sodium carbonate [22] or sodium hydrogen carbonate [23], or solid potassium carbonate [24, 28] to neutralize the catalyst. The yields of 3-(1-alkoxyethoxy)-prop-1-ynes **1** ranged from 49 to 92%.

We previously showed that perfluorinated carboxylic acids such as trifluoroacetic or perfluorobutyric are convenient and specific catalysts for electrophilic addition of hydroxy compounds to vinyl ethers [30, 31]. In this work, using trifluoroacetic acid as catalyst, from commercial alkoxyethenes and prop-2-yn-1-ol we obtained 3-(1-alkoxyethoxy)prop-1-ynes **1a** and **1b** in quantitative yield (Scheme 2).

The reactions were fast and were accompanied by a slight evolution of heat upon addition of the catalyst (~0.2 wt %) to a mixture of alkoxyethene and prop-2-yn-1-ol at a ratio of (1–1.2):1 and were complete in 20–30 min. To effect acetylene–allene isomerization, a solution of potassium *tert*-butoxide (10–11 wt %) in DMSO was added to the reaction mixture at room temperature, and the mixture was stirred for 6–12 min at 20–55°C. Allenyl acetals **2a** and **2b** were isolated by distillation in 68 and 77% yield (calculated on the initial prop-2-yn-1-ol), respectively.

1-(1-Ethoxyethoxy)allene **2a** was synthesized previously [21] by heating 3-(1-ethoxyethoxy)prop-1-yne **1a** in the presence of a catalytic amount of potassium *tert*-butoxide (without a solvent) at 70°C for 2–3 h. There are no published data on the synthesis of 1-(1-butoxyethoxy)allene **2b**.

Thus, the use of trifluoroacetic acid as catalyst in the reaction of prop-2-yn-1-ol with alkoxyethenes makes it possible to readily synthesize in a short time (20–40 min) in one preparative step both 3-(1-alkoxyethoxy)prop-1-ynes **1** and their allene isomers **2** that are synthetically important monomers and versatile building blocks [1–17, 32–35].

1-(1-Ethoxyethoxy)allene (2a). Trifluoroacetic acid 0.036 g (0.2 wt %) was added dropwise to a mixture of 10.82 g (0.150 mol) of ethyl vinyl ether and 7.01 g (0.125 mol) of prop-2-yn-1-ol with stirring on a magnetic stirrer at room temperature. The reaction was accompanied by evolution of heat, and the mixture quickly warmed up to 60°C. It was stirred for 20 min at 20→60→30°C with intermittent cooling. According to the NMR data, 3-(1-ethoxyethoxy)prop-1-yne (**1a**) was formed in quantitative yield. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.19 t (3H, $OCH_2C\mathbf{H}_3$, ^3J = 7.1 Hz), 1.32 d [3H, $OCH(C\mathbf{H}_3)O$, ^3J = 5.4 Hz], 2.41 t (1H, ≡CH, ^4J = 2.5 Hz), 3.51 d.q and 3.64 d.q (2H, $OC\mathbf{H}_2CH_3$, *AB* system, ^2J = 8.7, ^3J = 7.1 Hz), 4.19 d (2H, $OCH_2C\equiv$, ^4J = 2.5 Hz), 4.84 q [1H, $OC\mathbf{H}(CH_3)O$, ^3J = 5.4 Hz]. ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 15.05 ($OCH_2\mathbf{C}H_3$), 19.48 [$OCH(\mathbf{C}H_3)O$], 52.29 ($O\mathbf{C}H_2C\equiv$), 60.59 ($O\mathbf{C}H_2CH_3$), 73.63 (≡CH), 79.88 ($OCH_2\mathbf{C}\equiv$), 98.44 [$O\mathbf{C}H(CH_3)O$].

