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Highly Stereoselective Approach to Alk-2-yne-1,4-diols by Oxazaborolidine-Mediated Reduction of Alk-2-yne-1,4-diones†

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We performed the borane-mediated reduction of a series of symmetrical alk-2-yne-1,4-diones (**5**) in the presence of the oxazaborolidine (*R*)-**6** to afford (*R*,*R*)-alk-2-yne-1,4-diols ((*R*,*R*)-**1**) in good yields and high stereoselectivities (up to 99.9% ee). In some cases, the stereochemical purity of **1** was improved by a two-step process: (i) temporary transformation of **1** into its *vic*-dibromo derivatives **9**, which allowed us to remove the minor *meso* isomer by chromatography, and (ii) regeneration of the enantioenriched diols **1** with SmI_2. Reduction of the hexacarbonyldicobalt complexes **8** derived from **5** was also successful.

Introduction

In the course of studies directed toward the synthesis of paraconic acids and related metabolites,[1] we needed an efficient and stereoselective access to alk-2-yne-1,4-diols (**1**) as precursors of chiral (*E*)- or (*Z*)-alk-2-ene-1,4-diols (**2** or **3**).[2] The preparation of these unsaturated 1,4-diols (**1**−**3**) is a challenge not only because they are often present in natural products[3] but also because they are amenable to conversion into other functionalities in a stereoselective way.[4] In addition, the related C_2-symmetrical saturated 1,4-diols (**4**), easily derived from **1**−**3** by hydrogenation,[5] have been used in the preparation *inter alia* of *trans*-2,5-disubstituted pyrrolidines,[6] thiolanes,[7] and phosphine ligands of interest for asymmetric hydrogenation.[8]

In this context, we recently reported that the addition of chiral 1-alkyn-3-ols (or their protected derivatives) to α- or *β*-branched aldehydes mediated by zinc triflate, Et_3N, and (+)- or (−)-*N*-methylephedrine is a stereoselective, modular way to prepare chiral diols **1** (Scheme 1).[9] However, this approach is less satisfactory when α-unbranched aldehydes (RCHO, R = *n*-alkyl) are involved, resulting in lower yields and/or selectivities.[10]

On the other hand, the stereoselective reduction of alk-2-yne-1,4-diones (**5**) is an alternative, obvious approach to compounds **1**. On the basis of our success in the reduction of simpler acetylenic ketones with borane catalyzed by (*R*)- and (*S*)-*B*-methyl-4,5,5-triphenyl-1,3,2-oxazaborolidines, (*R*)- and (*S*)-**6**,[11] we concluded that

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(1) (a) Ariza, X.; Garcia, J.; López, M.; Montserrat, L. *Synlett* **2001**, 120−122. (b) Ariza, X.; Fernández, N.; Garcia, J.; López, M.; Montserrat, L.; Ortiz, J. *Synthesis* **2004**, 128−134.

(2) Allylic diols **2** and **3** are easily obtainable from **1** by $LiAlH_4$ reduction and partial hydrogenation, respectively (see ref 1).

(3) See, for example: (a) Grabley, S.; Granzer, E.; Huetter, K.; Ludwig, D.; Mayer, M.; Thiericke, R.; Till, G.; Phillipps, S.; Wink, J.; Zeeck, A. *J. Antibiot.* **1992**, *45*, 56−65. (b) Nagle, D. G.; Gerwick, W. H. *J. Org. Chem.* **1994**, *59*, 7227−7237. (c) Arnone, A.; Nasini, G.; de Pava, O. V. *Phytochemistry* **2000**, *53*, 1087−1090. (d) Bode, H. B.; Walker, M.; Zeeck, A. *Eur. J. Org. Chem.* **2000**, 1451−1456.

(4) For a review on substrate-directable chemical reactions, see: Hoveyda, A. H.; Evans, D. A.; Fu, G. C. *Chem. Rev.* **1993**, *93*, 1307−1370.

(5) Current preparations of enantiopure saturated 1,4-diols include: Enzymatic resolutions of mixtures of *meso* and racemic isomers: (a) Mattson, A.; Öhrner, N.; Hult, K.; Norin, T. *Tetrahedron: Asymmetry* **1993**, *4*, 925−930. (b) Kim, M.-J.; Lee, I. S. *Synlett* **1993**, 767−768. (c) Nagai, H.; Morimoto, T.; Achiwa, K. *Synlett* **1994**, 289−290. (d) Caron, G.; Kazlauskas, R. J. *Tetrahedron: Asymmetry* **1994**, *5*, 657−664. Dynamic kinetic resolution: (e) Persson, B. A.; Huerta, F. F.; Bäckvall, J.-E. *J. Org. Chem.* **1999**, *64*, 5237−5240 and references therein. Electrochemical Kolbe-type coupling of chiral *β*-hydroxy acids: (f) Ross, S. D.; Finkelstein, M.; Rudd, E. J. *Anodic Oxidation*; Academic Press: New York, 1975. (g) Burk, M. J.; Feaster, J. E.; Harlow, R. L. *Tetrahedron: Asymmetry* **1991**, *2*, 569−592. Microbial reduction of diketones using baker's yeast: (h) Lieser, J. K. *Synth. Commun.* **1983**, *13*, 765−767. Reduction of diketones using chiral reagents or auxiliaries: (i) Kuwano R.; Sawamura M.; Shirai J.; Takahashi M.; Ito Y. *Tetrahedron Lett.* **1995**, *36*, 5239−5242. (j) Quallich G. J.; Keavey K. N.; Woodall T. M.; *Tetrahedron Lett.* **1995**, *36*, 4729−4732.

(6) For a review on the synthesis of 2,5-disubstituted pyrrolidines, see: (a) Pichon, M.; Figadère, B. *Tetrahedron: Asymmetry* **1996**, *7*, 927−964. (b) Whitesell, J. K. *Chem. Rev.* **1989**, *89*, 1581−1590. (c) Chong, J. M.; Clarke, I. S.; Koch, I.; Olbach, P. C.; Taylor, N. J. *Tetrahedron: Asymmetry* **1995**, *6*, 409−418. See also ref 5b.

(7) (a) Otten, S.; Frölich, R.; Haufe, G. *Tetrahedron: Asymmetry* **1998**, *9*, 189−191. (b) Julienne, K.; Metzner, P.; Henryon, V.; Greiner, A. *J. Org. Chem.* **1998**, *63*, 4532−4534.

(8) (a) Burk, M. J. *J. Am. Chem. Soc.* **1991**, *113*, 8518−8519. (b) Fiaud, J.-C.; Legros, J.-Y. *Tetrahedron Lett.* **1991**, *32*, 5089−5092. (c) Burk, M. J.; Harper, T. G. P.; Kalberg, C. S. *J. Am. Chem. Soc.* **1995**, *117*, 4423−4424 and references therein. See also ref 5g.

