Highly Enantioenriched Propargylic Alcohols by Oxazaborolidine-Mediated Reduction of Acetylenic Ketones

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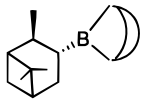
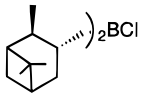
Development of new or improved methods for the asymmetric reduction of ketones has gained considerable significance during the past years,[1] not only because the optically active secondary alcohols are often present in natural products but also due to the fact that such compounds are valuable intermediates in organic synthesis. In this connection, α,*β*-alkynyl ketones such as **1** have achieved much importance since the acetylenic moiety of propargylic alcohols **2** can be transformed into many other functional groups (Scheme 1).[2]

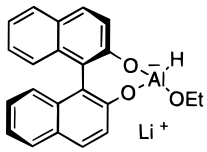
Midland's *B*-isopinocampheyl-9-borabicyclo[3.3.1]nonane (Alpine-Borane, **3**),[3a−c] Brown's *B*-chlorodiisopinocampheylborane (DIP-Chloride, **4**),[3d] and Noyori's Binal-H (**5**)[4] are excellent reagents for the conversion of **1** to **2**. Successful enantioselective reductions of a number of alkynyl ketones have also been reported by using other reagents.[5,6]



(−)-**3**



(−)-**4**



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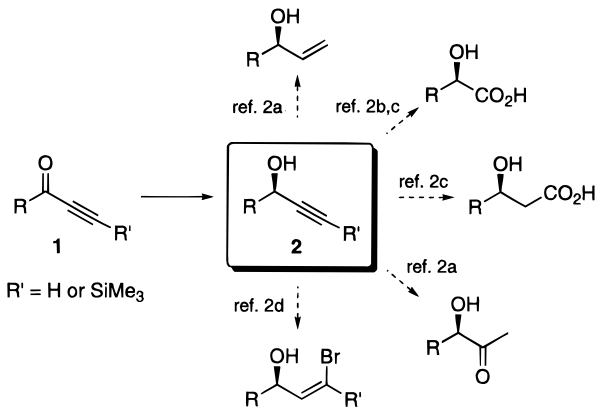
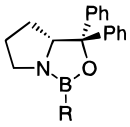
Nevertheless, none of these reagents are of general application and none afford alcohols with high optical purity (≥90% ee) from both unhindered and hindered alkynyl ketones.[7] Thus, a reagent which provides a general access to highly enantiomerically enriched propargylic alcohols would be desirable.

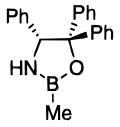
Scheme 1



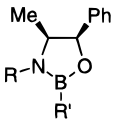
During the past recent years, oxazaborolidines have emerged as an important advance in the enantioselective reduction of ketones. Several research groups have developed chiral 1,3,2-oxazaborolidines (e.g., compounds **6**−**9**) which can act as efficient catalysts in the borane reduction of a wide range of structurally different ketones.[8] However, reports on reduction of α,*β*-acetylenic ketones are very scarce[9] and it is generally accepted that "the reduction of α,*β*-acetylenic ketones in the oxazaborolidine systems proceeds with only mediocre enantioselectivity".[2c]



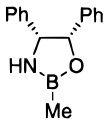
(*R*)-**6**



(*R*)-**7**



8a R = Me R' = H
8b R = H R' = Me
8c R = R' = H



(4*R*,5*S*)-**9**

In this connection, we have described (*R*)- and (*S*)-*B*-methyl-4,5,5-triphenyl-1,3,2-oxazaborolidine, (*R*)- and (*S*)-**7**, two catalysts derived from phenylglycine, which we have utilized in the borane-mediated reduction of aromatic, saturated, and α,*β*-alkenyl ketones.[10] Herein, we

(1) For leading reviews on enantioselective reduction of ketones, see: (a) Brown, H. C.; Cho, B. T.; Park, W. S.; Ramachandran, P. V. *J. Org. Chem.* **1987**, *52*, 5406. (b) Singh, V. K. *Synthesis* **1992**, 605. (c) Brown, H. C.; Ramachandran, P. V. *Acc. Chem. Res.* **1992**, *25*, 16. (d) Midland, M. M.; Morrell, L. A. In *Houben-Weyl Methods of Organic Chemistry*; Helmchen, G., Hoffmann, R. W., Mulzer, J., Schaumann, E., Eds.; Thieme Verlag: Stuttgart, 1995; Vol. E21d, p 4049.

(2) (a) Mukai, C.; Kataoka, O; Hanaoka, M. *J. Org. Chem.* **1993**, *58*, 2946. (b) Midland, M. M.; Lee, P. E. *J. Org. Chem.* **1981**, *46*, 3933. (c) Corey, E. J.; Helal, C. J. *Tetrahedron Lett.* **1995**, *36*, 9153. (d) Ohmori, K.; Nishiyama, S.; Yamamura, S. *Tetrahedron Lett.* **1995**, *36*, 6519. Enantiomerically enriched propargylic alcohols have been used as intermediates in many synthesis of natural and/or biologically active products: (e) Ramachandran, P. V.; Teodorovic, A. V.; Rangaishenvi, M. V.; Brown, H. C. *J. Org. Chem.* **1992**, *57*, 2379 and ref 6 therein. (f) Michelet, V.; Besnier, I.; Tanier, S.; Touzin, A. M.; Genet, J. P.; Demoute, J. P. *Synthesis* **1995**, 165 and refs 3−9 therein. (g) Roush, W. R.; Sciotti, R. J. *J. Am. Chem. Soc.* **1994**, *116*, 6457. (h) Zhu, G.; Lu, X. *J. Org. Chem.* **1995**, *60*, 1087. (i) Marshall, J. A.; Xie, S. *J. Org. Chem.* **1995**, *60*, 7230. (j) Borzilleri, R. M.; Weinreb, S. M.; Parvez, M. *J. Am. Chem. Soc.* **1995**, *117*, 10905. (k) Mukai, C.; Hanaoka, M. *Synlett* **1996**, 11.