A solution of 2.0 g (0.018 mol, 10.2 wt %) of potassium *tert*-butoxide in 12 mL of anhydrous DMSO was added to the mixture, and the mixture warmed up to 37°C. It was stirred for 6 min at 37–42°C and treated (without preliminary cooling) with 15 mL of a saturated aqueous solution of ammonium chloride. The organic layer was separated, and the aqueous phase was extracted with diethyl ether (4×30 mL). The extracts were combined with the organic phase, washed with a saturated aqueous solution of ammonium chloride (4×30 mL) to remove DMSO and *t*-BuOH, and dried over potassium carbonate. The solvent was removed under reduced pressure on a rotary evaporator, and the residue was distilled in a vacuum to isolate 10.92 g (68%) of allene **2a** as a colorless liquid, bp 54–58°C (36 mm), n_D^{20} = 1.4357. IR spectrum (film), ν, cm^{-1}: 3033, 2982, 2928, 2883, 2803, 1953 (C=C=C), 1447, 1383, 1342, 1276, 1184, 1135, 1080, 1048, 1016, 947, 883, 857, 821, 694, 670, 623, 522. ^{1}H NMR spectrum, δ, ppm: 1.20 t (3H, $OCH_2C\mathbf{H}_3$, ^3J = 7.1 Hz), 1.36 d [3H, $OCH(C\mathbf{H}_3)O$, ^3J = 5.1 Hz], 3.48 d.q and 3.75 d.q (2H, $OC\mathbf{H}_2CH_3$, *AB*, ^2J = 9.3, ^3J = 7.1 Hz), 4.92 q [1H, $OC\mathbf{H}(CH_3)O$, ^3J = 5.1 Hz], 5.34 d.d and 5.36 d.d (2H, CH_2=, *AB*, ^2J = 8.4, ^4J = 6.0 Hz), 6.67 t (1H, OCH=, ^4J = 6.0 Hz). ^{13}C NMR spectrum, δ_C, ppm: 15.02 ($OCH_2\mathbf{C}H_3$), 20.13 [$OCH(\mathbf{C}H_3)O$], 62.61 ($O\mathbf{C}H_2CH_3$), 88.81 (CH_2=), 99.68 [$O\mathbf{C}H(CH_3)O$], 116.95 (OCH=), 201.47 (=C=); the ^{13}C NMR signals were assigned on the basis of the 2D ^{1}H–^{13}C HSQC data. Found, %: C 65.48; H 9.57. $C_7H_{12}O_2$. Calculated, %: C 65.60; H 9.44.

1-(1-Butoxyethoxy)allene (2b). Trifluoroacetic acid, 0.04 g (0.2 wt %), was added dropwise to a mixture of 12.78 g (0.125 mol) of butyl vinyl ether and 7.01 g (0.125 mol) of prop-2-yn-1-ol with stirring on a magnetic stirrer at room temperature. The reaction was accompanied by evolution of heat, and the mixture slowly warmed up to 60°C. The mixture was stirred for 30 min at 20→60→30°C (without external cooling). According to the NMR data, 3-(1-butoxyethoxy)prop-1-yne (**1b**) was formed in quantitative yield. IR spectrum (film), ν, cm^{-1}: 3300 (≡C–H), 2957, 2932, 2872, 1456, 1388, 1344, 1265, 1237, 1201, 1133, 1094, 1042, 979, 913, 873, 837, 738, 664, 635, 510. ^{1}H NMR spectrum, δ, ppm: 0.91 t [3H, $O(CH_2)_3CH_3$, ^3J = 7.3 Hz], 1.32 d [3H, $OCH(CH_3)O$, ^3J = 5.4 Hz], 1.37 m [2H, $O(CH_2)_2CH_2CH_3$], 1.55 m [2H, $OCH_2CH_2C_2H_5$], 2.40 t (1H, ≡CH, ^4J = 2.4 Hz), 3.44 d.t and 3.58 d.t (2H, $OCH_2C_3H_7$, *AB*, ^2J = 9.3, ^3J = 6.6 Hz), 4.19 d (2H, OCH_2C≡, ^4J = 2.4 Hz), 4.84 q [1H, $OCH(CH_3)O$, ^3J = 5.4 Hz]. ^{13}C NMR spectrum, δ_C, ppm: 13.74 [$O(CH_2)_3CH_3$], 19.26 ($O(CH_2)_2CH_2CH_3$), 19.47 [$OCH(CH_3)O$], 31.77 [$OCH_2CH_2C_2H_5$], 52.37 (OCH_2C≡), 65.00 ($OCH_2C_3H_7$), 73.71 (≡CH), 79.92 (OCH_2C≡), 98.61 [$OCH(CH_3)O$]; signals in the ^{13}C NMR spectrum were assigned on the basis of the 2D ^{1}H–^{13}C HSQC data.

