

Intramolecular C–H Insertion Reactions of Boroxy Fischer Carbene Complexes. Regio- and Diastereoselective Modification of Terpenes

José Barluenga,^{*,†} Félix Rodríguez,[†] Jérôme Vadecard,[†] Maximilian Bendix,[†] Francisco J. Fañanás,[†] Fernando López-Ortiz,^{‡,⊥} and Miguel A. Rodríguez^{§,||}

Contribution from the Instituto Universitario de Química Organometálica “Enrique Moles”, Unidad Asociada al C.S.I.C., Universidad de Oviedo, Julián Clavería, 8, E-33071 Oviedo, Spain, Departamento de Geometría, Topología y Química Orgánica, Facultad de Ciencias Experimentales, Universidad de Almería, E-04120 Almería, Spain, and Departamento de Química, Universidad de La Rioja, E-26071 Logroño, Spain

Received April 12, 1999

Abstract: In-situ-generated dialkylboroxy and diamino-boroxy Fischer carbene complexes lead to oxaborolane or oxazaborolidine derivatives via an intramolecular C–H insertion reaction. Further oxidation of these intermediates yields 1,3-diol or 1,2-amino alcohol derivatives. Diastereoselectivities as high as 99% are reached when starting from boroxy Fischer carbene complexes derived from terpenes, which represents a regio- and diastereoselective modification of this type of natural product. The influence of the C_β substituents relative to the boron atom on the reaction path is studied, and a mechanism is proposed after identification of an intermediate by NMR. In addition, theoretical calculations show the presence of a boron–metal interaction, which could result as key step to the C–H insertion reaction.

Introduction

Fischer-type alkoxy and aminocarbene complexes have attracted much interest as useful synthons in organic and organometallic synthesis.¹ By contrast, the synthesis and chemistry of bimetallic systems, in which the carbene heteroatom is bound to a second, electron-deficient metal² (metal = Si,³ Ti,⁴ Zr,⁵ Hf,⁶ and Th⁷), have been much less explored. Such

complexes offer the opportunity to modulate the carbene reactivity by steric and electronic variation of the Lewis acidic component. In particular, only a few examples of boroxy Fischer carbene complexes have been described, and they were found to decompose to a mixture of unidentified products upon standing at room temperature.⁸ However, we have recently reported new synthetic applications of this type of complexes.⁹ On the other hand, whereas some C–H insertion reactions are known for cationic iron carbene complexes,¹⁰ only one example that involves group 6 non-heteroatom-stabilized Fischer carbene complexes has been reported.¹¹ In addition, Wulff et al. propose the formation of butanolide derivatives via a C–H insertion

[†] Universidad de Oviedo.

[‡] Universidad de Almería.

[§] Universidad de La Rioja.

[⊥] NMR studies.

^{||} Theoretical calculations studies.

(1) (a) Dötz, K. H. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 587. (b) Dötz, K. H. In *Organometallics in Organic Synthesis: Aspects of a Modern Interdisciplinary Field*; tom Dieck, H., de Meijere, A., Eds.; Springer: Berlin, 1988. (c) Wulff W. D. In *Comprehensive Organic Synthesis*, Vol. 5; Trost, B. M., Fleming, I., Eds.; Pergamon: New York, 1991; p 1065. (d) Doyle, M. P. In *Comprehensive Organometallic Chemistry II*, Vol. 12; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon: Oxford, 1995; p 387. (e) Wulff W. D. In *Comprehensive Organometallic Chemistry II*, Vol. 12; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon: Oxford, 1995; p 469. (f) Hegedus, L. S. In *Comprehensive Organometallic Chemistry II*, Vol. 12; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon: Oxford, 1995; p 549.

(2) Reviews: (a) Erker, G. In *Organometallics in Organic Synthesis*; de Meijere, A., tom Dieck, H., Eds.; Springer-Verlag: Berlin, 1987; p 143. (b) Erker, G. *Polyhedron* **1988**, *7*, 2451. (c) Erker, G. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 397.