(3) (a) Midland, M. M.; McDowell, D. C.; Hatch, R. L.; Tramontano, A. *J. Am. Chem. Soc.* **1980**, *102*, 867. (b) Brown, H. C.; Pai, G. G. *J. Org. Chem.* **1985**, *50*, 1384. (c) Midland, M. M.; McLoughlin, J. I.; Gabriel, J. *J. Org. Chem.* **1989**, *54*, 159. (d) Dhar, R. K. *Aldrichimica Acta* **1994**, *27*, 43. Also see ref 2e.

(4) (a) Noyori, R.; Tomino, I.; Yamada, M.; Nishizawa, M. *J. Am. Chem. Soc.* **1984**, *106*, 6717. (b) Bringmann, G.; Gassen, M.; Lardy, R. *Tetrahedron* **1994**, *50*, 10245.

(5) Enzymatic reductions: (a) Bradshaw, C. W.; Hummel, W.; Wong, C.-H. *J. Org. Chem.* **1992**, *57*, 1532. (b) Ansari, M. H.; Kusumoto, T.; Hiyama, T. *Tetrahedron Lett.* **1993**, *34*, 8271. Chiral aluminum or boron hydrides: (c) Cohen, N.; Lopresti, R. J.; Neukom, C.; Saucy, G. *J. Org. Chem.* **1980**, *45*, 582. (d) Vigneron, J. P.; Bloy, V. *Tetrahedron Lett.* **1980**, *21*, 1735. (e) Corey, E. J.; Boaz, N. W. *Tetrahedron Lett.* **1984**, *25*, 3055. (f) Wender, P. A.; Ihle, N. C.; Correia, C. R. D. *J. Am. Chem. Soc.* **1988**, *110*, 5904.

(6) For optically active propargylic alcohols prepared by other routes, see: (a) Mukaiyama, T.; Susuki, K. *Chem. Lett.* **1980**, 255. (b) Mori, A.; Ishihara, K.; Arai, I.; Yamamoto, H. A. *Tetrahedron* **1987**, *43*, 755. (c) Burgess, K.; Jennings, L. D. *J. Am. Chem. Soc.* **1991**, *113*, 6129. (d) Corey, E. J.; Cimprich, K. A. *J. Am. Chem. Soc.* **1994**, *116*, 3151. (e) Oguni, N.; Satoh, N.; Fujii, H. *Synlett* **1995**, 1043. (f) Lütjens, H.; Nowotny, S.; Knochel, P. *Tetrahedron: Asymmetry* **1995**, *6*, 2675. See also ref 2b.

(7) For instance, **3** cannot be applied to the reduction of *tert*-butyl alkynyl ketones whereas **4** reduces efficiently this type of hindered ketones but fails for other ketones with lower steric requeriments (see ref 2e).

(8) For recent reviews, see: Wallbaum, S.; Martens, J. *Tetrahedron: Asymmetry* **1992**, *3*, 1475. Deloux, L.; Srebnik, M. *Chem. Rev.* **1993**, *93*, 763. Also see: Franot, C.; Stone, G. B.; Engeli, P.; Spöndlin, C.; Waldvogel, E. *Tetrahedron: Asymmetry* **1995**, *6*, 2755 and references therein. Hong, Y.; Gao, Y.; Nie, X.; Zepp, C. M. *Tetrahedron Lett.* **1994**, *35*, 6631. Gajda, T. *Tetrahedron: Asymmetry* **1994**, *5*, 1965. Willems, J. G. H.; Dommerholt, F. J.; Hammink, J. B.; Vaarhorst, A. M.; Thijs, L.; Zwanenburg, B. *Tetrahedron Lett.* **1995**, *36*, 603. Dubois, L.; Fiaud, J.-C.; Kagan, H. B. *Tetrahedron: Asymmetry* **1995**, *6*, 1097. Meier, C.; Laux, W. H. G. *Tetrahedron* **1996**, *52*, 589. Schwink, L.; Knochel, P. *Tetrahedron Lett.* **1996**, *37*, 25.

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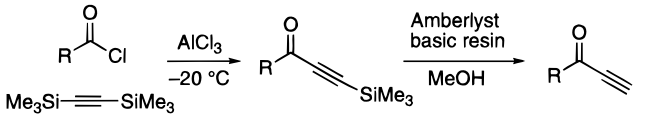
Scheme 2



a	R = $PhCH_2CH_2$	**10a**	(98% yield)	**11a**	(98% yield)
b	R = cyclohexyl	**10b**	(90% yield)	**11b**	(80% yield)
c	R = 1-adamantyl	**10c**	(86% yield)	**11c**	(90% yield)

report that oxazaborolidines **7** also efficiently catalyze the borane reduction of several α,*β*-acetylenic ketones. The relative performance of oxazaborolidines **6**−**9** with regard to the asymmetric reduction of sterically crowded carbonyl groups of α,*β*-acetylenic ketones and their dicobalthexacarbonyl complexes has also been investigated.

Results and Discussion

Preparation of α,*β*-Acetylenic Ketones. A representative set of trimethylsilyl acetylenic ketones (RC(O)C≡C$SiMe_3$, ketones **10a**−**c**) with different bulky alkyl groups (R) were prepared in good yields by reaction of bis(trimethylsilyl)acetylene with the corresponding acyl chloride under Friedel−Crafts conditions (Scheme 2).[11] We envisaged that the presence of the easily removable trimethylsilyl group[12] in the acetylenic moiety could be beneficial to prevention of undesirable additions to the triple bond. However, for the sake of comparison, the desilylated ketones **11a**−**c** (obtained from **10a**−**c**) were also included in the present reduction study.