A solution of 2.5 g (0.02 mol, 11.3 wt %) of potassium *tert*-butoxide in 12 mL of anhydrous DMSO was added to the resulting material, and the mixture was stirred for 8 min at room temperature and for 4 min at 50–55°C. It was then treated with 20 mL of a saturated aqueous solution of ammonium chloride, the organic layer was separated, and the aqueous phase was extracted with diethyl ether (2×30 mL) and diethyl ether–hexane (~1:1, 30 mL). The extracts were combined with the organic phase, washed with a saturated aqueous solution of ammonium chloride (3×30 mL), and dried over potassium carbonate. The solvent was removed under reduced pressure, and the residue was distilled in a vacuum to isolate 14.93 g (77%) of allene **2b** as a colorless liquid, bp 72–74°C (14 mm), n_D^{20} = 1.4395. IR spectrum (film), ν, cm^{-1}: 3034, 2985, 2957, 2934, 2873, 1953 (C=C=C), 1449, 1383, 1344, 1259, 1193, 1173, 1134, 1084, 1015, 985, 914, 886, 832, 741, 697, 670, 624, 541, 522, 472. ^{1}H NMR spectrum, δ, ppm: 0.91 t [3H, $O(CH_2)_3CH_3$, ^3J = 7.3 Hz], 1.35 d [3H, $OCH(CH_3)O$, ^3J = 5.1 Hz], 1.37 m [2H, $O(CH_2)_2CH_2CH_3$], 1.55 m [2H, $OCH_2CH_2C_2H_5$], 3.42 d.t and 3.69 d.t (2H, $OCH_2C_3H_7$, *AB*, ^2J = 9.4, ^3J = 6.9 Hz), 4.90 q [1H, $OCH(CH_3)O$, ^3J = 5.1 Hz], 5.33 d.d and 5.35 d.d (2H, CH_2=, *AB*, ^2J = 8.7, ^4J = 6.1 Hz), 6.66 t (1H, OCH=, ^4J = 6.1 Hz). ^{13}C NMR spectrum, δ_C, ppm: 13.67 [$O(CH_2)_3CH_3$], 19.18 [$O(CH_2)_2CH_2CH_3$], 19.99 [$OCH(CH_3)O$], 31.64 [$OCH_2CH_2C_2H_5$], 66.77 ($OCH_2C_3H_7$), 88.57 (CH_2=), 99.81 [$OCH(CH_3)O$], 116.88 (OCH=), 201.62 (=C=). Found, %: C 69.30; H 10.19. $C_9H_{16}O_2$. Calculated, %: C 69.19; H 10.32.

The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DPX-400 spectrometer at 400.13 and 100.62 MHz, respectively; heteronuclear ^{1}H–^{13}C HSQC correlations were obtained on a Bruker AV-400 instrument using $CDCl_3$ as solvent; the chemical shifts were measured relative to hexamethyldisiloxane (δ 0.05 ppm) and $CDCl_3$ (δ_C 77.00 ppm). The IR spectra were recorded on a Bruker Vertex 70 spectrometer. The elemental analyses were obtained with a Carlo Erba EA-1108 CHNS/O analyzer. The progress of reactions and the purity of the isolated compounds were monitored by TLC on Silica gel $60F_{254}$ plates, as well as by ^{1}H NMR. Dimethyl sulfoxide was dried by distillation over potassium *tert*-butoxide. Alkoxyethenes, prop-2-yn-1-ol, and other reagents and solvents used in this work were commercial products.

This study was performed using the equipment of the Baikal Joint Analytical Center (Siberian Branch, Russian Academy of Sciences).

REFERENCES

1. Nedolya, N.A., Ph.D. Thesis of Utrecht University, Utrecht, The Netherlands, 1999.
2. Nedolya, N.A. and Trofimov, B.A., *Khimiya geterotsiklicheskikh soedinenii. Sovremennye aspekty* (Chemistry of Heterocyclic Compounds. Modern Aspects), Kartsev, V.G., Ed., Moscow: MBFNP, 2014, vol. 1, p. 329.
3. Brandsma, L., Nedolya, N.A., and Trofimov, B.A., *Russ. Chem. Bull., Int. Ed*., 2000, vol. 49, p. 1634. doi 10.1007/BF02495172
4. Tarasova, O.A., Nedolya, N.A., Albanov, A.I., and Trofimov, B.A., *Russ. J. Org. Chem*., 2010, vol. 46, p. 773. doi 10.1134/S1070428010050337
5. Brandsma, L., Nedolya, N.A., Tolmachev, S.V., and Albanov, A.I., *Chem. Heterocycl. Compd*., 2001, vol. 37, p. 364.
6. Nedolya, N.A., Brandsma, L., and Tolmachev, S.V., *Russ. J. Org. Chem*., 2002, vol. 38, p. 907.
7. Nedolya, N.A., Tolmachev, S.V., and Brandsma, L., *Russ. J. Org. Chem*., 2007, vol. 43, p. 478. doi 10.1134/S1070428007030311
8. Nedolya, N.A., Brandsma, L., Shlyakhtina, N.I., and Fedorov, S.V., *Chem. Heterocycl. Compd*., 2002, vol. 38, p. 622. doi 10.1023/A:1019585802386

