Efficient Synthesis of Optically Active 2,3-Allenols via the Simple CuBr-Mediated Reaction of Optically Active Propargylic Alcohols with Paraformaldehyde

Shengming Ma,* Hairong Hou, Shimin Zhao, Guangwei Wang

State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Lu, Shanghai 200032, P. R. China
Fax +86(21)64166128; E-mail: masm@pub.sioc.ac.cn

Received 16 April 2002; revised 3 June 2002

Abstract: Enantiomerically enriched 2,3-allenols were prepared by the CuBr-mediated homologation of the relatively easily available optically active terminal propargylic alcohols with paraformaldehyde in the presence of diisopropylamine.

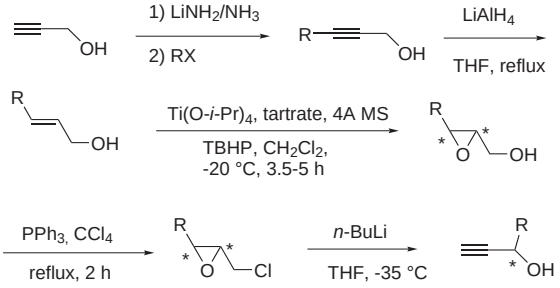
Key words: propargylic alcohols, 2,3-allenols, copper

2,3-Allenols are an important class of functionalized allenes, which can be used as the starting materials for the synthesis of oxiranes,[1] 2,5-dihydrofurans,[2] α-methylenelactone,[3] α- or γ-amino alcohols,[4] and α,β-unsaturated ketones.[5] For the synthesis of oxygen-containing heterocycles, it should be possible to transfer the chirality of the optically active 2,3-allenols into the corresponding final products. Thus, the syntheses of optically active 2,3-allenols are of current interest. In this paper, we wish to report a facile synthesis of terminally unsubstituted 2,3-allenols with the chirality at the carbon atom connected to the hydroxyl group.

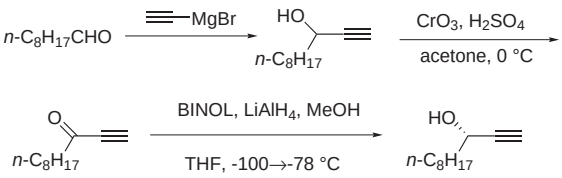
These optically active 2,3-allenols are usually prepared via the reaction of optically active 1,2-allenylboron reagents with aldehydes[6] or the (*S*)-BINOL(2,2′-dihydroxy-1,1′-binaphthyl)-Ti(IV)-catalyzed reaction of propargylictin with aldehydes.[7] Recently, we have prepared the optically active 2,3-allenols via the SN_2-type reduction of optically active 1-OTHP-alk-2-yn-4- ols with $LiAlH_4$.[1a]

Since optically active propargylic alcohols are relatively easily available by several approaches,[8] we reasoned that the optically active 2,3-allenols with the chiral centers connected to the hydroxyl group can be synthesized via the CuBr-mediated reaction of optically active terminal propargylic alcohols with paraformaldehyde in the presence of diisopropylamine.[9]

The optically active propargylic alcohols used in this study were prepared via the treatment of corresponding optically active chloromethylepoxide with BuLi in THF (Scheme 1)[10] or the enantioselective reduction of 1-ethynyl ketones (Scheme 2).[8a]



Scheme 1



Scheme 2

In this study, (*R*)- or (*S*)-undecyn-3-ols were also prepared by the catalytic enantioselective reduction of 1-trimethylsilylundec-1-yn-3-one followed by desilylation (Scheme 3).[8e]

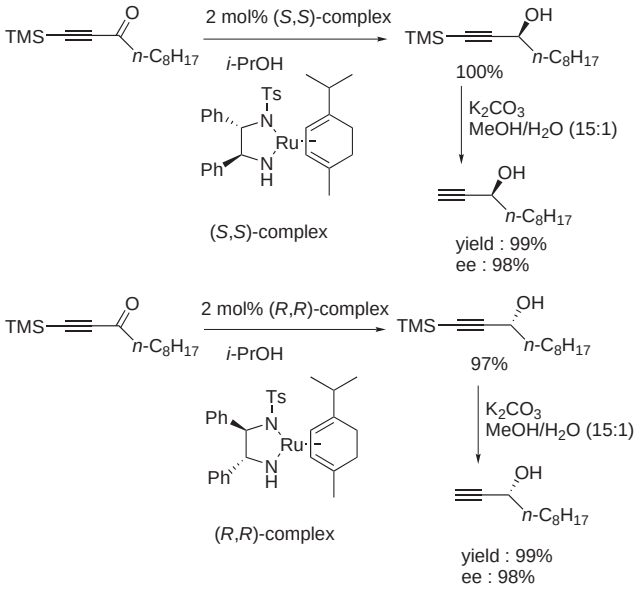
Using these above synthesized optically active propargylic alcohols as the starting materials, the results of CuBr-mediated reaction of optically active terminally unsubstituted propargylic alcohols with paraformaldehyde were summarized in Table 1.