(9) (a) Amador, M.; Ariza, X.; Garcia, J.; Ortiz, J. *Tetrahedron Lett.* **2002**, *43*, 2691−2694. See also: (b) Diez, R. S.; Adger, B.; Carreira, E. M. *Tetrahedron* **2002**, *58*, 8341−8344.

(10) In many cases, the aldehyde is partially consumed in the formation of self-condensation aldol products.

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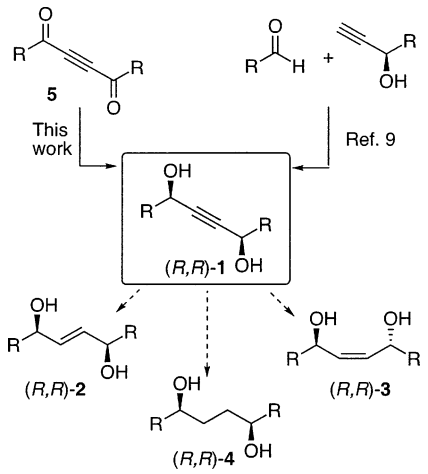
SCHEME 1



compounds **5** could be suitable substrates for such reductions.[12] This was based on two facts: (i) our previous experience in simpler ketones indicated that the presence of the triple bond could cause a sufficient difference in steric requirements on both sides of the carbonyl group since the acetylenic moiety behaves as an even "smaller" group than a linear saturated chain in oxazaborolidine-mediated reductions; (ii) from a statistical point of view, one might expect much higher enantioselectivities in the reduction of diketones **5** than those noted for related monoketones, since most of the minor enantiomer formed in the reduction of the first carbonyl group would become a *meso* compound after the second reduction. Thus, the enantiopurity of the final diols would be enhanced at the expense of the formation of potentially removable *meso* byproducts.[13]

The present work details the performance of oxazaborolidines **6** in the reduction of diketones **5** with BH_3/SMe_2 (Figure 1). The extension of this asymmetric process to the hexacarbonyldicobalt complexes **8** (acting as synthetic equivalents of **5**) was also investigated.[14] We also report that the temporary transformation of **1** (arising from reduction of **5** or **8**) into their *vic*-dibromo derivatives **9** facilitated removal of the minor *meso*-**1** isomer by chromatography. The process provides an attractive and general route to highly enantioenriched diols **1**.

Results and Discussion

Preparation of Symmetrical 1,4-Diketones. A representative set of alk-2-yne-1,4-diones, **5a**−**f**, with increasing steric demand in going from **5a** (R = Me) to **5e** (R = *t*-Bu), was synthesized by Jones oxidation of the corresponding alk-2-yne-1,4-diols **1** (mixture of stereoisomers) as shown in Scheme 2. Among the diols required, only hex-3-yne-2,5-diol, **1a**, was commercially available. Compound **1b** was obtained by allylic oxidation (SeO_2/*t*-BuOOH) of commercial oct-4-yne according to a Sharpless procedure.[15] Similarly, the adaptation of this protocol to dec-5-yn-4-ol, **10**, allowed the synthesis of propargylic diol **1c**. However, compounds **1d**−**f** were better obtained by one-pot double addition of dilithium acetylide to aldehydes.[16] Further transformation of diketones **5** into the corresponding hexacarbonyldicobalt complexes **8** was achieved by treatment with $Co_2(CO)_8$ in pentane/CH_2Cl_2.

Reduction of Diketones. Having in hand diketones **5** and **8**, we undertook their oxazaborolidine-mediated reduction. First, we performed the slow addition of a solution of diketone **5a** (1.0 mmol) to an ice-cooled THF solution of BH_3/SMe_2 (2.2 mmol) and (*R*)-**6** (2.0 mmol) in THF to afford cleanly the propargylic diol (*R*,*R*)-**1a** in good yield (85%) but in moderate stereoselectivity

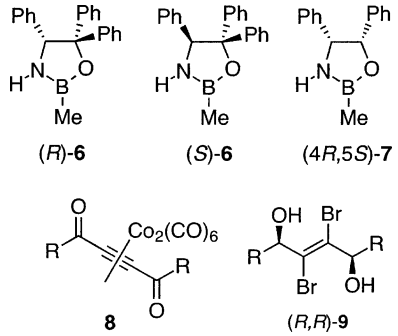
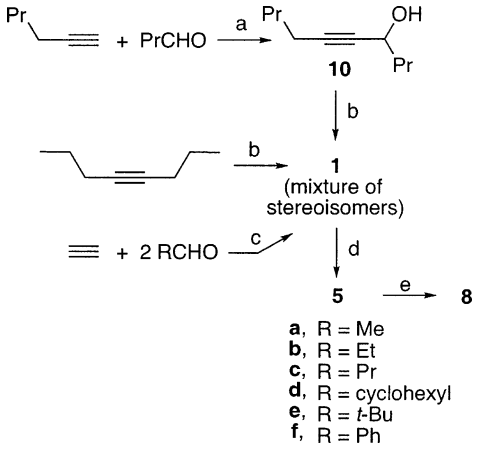


FIGURE 1.

SCHEME 2[a]



[a] Reagents and conditions: (a) (i) *n*-$C_4H_9C{\equiv}CH$, BuLi, THF, −78 °C, (ii) *n*-C_3H_7CHO, THF, −78 °C; (b) (i) *t*-BuOOH, SeO_2, CH_2Cl_2, rt, 24 h, (ii) $NaBH_4$, MeOH, 0 °C; (c) ref 16; (d) CrO_3, aq H_2SO_4, 0 °C; (e) $Co_2(CO)_8$, pentane/CH_2Cl_2, rt.

(11) (a) Bach, J.; Berenguer, R.; Garcia, J.; Loscertales, T.; Vilarrasa, J. *Org. Chem.* **1996**, *61*, 9021−9025. For related reductions, see: (b) Corey, E. J., Helal, C. J. *Tetrahedron Lett.* **1995**, *36*, 9153−9156. (c) Parker, K. A.; Ledeboer, M. W. *J. Org. Chem.* **1996**, *61*, 3214−3127.

(12) In this connection, it should be noted that the oxazaborolidine-mediated reduction of the related (*E*)-alk-2-ene-1,4-diones affords 1,4-diols **2** in good yields and enantioselectivities but, in general, suffers from low diastereoselectivities (*dl*/*meso* ratio from 5.6:1 to ∼1:1). In contrast, (*Z*)-alk-2-ene-1,4-diones give low yields of the desired (*Z*)-1,4-diol **3** under the same conditions. See: Bach, J.; Berenguer, R.; Garcia, J.; López, M.; Manzanal, J.; Vilarrasa, J. *Tetrahedron* **1998**, *54*, 14947−14962.