(3) (a) Moser, E.; Fischer, E. O. *J. Organomet. Chem.* **1969**, *16*, 275. (b) Fischer, E. O.; Selmayr, T.; Kreissl, F. R.; Schubert, U. *Chem. Ber.* **1977**, *110*, 2574. (c) Fischer, E. O.; Schubert, U.; Kleine, W.; Fischer, H. *Inorg. Synth.* **1979**, *19*, 164. (d) Voran, S.; Blau, H.; Malisch, W.; Schubert, U. *J. Organomet. Chem.* **1982**, *232*, C33. (e) Balzer, B. L.; Cazanoue, M.; Finn, M. G. *J. Am. Chem. Soc.* **1992**, *114*, 8735. (f) Gross, M. F.; Finn, M. G. *J. Am. Chem. Soc.* **1994**, *116*, 10921.

(4) (a) Raubenheimer, H. G.; Fischer, E. O. *J. Organomet. Chem.* **1975**, *91*, C23. (b) Mashima, K.; Jyodoi, K.; Ohyoshi, A.; Takaya, H. *J. Chem. Soc., Chem. Commun.* **1986**, 1145. (c) Sabat, M.; Gross, M. F.; Finn, M. G. *Organometallics* **1992**, *11*, 745. (d) Balzer, B. L.; Cazanoue, M.; Sabat, M.; Finn, M. G. *Organometallics* **1992**, *11*, 1759. (e) Beckhaus, R.; Oster, J.; Kempe, R.; Spannenberg, A. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1565.

(5) (a) Wolczanski, P. T.; Threlkel, R. S.; Bercaw, J. E. *J. Am. Chem. Soc.* **1979**, *101*, 218. (b) Threlkel, R. S.; Bercaw, J. E. *J. Am. Chem. Soc.* **1981**, *103*, 2650. (c) Erker, G.; Dorf, U.; Benn, R.; Reinhardt, R. D. *J. Am. Chem. Soc.* **1984**, *106*, 7649. (d) Erker, G.; Dorf, U.; Mynott, R.; Tsay, Y. H.; Krüger, C. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 584. (e) Beckhaus, R.; Thiele, K. H. *J. Organomet. Chem.* **1989**, *368*, 31. (f) Erker, G.; Sosna, F.; Zwettler, R.; Krüger, C. *Organometallics* **1989**, *8*, 450. (g) Erker, G.; Sosna, F.; Petersen, J. L.; Benn, R.; Grondey, H. *Organometallics* **1990**, *9*, 2462. (h) Erker, G.; Sosna, F.; Betz, P.; Werner, S.; Krüger, C. *J. Am. Chem. Soc.* **1991**, *113*, 564. (i) Erker, G.; Berlekamp, M.; López, L.; Grehl, M.; Schönecker, B.; Krieg, R. *Synthesis* **1994**, 212.

(6) (a) Erker, G.; Lecht, R. *J. Organomet. Chem.* **1986**, *311*, 45. (b) Erker, G.; Lecht, R.; Schlund, K. A.; Krüger, C. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 666. See also ref 5i.

(7) Erker, G.; Mühlendernd, T.; Benn, R.; Rufinska, A. *Organometallics* **1986**, *5*, 402. See also ref 6a.

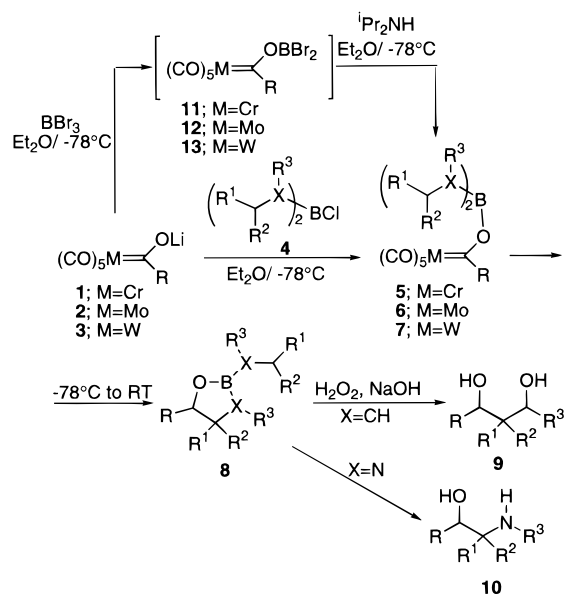
(8) (a) Fischer, E. O.; Gibbins, S. G.; Kellerer, W. *J. Organomet. Chem.* **1981**, *218*, C51. (b) Petz, W. *Z. Naturforsch.* **1981**, *36b*, 335.