Oxazaborolidine-Mediated Reductions of Ynones 10 and 11. Treatment of ketones **10a**−**c** and **11a**−**c** with BH_3·SMe_2 in the presence of (*R*)-**7**, in THF at 0 °C, gave a clean conversion into propargylic alcohols **12a**−**c** and **13a**−**c**, respectively, within a few minutes.[13] The results are summarized in Table 1. It is worth noting that even a very hindered ketone like **10c** is reduced quite fast under these conditions.[14,15]

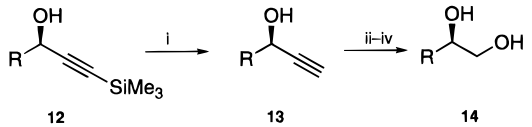
The absolute configurations of propargylic alcohols **12** and **13** were determined by chemical correlation with the known chiral 1,2-diols **14** (Scheme 3),[16] except for the configuration of **13c** (and also **12c** after desilylation), which was determined by comparison of the sign of specific rotation with that given in the literature.[17]

Table 1. Reduction of Acetylenic Ketones 10 and 11 with BH_3·SMe_2 in the Presence of (*R*)-7, in THF at 0 °C[a]

entry	ketone	alcohol	yield (%)[b]	ee (%)[b]
1	**10a**	(*R*)-**12a**	92 (80)	90[c] (84)
2	**11a**	(*R*)-**13a**	73 (65)	90[d] (80)
3	**10b**	(*R*)-**12b**	65 (70)	93[d] (85)
4	**11b**	(*R*)-**13b**	60 (65)	90[d] (88)
5	**10c**	(*R*)-**12c**	80 (71)	95[d] (95)
6	**11c**	(*R*)-**13c**	70 (75)	97[d] (95)

[a] Reactions, monitored by TLC (silica gel, CH_2Cl_2), finished in <5 min. [b] Isolated yields, with 1.2 equiv of BH_3·SMe_2 and 1.0 equiv of (*R*)-**7**. Within parentheses, yields and ee values using 0.2 equiv of (*R*)-**7**. [c] Determined by HPLC analysis of the benzoate derivatives with a Chiralcel OD-H chiral column. [d] Determined by HPLC (Tracer Spherisorb column) and/or ^{19}F NMR analysis of the corresponding Mosher esters.

Scheme3[a]



12 13 14

[a] (i) K_2CO_3, MeOH/H_2O; (ii) H_2, Lindlar cat., MeOH; (iii) O_3, CH_2Cl_2-MeOH (1:1); (iv) $NaBH_4$.

As shown in Table 1, reduction of α,*β*-acetylenic ketones with very different steric requirements proceeds with consistency and predictable stereochemistry to give propargylic alcohols of high optical purity (90−97% ee when 1 equiv of (*R*)-**7** is used). Apparently, the presence of Me_3Si does not change significantly the selectivities (compare entries 1, 3, and 5 to entries 2, 4, and 6, respectively). An increase of the steric requirements around the carbonyl group (from ketone **10a** to ketone **10c**) causes a rise in the enantioselectivity. This and the fact that alcohols of the *R* configuration are mainly obtained may be explained—according to the mechanism proposed by Corey et al.[18] for analogous oxazaborolidine-mediated reactions—by a transition state in which the acetylenic moiety acts as the smaller group (see Scheme 4).

Reduction of Masked Acetylenic Ketones. Despite the good performance of (*R*)-**7** in the reduction of acetylenic ketones, we have also explored the possibility of improving these results (which was specially desirable for unbranched or α-monobranched ketones **10a**,**b** and **11a**,**b**) by temporary transformation of the acetylenic moiety in a bulkier group that could enhance (or reverse) the selectivity. In this regard, the hexacarbonyldicobalt complexes of the ynones seemed a very attractive choice[19] since these compounds are easy to obtain and, after the carbonyl reduction step, the triple bond can be regenerated with the aid of a mild oxidant as Ce(IV) (see Scheme 5). Very recently, Corey et al. reported[2c] the reduction of

(9) Morita et al. have recently reported the reduction of an acetylenic ketone catalyzed by proline-derived oxazaborolidine [(*S*)-**6**, R = Me and Bu] in low yields and enantioselectivity: Morita, S.; Otsubo, K.; Matsubara, J.; Ohtani, T.; Uchida, M. *Tetrahedron: Asymmetry* **1995**, *6*, 245. See also ref 2c. During the preparation of this manuscript a Note has appeared reporting the efficient reduction of a few acetylenic ketones with an excess of (*S*)-**6** (R = Me) at −30 °C: Parker, K. A.; Ledeboer, M. W. *J. Org. Chem.* **1996**, *61*, 3214.

(10) (a) Berenguer, R.; Garcia, J.; Gonzàlez, M.; Vilarrasa, J. *Tetrahedron: Asymmetry* **1993**, *4*, 13. (b) Berenguer, R.; Garcia, J.; Vilarrasa, J. *Tetrahedron: Asymmetry* **1994**, *5*, 165. (c) Bach, J.; Berenguer, R.; Garcia, J.; Vilarrasa, J. *Tetrahedron Lett.* **1995**, *36*, 3425. (d) Bach, J.; Berenguer, R.; Farràs, J.; Garcia, J.; Meseguer, J.; Vilarrasa, J. *Tetrahedron: Asymmetry* **1995**, *6*, 2683.

(11) (a) Birkofer, L.; Ritter, A.; Uhlenbrauck, H. *Chem. Ber.* **1963**, *96*, 3280. (b) Karpf, M.; Dreiding, A. S. *Helv. Chim. Acta* **1979**, *62*, 852.

(12) (a) Wender, P. A.; McKinney, J. A.; Mukai, C. *J. Am. Chem. Soc.* **1990**, *112*, 5369. (b) Schmidt, H.; Arens, J. F. *Recl. Trav. Chim. Pays-Bas* **1967**, *86*, 1138.

(13) Reactions were monitored by TLC. Triple-bond hydroboration byproducts were not detected. Temperature appeared to be crucial: an attempt to reduce **10a** at rt lead to a complex mixture of products, whereas reduction at −40 °C was much slower and gave alcohol **12a** in lower yield and stereoselectivity (64%, 39% ee.).

(14) In this connection it is timely to point out that, in our hands, reduction of **10c** with neat (−)-DIP-Chloride at rt yielded a 70% of alcohol (−)-**12c** (97% ee.) after 2 days. The *R* configuration was assumed for the resulting alcohol in agreement with the mechanism accepted for such reductions.

(15) A similarly crowded ketone, 4,4-dimethyl-1-(trimethylsilyl)-1-pentyn-3-one (**10d**, R = Bu^t) was subjected to identical reduction conditions, with parallel results: 97% ee and 93% ee (using 1 equiv and 0.2 equiv of (*R*)-**7**, respectively).