From the results listed in Tables 1 and 2, it is obvious that the reaction afforded 2,3-allenols in moderate yields and the enantiopurity of the chiral center remained essentially unchanged. Due to the synthetic importance of (*S*)- or (*R*)-2,3-allenols, this route will show its utility in organic synthesis.

All reactions were carried out under argon unless otherwise noted. All solvents were distilled prior to use. 1,4-Dioxane was distilled from sodium ketyl. ^1H NMR spectra were recorded in $CDCl_3$ on a Varian 300 MHz spectrometer. IR spectra were obtained using a Perkin-Elmer 983 instrument. Mass spectra were obtained using a HP 5989A mass spectrometer. GC spectra were obtained using a Perkin-Elmer Autosystem XL Gas Chromatograph instrument(RT-βDEXcst, 30 meter, 0.25 m ID, 0.25 μm DF).

Synthesis 2002, No. 12, Print: 06 09 2002.
Art Id.1437-210X,E;2002,0,12,1643,1645,ftx,en;F02802SS.pdf.

ISSN 0039-7881



Scheme 3

(*R*)-Octa-1,2-dien-4-ol [(*R*)-2a]; Typical Procedure

In a reaction flask containing CuBr (142 mg, 0.99 mmol) and paraformaldehyde (144 mg, 4.8 mmol) were added subsequently *i*-Pr_2NH (0.51 mL, 364 mg, 3.6 mmol), (*R*)-hept-1-yn-3-ol [336 mg, 3.0 mmol; purity: 97% ee; GC conditions: carrier N_2; 8.0 psi; injector 250 °C; detector (FID, H_2, 0.218 MPa) 250 °C; oven temperature 120 °C (20 min), 1 °C min^{-1} to 140 °C (20 min); t_1 (*S*) 10.877 min, t_2 (*R*) 11.257 min], and 1,4-dioxane (4.0 mL). The mixture was heated at 120 °C for 2 h. After cooling, the mixture was evaporated and the crude product was submitted to chromatography on silica gel (petroleum ether–EtOAc, 10:1) to afford 242 mg (64%) of (*R*)-**2a**[11] with 97% ee [GC conditions: carrier N_2; 6.8 psi; injector 250 °C; detector (FID, H_2, 0.218 MPa) 250 °C; oven temperature 100 °C (10 min), 1 °C min^{-1} to 120 °C, 2 °C min^{-1} to 180 °C; t_1 (*S*) 28.867 min, t_2 (*R*) 29.428 min].

IR (neat): 3360, 1957, 842 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 5.23 (q, *J* = 6.5 Hz, 1 H), 4.86–4.83 (m, 2 H), 4.18–4.16 (m, 1 H), 1.57–1.53 (m, 2 H), 1.39–1.18 (m, 4 H), 0.89 (t, *J* = 6.9 Hz, 3 H).

MS: *m*/*z* (%) = 126 (M^+, 21.21), 87 (8.03), 69 (61.57), 57 (30.82), 43 (100.00), 41 (39.90).

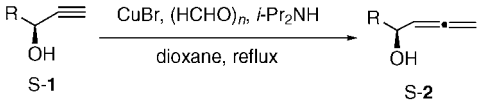
(*S*)-Octa-1,2-dien-4-ol [(*S*)-2a)]

The typical procedure given above was followed starting from CuBr (96 mg, 0.67 mmol), paraformaldehyde (98 mg, 3.3 mmol), *i*-Pr_2NH (0.35 mL, 250 mg, 2.5 mmol), (*S*)-hept-1-yn-3-ol (221 mg, 2.0 mmol, 80% ee), and 1,4-dioxane (3.5 mL) to afford 196 mg (79%, 80% ee) of (*S*)-**2a**.[11]