(9) (a) Barluenga, J.; Canteli, R. M.; Flórez, J.; García-Granda, S.; Gutiérrez-Rodríguez, A. *J. Am. Chem. Soc.* **1994**, *116*, 6949. (b) Barluenga J.; Rodríguez, F.; Fañanás, F. *J. Organometallics* **1997**, *16*, 5384. (c) Barluenga, J.; Canteli, R. M.; Flórez, J.; García-Granda, S.; Gutiérrez-Rodríguez, A.; Martín, E. *J. Am. Chem. Soc.* **1998**, *120*, 2514.

(10) (a) Zhao, S. K.; Knors, C.; Helquist, P. *J. Am. Chem. Soc.* **1989**, *111*, 8527. (b) Zhao, S. K.; Helquist, P. *J. Org. Chem.* **1990**, *55*, 5820. (c) Zhao, S.; Mehta, G.; Helquist, P. *Tetrahedron Lett.* **1991**, *32*, 5753.

(11) (a) Fischer, H.; Schmid, J.; Maerkl, R. *J. Chem. Soc., Chem. Commun.* **1985**, 572. (b) Fischer, H.; Schmid, J. *J. Mol. Catal.* **1988**, *46*, 277. (c) Fischer, H.; Jungklaus, H. *J. Organomet. Chem.* **1999**, *572*, 105.

Scheme 1



reaction of an in-situ-generated non-heteroatom-stabilized chromium carbene complex.¹² Recently, two examples of C–H insertion reactions involving stabilized Fischer carbene complexes have been reported.¹³ Previously, we described, for the first time, the preparation of boroxycarbene complexes and their transformation into oxaborolane or oxazaborolidine derivatives via a C–H insertion process.¹⁴ In the present paper, we describe in full our findings on the intramolecular C–H insertion reactions of boroxycarbene complexes and mechanistic aspects of this reaction on the basis of both experimental and theoretical investigations. This process has been widely applied to the regio- and diastereoselective modification of terpenes. The scope and limitations of this methodology are defined.

Results and Discussion

The treatment of pentacarbonylmetal acylate intermediates **1**–**3**, formed by reaction of metal hexacarbonyl and the corresponding organolithium compound,¹⁵ with dialkylchloroboranes **4** (X = CH)¹⁶ in diethyl ether at -78°C readily led to dialkylboroxycarbene complexes **5**–**7**. On warming to room temperature, these compounds underwent loss of the metal fragment affording the oxaborolane derivatives **8** (X = CH). This transformation involves the insertion of the carbene ligand into the boron $\text{C}_\beta\text{–H}$ bond. Further oxidation of **8** (X = CH) with hydrogen peroxide in basic media yielded 1,3-diols **9** as mixtures of diastereoisomers (Scheme 1 and Table 1). We have observed that oxaborolanes **8** (X = CH) are produced in moderate yield when either R^1 and R^2 are alkyl groups (Table 1, entries 1–6) or R^1 and R^2 are H and a donor group, respectively (Table 1, entries 7–11). Conversely, the reaction does not work for $\text{R}^1 = \text{H}$ and $\text{R}^2 = \text{alkyl}$ ($n\text{-C}_6\text{H}_{11}$ or $n\text{-C}_6\text{H}_{13}$) or electron-withdrawing groups ($4\text{-ClC}_6\text{H}_4$), and complex

(12) Wang, S. L. B.; Su, J.; Wulff, W. D.; Hoogsteen, K. *J. Am. Chem. Soc.* **1992**, *114*, 10665.