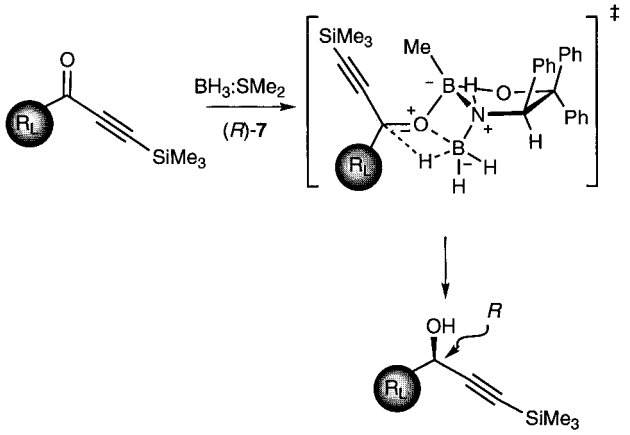
(16) (a) Compound **14a**: Jeong K.-S.; Sjö, P.; Sharpless, K. B. *Tetrahedron Lett.* **1992**, *33*, 3833. (b) Compound **14b**: Naemura, K.; Mizo-oku, T.; Kamada, K.; Hirose, K.; Tobe, Y.; Sawada, M.; Takai, Y. *Tetrahedron: Asymmetry* **1994**, *5*, 1549. (c) Compound **14c**: Huszthy, P.; Bradshaw, J. S.; Zhu, C. Y.; Izatt, R. M. *J. Org. Chem.* **1991**, *56*, 3330.

(17) Kluge, A. F.; Kertesz, D. J.; O-Yang, C.; Wu, H. Y. *J. Org. Chem.* **1987**, *52*, 2860.

(18) Corey, E. J.; Bakshi, R. K.; Shibata, S.; Chen, C.-P.; Singh, V. K. *J. Am. Chem. Soc.* **1987**, *109*, 7925.

(19) Nicholas, K. M. *Acc. Chem. Res.* **1987**, *20*, 207.

Scheme 4



Scheme 5

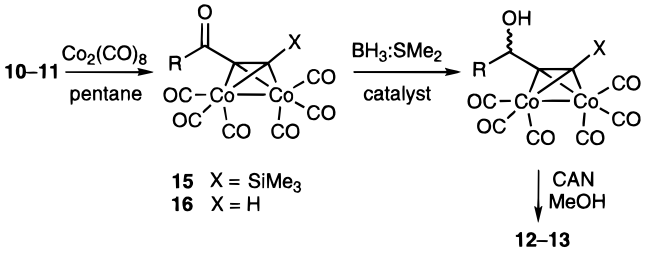


Table 2. Reduction of Hexacarbonyldicobalt Complexes 15 and 16 with $BH_3{\cdot}SMe_2$ in the Presence of Oxazaborolidines, in THF at 0 °C[a]

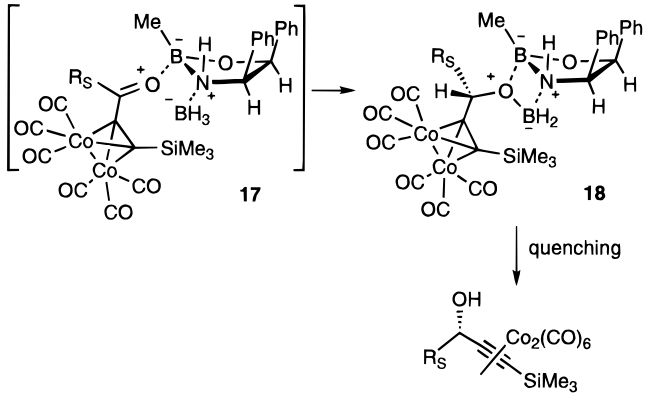
entry	ketone	oxazaborolidine	reactn time	alcohol (overall yield, %)	confign, % ee[b]
1	**15a**	(*R*)-**7**	3 h	**12a** (34)	*S*, 89
2[c]	**15a**	(*R*)-**7**	1 h	**12a** (65)	*S*, 92
3[d]	**15a**	(*R*)-**6**	48 h	**12a** (35)	*S*, 10
4	**15a**	(4*S*,5*R*)-**8a**	20 min	**12a** (90)	*R*, 85
5	**15a**	(4*S*,5*R*)-**8b**	25 min	**12a** (77)	*R*, 81
6	**15a**	(4*R*,5*S*)-**9**	30 min	**12a** (88)	*S*, 97
7	**15b**	(4*R*,5*S*)-**9**	1 h	**12b** (85)	*S*, 97
8	**16a**	(4*R*,5*S*)-**9**	45 min	**13a** (86)	*S*, 85
9	**16b**	(4*R*,5*S*)-**9**	1 h	**13b** (93)	*S*, 82

[a] 1.1 equiv of oxazaborolidine and 1.2 equiv of $BH_3{\cdot}SMe_2$, in THF, unless otherwise indicated; deprotection with CAN/MeOH (see Experimental Section). [b] Determined as indicated in Table 1. [c] 2.2 equiv of $BH_3{\cdot}SMe_2$ was used in this case. [d] Catecholborane as the reducing agent, in toluene at −57 °C.

the $Co_2(CO)_6$ adduct of non-3-yn-2-one (**1**, R = Me, R′ = pentyl in Scheme 1) to the corresponding alcohol with 97% ee using a modified proline-derived oxazaborolidine [(*R*)-**6**, R = Me_3SiCH_2].

Ketones **10** and **11** were easily and quantitatively transformed into their hexacarbonyldicobalt complexes (**15** and **16**, respectively) with octacarbonyldicobalt in pentane. The α-unbranched ketone **15a** was chosen as a representative model to optimize the oxazaborolidine-mediated reduction step. As shown in Table 2, an experiment of reduction of **15a** with $BH_3{\cdot}SMe_2$ in the presence of 1.2 equiv of (*R*)-**7** gave a low yield of alcohol (entry 1). Some improvement was observed when 2.2 equiv of borane was used (entry 2). Moreover, reduction with a proline-derived oxazaborolidine [(*R*)-**6**, R = Me] was also unsuccessful under the conditions reported for α,β-enones (entry 3).[8] Apparently, steric requirements of ketone **15a** prevented an efficient complexation with oxazaborolidines **6** and **7**. We supposed that a less congested catalyst could be more appropiate.