9. Nedolya, N.A., Schlyakhtina, N.I., Klyba, L.V., Ushakov, I.A., Fedorov, S.V., and Brandsma, L., *Tetrahedron Lett*., 2002, vol. 43, p. 9679.
10. Tarasova, O.A., Nedolya, N.A., Albanov, A.I., and Trofimov, B.A., *Russ. J. Org. Chem*., 2015, vol. 51, p. 740. doi 10.1134/S1070428015050279
11. Nedolya, N.A., Tarasova, O.A., Albanov, A.I., Volostnykh, O.G., Brandsma, L., and Trofimov, B.A., *Mendeleev Commun*., 2008, vol. 18, p. 164.
12. Nedolya, N.A., Tarasova, O.A., Brandsma, L., and Trofimov, B.A., *Russ. J. Org. Chem*., 2009, vol. 45, p. 626. doi 10.1134/S1070428009040289
13. Tarasova, O.A., Nedolya, N.A., Albanov, A.I., Brandsma, L., and Trofimov, B.A., *Russ. J. Org. Chem*., 2009, vol. 45, p. 939. doi 10.1134/S1070428009060244
14. Nedolya, N.A., Tarasova, O.A., Albanov, A.I., and Trofimov, B.A., *J. Org. Chem*., 2017, vol. 82, p. 7519.
15. Nedolya, N.A., Tarasova, O.A., Albanov, A.I., and Trofimov, B.A., *Synthesis*, 2018, vol. 50, p. 1891.
16. Nedolya, N.A., Tarasova, O.A., Albanov, A.I., and Trofimov, B.A., *Synthesis*, 2015, vol. 47, p. 3593.
17. Nedolya, N.A., Tarasova, O.A., Albanov, A.I., Klyba, L.V., and Trofimov, B.A., *Tetrahedron*, 2017, vol. 73, p. 1085.
18. Yanovskaya, L.A., Yufit, S.S., and Kucherov, V.F., *Khimiya atsetalei* (Chemistry of Acetals), Moscow: Nauka, 1975.
19. Bogomazova, A., Mikhailova, N., and Zlotskii, S., *Sovremennaya khimiya tsiklicheskikh atsetalei. Poluchenie. Reaktsii. Svoistva* (Modern Chemistry of Cyclic Acetlas. Syntheis, Reactions, and Properties), Lambert Academic, 2012.
20. Kleinschmidt, R.F., US Patent no. 2641615, 1953; *Chem. Abstr*., 1954, vol. 48, p. 18408.
21. Hoff, S., Brandsma, L., and Arens, J.F., *Recl. Trav. Chim. Pays–Bas*, 1968, vol. 87, p. 916.
22. Hoffmeister, L., Fukuda, T., Pototschnig, G., and Fürstner, A., *Chem. Eur. J*., 2015, vol. 21, p. 4529.
23. Blouin, S., Gandon, V., Blond, G., and Suffert, J., *Angew. Chem., Int. Ed*., 2016, vol. 55, p. 7208.
24. Mames, A., Stecko, S., Mikołajczyk, P., Soluch, M., Furman, B., and Chmielewski, M., *J. Org. Chem*., 2010, vol. 75, p. 7580.
25. Shostakovskii, M.F., Vlasov, V.M., and Grenovskii, P.I., *Zh. Obshch. Khim*., 1964, vol. 34, p. 1403.
26. Zakharkin, L.I., Stanko, V.I., and Brattsev, V.A., *Bull. Acad. Sci. USSR, Div. Chem. Sci*., 1964, vol. 13, no. 5, p. 871.
27. Lisovin, E.G. and Komarov, N.V., *Zh. Obshch. Khim*., 1980, vol. 50, p. 854.
28. Karaev, S.F., Guseinov, Sh.O., and Garaeva, Sh.V., *Russ. J. Gen. Chem*., 1994, vol. 64, p. 632.
29. Iqbal, J., Srivastava, R.R., Gupta, K.B., and Khan, M.A., *Synth. Commun*., 1989, vol. 19, p. 901.
30. Nedolya, N.A., *Cand. Sci. (Chem.) Dissertation*, Irkutsk, 1982.
31. Nedolya, N.A. and Trofimov, B.A., *J. Org. Chem. USSR*, 1985, vol. 21, p. 680.
32. Stork, G. and Nakamura, E., *J. Am. Chem. Soc*., 1983, vol. 105, p. 5510.
33. Buynak, J.D., Strickland, J.B., Lamb, G.W., Khasnis, D., Modi, S., Williams, D., and Zhang, H., *J. Org. Chem*., 1991, vol. 56, p. 7076.
34. Ricci, A., Degl'Innocenti, A., Capperucci, A., Reginato, G., and Mordini, A., *Tetrahedron Lett*., 1991, vol. 32, p. 1899.
35. Friesen, R.W., *J. Chem. Soc., Perkin Trans. 1*, 2001, p. 1969.