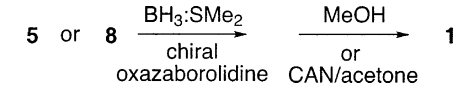
(13) For a discussion of this statistical effect applied to two-directional chain syntheses, see: Poss C. S.; Schreiber S. L. *Acc. Chem. Res.* **1994**, *27*, 9−17. See also: Magnuson, S. R. *Tetrahedron* **1995**, *51*, 2167−2213.

(14) A part of this work appeared as a preliminary communication: Bach, J.; Berenguer, R.; Garcia, J.; Loscertales, T.; Manzanal, J.; Vilarrasa, J. *Tetrahedron Lett.* **1997**, *38*, 1091−1094.

(15) Chabaud, B.; Sharpless, K. B. *J. Org. Chem.* **1979**, *44*, 4202−4204.

(16) Sudweeks, W. B.; Broadbent, H. S. *J. Org. Chem.* **1975**, *40*, 1131−1136. These authors described the preparation of **1d** and **1e** in 32% and 31% using the magnesium acetylide. We obtained better results (76% and 98% yield, respectively) by using the dilithium acetylide. However, when α-unbranched aldehydes as propanal were used, much lower yields were recorded.

TABLE 1. Reduction of Diketones 5 and 8 with BH_3/SMe_2 in the Presence of Oxazaborolidines (*R*)-6 and (4*R*,5*S*)-7[a]



entry	diketone	catalyst	product	yield[b] (%)	*dl*/*meso* ratio[b,c]	ee[b,c] (%)
1	**5a**, R = Me	(*R*)-**6**	(*R*,*R*)-**1a**	85 (65)	72:28 (62:38)	85 (80)
2	**5b**, R = Et	(*R*)-**6**	(*R*,*R*)-**1b**	85 (81)	87:13 (72:18)	98 (96)
3[d]	**5c**, R = Pr	(*R*)-**6**	(*R*,*R*)-**1c**	86 (77)	90:10 (75:25)	99 (98)
4	**5d**, R = cyclohexyl	(*R*)-**6**	(*R*,*R*)-**1d**	90 (90)	88:12 (84:16)	97 (96)
5	**5e**, R = *t*-Bu	(*R*)-**6**	(*R*,*R*)-**1e**	98 (95)	99.9:0.1 (97:3)	99.9 (99)
6	**5f**, R = Ph	(*R*)-**6**	(*R*,*R*)-**1f**	75 (23)	91:9 (86:14)	98 (98)
7	**8a**, R = Me	(4*R*,5*S*)-**7**	(*S*,*S*)-**1a**	72	90:10	98
8	**8b**, R = Et	(4*R*,5*S*)-**7**	(*S*,*S*)-**1b**	96	98.6:1.4	98
9[e]	**8c**, R = Pr	(4*R*,5*S*)-**7**	(*S*,*S*)-**1c**	95	92:8	98
10	**8d**, R = cyclohexyl	(4*R*,5*S*)-**7**	(*S*,*S*)-**1d**	71	95:5	96

[a] Reactions were carried out by slow addition of diketone (1 mmol) to a mixture of BH_3/SMe_2 (2.2 mmol) and oxazaborolidine (2 mmol) in ice-cooled THF. Yields and stereochemical results for diketones **8** are referred to diols **1** (after treatment of the diols arising from the carbonyl reduction with CAN in acetone). [b] Within parentheses, values using 0.2 mmol of catalyst. [c] Determined by HPLC and/or ^{19}F NMR analysis of the corresponding Mosher diesters. [d] Better results were obtained than those reported in our preliminary communication (ref 14). [e] Excesses of BH_3/SMe_2 (3 mmol) and (4*R*,5*S*)-**7** (4 mmol) were needed to complete the reduction.

(72:28 *dl*/*meso* ratio, 85% ee). Despite this disappointing result, we reduced the remaining diketones. To our satisfaction, better results (>96% ee) were observed in the reduction of **5b**−**f** where the R group was bigger than Me (entries 2−5 in Table 1). However, a small amount of the concomitant, inseparable *meso* isomer was always produced in such reductions, especially if only 0.2 mmol of catalyst was used.[17] As shown in Table 1, the best result was obtained for **5e** (R = *t*-Bu, 99.9:0.1 *dl*/*meso* ratio, 99.9% ee).

The configuration of alcohols **1**[18] and the fact that higher selectivities were noted in diketones with sterically demanding R groups may be explained according to the mechanism proposed by Corey et al.[19] for similar processes. Thus, the *R* configuration in diols **1** could arise from an arrangement like **11a**, in which the R group, which is larger than the acetylenic moiety, is located far from the Me group on the boron atom (see Figure 2). The alternative arrangement, **11b**, which would lead to the *S* isomer, is clearly less attainable. An increase of the steric requirements in the R group may increase the energetic difference between **11a** and **11b** and raise the stereoselectivities. Obviously, synthesis of diols (*S*,*S*)-**1** using oxazaborolidine (*S*)-**6** is also feasible.

Looking for a better diastereoselectivity (especially for diketones with R = Me or *n*-alkyl), we turned our attention to the reduction of the hexacarbonyldicobalt complexes **8**, derived from **5**. Since our previous experience[11a,20] indicated that oxazaborolidines **6** were inefficient for the reduction of very crowded ketones, we treated **8a**−**d** with BH_3/SMe_2 in the presence of the less sterically demanding oxazaborolidine (4*R*,5*S*)-**7**.[21] As

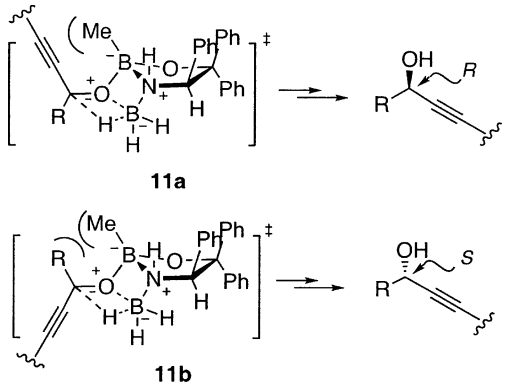


FIGURE 2.