Scheme 6



We carried out the reduction of **15a** using oxazaborolidines **8a**, derived from (−)-ephedrine, and **8b**, derived from (−)-norephedrine,[10a] in which the lack of a phenyl group at the α-face (in comparison to **6** and **7**) makes that α-face more available for complexation. Reductions were almost complete in both experiments in <10 min at 0 °C but with moderate stereoselectivities (entries 4 and 5). In light of these results, it seemed reasonable to investigate an oxazaborolidine such as **8c** in which not only the nitrogen but also the boron atom was unsubstituted. Unfortunately, in this case the reduction did not work well. It should be borne in mind that, unlike **8a** and **8b**, oxazaborolidine **8c** must be prepared at rt (the reaction cannot be carried to completion by heating since trimerization to borazine predominates) and the probable presence of several boron species can cut down yield and selectivity. Finally, looking for a catalyst in which the β-face was more blocked, we studied the oxazaborolidine (4*R*,5*S*)-**9**, derived from commercially available (1*S*,2*R*)-2-amino-1,2-diphenylethanol.[20] A fast reduction of both linear ketone **15a** and α-monobranched ketone **15b**, with a gratifying 97% ee, was observed (entries 6 and 7). With nonsilylated ketones **16a** and **16b** the results, although not so good, were satisfactory (entries 8 and 9).[21] With regard to ketones **15c** and **16c**, oxazaborolidines **7** and **9** did not show any catalytic effect (no reaction occurred), probably due to the fact that the steric hindrance around the carbonyl groups of these substrates was too great.

The origin of the enantioselectivity observed in the cases shown in Table 2 can be explained by an *exo* complex like **17** in which the huge cobalt complex moiety is located far from the Me group on the boron atom (Scheme 6). On the other hand, the fact that at least 1 equiv of oxazaborolidine is needed to complete the reduction suggests that, in contrast with reduction of ynones, the first expected product is a complex (**18**) which does not liberate easily the oxazaborolidine (**7** or **9**) in the reaction mixture, so that a true catalytic cycle is lacking.[22]

In summary, we have achieved an efficient and general approach to highly enantiomerically enriched propargylic alcohols by borane-mediated, oxazaborolidine-catalyzed reduction of ketones. A judicious choice of the catalyst

(20) Quallich, G. J.; Woodall, T. M. *Tetrahedron Lett.* **1993**, *34*, 4145. Its enantiomer, (1*R*,2*S*)-2-amino-1,2-diphenylethanol, is also commercially available.

(21) By contrast, oxazaborolidine **9** showed a less satisfactory performance in the reduction of noncomplexed acetylenic ketones (74% yield, 69% ee, for ketone **10a**). In the same way, reduction of **10a** with catecholborane in the presence of (*R*)-**6** at −57 °C showed an acceptable yield but a moderate selectivity (82% yield, 81% ee).

(**7** or **9**) and ketone (either in its acetylenic or hexacarbonyldicobalt complex form) allows one to obtain diverse homochiral propargylic alcohols. Thus, while ynones **10** and **11** give propargylic alcohols of the *R* configuration (>90% ee) with (*R*)-**7**, their cobalt complexes afford propargylic alcohols of the *S* configuration with (*R*)-**7** (moderate yields, excellent ee) as well as with (4*R*,5*S*)-**9** (excellent yields and ee for **15a** and **15b**).

Experimental Section

All the solvents were distilled from an appropiate drying agent and stored under a nitrogen atmosphere. The crude products were purified by column chromatography on silica gel of 230−400 mesh (flash chromatography). Thin-layer chromatograms were performed on HF 254 silica gel plates (using CH_2Cl_2, CH_2Cl_2/MeOH, or CH_2Cl_2/hexane as the eluent, as indicated after the R_f values). Melting points are uncorrected. ^{1}H, ^{13}C, and ^{19}F NMR spectra were obtained in $CDCl_3$ at 200, 50.3, and 282.2 MHz, respectively; chemical shifts are given in ppm with respect to internal TMS, and *J* values are quoted in hertz. ^{11}B NMR spectra were recorded in THF at 96.2 MHz, with respect to an external standard of $BF_3{\cdot}Et_2O$ in C_6D_6. Infrared spectra were measured on a Perkin-Elmer 681 on NaCl plates (film) or in KBr; only the most significant absortions, in cm^{-1}, are indicated. Microanalyses were performed by the Serveis Científico-Tècnics (Universitat de Barcelona). Chemical ionization mass spectra (NH_3) are given in *m*/*z*. Acetylenic ketones **10b**[11b] and **10d**,[11b] as well as oxazaborolidines **6** (R = Me),[23] **8a**,[24] **8b**,[25] and **9**,[20] were prepared according to published procedures.

(*R*)-1,1,2-Triphenyl-2-aminoethanol.[26] Methyl (*R*)-phenylglycinate hydrochloride (10.0 g, 0.050 mol) was added portionwise to phenylmagnesium bromide (150 mL, 3 M in Et_2O) at 0 °C under Ar over 2 h. The cooling bath was removed, and the reaction mixture was stirred at room temperature for 7 h. The solution was poured into crushed ice (300 g) and concd HCl (50 mL) with mechanical stirring. The mixture was stirred vigorously for 1 h, and the precipitate, amino alcohol hydrochloride, was collected by filtration and washed with water and then diethyl ether. The filtrate was stirred in 1.5 M NaOH (150 mL) for 1 h. Afterward, 200 mL of diethyl ether was added and the resulting mixture was stirred for 3 h. The organic layer was decanted, washed with small portions of water until *p*H ~7, and dried. The solvent was removed, and the solid was recrystallized from ethanol to afford the product as a white solid (10.5 g, 73%). Enantiomeric purity (>99.8:0.2) was determined by HPLC (Chiralcel OD-H, hexane/isopropyl alcohol, 95:5, $t_R(R)$ = 18.4 min, $t_R(S)$ = 22.0 min); R_f 0.52 (CH_2Cl_2/MeOH, 95:5); mp 131.1−132.1 °C; $[\alpha]^{20}_D$ +248.0 (*c* 1, $CHCl_3$); ^{1}H NMR δ 1.64 (br s, 3 H), 4.99 (s, 1 H), 6.95−7.45 (m, 13 H), 7.76 (m, 2 H); ^{13}C NMR δ 61.7, 79.5, 126.0, 126.2, 126.5, 127.0, 127.2, 127.3, 127.4, 128.5, 128.6, 140.0, 143.8, 146.4.