(13) (a) Barluenga, J.; Aznar, F.; Fernández, M. *Chem. Eur. J.* **1997**, *3*, 1629. (b) Takeda, K.; Okamoto, Y.; Nakajima, A.; Yoshii, E.; Koizumi, T. *Synlett* **1997**, 1181.

(14) Barluenga, J.; Rodríguez, F.; Vadeкарd, J.; Bendix, M.; Fañanás, F. J.; López-Ortiz, F. *J. Am. Chem. Soc.* **1996**, *118*, 6090.

(15) (a) Fischer, E. O.; Maasböl, A. *Chem. Ber.* **1967**, *100*, 2445.

(16) Dialkylchloroboranes have been prepared as described in the literature, see: Brown, H. C.; Ganesan, K.; Dhar, R. K. *J. Org. Chem.* **1992**, *57*, 3767.

mixtures are obtained. On the other hand, starting from diaminochloroborane **4g** (X = N),¹⁷ oxazaborolidine **8g** (X = N) and 1,2-amino alcohol **10** can be prepared (Table 1, entries 12–14). Carbene complexes **5g**–**7g** (X = N) and, therefore, oxazaborolidine **8g** and 1,2-amino alcohol **10** can be also indirectly obtained by reaction of acylmetalates **1**–**3** with boron tribromide at -78°C , presumably leading to the corresponding dibromoboroxycarbene complex **11**–**13**, and further treatment with an excess of diisopropylamine at the same temperature (Table 1, entries 12–14). It is interesting to note that the nature of the metal plays a role in the reaction rate, while the product distribution remains unaffected (Table 1, entries 1–3, 4–6, and 12–14). Thus, 2 or 3 h and around 12 h were required for the formation of oxaborolanes **8a,b** at room temperature by starting from carbenes **6a,b** (M = Mo) and **7a,b** (M = W), respectively.

A mechanistic proposal that accounts for the formation of oxaborolanes **8** is outlined in Scheme 2 and involves intramolecular hydride transfer to the carbene carbon atom in the complex **7**, favored presumably by an initial interaction between the boron atom and the metal of carbene complex, as depicted in the transition state **I**, to give formally the carbocation intermediate **II**, which rapidly affords the oxaborolane derivatives **8** likely by simultaneous formation of a carbon–carbon bond and loss of the metal fragment.¹⁸ The results are in agreement with the proposed mechanism. In fact, the hydride transfer is observed only in the cases in which the early-developing carbocation can be stabilized. Moreover, NMR monitoring of the reaction course of **7g** (X = N) at -50°C allowed identification of the intermediate **III** (Scheme 2). The 2D ^1H , ^{13}C HMBC spectrum¹⁹ showed correlations of the methyne proton at 5.31 ppm with aromatic carbons (119.4, 157.3 ppm) and one of the carbonyl groups bound to tungsten (203.6 ppm), while the diastereotopic methyl groups (2.68, 2.74 ppm) correlate with a carbon at 189.2 ppm. The ^{183}W chemical shift of **III** (-66.8 ppm) measured from the ^1H , ^{183}W HMBC spectrum²⁰ is unusually high ($\Delta\delta \approx 2600$ ppm) compared with those of other related tungsten complexes,²¹ implying a strong variation in the electronic surrounding around the tungsten atom,²² and suggests that the metal actually coordinates to the boron atom.

Ab Initio Calculations. To corroborate the proposed intramolecular interaction between the boron atom and the metal of the carbene complex, we carried out theoretical calculations on boroxycarbene complexes. To the best of our knowledge, no ab initio calculations have been described for this kind of complexes. The size of the molecule under study

(17) Diaminochloroboranes have been prepared as described in the literature, see: Aubrey, D. W.; Lappert, M. F.; Majumdar, M. K. *J. Chem. Soc.* **1962**, 4088.