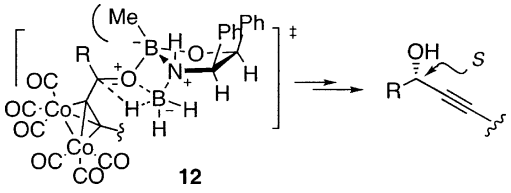


FIGURE 3.

expected, the temporary transformation of the acetylenic moiety in a much bulkier group not only enhanced but also reversed the selectivity, leading to propargylic alcohols (*S*,*S*)-**1a**−**d**, in good yields and selectivities after regeneration of the triple bond with the aid of a mild oxidant like Ce(IV). However, an excess of BH_3/SMe_2 (3 mmol) and catalyst (4 mmol) were needed to complete the reduction of **8d**. The origin of the configuration of the new stereocenters can be explained by a complex like **12** in which the huge cobalt complex is placed far from the Me group on the boron atom (see Figure 3). It should be noted that in contrast to reduction of diketones **5**, at least 2 mmol of (4*R*,5*S*)-**7** is needed to complete the reduction. This fact suggests that the oxazaborolidine is not easily liberated after reduction and it does not enter

(17) Reduction of diketone **5f** using 0.2 mmol of catalyst led to a complex mixture from which diol (*R*,*R*)-**1f** was isolated in low yield. This disappointing result was not completely unexpected in the light of our previous experience in the reduction of the related 1,4-diphenylbut-2-ene-1,4-dione (see ref 12).

(18) Absolute configurations were established by comparison of the sign of specific rotation of saturated diols arising from hydrogenation (H_2, Pt/C) of **1** with that given in the literature (see refs 12 and 14 and references therein).

(19) For a review, see: Corey, E. J.; Helal, *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 1986−2012.

(20) Alemany, C.; Bach, J.; Garcia, J.; López, M.; Rodriguez, A. B. *Tetrahedron* **2000**, *56*, 9305−9312.

(21) (a) Quallich, G. J.; Woodall, T. M. *Tetrahedron Lett.* **1993**, *34*, 4145−4148. (b) Quallich, G. J.; Blake, J. F.; Woodall, T. M. *J. Am. Chem. Soc.* **1994**, *116*, 8516−8525.

into a true catalytic cycle.[11a] Finally, when we attempted to extend this strategy to the more crowded ketones **8e** and **8f**, they remained unchanged under similar conditions. In conclusion, the reduction of the Co complexes of acetylenic diketones could gave excellent stereoselectivities but this process is unsuitable for substrates with high steric requirements.

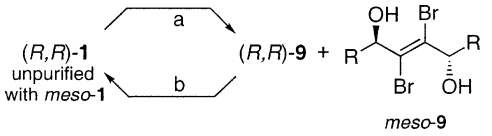
Temporary Transformation of Diols 1 into *vic*-Dibromoalkenes 9. The main drawback of the abovementioned approach to enantioenriched alk-2-yne-1,4-diols lies in the difficulty in removing the undesired *meso*-**1** diols from their chiral isomers (*R*,*R*)- or (*S*,*S*)-**1** either by fractional crystallization (for solid diols **1d** and **1e**) or by column chromatography. In contrast, our previous experience indicates that the *dl* and *meso* isomers of allylic diols **2** arising from **1** can be, in general, readily separated by chromatography. Looking for a temporary transformation of **1** into a kind of compound that allows us the separation of diastereomers, our interest was drawn to *vic*-dibromides **9**. The treatment of samples of (*R*,*R*)-**1** contaminated with *meso* isomer with pyridinium tribromide in CH_2Cl_2, smoothly furnished **9** in >90% overall yield.[22] However, the sterically more demanding **1e** remained unchanged under similar conditions and a more vigorous brominating agent (Br_2 in CH_2Cl_2) was needed to attain **9e** but in low yield (31%).

To our satisfaction, chromatographic behaviors of *meso*- and (*R*,*R*)-**9** were quite dissimilar, even more than those noted for the parent allylic diols **2**.[23] Thus, we were able to remove easily by flash chromatography on silica gel the minor *meso*-**9** isomers, these being eluted first in all the cases studied. Having in hand highly stereoenriched diols **9**, the study of their transformation back to chiral diols **1** (free of *meso* isomer) was next addressed. A variety of methods has been devised to accomplish the reductive dehalogenation of *vic*-dibromides to alkynes, including metallic samarium,[24] Zn powder,[22c,d] Ni catalysts,[25] sodium sulfide in dimethylformamide,[26] and diorganotellurides.[27] Although in our hands (*R*,*R*)-**9a** was efficiently transformed in (*R*,*R*)-**1a** either with Zn/AcOH[22c] or Sm(0), for the rest of compounds **9** even better and more reproducible results were obtained by using freshly prepared SmI_2 in THF,[28] to yield enantioenriched (*R*,*R*)-**1** in high yield (Scheme 3).

A Special Case: Cyclododec-2-yne-1,4-diol. We then examined the cyclic propargylic 1,4-diols. Cyclododec-2-yne-1,4-diol, **1g**, was chosen as a representative model since its preparation by allylic oxidation of cyclododecyne[29] with SeO_2/*t*-BuOOH had been described by Chabaud and Sharpless.[15] Thus, we carried out the reported protocol assuming that the obtained diol **1g** was a mixture of diastereomers. However, when we transformed an analytical sample of the diol into its Mosher's diester, we obtained only two singlets of equal intensity in its ^{19}F NMR spectrum (instead of four expected signals: two singlets for the *meso* isomer and one more for each enantiomer) and we could not separate either of the assumed diastereomers by HPLC. In addition, the treatment of **1g** with pyridinium tribromide in CH_2Cl_2 led to a single dibromoderivative. These unexpected results suggest that we had obtained a single diastereomer. To confirm this we transformed the diol into its monoacetate **14** and then inverted the configuration of the remaining hydroxyl group using Mitsunobu's protocol with benzoate as nucleophile.[30] After removal of the benzoate group the other diastereomer of **1g** was isolated (see Scheme 4).

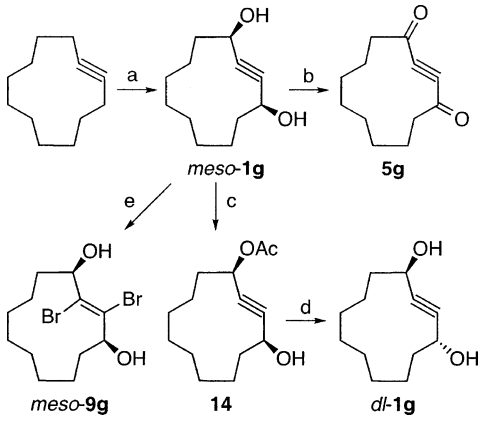
Oxidation of **1g** with Jones reagent gave diketone **5g**, which in turn was subjected to the borane-mediated reduction in the presence of oxazaborolidine (*R*)-**6**.[31] Unfortunately, reduction of **5g** was less efficient than that noted for acyclic alkynediones **5a**−**f**, leading to (*R*,*R*)-**1g** in acceptable enantioselectivity (90% ee) but unpurified by a considerable amount of *meso* diol (2.1:1 *dl*/*meso*

SCHEME 3[a]



[a] Reagents and conditions:(a) pyridinium tribromide, CH_2Cl_2, rt; (b) SmI_2, THF, rt.