(*R*)-*B*-Methyl-4,5,5-triphenyl-1,3,2-oxazaborolidine [(*R*)-7].[26] Trimethylboroxine (0.87 g, 7.0 mmol) was added to a solution of (*R*)-(+)-2-amino-1,1,2-triphenylethanol (3.00 g, 10.4 mmol) in 20 mL of dry toluene, and the mixture was stirred under Ar at rt for 1 h. The solution was concentrated (1 atm) to ca. 5 mL. Toluene (20 mL) was added, and the solution was concentrated again at 1 atm. The process was repeated once more. This last solution was diluted with toluene up to 25 mL and stored under Ar: ^{1}H NMR δ 0.48 (s, 3 H), 3.65 (br s, 1 H), 5.38 (s, 1 H), 6.8−7.4 (m, 15 H); ^{13}C NMR δ 69.0, 91.3, 126.0, 126.2, 126.8, 126.9, 127.1, 127.3, 127.5, 127.9, 128.0, 142.1, 142.7, 147.6; ^{11}B NMR δ 39.

General Procedure for Reduction of Acetylenic Ketones with Borane Catalyzed by (*R*)-7: Reduction of Ketone 10a. A solution of **10a** (115 mg, 0.50 mmol) in THF (0.5 mL) was slowly (ca. 1 mmol/h) added to a solution of (*R*)-**7** (0.5 mmol) and $BH_3{\cdot}SMe_2$ (60 μL, 0.60 mmol) in THF (1 mL) at 0 °C under Ar. Upon completion of the addition, TLC revealed the disappearance of the starting ketone. Reaction was cautiously quenched by addition of MeOH (1 mL) at 0 °C. The solution was stirred for 15 min at rt and then concentrated under vacuum. The residue was purified by flash chromatography (SiO_2, CH_2Cl_2) to yield 107 mg (92%) of (*R*)-5-phenyl-1-(trimethylsilyl)-1-pentyn-3-ol,[27] (*R*)-**12a**: oil; R_f 0.40 (CH_2Cl_2); ^{1}H NMR δ 0.22 (s, 9H), 1.62 (bs, 1H), 2.02 (m, 2 H), 2.81 (m, 2H), 4.40 (t, *J* = 7.2 Hz, 1 H), 7.20−7.40 (m, 5H); ^{13}C NMR δ 0.0, 31.5, 39.2, 62.3, 90.0, 106.5, 126.1, 128.5, 128.6, 141.4; IR (neat) 845, 1245, 1610, 2120, 3590−3100; $[\alpha]^{20}_D$ −20.2 (*c* 3, $CHCl_3$); MS (NH_3/CI) 250 (100) ([M + NH_4^+]). Anal. Calcd for $C_{14}H_{20}$OSi: C, 72.36; H, 8.67. Found: C, 72.24; H, 8.52.

An analytical sample of **12a** was benzoylated (PhCOCl, Et_3N, DMAP cat., CH_2Cl_2). The analysis of this derivative by HPLC (Chiralcel OD-H, hexane/isopropyl alcohol, 99.8:0.2, $t_R(S)$ = 9.3 min, $t_R(R)$ = 13.7 min) revealed 90% ee.

(*R*)-1-Cyclohexyl-3-(trimethylsilyl)-2-propyn-1-ol ((*R*)-12b): 65% yield; oil; R_f 0.48 (CH_2Cl_2); ^{1}H NMR δ 0.22 (s, 9H), 1.05−1.40 (m, 5 H), 1.45−2.10 (m, 7 H), 4.18 (d, *J* = 7.3 Hz, 1 H); ^{13}C NMR δ 0.0, 26.0, 28.2, 28.6, 44.1, 67.7, 90.2, 105.9; IR (neat) 820, 1200, 1420, 2120, 3500−3010; $[\alpha]^{20}_D$ −3.5 (*c* 3, $CHCl_3$); CIMS 228 (100) ([M + NH_4^+]). Anal. Calcd for $C_{12}H_{22}$OSi: C, 68.51; H, 10.54. Found: C, 68.33; H, 10.60.

An analytical sample was converted into the corresponding Mosher ester derived from (*R*)-Mosher acid. HPLC analysis of the sample (Tracer Spherisorb column, hexane/THF, 99.9:0.1, $t_R(R,R)$ = 9.3 min, $t_R(R,S)$ = 11.4 min) revealed 93% ee.

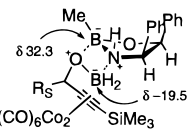
(*R*)-1-(Tricyclo[3.3.1.1^{3,7}]dec-1-yl)-3-(trimethylsilyl)-2-propyn-1-ol ((*R*)-12c): 80% yield; mp 60.1−61.0 °C; R_f 0.44 (CH_2Cl_2); ^{1}H NMR δ 0.22 (s, 9 H), 2.05 (m, 3 H), 1.59−1.80 (m, 13 H), 3.88 (s, 1H); ^{13}C NMR δ 0.1, 28.2, 37.0, 37.9, 37.6, 52.8, 71.9, 90.7, 104.8; IR (KBr) 835, 1240, 2110, 3510−3090; $[\alpha]^{20}_D$ −2.47 (*c* 1, $CHCl_3$); CIMS 280 (100) ([M + NH_4^+]). Anal. Calcd for $C_{16}H_{26}$OSi: C, 73.22; H, 9.98. Found: C, 73.22; H, 10.02. ^{19}F NMR analysis of the corresponding Mosher ester revealed 95% ee.

(*R*)-4,4-Dimethyl-1-(trimethylsilyl)-1-pentyn-3-ol ((*R*)-12d): 60% yield; mp 45.1−46.0 °C; R_f 0.45 (CH_2Cl_2); ^{1}H NMR δ 0.27 (s, 9 H), 1.09 (s, 9 H), 1.95 (bs, 1H), 4.02 (s, 1H); ^{13}C NMR δ 0.0, 25.3, 35.8, 71.8, 90.3, 105.7; IR (KBr) 825, 1235, 2120, 3590−3080; $[\alpha]^{20}_D$ +3.9 (*c* 1, $CHCl_3$). Anal. Calcd for $C_{10}H_{20}$OSi: C, 65.15; H, 10.93. Found: C, 64.85; H, 10.83.