(*R*)-1,2-Undeca-1,2-dien-4-ol [(*R*)-2b]

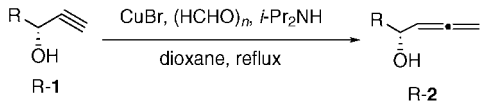
The typical procedure given above was followed starting from CuBr (94 mg, 0.66 mmol), paraformaldehyde (96 mg, 3.2 mmol), *i*-Pr_2NH (242 mg, 2.4 mmol, 0.34 mL), (*R*)-dec-1-yn-3-ol [308 mg, 2.0

Table 1 Homologation of (*S*)-Propargylic Alcohols (*S*)-**1** to (*S*)-2,3-Allenols (*S*)-**2**



Entry	(*S*)-**1**	ee of (*S*)-**1** (%)	Yield of (*S*)-**2** (%)	ee of (*S*)-**2** (%)	$[\alpha]_D^{20}$ (MeOH)
1	Bu [(*S*)-**1a**]	80	79 [(*S*)-**2a**]	80	–17.8 (*c*, 1.00)
2	C_7H_{15} [(*S*)-**1b**]	92	79 [(*S*)-**2b**]	92	–16.5 (*c*, 0.95)
3	C_8H_{17} [(*S*)-**1c**]	96	72 [(*S*)-**2c**]	95	–19.6 (*c*, 0.95)
4	Ph [(*S*)-**1d**]	96	77 [(*S*)-**2d**]	96	–130.6 (*c*, 0.95)

Table 2 Homologation of (*R*)-Propargylic Alcohols to (*R*)-2,3-Allenols



Entry	(*R*)-**1**	ee of (*R*)-**1** (%)	Yield of (*R*)-**2** (%)	ee of (*R*)-**2** (%)	$[\alpha]_D^{20}$ (MeOH)
1	Bu [(*R*)-**1a**]	97	64 [(*R*)-**2a**]	97	+22.8 (*c*, 1.05)
2	C_7H_{15} [(*R*)-**1b**]	89	70 [(*R*)-**2b**]	89	+18.9 (*c*, 0.95)
3	C_8H_{17} [(*R*)-**1c**]	94	69 [(*R*)-**2c**]	97	+15.3 (*c*, 1.05)
4	Ph [(*R*)-**1d**]	96	69 [(*R*)-**2d**]	97	+121.4 (*c*, 1.10)
5	C_8H_{17} [(*R*)-**1c**]	98	71 [(*R*)-**2c**]	98	+20.3 (*c*, 1.30)

mmol; purity: 89% ee; GC conditions: carrier N_2; 8.0 psi; injector 250 °C; detector (FID, H_2, 0.218 MPa) 250 °C; oven temperature 130 °C (10 min), 1 °C min^{-1} to 180 °C (10 min); t_1 (*S*) 23.815 min, t_2 (*R*) 24.292 min], and 1,4-dioxane (3.0 mL) to afford 234 mg (70%) of (*R*)-**2b**[12] with 89% ee [GC conditions: carrier N_2, 6.8 psi; injector 250 °C; detector (FID, H_2, 0.218 MPa) 250 °C; oven temperature 100 °C (10 min), 1 °C min^{-1} to 120 °C, 2 °C min^{-1} to 180 °C; t_1 (*S*) 52.345 min, t_2 (*R*) 52.863 min].

IR (neat): 3345, 1957, 842 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 5.24 (q, *J* = 6.5 Hz, 1 H), 4.87–4.84 (m, 2 H), 4.18–4.16 (m, 1 H), 1.70–1.53 (m, 2 H), 1.39–1.18 (m, 10 H), 0.89 (t, *J* = 6.9 Hz, 3 H).

MS: *m*/*z* (%) = 169 (M^+ + 1, 0.43), 109 (10.33), 95 (20.11), 81 (15.96), 69 (100.00).