SCHEME 4[a]



[a] Reagents and conditions: (a) ref 15; (b) CrO_3, aq H_2SO_4, acetone, 0 °C; (c) Ac_2O (1 equiv), 4-(dimethylamino)pyridine cat., pyridine, CH_2Cl_2, 0 °C; (d) (i) Ph_3P, $PhCO_2H$, diethyl azodicarboxylate, THF, 0 °C, (ii) NH_3, MeOH, rt; (e) pyridinium tribromide, CH_2Cl_2, rt.

(22) Transformation of **1a** into **9a** by treatment with bromine in chloroform was described almost a century ago: (a) Dupont, M. G. *C. R. Acad. Sci.* **1909**, *149*, 1381−1383. See also: (b) Hermann, H.; Luttke, W. *Chem. Ber.* **1971**, *104*, 479−491. (c) Schoepfer, J.; Eichenberger, E.; Neier, R. *J. Chem. Soc., Chem. Commun.* **1993**, 246−248. The use of bromine in the presence of Hünig's base has been also reported: (d) Adjé, N.; Breuilles, P.; Uguen, D. *Tetrahedron Lett.* **1993**, *34*, 4631−4634.

(23) Ab initio calculations at 6-311G level of theory using Gaussian-04 series of programs indicate that the minimum energy conformations of *meso*-**2a** and *meso*-**9a** are apolar ($\mu = 0$ D, C_i symmetry). In contrast, the dipole moment for the minimum energy conformations of *dl*-**2a** and *dl*-**9a** are 0.01 and 2.46 D, respectively.

(24) Yanada, R.; Negoro, N.; Yanada, K.; Fujita, T. *Tetrahedron Lett.* **1996**, *37*, 9313−9316.

(25) Malanga, C.; Mannucci, S.; Lardicci, L. *Tetrahedron* **1998**, *54*, 1021−1028.

(26) Fukunaga, K.; Yamaguchi, H. *Synthesis* **1981**, 879−880.

(27) Butcher, T. S.; Zhou, F.; Detty, M. R. *J. Org. Chem.* **1998**, *63*, 169−176.

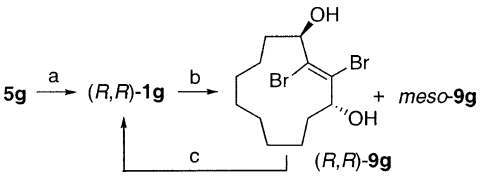
(28) Girard, P.; Namy, J. L.; Kagan, H. B. *J. Am. Chem. Soc.* **1980**, *102*, 2693−2698. It is worth noting that diol **1f** was sensitive to epimerization when a large amount of SmI_2 was used.

(29) (a) Lalezari, I.; Shafiee, A.; Yalpani, M. *J. Heterocycl. Chem.* **1972**, 1411−1412. (b) Lalezari, I.; Shafiee, A.; Yalpani, M. *J. Org. Chem.* **1971**, *36*, 2836−2838.

(30) Mitsunobu, O. *Synthesis* **1981**, 1−28.

(31) It is worth noting that $NaBH_4$ reduction of diketone **5g** gave a ~1:1 mixture of *dl*-**1g** and *meso*-**1g**.

SCHEME 5[a]



[a] Reagents and conditions: (a) BH_3:SMe_2 (2.2 mmol), (*R*)-**6** (2 mmol), THF, 0 °C; (b) pyridinium tribromide, CH_2Cl_2, rt; (c) SmI_2, THF, rt.

ratio, see Scheme 5). Fortunately, the *meso* isomer could be removed easily by transformation of the mixture of diols **1g** into their dibromo derivatives **9g** followed by reductive debromination of the isolated (*R*,*R*)-**9g** (Scheme 5). As far as the amount of catalyst is concerned, a decrease in the ratio of oxazaborolidine/diketone to 0.2 reduced the yield and the stereoselectivity (32%, ~1:1 *dl*/*meso* ratio, 65% ee). Apparently, the lack of conformational flexibility in the cyclic diketone makes the stereoselective reduction slower since an arrangement such as **11a** (Figure 2), assumed in the noncyclic diketones **1a**−**f**, is now less favorable. Accordingly, we can expect an increasing significance of the uncatalyzed reduction by borane as the relative amount of oxazaborolidine decreases.

Conclusion

This paper describes a preparative approach to enantioenriched alk-2-yne-1,4-diols based on the borane-mediated reduction of the parent alk-2-yne-1,4-diones (or their $Co_2(CO)_6$ complexes) in the presence of a chiral oxazaborolidine. The temporary transformation of such diols into their *vic*-dibromo derivatives allowed us to remove the *meso* isomer to afford highly enantioenriched propargylic diols. This methodology seems especially valuable for linear diols in which the alternative approach by direct addition of an alkynol to the aldehyde is less suitable. However, this reduction gave lower stereoselectivity when it was applied to a cyclic diketone as cyclodec-2-yne-1,4-dione.

Experimental Section

General Procedure for Preparation of Diketones 5: Oct-4-yne-3,6-dione (5b). To a stirred solution of oct-4-yne-3,6-diol (**1b**) (0.524 g, 3.68 mmol) in acetone (20 mL) in an ice bath was added dropwise a solution of Jones reagent (8.0 g of CrO_3/7.6 mL of concd H_2SO_4/20 mL H_2O) until an orange color persisted. The reaction mixture was partitioned by adding H_2O (20 mL) and CH_2Cl_2 (50 mL). The phases were separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic phases were washed with brine, dried (Na_2SO_4), and concentrated under reduced pressure. The residue was purified by flash chromatography (CH_2Cl_2) to give 400 mg (79%) of oct-4-yne-3,6-dione, **5b**, as a yellow oil: R_f 0.58 (CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.20 (t, 6H, J = 7.4 Hz), 2.68 (q, 4H, J = 7.4 Hz); ^{13}C NMR δ 7.1, 38.6, 84.1 (C≡C), 186.8 (CO); IR (neat) 2980, 2200, 1710, 1680, 1450. Anal. Calcd for $C_8H_{10}O_2$: C, 69.55; H, 7.29. Found: C, 69.38; H, 7.51.

