Electronic supplementary materials *Mendeleev Commun*., 2011, **21**, 339–340

Convenient synthesis of diarylpropargyl alcohols

Valerii Z. Shirinian,* Alexey A. Shimkin, Arthur K. Mailyan, Evgenya S. Leonova and Mikhail M. Krayushkin

General

^{1}H NMR spectra were recorded on a Bruker AM-300 spectrometer. Mass spectra were obtained on a Kratos mass spectrometer (70 eV) with direct sample inlet into the ion source. Melting points were measured on a Boetius hot stage and were not corrected. Commercially available (Acros, Merck) reagents and solvents were used. Chromatography materials were purchased from Merck. Benzophenones **1a-c,j** were prepared according to literature procedures,[1] others were synthesized by nucleophilic substitution of fluorine atom in (2,4-dimethoxyphenyl)(4-fluorophenyl)methanone (**1a**)[1a] or (4-fluorophenyl)(naphthalen-1-yl)methanone[2] with the appropriate amines as described elsewhere.[3]

Synthesis of diarylpropargyl alcohols (general procedure)

To a stirred mixture of sodium acetylide (18% suspension in xylene, 8 g, 30 mmol) in anhydrous THF (50 ml) benzophenone **1** (15 mmol or 7.5 mmol for **1g**) and 18-crown-6 (0.27 g, 1 mmol) were added. The flask was closed with a stopper, and the reaction mixture was stirred for 7 days at room temperature, and then poured into crushed ice (200 g). The precipitate was filtered off, washed with water (3×50 ml), and dried in air. If an oil instead of precipitate emerged, the mixture was extracted with ethyl acetate (3×50 ml). The combined extracts were washed with water (3×50 ml) and evaporated *in vacuo*. The crude material was purified by flash chromatography.

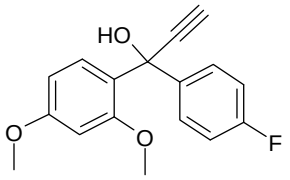
---

[1] (*a*) D. N. Gray and R. D. Knight, *J. Chem. Eng. Data*, 1966, **11**, 446; (*b*) A. Arnone, L. Camarda, L. Merlini and G. Nasini, *J. Chem. Soc., Perkin Trans. 1*, 1975, 186; (*c*) P. A. J. Janssen, G. H. P. Van Daele and J. M. Boey, *US* 4,035,376 (1977).

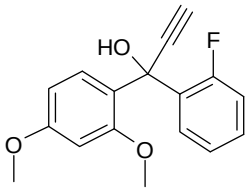
[2] M. Artico, G. Stefancich, R. Silvestri, S. Massa, G. Apuzzo, M. Artico and G. Simonetti, *Eur. J. Med. Chem.*, 1992, **27**, 693.

[3] S. Spange, M. El-Sayed, H. Mueller, G. Rheinwald, H. Lang and W. Poppitz, *Eur. J. Org. Chem.*, 2002, **24**, 4159.

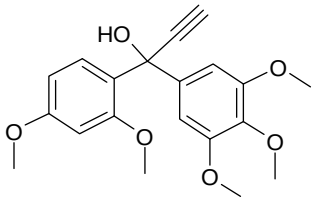
1-(2,4-Dimethoxyphenyl)-1-(4-fluorophenyl)prop-2-yn-1-ol **2a**: yellow oil, 4.25 g (99%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.82 (s, 1H, CH), 3.77 (s, 3H, CH_3), 3.82 (s, 3H, CH_3), 4.76 (s, 1H, OH), 6.45 (dd, J = 2.2, 8.4, 1H, H^{arom}), 6.51 (d, J = 2.2, 1H, H^{arom}), 6.98–7.07 (m, 2H, H^{arom}), 7.24 (d, J = 8.4, 1H, H^{arom}), 7.52 (dd, J = 5.5, 8.8, 1H, H^{arom}). MS, *m/z* (%): 286 (35, $[M]^+$), 271 (38, $[M–Me]^+$), 255 (100, $[M–OMe]^+$), 191 (74, $[M–C_6H_4F]^+$). Found (%): C, 71.40; H, 5.35. Calc. for $C_{17}H_{15}FO_3$ (%): C, 71.32; H, 5.28.