An analytical sample was transformed into the corresponding Mosher ester derived from (*R*)-Mosher acid. HPLC analysis of the sample (Tracer Spherisorb column, hexane/THF, 99.9:0.1, $t_R(R,R)$ = 8.9 min, $t_R(R,S)$ = 11.3 min) revealed 97% ee.

(*R*)-5-Phenyl-1-pentyn-3-ol[27] **((*R*)-13a):** 73% yield; oil; R_f 0.26 (CH_2Cl_2); ^{1}H NMR δ 1.80 (bs, 1H), 2.00−2.13 (m, 2 H), 2.70−2.85 (m, 2H), 2.52 (d, *J* = 2.2 Hz, 1H) 4.32 (m, 1 H), 7.10−7.35 (m, 5H); ^{13}C NMR δ 31.8, 39.6, 62.0, 73.8, 85.2, 126.6, 129.0, 141.6; IR (neat) 1010, 1420, 2100, 3400−3010; $[\alpha]^{20}_D$ +4.0 (*c* 0.7,

(22) A ^{11}B NMR experiment ($BF_3{\cdot}Et_2O$ as the external reference) was carried out by mixing a sample of ketone **15a** with 1.1 equiv of oxazaborolidine **9** and 1.2 equiv of $BH_3{\cdot}SMe_2$ in THF. We observed that the sharp signal corresponding to $BH_3{\cdot}SMe_2$ (ca. δ −20) and that one corresponding to **9** (δ 35.1) were gradually replaced by two new peaks at δ 32.3 and −19.5, which may be attributed to structure **18**. Addition of an excess of $BH_3{\cdot}SMe_2$ to the sample did not modify the observed ^{11}B NMR shifts. However, in a parallel experiment, when an excess of Et_3N was added, besides a fast formation of the $BH_3{\cdot}NEt_3$ complex (ca. δ −15) with the remaining borane, a slower transformation of the peak at δ 32.3 to the former at δ 35.1 (corresponding to **9**) and the disappearance of the peak at δ −19.5 was observed. In summary, oxazaborolidine **9** is regenerated by Et_3N (a good Lewis base) but not by the excess of borane present in the reaction mixture.



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$CHCl_3$); CIMS 178 (100) ([M + NH_4^+]). ^{19}F NMR analysis of the corresponding Mosher ester revealed 90% ee.

(*R*)-1-Cyclohexyl-2-propyn-1-ol[17] **((*R*)-13b).** Compound (*R*)-**13b** was prepared as above for (*R*)-**12a**: 60% yield; oil; R_f 0.31 (CH_2Cl_2); ^1H NMR δ 1.10−1.38 (m, 5 H), 1.55−1.95 (m, 6 H), 2.21 (bs, 1 H), 2.46 (d, J = 2.2 Hz, 1 H), 4.18 (dd, J = 2.2, 6.3 Hz, 1 H); ^{13}C NMR δ 25.7, 25.8, 26.3, 27.9, 28.4, 43.8, 66.9, 73.6, 83.9; IR (neat) 1015, 1430, 2105, 3280, 3400−3000; $[\alpha]^{20}_D$ +9.9 (*c* 1, diethyl ether) [lit.[17] $[\alpha]^{25}_D$ −11.2 (*c* 1, Et_2O) for *S* isomer]; CIMS 156 (25) ([M + NH_4^+]), 173 (100) ([M + $N_2H_7^+$]). ^{19}F NMR analysis of the corresponding Mosher ester revealed 90% ee.

(*R*)-1-(Tricyclo[3.3.1.1^{3,7}]dec-1-yl)-2-propyn-1-ol ((*R*)-13c): 70% yield; mp 79.0−80.0 °C; R_f 0.44 (CH_2Cl_2); ^1H NMR δ 1.45−1.90 (m, 13 H), 2.03 (s, 3 H), 2.47 (d, J = 1.0 Hz, 1H), 3.88 (s, 1 H); ^{13}C NMR δ 28.1, 36.9, 37.0, 37.5, 53.4, 71.4, 74.2, 82.8; IR (KBr) 1330, 1440, 2330, 3000−3400; $[\alpha]^{20}_D$ +14.3 (*c* 0.2, EtOH); CIMS 208 (84) ([M + NH_4^+]), 225 (100) ([M + $N_2H_7^+$]). Anal. Calcd for $C_{13}H_{18}O$: C, 82.06; H, 9.53. Found: C, 81.88; H, 9.65. ^{19}F NMR analysis of the corresponding Mosher ester revealed 97% ee.

General Procedure for Conversion of Propargylic Alcohols into 1,2-Diols: (*R*)-4-Phenyl-1,2-butanediol[16a] **((*R*)-14a).** A mixture of 86 mg (0.53 mmol) of (*R*)-**13a**, 5 mg of Pd/$CaCO_3$, and 5 μL of quinoline in 2 mL of benzene was shaken at rt under a hydrogen atmosphere for 40 min. Within this time, 12.1 mL (∼0.5 mmol) of hydrogen had been consumed. The mixture was filtered through a pad of Celite, and the filtrate was diluted with 120 mL of CH_2Cl_2. After being washed with 0.1 M aqueous HCl (5 mL) and brine (20 mL), the solution was dried over Na_2SO_4 and the solvent removed *in vacuo*. The residue, containing almost pure allylic alcohol, was dissolved in 3 mL of CH_2Cl_2/MeOH 1:1, and the solution was then treated with a stream of ozone at −78 °C. The progress of the reaction was monitored by TLC. When the reaction was complete, the excess of ozone was removed by a stream of N_2 and 76 mg (2 mmol) of $NaBH_4$ was added at −78 °C. After 15 min at this temperature, the reaction mixture was allowed to warm to rt over 1 h. The suspension was recooled in an ice-water bath, 1% AcOH (2 mL) was added, and the solution then was stirred for 15 min. The mixture was extracted with CH_2Cl_2 (3 × 5 mL), and the organic layer was washed with saturated $NaHCO_3$ (5 mL). The organic extracts were dried (Na_2SO_4) and evaporated *in vacuo*. The residue was chromatographed on silica gel (CH_2Cl_2/MeOH, 95:5) to afford 43 mg (0.26 mmol, 50% overall yield) of (*R*)-**14a** as a colorless oil: R_f 0.11 (CH_2Cl_2/MeOH, 95:5); ^1H NMR δ 1.60−1.75 (m, 2 H), 2.55−2.80 (m, 2 H), 3.40−3.75 (m, 5 H), 7.15−7.30 (m, 5 H); ^{13}C NMR δ 31.7, 34.5, 66.6, 71.5, 125.9, 128.3, 128.4, 141.6; IR (neat) 1020, 1050, 1080, 1440, 1590, 3010−3700; $[\alpha]^{20}_D$ +27.1 (*c* 1, EtOH) (lit.[15a] $[\alpha]^{20}_D$ −34.1 (*c* 1, EtOH) for isomer *S*).

