Pergamon

Tetrahedron Letters, Vol. 38, No. 39, pp. 6921-6924, 1997
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0040-4039/97 $17.00 + 0.00

PII: S0040-4039(97)01622-5

Chiral *(E,E)*-1,4-Dialkoxy-1,3-butadienes. 1. Stereoselective Synthesis

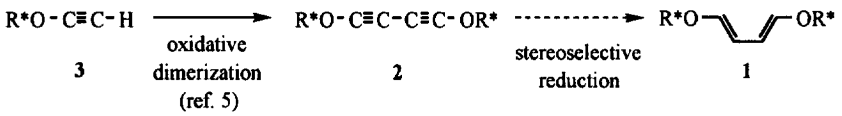
Marina Virgili, Albert Moyano*, Miquel A. Pericàs*, Antoni Riera

Unitat de Recerca en Síntesi Asimètrica, Departament de Química Orgànica, Universitat de Barcelona, c/ Martí i Franquès, 1-11.
08028-Barcelona, Spain

Abstract: A two step, totally stereoselective synthesis of *(E,E)*-1,4-dialkoxy-1,3-butadienes from chiral secondary alcohols has been developed. The key step involves the regio- and stereoselective hydrozirconation of alkoxyethynes derived from chiral alcohols; the intermediate *(E)*-(2-alkoxyvinyl)zirconium compounds, after treatment with cuprous chloride and thermally induced decomposition of the corresponding (2-alkoxyvinyl)copper, give the dialkoxybutadienes in moderate yield but with complete *(E,E)* diastereoselectivity. © 1997 Published by Elsevier Science Ltd.

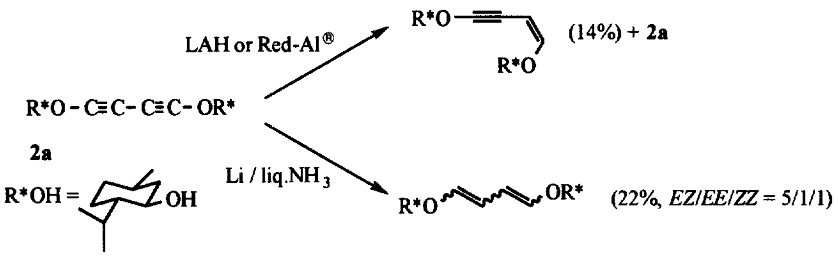
Contrasting to other heterosubstituted dienes, which have been studied mainly in connection with their use in Diels-Alder cycloadditions,[1] *(E,E)*-1,4-dialkoxy-1,3-butadienes still constitute a class of largely unknown compounds. In fact, with the exception of the six-step synthesis of *(E,E)*-1,4-dimethoxy-1,3-butadiene described by Meister more than thirty years ago,[2] only a few, mostly non-stereoselective approaches to a small number of these dienes, derived from simple, achiral alcohols can be found in the literature.[3,4] We wish to report in this communication a two-step, general and totally stereoselective synthesis of *(E,E)*-1,4-dialkoxy-1,3-butadienes derived from chiral secondary alcohols (**1**).

In our initial strategy, we planned to obtain the dialkoxydienes **1** by the stereoselective reduction of 1,4-dialkoxy-1,3-butadiynes **2**,[5] which are readily available through the oxidative dimerization of the corresponding alkoxyethynes **3** (Scheme 1).[6]



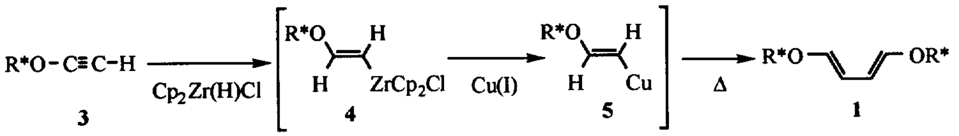
Scheme 1

All attempts to effect the transformation depicted in Scheme 1 on the 1,4-di (*l*-menthyloxy)-1,3-butadiyne **2a**, chosen as a model, were however unsuccessful. In effect, the reaction of **2a** either with aluminum hydrides or with liquid ammonia solutions of alkaline metals led respectively to the formation of partially reduced products or to complex mixtures of stereoisomers (Scheme 2). This behavior contrasts to that of *C*-substituted monoalkoxyacetylenes, which are stereoselectively converted to *(E)*-*O*-alkyl enol ethers under both of these reaction conditions.[6,7]



Scheme 2

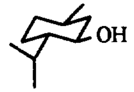
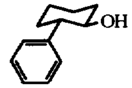
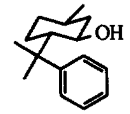
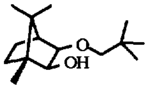
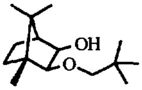
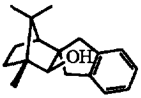
At the light of these results, and inspired both by the hydrozirconation of ethoxyethyne reported by Negishi[8] and by the Zr(IV) to Cu(I) transmetallation of alkenylzirconocene complexes described by Schwartz,[9] we turned our attention to an alternative strategy, the metal-mediated reductive dimerization of alkoxyethynes. According to these literature precedents, the hydrozirconation of an alkoxyethyne **3** should lead to an *(E)*-(2-alkoxyvinyl)zirconocene **4**; subsequent treatment of this complex with a Cu(I) salt would give the corresponding alkenylcopper(I) **5**, whose thermally-induced decomposition would produce the desired *(E,E)*-1,4-dialkoxy-1,3-butadiene **1** (Scheme 3).