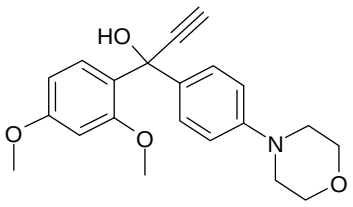
1-(2,4-Dimethoxyphenyl)-1-(2-fluorophenyl)prop-2-yn-1-ol **2b**: white solid, 4.12 g (96%), mp 103–104°C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.82 (s, 1H, CH), 3.74 (s, 3H, CH_3), 3.81 (s, 3H, CH_3), 4.78 (s, 1H, OH), 6.45–6.55 (m, 2H, H^{arom}), 6.95–7.06 (m, 1H, H^{arom}), 7.12–7.20 (m, 1H, H^{arom}), 7.27–7.35 (m, 1H, H^{arom}), 7.50 (d, J = 8.8, 1H, H^{arom}), 7.69–7.78 (m, 1H, H^{arom}). MS, *m/z* (%): 286 (45, $[M]^+$), 271 (35, $[M–Me]^+$), 255 (100, $[M–OMe]^+$), 191 (80, $[M–C_6H_4F]^+$). Found (%): C, 71.39; H, 5.32. Calc. for $C_{17}H_{15}FO_3$ (%): C, 71.32; H, 5.28.



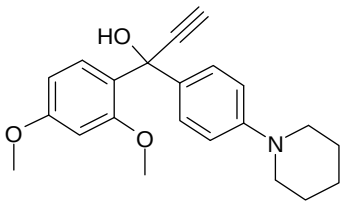
1-(2,4-Dimethoxyphenyl)-1-(3,4,5-trimethoxyphenyl)prop-2-yn-1-ol **2c**: yellow oil, 4.72 g (88%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.81 (s, 1H, CH), 3.82 (s, 12H, $4CH_3$), 3.86 (s, 3H, CH_3), 4.89 (s, 1H, OH), 6.43 (d, J = 8.1, 1H, H^{arom}), 6.52 (s, 1H, H^{arom}), 6.82 (s, 2H, H^{arom}), 7.11 (d, J = 8.1, 1H, H^{arom}). MS, *m/z* (%): 358 (71, $[M]^+$), 343 (44, $[M–Me]^+$), 255 (47), 191 (81), 165 (100). Found (%): C, 67.12; H, 6.25. Calc. for $C_{20}H_{22}O_6$ (%): C, 67.03; H, 6.19.



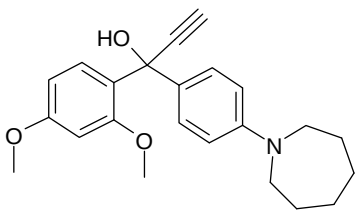
1-(2,4-Dimethoxyphenyl)-1-[4-(morpholin-4-y)lphenyl]prop-2-yn-1-ol **2d**: yellowish solid, 5.08 g (96%), mp 171–172°C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.78 (s, 1H, CH), 3.17 (t, J = 4.6, 4H, $2CH_2$), 3.78 (s, 3H, CH_3), 3.80 (s, 3H, CH_3), 3.86 (t, J = 4.6, 4H, $2CH_2$), 4.74 (s, 1H, OH), 6.43 (dd, J = 2.0, 8.5, 1H, H^{arom}), 6.51 (d, J = 2.0, 1H, H^{arom}), 6.88 (d, J = 8.5, 2H, H^{arom}), 7.20 (d, J = 8.5, 1H, H^{arom}), 7.44 (d, J = 8.5, 2H, H^{arom}). MS, *m/z* (%): 353 (55, $[M]^+$), 338 (29, $[M–Me]^+$), 336 (63, $[M–OH]^+$), 322 (100), 310 (62), 165 (62). Found (%): C, 71.42; H, 6.65; N, 3.95. Calc. for $C_{21}H_{23}NO_4$ (%): C, 71.37; H, 6.56; N, 3.96.