General Procedure for Oxazaborolidine-Mediated Reduction of Diketones 5 and 8: Preparation of (*R*,*R*)-Hex-3-yne-2,5-diol [(*R*,*R*)-1a]. A solution of hex-3-yne-2,5-dione **5a**[32] (110 mg, 1.0 mmol) in THF (3 mL) was added slowly (~1 h) to a solution of oxazaborolidine (*R*)-**6** (2 mmol, from a toluene solution after removing the solvent under reduced pressure) and BH_3/SMe_2 (222 μL, 2.2 mmol) in THF (3 mL) at 0 °C under Ar. Upon completion of the addition, TLC revealed the disappearance of the starting diketone. The reaction was cautiously quenched by slow addition of MeOH (1 mL) at 0 °C. The solution was stirred for 15 min at rt and then concentrated under reduced pressure. The residue was purified by flash chromatography (CH_2Cl_2/MeOH 95:5) to yield 97 mg (85%) of enantioenriched (*R*,*R*)-hex-3-yne-2,5-diol, (*R*,*R*)-**1a**. An analytical sample of the crude was treated with an excess of (*S*)-Mosher acid chloride (derived from (*R*)-acid)[33] to give a mixture of Mosher diesters. The analysis by HPLC (Tracer Spherisorb S3W column, 0.9 mL/min, hexane/THF 98:2, t_R (*R*,*R*) = 13.4 min, t_R (*R*,*S*) = 16.6 min, t_R (*S*,*S*) = 19.6 min) revealed a 72:28 *dl*/*meso* ratio and 85% ee. A similar reduction using a molar ratio (*R*)-**6**/diketone = 0.2 led to (*R*,*R*)-**1a** in 65% yield, with a *dl*/*meso* ratio of 62:38 and 80% ee.

(*S*,*S*)-Hex-3-yne-2,5-diol [(*S*,*S*)-1a]. Alternatively, to a solution of $Co_2(CO)_8$ (376 mg, 1.1 mmol) in anhyd pentane (5 mL) under Ar at rt was added a solution of diketone **5a** (110 mg, 1.0 mmol) in anhyd pentane (3 mL) and CH_2Cl_2 (0.5 mL) via cannula. The dark red solution was stirred at rt. After 1 h, TLC revealed the disappearance of the starting ketone. The solution was filtered through silica gel (CH_2Cl_2). The solvent was removed under reduced pressure to afford **8a** (335 mg, 85%) as a brown oil which was stored under Ar and used in the reduction step without further purification: R_f 0.38 (CH_2Cl_2); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 2.51 (s, 6H); ^{13}C NMR δ 30.8 (CH_3), 86.2 (C≡C), 197.1 (CO), 199.4 (CO); IR (film) 2980, 2050, 1680, 1550, 1210, 1150. A solution of diketone **8a** (316 mg, 0.80 mmol) in THF (1 mL) was added dropwise over ~50 min to a solution of BH_3/SMe_2 (176 μL, 1.76 mmol) and (4*R*,5*S*)-**7** (1.6 mmol, from a toluene solution after removing the solvent under reduced pressure) in THF (1 mL), at 0 °C under Ar. Upon completion of the addition, TLC revealed the disappearance of the starting diketone. The reaction was then cautiously quenched by adding 1 mL of MeOH, stirred for an additional 10 min, and allowed to warm to rt. The mixture was evaporated under reduced pressure. The crude propargylic diol complex was dissolved in dry acetone (4 mL), and solid CAN was cautiously added at 0 °C until the vigorous gas release had finished. After 5 min (TLC monitoring), the volatiles were removed and the residue was partitioned with CH_2Cl_2 (20 mL) and saturated aqueous $NaHCO_3$ (5 mL). The aqueous layer was extracted with CH_2Cl_2 (4 × 20 mL). The combined organic phases were dried over $MgSO_4$. Evaporation of the solvent and purification by *flash* chromatography (hexane/EtOAc 6:4) yielded 66 mg (0.58 mmol, 72%) of (*S*,*S*)-**1a**. An analytical sample of (*S*,*S*)-**1a** was transformed into the corresponding Mosher ester derived from Mosher's (*R*)-acid. The analysis by HPLC revealed a 90:10 *dl*/*meso* ratio and 98% ee. (*S*,*S*)-Hex-3-yne-2,5-diol: mp 53−4 °C (lit.[34] mp 58−60 °C); R_f 0.40 (EtOAc); $[\alpha]_D^{20}$ −50.6 (*c* = 2.1, $CHCl_3$) [lit.[34] $[\alpha]_D^{25}$ −57.3 (*c* = 1.53, $CHCl_3$)]; ^{1}H NMR ($CDCl_3$, 200 MHz) δ 1.45 (d, 6H, J = 6.4 Hz), 2.40 (bs, 2H, OH), 4.57 (q, 2H, J = 6.4 Hz); ^{13}C NMR δ 24.0 (CH_3), 57.8 (CHOH), 85.9 (C≡C); IR (neat) 3400, 2960, 2920, 1020.

Typical Procedure for the Preparation of *vic*-Dibromo Diols 9: (*E*)-2,3-Dibromo-1,4-dicyclohexylbut-2-ene-1,4-diol (9d). Pyridinium tribromide (600 mg, 1.88 mmol) was slowly added to a solution of 470 mg (1.88 mmol) of (*S*,*S*)-dicyclohexylbut-2-yne-1,4-diol, (*S*,*S*)-**1d** (95:5 *dl*/*meso* ratio and 96% ee) in 20 mL of CH_2Cl_2 cooled in an ice bath. The solution was stirred at rt overnight. Then, TLC revealed the disappearance of the starting propargylic diol. Reaction was cautiously quenched by addition of satd aq $NaHSO_3$ (10 mL), and

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(33) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543−2549.

(34) Kim, M.-J.; Lee, I. S.; Jeong, N.; Choi, Y. K. *J. Org. Chem.* **1993**, *58*, 6483−6485.

the aqueous layer was extracted with more CH_2Cl_2. The combined organic layers were dried ($MgSO_4$), and the solvent was eliminated under reduced pressure. The residue was purified by flash chromatography (CH_2Cl_2 and then CH_2Cl_2/MeOH 99:1) to give (*S*,*S*)-**9d** (693 mg, 1.69 mmol) along with *meso*-**9d** (35 mg, 0.09 mmol) (94% overall yield). (1*S*,2*E*,4*S*)-2,3-Dibromo-1,4-dicyclohexylbut-2-ene-1,4-diol [(*S*,*S*)-**9d**]: mp 118−120 °C; R_f 0.10 (CH_2Cl_2/MeOH 95:5); $[\alpha]^{20}_D$ −15.1 (*c* = 1.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.90−1.21 (m, 12H, CH_2), 1.44−1.76 (m, 10H, CH_2 and CH), 2.06 (bs, 2H, OH), 4.56 (d, 2H, *J* = 9.0 Hz, C*H*OH); ^{13}C NMR δ 25.6, 25.8, 26.2, 28.1 and 29.1 (CH_2), 42.5 (CH), 78.3 (CHOH), 127.4 (CBr=); IR (KBr) 3855, 2923, 2830, 1440, 680. MS (NH_3/CI) *m*/*z* (rel int) 428 (100, $^{79}Br^{81}Br$, [M + NH_4^+]); HRMS (EI) calcd for $C_{16}H_{26}O_2{}^{79}Br^{81}Br$ (M^+) 410.0279, found 410.0285. Anal. Calcd for $C_{16}H_{26}O_2Br_2$: C, 46.85; H, 6.39; Br, 38.96. Found: C, 46.85; H, 6.42; Br, 38.88.