(18) According to the suggestion of a reviewer and in order to establish the intramolecular nature of the process, we carried out a crossover experiment with carbene complexes **16e** and **21e**, which after usual workup resulted in the exclusive formation of diols **18e** and **22e**.

(19) Bax, A.; Summers, M. F. *J. Am. Chem. Soc.* **1986**, *108*, 2093.

(20) (a) Benn, R.; Brenneke, H.; Heck, J.; Rufinska, A. *Inorg. Chem.* **1987**, *26*, 2826. (b) Benn, R.; Rufinska, A.; King, M. A.; Osterberg, C. E.; Richmond, T. *J. Organomet. Chem.* **1989**, *376*, 359. (c) Machioni, A.; Pregosin, P. S.; Rüegger, H.; van Koten, G.; van der Schaaf, P. A.; Abbenhuis, R. A. T. *Magn. Reson. Chem.* **1994**, *235*, 32.

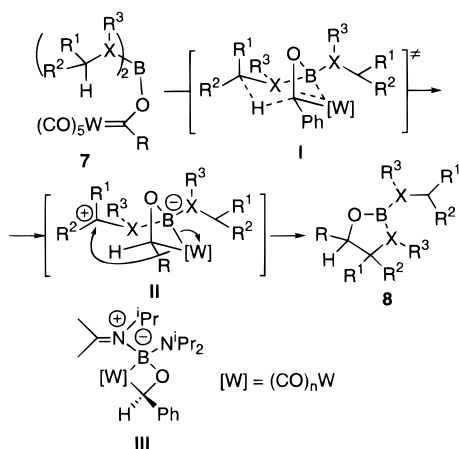
(21) We could obtain the ^{183}W chemical shift (-2769 ppm) for carbene complex **16d** through a ^1H , ^{183}W HMQC experiment. For other ^{183}W δ values of related tungsten complexes, see: (a) Minelli, M.; Enemark, J. H.; Brownlee, T. T. C.; O'Connor, M. J.; Wedd, A. G. *Coord. Chem. Rev.* **1985**, *68*, 169. (b) Barluenga, J.; Tomás, M.; Ballesteros, A.; Santamaría, J.; Carbajo, R. J.; López-Ortiz, F.; García-Granda, S.; Pertierra, P. *Chem. Eur. J.* **1996**, *2*, 88.

(22) We could not measure the ^{11}B NMR spectrum for **III** because, at the low temperature needed (-50°C), the quadrupolar nature of the boron resulted in an exceedingly large line width.

Table 1. Diols **9** and Amino Alcohol **10** from C–H Insertion in the Boroxo Fischer Carbene Complexes **5–7**, and Further Oxidation

entry	carbene complex	R	X	R ¹	R ²	R ³	diol	yield (%) ^a	de (%) ^b
1	5a	(<i>E</i>)-PhCH=CH	CH	Me	Me	Me	9a	51	11
2	6a	(<i>E</i>)-PhCH=CH	CH	Me	Me	Me	9a	53	12
3	7a	(<i>E</i>)-PhCH=CH	CH	Me	Me	Me	9a	50	12
4	5b	Ph	CH	Me	Me	Me	9b	53	31
5	6b	Ph	CH	Me	Me	Me	9b	55	33
6	7b	Ph	CH	Me	Me	Me	9b	55	30
7	6c	Ph	CH	H	Ph	H	9c	52	10
8	7c	Ph	CH	H	Ph	H	9c	57	10
9	6d	(<i>E</i>)-PhCH=CH	CH	H	Ph	H	9d	64	32
10	6e	Me	CH	H	4-MeOC ₆ H ₄	H	9e	49	20
11	6f	2-Naph ^c	CH	H	4-MeOC ₆ H ₄	H	9f	59	24
12	5g	Ph	N	Me	Me	ⁱ Pr	10	67 (66) ^d	
13	6g	Ph	N	Me	Me	ⁱ Pr	10	65 (68) ^d	
14	7g	Ph	N	Me	Me	ⁱ Pr	10	70 (60) ^d	

^a Based on M(CO)₆. ^b Determined by NMR. ^c 2-Naph = 2-naphthyl. ^d In parentheses are represented the yields obtained in the indirect reaction of acylmetalates **1**, **2**, or **3** with BBr₃ and further treatment with ⁱPr₂NH.