Scheme 3

The reaction conditions corresponding to this transformation were thoroughly optimized (with respect to solvent, concentration, source of Cu(I) and temperature) for the di-*l*-menthyloxy derivative **1a**, and extended to a set of chiral dialkoxybutadienes **1b-f** with the results summarized in the Table.[10] As it can be seen, the yields are generally higher than 40%, except in the case of the very hindered camphor-derived alcohol **f**. In this instance, the low yield can be ascribed to the low dimerization rate of the intermediate vinyl copper, since the main product of the reaction (50%) was the vinyl ether, probably arising from hydrogen abstraction in the thermal decomposition of **5**. In any case, this alkoxyvinyl ether can be conveniently separated by column chromatography. Smaller quantities (10-20%) of vinyl ethers were also isolated in the reactions leading to compounds **1c**, **1d** and **1e**. Although these dialkoxydienes appear to be very sensitive both to acid-catalyzed hydrolysis and to oxidation by atmospheric oxygen, they can be stored at -18°C for extended periods of time (1-2 months) without appreciable decomposition *when obtained in pure state*. In that the requisite alkoxyethynes **3a-f** can be obtained in one step from the corresponding chiral alcohols **a-f**[12] by means of a well established methodology[6] with the yields shown in the Table, the present approach constitutes a synthetically efficient route to chiral *(E,E)*-1,4-dialkoxy-1,3-butadienes, taking place in just two steps from the starting chiral alcohols. The use of chiral *(E)*-1-alkoxy-2-zirconaalkenes in the synthesis of chiral *(E,E)*-1-alkoxy-1,3-dienes and the diastereoselective Diels-Alder cycloadditions of these two types of chiral dienes have also been studied in our laboratories and will be the subject of forthcoming publications.

Table. Two-step synthesis of *(E,E)*-1,4-dialkoxy-1,3-butadienes **1a-f** from chiral alcohols.

R*OH	R*O-C≡C-H (yield)[a]	Thermolysis time[b]	 (yield)[c]
 **a**	**3a** (82%)	2 h	**1a** (74%)
 **b**	**3b** (72%)	1.5 h	**1b** (50%)
 **c**	**3c** (74%)	2 h	**1c** (62%)
 **d**	**3d** (81%)	1.75 h	**1d** (42%)
 **e**	**3e** (77%)	3.5 h	**1e** (47%)
 **f**	**3f** (78%)	45 min	**1f** (25%)

[a]Yields of pure alkoxyethynes obtained according to the general procedure described in ref. 6 [b]Time necessary for the complete decomposition (in refluxing THF) of the alkoxyvinyl copper (**5**) obtained upon addition of the alkoxyvinyl zirconium (**4**) to a suspension of CuCl. See note 10 for a representative experimental procedure. [c]Yields of isolated product after chromatographic purification. All dienes gave correct analytical and/or spectral data.

Acknowledgments: Financial support from CIRIT-CICYT (QFN93-4407) is gratefully acknowledged. Marina Virgili is grateful to CIRIT for a pre-doctoral fellowship.

References and Notes:

1. Fringuelli, F.; Taticchi, A. *Dienes in the Diels-Alder Reaction*; John Wiley, New York: 1990.
2. Meister, H. *Chem. Ber.* **1963**, *96*, 1688.
3. Symmetrical 1,4-dialkoxy-1,3-butadienes: (a) Scheeren, J. W.; Marcelis, A. T. M.; Aben, R. W.; Nivard, R. J. F. *Recl. Trav. Chim. Pays-Bas* **1975**, *94*, 196. (b) Keana, J. F. W.; Eckler, P. E. *J. Org. Chem.* **1976**, *41*, 2625. (c) Kirmse, W.; Scheidt, F.; Vater, H.-J. *J. Am. Chem. Soc.* **1978**, *100*, 3945. (d) Boeckman, R. K., Jr.; Dolak, T. M.; Culos, K. O. *J. Am. Chem. Soc.* **1978**, *100*, 7098. (e) van Rijn, P.; Everhardus, R. H.; van der Ven, J.; Brandsma, L. *Recl. Trav. Chim. Pays-Bas* **1981**, *100*, 372. (f)

Hiranuma, H.; Miller, S. I. *J. Org. Chem.* **1982**, *47*, 5083. (g) Hiranuma, H.; Miller, S. I. *J. Org. Chem.* **1983**, *48*, 3096.