(1*R*,2*E*,4*S*)-2,3-Dibromo-1,4-dicyclohexylbut-2-ene-1,4-diol (*meso*-9d): mp 185−187 °C; R_f 0.65 (CH_2Cl_2/MeOH 95:5); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.90−1.21 (m, 12H, CH_2), 1.44−1.75 (m, 10H, CH_2 and CH), 2.12 (bs, 2H, OH), 4.56 (d, 2H, *J* = 9.0 Hz, C*H*OH); ^{13}C NMR δ 25.7, 25.8, 26.2, 28.3 and 29.1 (CH_2), 42.5 (CH), 78.3 (CHOH), 127.2 (CBr=); IR (KBr) 3855, 2920, 2830, 1440, 685. MS (NH_3/CI) *m*/*z* (rel int) 428 (100, $^{79}Br^{81}Br$, [M + NH_4^+]); HRMS (EI) calcd for $C_{16}H_{26}O_2{}^{79}Br^{81}Br$ (M^+) 410.0279, found 410.0283. Anal. Calcd for $C_{16}H_{26}O_2Br_2$: C, 46.85; H, 6.39; Br, 38.96. Found: C, 46.73; H, 6.45; Br, 38.83.

Representative Procedure of Transformation of *vic*-Dibromo Compounds 9 into Propargylic Diols 1: Preparation of (*S*,*S*)-1d. To a freshly prepared 0.1 M THF solution of SmI_2[27] (13 mL, 1.3 mmol) was added a solution of (1*S*,2*E*,4*S*)-2,3-dibromo-1,4-dicyclohexylbut-2-ene-1,4-diol, (*S*,*S*)-**9d**, (135 mg, 0.33 mmol) in dry THF (3 mL) under Ar at rt. The progress of the reaction was monitored by TLC. After 20 min, the mixture was filtered, the solvent was removed under reduced pressure, and the crude was purified by flash chromatography (CH_2Cl_2/MeOH 97:3) to yield (*S*,*S*)-**1d** (82 mg, 96%). (*S*,*S*)-Dicyclohexylbut-2-yne-1,4-diol, (*S*,*S*)-**1d**: mp 105−106 °C [lit.[16] mp 102−106 °C for a mixture of stereoisomers]; R_f 0.18 (CH_2Cl_2/MeOH 95:5); $[\alpha]^{20}_D$ −63.0 (*c* = 4.0, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 200 MHz) δ 0.60−1.30 (m, 10H, CH_2), 1.35−1.95 (m, 12H, CH_2 and CH), 4.11 (d, 2H, *J* = 8.8 Hz, C*H*OH); ^{13}C NMR δ 23.4, 25.9, 26.4, 28.1 and 28.6 (CH_2), 44.0 (CH), 67.1 (CHOH), 73.6 (C≡C); IR (KBr) 3400, 2910, 2830, 1450. MS (NH_3/CI) *m*/*z* (rel int) 268 (100, [M + NH_4^+]); HRMS (EI) calcd for $C_{16}H_{26}O_2$ (M^+) 250.1933, found 250.1936. Anal. Calcd for $C_{16}H_{26}O_2$: C, 76.75; H, 10.47. Found: C, 76.45; H, 10.47.

Preparation of (*RS*,*SR*)-Cyclododec-2-yne-1,4-diol (*dl*-1g). Acetic anhydride (100 μL, 1.06 mmol) was added to a stirred solution of 200 mg (1.02 mmol) of *meso*-**1g**,[15] pyridine (100 μL, 1.25 mmol), and a catalytic amount of 4-(*N*,*N*-dimethylamino)pyridine (DMAP) in dry CH_2Cl_2 (2 mL) at 0 °C. The progress of the reaction was monitored by TLC. When TLC revealed the disappearance of the starting diol (3 h), more CH_2Cl_2 (20 mL) was added and the solution was washed with 0.5 M aq HCl, satd aq $NaHCO_3$, and brine. The organic phase was dried (Na_2SO_4) and concentrated under reduced pressure. The residue was purified by flash chromatography (CH_2Cl_2/MeOH 98:2) to give 52 mg (0.18 mmol, 18%) of the diacetate of *meso*-**1g** and 114 mg (0.48 mmol, 47%) of the desired 4-hydroxycyclododec-2-ynyl acetate, **14**:[35] colorless oil; R_f 0.23 (CH_2Cl_2/MeOH 98:2); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.38-1.85 (m, 16H, CH_2), 2.17 (s, 3H, CH_3), 4.51 (m, 1H, C*H*OH), 5.46 (td, 1H, *J* = 8.7, 1.8 Hz, C*H*OAc); ^{13}C NMR δ 21.0 (CH_3), 21.7, 21.8, 24.0, 24.1, 25.3, 25.5, 31.2 and 34.6 (CH_2), 62.7 and 64.6 (CHO-), 82.6 and 87.1 (C≡C), 169.1 (CO); IR (film) 3435, 1735, 1234; Anal. Calcd for $C_{14}H_{22}O_3$: C, 70.56; H, 9.30. Found: C, 70.92; H, 9.12.

(35) Saimoto, H.; Shinoda, M.; Matsubara, S.; Oshima, K.; Hiyama, T.; Nozaki, H. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 3088−3092.

Diethyl azadicarboxylate (DEAD, 0.66 mmol) in THF (1 mL) was slowly added to a solution of **14** (106 mg, 0.44 mmol), Ph_3P (173 mg, 0.66 mmol), and benzoic acid (81 mg, 0.66 mmol) in THF (2 mL) at 0 °C under Ar. After 30 min, the reaction was quenched by addition of EtOH (1 mL). The reaction mixture was filtered, and the volatiles were removed under reduced pressure. The residue was purified by flash chromatography through a short pad of silica gel (hexane/CH_2Cl_2 1:1) to afford a crude benzoate derivative (R_f 0.11, hexane/CH_2Cl_2 1:1), which was treated with 5 M NH_3 in MeOH (1 mL, 5 mmol) without further purification. After 3 days at rt, the solvent was removed and the residue was purified by flash chromatography to afford *dl*-**1g** (59 mg, 0.30 mmol, 68% overall yield).