(*S*)-Undeca-1,2-dien-4-ol [(*S*)-2b]
The typical procedure given above was followed starting from CuBr (142 mg, 0.99 mmol), paraformaldehyde (144 mg, 4.8 mmol), *i*-Pr_2NH (0.51 mL, 364 mg, 3.6 mmol), (*S*)-dec-1-yn-3-ol (462 mg, 3.0 mmol, 92% ee) and 1,4-dioxane (3.5 mL) to afford 395 mg (79%, 92% ee) of (*S*)-**2b**.[12]

(*R*)-Dodeca-1,2-dien-4-ol [(*R*)-2c]
The typical procedure given above was followed starting from CuBr (94 mg, 0.66 mmol), paraformaldehyde (96 mg, 3.2 mmol), *i*-Pr_2NH (0.34 mL, 242 mg, 2.4 mmol), (*R*)-undec-1-yn-3-ol [331 mg, 2.0 mmol; purity: 94% ee; GC conditions: carrier N_2; 8.0 psi; injector 250 °C; detector (FID, H_2, 0.218 MPa) 250 °C; oven temperature 140 °C, t_1 (*S*) 30.770 min, t_2 (*R*) 31.232 min], and 1,4-dioxane (3.0 mL) to afford 248 mg (69%) of (*R*)-**2c**[13] with 97% ee [GC conditions: carrier N_2; 8.0 psi; injector 250 °C; detector (FID, H_2, 0.218 MPa) 250 °C; oven temperature 140 °C; t_1 (*S*) 44.560 min, t_2 (*R*) 45.055 min].

When the same experiment was carried out with (*R*)-undec-1-yn-3-ol of 98% ee (332 mg, 2.0 mmol) (*R*)-**2c**[13] of 98% ee was obtained; yield: 256 mg (71%).

IR (neat): 3344, 1957, 842 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 5.18 (q, *J* = 6.5 Hz, 1 H), 4.80–4.77 (m, 2 H), 4.11–4.10 (m, 1 H), 1.54–1.44 (m, 2 H), 1.38–1.21 (m, 12 H), 0.81 (t, *J* = 6.7 Hz, 3 H).

MS: *m*/*z* (%) = 183 (M^+ + 1, 0.21), 109 (6.07), 95 (10.76), 69 (100.00), 57 (19.14).

(*S*)-Dodeca-1,2-dien-4-ol [(*S*)-2c]
The typical procedure given above was followed starting from CuBr (94 mg, 0.66 mmol), paraformaldehyde (96 mg, 3.2 mmol), *i*-Pr_2NH (0.34 mL, 242 mg, 2.4 mmol), (*S*)-undec-1-yn-3-ol (336 mg, 2.0 mmol, 96% ee) and 1,4-dioxane (3.0 mL) afforded 262 mg (72%, 95% ee) of (*S*)-**2c**.[13]

(*R*)-1-Phenylbuta-2,3-dien-1-ol [(*R*)-2d]
The typical procedure given above was followed starting from CuBr (94 mg, 0.66 mmol), paraformaldehyde (96 mg, 3.2 mmol), *i*-Pr_2NH (0.34 mL, 242 mg, 2.4 mmol), (*R*)-1-phenylprop-2-yn-1-ol [264 mg, 2.0 mmol; purity: 97% ee; GC conditions: carrier N_2; 6.4 psi; injector 250 °C; detector (FID, H_2, 0.218 MPa) 250 °C; oven temperature 130 °C (2 min), 1 °C min^{-1} to 180 °C (20 min); t_1 (*S*): 31.365 min, t_2 (*R*): 31.753 min], and 1,4-dioxane (3.0 mL) to afford 182 mg (69%) of (*R*)-**2d**[14] with 97% ee [GC conditions: carrier N_2; 8.0 psi; injector 250 °C; detector (FID, H_2, 0.218 MPa) 250 °C; oven temperature 140 °C; t_1 (*S*) 41.060 min, t_2 (*R*) 41.372 min].

IR (neat): 3361, 1956, 850, 700 cm^{-1}.

^{1}H NMR ($CDCl_3$): δ = 7.36–7.20 (m, 5 H), 5.39 (q, *J* = 6.5 Hz, 1 H), 5.23–5.22 (m, 1 H), 4.90–4.85 (m, 2 H), 2.10 (s, 1 H).

MS: *m*/*z* (%) = 145 (M^+ – 1, 4.09), 129 (100.00).