Scheme 2

necessitates the use of (CO)₅M=CH(OBH₂) as a model for the ab initio calculations. All calculations were carried out using the Gaussian 94 program package.²³ The molecular geometries were initially optimized, within appropriate molecular symmetry constraints (C_s), at the Hartree–Fock self-consistent field (HF) level of theory, and electron correlation, keeping the core orbitals frozen, was included in further optimizations using Møller–Plesset perturbation theory^{24,25} with second-order corrections (MP2) employing Schlegel’s analytical gradient procedure.²⁶ All optimized structures reported in this paper are minima on the potential energy surface (all eigenvalues of the Hessian matrix are positive).²⁵

The following basis set combination has been employed: for C, O, B, and H, the standard split-valence 6-31G(d) basis set,^{27,28} with six d functions, and for W and Mo, the Hay–Wadt small-core effective core potential,²⁹ where the minimal basis set has

(23) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Gill, P. M. W.; Johnson, B. G.; Robb, M. A.; Cheeseman, J. R.; Keith, T. A.; Petersson, G. A.; Montgomery, J. A.; Raghavachari, K.; Al-Laham, M. A.; Zakrzewski, V. G.; Ortiz, J. V.; Foresman, J. B.; Cioslowski, J.; Stefanov, B.; Nanayakkara, A.; Challacombe, M.; Peng, C. Y.; Ayala, P. Y.; Chen, W.; Wong, M. W.; Andres, J. L.; Replogle, E. S.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Binkley, J. S.; Defrees, D. J.; Baker, J.; Stewart, J. P.; Head-Gordon, M.; Gonzalez, C.; Pople, J. A. *Gaussian 94* (Revision C.3); Gaussian, Inc.: Pittsburgh, PA, 1995.

(24) Møller, C.; Plesset, M. S. *Phys. Rev.* **1934**, *46*, 618.

(25) Hehre, W. J.; Radom, L.; Schleyer, P. v. R.; Pople, J. A. *Ab Initio Molecular Orbital Theory*; J. Wiley: New York, 1986.

(26) Schlegel, H. B. *J. Comput. Chem.* **1982**, *3*, 214.

(27) Hariharan, P. C.; Pople, J. A. *Theor. Chim. Acta* **1973**, *28*, 213.

(28) Hehre, W. J.; Ditchfield, R.; Pople, J. A. *J. Chem. Phys.* **1972**, *56*, 2257.

(29) Hay, P. J.; Wadt, W. R. *J. Chem. Phys.* **1985**, *82*, 299.

been split to [441/2111/21] and [341/3111/31], respectively.³⁰ This basis set combination will hereafter be referred to as II. The accuracy of the HF/II and MP2/II levels of theory has already been demonstrated in the calculation of the optimized geometries of metal carbene complexes.³⁰ Improved energies were obtained from single-point calculations at the MP2 level using the II basis set augmented with one diffuse function for C, O, and B³¹ and one set of f functions for W ($\zeta_f = 0.823$) and Mo ($\zeta_f = 1.043$).³² This basis set combination will hereafter be denoted IIID, where D stands for diffuse functions.

The most relevant geometrical parameters of the optimized structures of (CO)₅W=CH(OBH₂) with the HF/II and MP2/II wave functions are given in Figure 1. Several features are noteworthy. At the HF/II level of theory, the W–B interatomic distance is very large (3.773 Å). Thus, the experimental coordination is not reproduced at this level. After inclusion of correlation at the MP2/II level, the W–B interatomic distance and the C2–O3–B4 bond angle are drastically reduced to 2.908 Å and 101.8°, respectively, which indicates that correlation effects are attractive due to the W–B interaction. Moreover, the tungsten–carbene carbon bond length is larger at the HF/II level than at the MP2/II level [from 2.149 (HF/II) to 2.109 Å (MP2/II), $\Delta = 0.040$ Å].