4. Unsymmetrical 1,4-dialkoxy-1,3-butadienes: (a) David, S.; Eustache, J. *J. Chem. Soc., Perkin Trans. 1* **1979**, 2230. (b) Maddaluno, J.; Gaonac'h, O.; Le Gallic, Y.; Duhamel, L. *Tetrahedron Lett.* **1995**, *36*, 8591. (c) Guillam, A.; Maddaluno, J.; Duhamel, L. *Chem. Commun.* **1996**, 1295.
5. Valentí, E.; Pericàs, M. A.; Serratosa, F. *J. Am. Chem. Soc.* **1990**, *112*, 7405.
6. Moyano, A.; Charbonnier, F.; Greene, A. E. *J. Org. Chem.* **1987**, *52*, 2919.
7. Solà, L.; Castro, J.; Moyano, A.; Pericàs, M. A.; Riera, A. *Tetrahedron Lett.* **1992**, *33*, 2863.
8. Negishi, E.; Van Horn, D. E. *J. Am. Chem. Soc.* **1977**, *99*, 3168.
9. Yoshifuji, M.; Loots, M. J.; Schwartz, J. *Tetrahedron Lett.* **1977**, *18*, 1303.
10. **Representative experimental procedure: *(E,E)*-1,4-bis(*l*-menthyloxy)-1,3-butadiene, 1a:** To a stirred suspension of freshly prepared zirconocene hydrochloride[11] (1.44 g, 5.55 mmol) in anhydrous, degassed THF (6 mL), under argon atmosphere, a solution of *l*-menthyloxyethyne **3a** (1.00 g, 5.55 mmol) in THF (10 mL) was added dropwise; the resulting mixture was stirred at room temperature for a few minutes, until the zirconocene hydrochloride dissolved completely; this solution was then transferred via cannula to an stirred suspension of previously purified cuprous chloride (0.60 g, 6.0 mmol) in anhydrous, degassed THF (9 mL). The resulting dark brown mixture was heated at 70°C during 2 h, after which time a bright copper mirror had deposited at the walls of the reaction vessel, together with some black precipitate. After cooling at room temperature, and diluting with hexane (25 mL), the clear supernatant liquid was filtered through a short pad of triethylamine-pretreated (2.5% v/v) silicagel, and the solvents were distilled off at reduced pressure. The resulting crude product was immediately purified by column chromatography on triethylamine-pretreated silicagel (2.5% v/v), eluting with hexane/ethyl ether mixtures, to give 0.74 g (74% yield) of the title compound as a white yellowish solid, and 0.133 g (15% yield) of *l*-menthyl alcohol. m. p. 59-60°C. $[\alpha]_D^{20} = -18.0$ (c=4.5, hexane). IR (NaCl film) ν_{max}: 3030, 2960, 2920, 2870, 1625, 1460, 1380, 1350, 1250, 1185, 1165, 1120, 1060, 1055, 1020, 995, 940, 850 cm^{-1}. ^{1}H NMR (200 MHz, CDCl$_3$) δ: 0.76 (d, J=6.9 Hz, 6H), 0.89 (d, J=7.0 Hz, 6H), 0.91 (d, J=6.5 Hz, 6H), 0.75-1.80 (m, 14H), 1.97-2.20 (m, 4H), 3.40 (td, J=11 Hz, J'=4 Hz, 2H), 5.48 (m, 2H), 6.23 ppm (m, 2H). ^{13}C NMR (50 MHz, C$_6$D$_6$) δ: 16.3 (q), 20.9 (q), 22.3 (q), 23.9 (t), 26.2 (d), 31.6 (d), 34.6 (t), 41.6 (t), 48.1 (d), 80.9 (d), 104.9 (d), 145.7 ppm (d). MS (CI-NH$_3$) *m/e*: 363 (M+1, 78%),380 (M+14, 14%), 224 (100%). Anal. Found: C, 79.65; H, 11.70. (Calc. for $C_{24}H_{42}O_2$: C, 79.50; H, 11.68). (NOTE: Due to the high sensitivity of the dialkoxydiene, the reaction glassware was washed with aqueous NaOH and oven-dried prior to use).
11. Buchwald, S. L.; La Maire, S. J.; Nielsen, R. B.; Watson, B. T.; King, S. M. *Tetrahedron Lett.* **1987**, *28*, 3895.
12. These chiral alcohols are either commercially available or can be obtained according to published literature procedures. **b**: Schwartz, A.; Madan, P.; Whitesell, J. K.; Lawrence, R. M. *Org. Synth.* **1990**, *69*, 1. **c**: Ort, O. *Org. Synth.* **1987**, *62*, 203. **d**: Oppolzer, W.; Chapuis, C.; Dao, G. M.; Reichlin, D.; Godel, T. *Tetrahedron Lett.* **1982**, *23*, 4781. **e**: Oppolzer, W.; Chapuis, C.; Dupuis, D.; Guo, H. *Helv. Chim. Acta* **1985**, *68*, 2100. **f**: Oghikawa, T.; Yamashita, M. *Bull. Chem. Soc. Jpn.* **1989**, *62*, 3177.

(*Received in UK* 20 *May* 1997; *revised* 5 *August* 1997; *accepted* 8 *August* 1997)