(*S*)-1-Phenylbuta-2,3-dien-1-ol [(*S*)-2d]
The typical procedure given above was followed starting from CuBr (94 mg, 0.66 mmol), paraformaldehyde (96 mg, 3.2 mmol), *i*-Pr_2NH (242 mg, 2.4 mmol, 0.34 mL), (*S*)-1-phenylprop-2-yn-1-ol (96% ee, 264 mg, 2.0 mmol), and 1,4-dioxane (3.0 mL), the reaction afforded 225 mg (77 mg, 96% ee) of (*S*)-**2d**.[14]

Acknowledgements

Financial support from the Major State Basic Research Development Program (Grant No. 2000077500), National Natural Science Foundation of China, Chinese Academy of Sciences, and Shanghai Municipal Committee of Science and Technology are greatly appreciated. Shengming Ma is the recipient of 1999 Qiu Shi Award for Young Scientific Workers issued by Hong Kong Qiu Shi Foundation of Science and Technology (1999–2003).

References

(1) (a) Ma, S.; Zhao, S. *J. Am. Chem. Soc.* **1999**, *121*, 7943. (b) Kang, S.-K.; Yamaguchi, T.; Pyun, S.-J.; Lee, Y.-T.; Baik, T.-G. *Tetrahedron Lett.* **1998**, *39*, 2127.
(2) (a) Olsson, L.-I.; Claesson, A. *Synthesis* **1979**, 743. (b) Marshall, J. A.; Pinney, K. G. *J. Org. Chem.* **1993**, *58*, 7180. (c) Marshall, J. A.; Yu, R. H.; Perkins, J. F. *J. Org. Chem.* **1995**, *60*, 5550. (d) Ma, S.; Gao, W. *Tetrahedron Lett.* **2000**, *41*, 8933.
(3) Yoneda, E.; Kaneko, T.; Zhang, S.-W.; Onitsuka, K.; Takahashi, S. *Org. Lett.* **2000**, *2*, 441.
(4) Ma, S.; Zhao, S. *J. Am. Chem. Soc.* **2001**, *123*, 5578.
(5) Shimizu, I.; Sugiura, T.; Tsuji, J. *J. Org. Chem.* **1985**, *50*, 537.
(6) Corey, E. J.; Yu, C.-M.; Lee, D.-H. *J. Am. Chem. Soc.* **1990**, *112*, 878.
(7) Yu, C.-M.; Yoon, S.-K.; Baek, K.; Lee, J.-Y. *Angew. Chem. Int. Ed.* **1998**, *37*, 2392.
(8) For some typical methods, see: (a) Noyori, R.; Tomino, I.; Yamada, M.; Nishizawa, M. *J. Am. Chem. Soc.* **1984**, *106*, 6717. (b) Frantz, D. E.; Fässler, R.; Carreira, E. M. *J. Am. Chem. Soc.* **2000**, *122*, 1806. (c) Corey, E. J.; Cimprich, K. A. *J. Am. Chem. Soc.* **1994**, *116*, 3151. (d) Lütjens, H.; Nowotny, S.; Knochel, P. *Tetrahedron: Asymmetry* **1995**, *6*, 2675. (e) Matsumura, K.; Hashiguchi, S.; Ikariya, T.; Noyori, R. *J. Am. Chem. Soc.* **1997**, *119*, 8738. (f) He, Q.; Ma, S. *Chin. J. Org. chem.* **2002**, *22*, 375.
(9) (a) Crabbé, P.; Fillion, H.; André, D.; Luche, J.-L. *J. Chem. Soc., Chem. Commun.* **1979**, 859. (b) Crabbé, P.; Nassim, B.; Robert-Lopes, M.-T. *Org. Synth.* **1985**, *63*, 203.
(10) (a) Gao, Y.; Hanson, R. M.; Klunder, J. M.; Ko, S. Y.; Masamune, H.; Sharpless, K. B. *J. Am. Chem. Soc.* **1987**, *109*, 5765. (b) Aoyagi, S.; Wang, T.-C.; Kibayashi, C. *J. Am. Chem. Soc.* **1993**, *115*, 11393.
(11) Bogentoft, C.; Olsson, L.-I.; Claesson, A. *Acta Chem. Scand.* **1974**, *28B*, 163.
(12) Lautens, M.; Delanghe, P. H. M. *J. Am. Chem. Soc.* **1994**, *116*, 8526.
(13) Tomooka, K.; Komine, N.; Nakai, T. *Synlett* **1997**, 1045.
(14) (a) Yu, C.-M.; Choi, H.-S.; Yoon, S.-K.; Jung, W.-H. *Synlett* **1997**, 889. (b) For a recent review see: Brown, H. C.; Khire, U. R.; Narla, G. *J. Org. Chem.* **1995**, *60*, 8130.