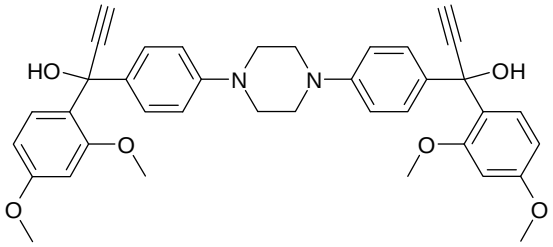
1-(2,4-Dimethoxyphenyl)-1-[4-(piperidin-1-yl)phenyl]prop-2-yn-1-ol **2e**: brownish solid, 4.74 g (90%), mp 66–67°C (light-yellow oil[4]). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.53–1.63 (m, 2H, CH_2), 1.65–1.76 (m, 4H, $2CH_2$), 2.77 (s, 1H, CH), 3.18 (t, J = 5.5, 4H, $2CH_2$), 3.79 (s, 3H, CH_3), 3.80 (s, 3H, CH_3), 4.76 (br. s, 1H, OH), 6.42 (dd, J = 2.2, 8.8, 1H, H^{arom}), 6.51 (d, J = 2.2, 1H, H^{arom}), 6.90 (d, J = 8.8, 2H, H^{arom}), 7.19 (d, J = 8.8, 1H, H^{arom}), 7.41 (d, J = 8.8, 2H, H^{arom}). MS, *m/z* (%): 351 (100, $[M]^+$), 336 (35, $[M–Me]^+$), 334 (33, $[M–OH]^+$), 320 (31), 191 (38).



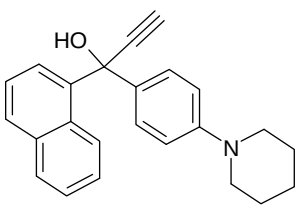
1-[4-(Azepan-1-yl)phenyl]-1-(2,4-dimethoxyphenyl)prop-2-yn-1-ol **2f**: brownish solid, 4.98 g (91%), mp 110–111.5°C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.50–1.61 (m, 4H, $4CH_2$), 1.73–1.86 (m, 4H, $2CH_2$), 2.77 (s, 1H, CH), 3.46 (t, J = 5.5, 4H, $2CH_2$), 3.80 (s, 3H, CH_3), 3.82 (s, 3H, CH_3), 4.77 (br. s, 1H, OH), 6.43 (dd, J = 2.2, 8.8, 1H, H^{arom}), 6.53 (d, J = 2.2, 1H, H^{arom}), 6.66 (d, J = 8.8, 2H, H^{arom}), 7.19 (d, J = 8.8, 1H, H^{arom}), 7.37 (d, J = 8.8, 2H, H^{arom}). MS, *m/z* (%): 365 (100, $[M]^+$), 350 (28, $[M–Me]^+$), 348 (29, $[M–OH]^+$), 334 (72), 165 (53). Found (%): C, 75.65; H, 7.50; N, 3.90. Calc. for $C_{23}H_{27}NO_3$ (%): C, 75.59; H, 7.45; N, 3.83.



1,4-Bis(4-{4-[1-(2,4-dimethoxyphenyl)-1-hydroxyprop-2-yn-1-yl]phenyl}piperazin) **2g**: yellow solid, 4.03 g (87%), mp 231–233°C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.83 (s, 2H, CH), 3.19–3.33 (m, 8H, $4CH_2$), 3.58 (s, 6H, $2CH_3$), 3.71 (s, 6H, $2CH_3$), 6.28–6.47 (m, 4H, H^{arom}), 6.72–6.91 (m, 4H, H^{arom}), 7.23–7.35 (m, 4H, H^{arom}), 7.36–7.48 (m, 2H, H^{arom}). MS, *m/z* (%): 618 (100, $[M]^+$), 603 (10, $[M–Me]^+$), 601 (9, $[M–OH]^+$), 593 (18), 165 (68). Found (%): C, 73.85; H, 6.22; N, 4.60. Calc. for $C_{38}H_{38}N_2O_6$ (%): C, 73.77; H, 6.19; N, 4.53.