Preparation of (*R*,*R*)-Cyclododec-2-yne-1,4-diol [(*R*,*R*)-1g]. Oxidation of *meso*-**1g**,[15] according to the above-described general procedure, gave diketone **5g** in 70% yield as a yellowish oil. Cyclododec-2-yne-1,4-dione (**5g**): R_f 0.84 (CH_2Cl_2/MeOH 95:5); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.56 (m, 8H, CH_2), 1.87 (m, 4H, CH_2), 2.60-2.65 (m, 4H, COC*H*$_2$); ^{13}C NMR δ 23.8, 25.3 and 25.8 (*C*H$_2$), 43.4 (CO*C*H$_2$), 85.2 (C≡C), 188.2 (CO); IR (neat) 3334, 2361, 1682; MS (NH_3/CI) *m*/*z* (rel int) 210 (8, [M + NH_4^+]). Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.81; H, 8.12. Reduction of diketone **5g** (192 mg, 1 mmol) was performed with oxazaborolidine (*R*)-**6** (2 mmol) and BH_3/SMe_2 (222 μL, 2.2 mmol) according to the procedure employed for **5a** to yield enantioenriched (*R*,*R*)-**1g** in 71% yield. An analytical sample of the crude was treated with an excess of (*S*)-Mosher acid chloride (derived from (*R*)-acid) to give a mixture of Mosher diesters. A careful analysis by ^{19}F NMR revealed a 2.1:1 *dl*/*meso* ratio and 90% ee. When the same reaction was carried out using a molar ratio of (*R*)-**6**/diketone = 0.2 the compound (*R*,*R*)-**1g** was obtained in only 32% yield, with a *dl*/*meso* ratio ∼1:1 and 65% ee.

Pyridinium tribromide (283 mg, 0.88 mmol) was slowly added to a solution of 144 mg (0.73 mmol) of (*R*,*R*)-**1g** (2.1:1 *dl*/*meso* ratio and 90% ee) in 10 mL of CH_2Cl_2 according to the procedure described for **1d.** The mixture of dibromo derivatives was purified by flash chromatography to afford (*R*,*R*)-**9g** (167 mg, 0.47 mmol, 64%) along with *meso*-**9g** (78 mg, 0.22 mmol, 30%). (1*R*,2*E*,4*R*)-2,3-Dibromocyclododec-2-ene-1,4-diol, (*R*,*R*)-**9g**: mp 139−141 °C; R_f 0.21 (CH_2Cl_2/MeOH 95:5); $[\alpha]^{20}_D$ +18.2 (*c* = 0.8, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.21 (m, 10H, CH_2), 1.60 (m, 2H, CH_2), 1.77 (m, 2H), 1.89 (m, 2H), 2.10 (bs, 2H, OH), 5.02 (dd, 2H, *J* = 10.2, 4.5 Hz, C*H*OH); ^{13}C NMR δ 22.7, 23.0, 23.2, 25.2, 26.0, 26.3, 33.1 and 34.6 (CH_2), 74.0 (CHOH), 128.7 (CBr=); IR (KBr) 3346, 2925, 2854, 1465, 1038, 693. MS (NH_3/CI) *m*/*z* (rel int) 374 (20, $^{79}Br^{81}Br$, [M + NH_4^+]); HRMS (EI) calcd for $C_{12}H_{20}O_2{}^{79}Br^{81}Br$ (M^+) 355.9810, found 355.9815. Anal. Calcd for $C_{12}H_{20}O_2Br_2$: C, 40.48; H, 5.66; Br, 44.88. Found: C, 40.41; H, 5.51; Br, 45.10.

(1*R*,2*E*,4*S*)-2,3-Dibromocyclododec-2-ene-1,4-diol (*meso*-9 g): mp 149−150 °C; R_f 0.30 (CH_2Cl_2/MeOH 95:5); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.34 (m, 10H, CH_2), 1.62 (m, 2H, CH_2), 1.81 (m, 2H), 1.95 (m, 1H), 2.42 (m, 1H), 5.00 (m, 2H, C*H*OH); ^{13}C NMR δ 21.7, 23.0, 23.2, 25.7, 26.0, 26.3, 33.1 and 34.0 (CH_2), 74.4 and 82.5 (CHOH), 122.5 and 126.1 (CBr=); IR (KBr) 3210, 2925, 2856, 1463, 1057, 708; MS (NH_3/CI) *m*/*z* (rel int) 374 (15, $^{79}Br^{81}Br$, [M + NH_4^+]); HRMS (EI) calcd for $C_{12}H_{20}O_2{}^{79}Br^{81}Br$ (M^+) 355.9810, found 355.9818.

A sample of (*R*,*R*)-**9g** (arising from **1g** of 90% ee, free of *meso*-**9g**) was treated with SmI_2 according to the procedure described for **9d** to give (*R*,*R*)-**1g** in 93% yield. An analytical sample of the crude was treated with an excess of (*S*)-Mosher acid chloride to give a mixture of Mosher diesters. A careful analysis by ^{19}F NMR revealed 94:6 *R*,*R*/*S*,*S* ratio in the sample. (*R*,*R*)-Cyclododec-2-yne-1,4-diol [(*R*,*R*)-**1g**]: mp 103−4 °C; R_f 0.10 (CH_2Cl_2/MeOH 95:5); $[\alpha]^{20}_D$ +32.6 (*c* = 2.3, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.37−1.85 (m, 16H, CH_2), 4.35 (m, 2H, C*H*OH); ^{13}C NMR δ 21.5, 24.0, 26.0 and 35.2 (CH_2), 62.9 (CHOH), 86.7 (C≡C); IR (KBr) 3345, 2932, 2850, 1465, 1038;

MS (NH_3/CI) *m*/*z* (rel int) 214 (100, [M + NH_4^+]); HRMS (EI) calcd for $C_{12}H_{20}O_2$ (M^+) 196.1463, found 196.1467.

In a similar way, reduction of *meso*-**9g** afforded propargylic diol *meso*-**1g** in 95% yield. *meso*-Cyclododec-2-yne-1,4-diol (*meso*-**1g**): mp 123−4 °C (lit.[15] mp 122−123 °C); R_f 0.10 (CH_2Cl_2/MeOH 95:5); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.37−1.84 (m, 16H, CH_2), 4.52 (td, 2H, J = 4.5, 3.9 Hz, C*H*OH); ^{13}C NMR δ 21.6, 21.7, 24.0, 24.1, 25.6, 25.9 and 35.0 (CH_2), 62.7 (CHOH), 86.2 (C≡C); IR (KBr) 3276, 2925, 2853, 1447, 1050. MS (NH_3/CI) *m*/*z* (rel int) 214 (100, [M + NH_4^+]).

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Supporting Information Available: Experimental details for preparation of compounds **1b**−**e** (mixture of stereoisomers), enantioenriched diols **1b**−**f**, and characterization data for compounds **5c**−**e** and **9a**−**c**,**e**,**f**. This material is available free of charge via the Internet at http://pubs.acs.org.

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