(*R*)-1-(Tricyclo[3.3.1.1^{3,7}]dec-1-yl)-1,2-ethanediol[16b] **((*R*)-14c)**: overall yield 32%; mp 108.0−109.2 °C; R_f 0.36 (CH_2Cl_2/MeOH, 9:1); ^1H NMR δ 1.57−1.85 (m, 12 H), 1.97 (m, 3 H), 3.22 (dd, J = 9.0, 3.3 Hz, 1 H), 3.43−3.60 (m, 1 H), 3.70 (dd, J = 10.8, 3.3 Hz, 1 H); ^{13}C NMR δ 28.2, 37.2, 38.2, 53.4, 62.3, 80.1; IR (neat) 1090, 1340, 1450, 3010−3550; $[\alpha]^{20}_D$ −9.2 (*c* 0.5, EtOH) (lit.[15b] $[\alpha]^{22}_D$ +19.2 (*c* 1, EtOH) for isomer *S*).

(*R*)-3,3-Dimethyl-1,2-butanediol[16c] **((*R*)-14d)**: overall yield 22%; mp 40−42 °C (lit.[15c] 41−42 °C); R_f 0.25 (CH_2Cl_2/MeOH 9:1); ^1H NMR δ 0.90 (s, 9 H), 2.80 (bs, 2 H), 3.44 (dd, J = 2.7, 9.6 Hz, 1 H), 3.55 (t, J = 9.6 Hz, 1 H), 3.79 (dd, J = 2.7, 9.6 Hz, 1 H); ^{13}C NMR δ 25.8, 29.7, 63.2, 77.2; IR (neat) 1090, 1653, 2840, 2918, 3080−3490; $[\alpha]^{20}_D$ −16.2 (*c* 0.2, $CHCl_3$) (lit.[15c] $[\alpha]^{20}_D$ −25.88 (*c* 0.77, $CHCl_3$)).

General Procedure for Reduction of Hexacarbonyldicobalt Complexes of Acetylenic Ketones with BH_3·SMe_2 Catalyzed by Oxazaborolidines 7, 8a, 8b, and 9. Reduction of Ketone 15a Catalyzed by (4*R*,5*S*)-9. A solution of 215 mg (0.42 mmol) of ketone **15a** in 1 mL of THF was added dropwise over ∼30 min to a solution of 50 μL (0.5 mmol) of BH_3·SMe_2 and 0.46 mmol of (4*R*,5*S*)-**9** (from a toluene solution after removing the solvent under vacuum) in 1 mL of THF, at 0 °C under Ar. After 30 min, the reaction was cautiously quenched (TLC monitoring) by adding 0.5 mL of MeOH, and then the mixture was stirred for additional 30 min. The mixture was carried to dryness, and the residue was filtered through a pad of silica gel (hexane/CH_2Cl_2, 1:1) to afford, after removing the solvent under vacuum, a crude containing the hexacarbonyldicobalt complex of the propargylic alcohol derived from **15a**. The residue was dissolved in 5 mL of MeOH, and an excess (∼5 equiv) of CAN was added at rt. After 30 min, 3 mL of H_2O was added and the aqueous layer was extracted with diethyl ether (3 × 8 mL). The organic phase was washed with brine and then dried over Na_2SO_4. Evaporation of solvent yielded 86 mg (0.36 mmol, 88%) of **12a**. An analytical sample of the alcohol was transformed into its benzoyl derivative and then analyzed by HPLC (97% ee).

Reduction of Ketone 15a with Borane Catalyzed by (4*S*,5*R*)-8c. To a solution of (−)-norephedrine (47 mg, 0.31 mmol) of in THF (2 mL) was added BH_3·SMe_2 (68 μL, 0.68 mmol) under Ar at rt, and the mixture was stirred overnight. The solution was then cooled at 0 °C, and a solution of 161 mg (0.31 mmol) of ketone **15a** in 1 mL of THF was added dropwise over ∼30 min. After an additional 45 min stirring at this temperature, reaction was cautiously quenched with 0.5 mL of MeOH. Workup as above afforded 15 mg (22%) of alcohol **12a**. An analytical sample of the alcohol was transformed into its benzoyl derivative and then analyzed by HPLC (20% ee.).

Reduction of Ketone 15a Catalyzed by (*R*)-6. To a stirred solution of 0.06 mmol of (*R*)-**6** and 159 mg (0.30 mmol) of ketone **15a** in 3 mL of toluene was added dropwise 68 μL (0.6 mmol) of catecholborane in 0.5 mL of toluene at −78 °C under Ar. The solution was allowed to warm to −57 °C and stirred for 48 h. The reaction was then quenched by addition of 0.5 mL of MeOH, and the solvent was removed *under vacuo*. Flash chromatography of the crude afforded 57 mg (35%) of the desired alcohol, recovering 95 mg (60%) of the starting ketone **15a**. Oxidative treatment of alcohol (CAN, MeOH) as described above yielded 24 mg (35%) of alcohol **12a**. An analytical sample of the alcohol was transformed into its benzoyl derivative and then analyzed by HPLC (ca. 10% ee.).

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Supporting Information Available: Preparation and physical and spectroscopical data of acetylenic ketones **10a**−**d** **11a**−**c** and of hexacarbonyldicobalt complexes **11a**−**c** and **16a**−**c** (2 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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