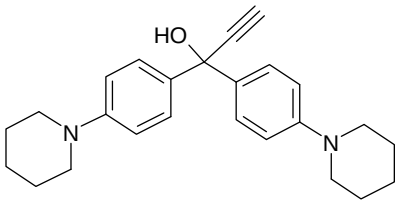
1-(Naphthalen-1-yl)-1-[4-(piperidin-1-yl)phenyl]prop-2-yn-1-ol **2h**: yellowish solid, 4.70 g (92%), mp 181–183°C. ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.51–1.62 (m, 2H, CH_2), 1.63–1.75 (m, 4H, $2CH_2$), 2.90 (s, 1H, CH), 2.92 (s, 1H, OH), 3.15 (t, J = 5.5, 4H, $2CH_2$), 6.85 (d, 8.4, 2H, H^{arom}), 7.31 (d, J = 8.1, 1H, H^{arom}), 7.36–7.45 (m, 3H, H^{arom}), 7.52 (t, J = 7.7, 1H, H^{arom}),



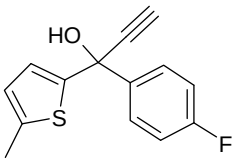
[4] V. D. Arsenov, A. M. Gorelik, V. A. Barachevsky and M. V. Alfimov, *EP* 1,038,870 A1, 2000.

7.81–7.90 (m, 2H, H^{arom}), 8.06–8.15 (m, 2H, H^{arom}). MS, *m/z* (%): 341 (100, $[M]^+$), 324 (52, $[M–OH]^+$), 313 (25), 239 (23), 214 (41), 210 (50), 181 (34), 161 (41), 160 (48). Found (%): C, 84.32; H, 6.75; N, 4.13. Calc. for $C_{24}H_{23}NO$ (%): C, 84.42; H, 6.79; N, 4.10.

1,1-Bis[4-(piperidin-1-yl)phenyl]prop-2-yn-1-ol **2i**: yellowish solid, 4.77 g (85%), mp 152–153°C (lit.[5] 151.5–153°C). ^1H NMR (300 MHz, $CDCl_3$): δ 1.52–1.63 (m, 4H, $2CH_2$), 1.64–1.76 (m, 8H, $4CH_2$), 2.82 (s, 1H, OH), 2.88 (s, 1H, CH), 3.11–3.20 (m, 8H, $4CH_2$), 6.87 (d, J = 8.0, 4H, H^{arom}), 7.43 (d, J = 8.0, 4H, H^{arom}). MS, *m/z* (%): 374 (100, $[M]^+$), 357 (34, $[M–OH]^+$), 348 (19), 346 (21).



1-(4-Fluorophenyl)-1-(5-methylthiophen-2-yl)prop-2-yn-1-ol **2j**: yellow oil, 3.32 g (90%). ^1H NMR (300 MHz, $CDCl_3$): δ 2.43 (s, 3H, CH_3), 2.88(s, 1H, CH), 3.09 (br. s, 1H, OH), 6.57 (dd, J = 1.3, 2.6, 1H, H^{thioph}), 6.88 (d, J = 2.6, 1H, H^{thioph}), 7.00–7.09 (m, 2H, H^{arom}), 7.67 (dd, J = 5.3, 7.8, 2H, H^{arom}). MS, *m/z* (%): 246 (24, $[M]^+$), 220 (68), 125 (100). Found (%): C, 68.32; H, 4.55; S, 12.95. Calc. for $C_{14}H_{11}FOS$ (%): C, 68.27; H, 4.50; S, 13.02.



[5] C. D. Gabbutt, J. D. Hepworth, B. M. Heron, S. M. Partington and D. A. Thomas, *Dyes Pigm.*, 2001, **49**, 65.