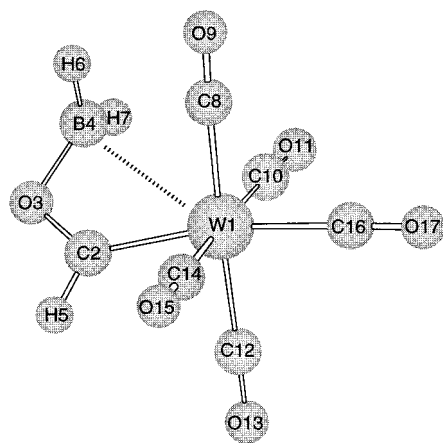
In view of the observed structural changes due to the W–B interaction, and taking into account that the atomic radius for coordinated tungsten is identical to that for molybdenum (1.39 Å for both metals),³³ we found it of interest to compare the W–B interaction with the Mo–B interaction. The MP2/II-optimized structure for (CO)₅Mo=CH(OBH₂) is represented in Figure 2. It can be observed that the replacement of W by Mo causes a reduction in the metal–boron interatomic distance (2.848 Å, $\Delta = -0.060$ Å), and the effect of this is transmitted through the rest of the structure: an increase in the metal–carbene carbon (2.111 Å, $\Delta = +0.002$ Å) and O–B (1.478 Å, $\Delta = +0.011$ Å) bond lengths and a reduction in the carbene carbon–oxygen distance (1.302 Å, $\Delta = -0.006$ Å) and C2–O3–B4 bond angle (98.6°, $\Delta = -3.2^\circ$). All these structural

(30) Frenking, G.; Antes, I.; Böhme, M.; Dapprich, S.; Ehlers, A. W.; Jonas, V.; Neuhaus, A.; Otto, M.; Stegmann, R.; Veldkamp, A.; Vyboshchikov, S. F. In *Reviews in Computational Chemistry*; Lipkowitz, K. B., Boyd, D. B., Eds.; VCH: New York, 1996; Vol. 8.

(31) Clark, T.; Chandrasekhar, J.; Spitznagel, G. W.; Schleyer, P. v. R. *J. Comput. Chem.* **1983**, *4*, 294.

(32) Ehlers, A. W.; Böhme, M.; Dapprich, S.; Gobbi, A.; Höllwath, A.; Jonas, V.; Köhler, K. F.; Stegmann, R.; Veldkamp, A.; Frenking, G. *Chem. Phys. Lett.* **1993**, *208*, 111.

(33) Müller, U. *Inorganic Structural Chemistry*; Wiley: Chichester, UK, 1993.



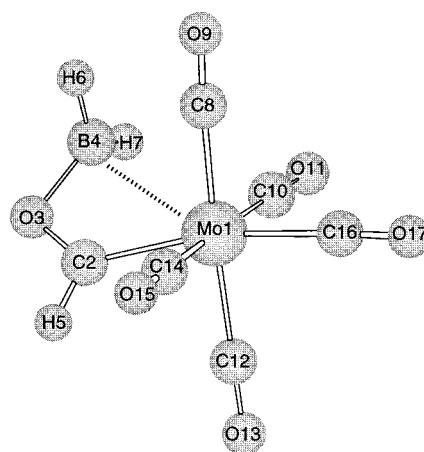
Bond Lengths, Å	
W1-B4	2.908 (3.773)
W1-C2	2.109 (2.149)
C2-O3	1.308 (1.298)
O3-B4	1.467 (1.377)
W1-C8	2.054 (2.096)
W1-C12	2.063 (2.104)
W1-C16	2.082 (2.107)
Bond Angles, deg	
W1-C2-O3	127.7 (132.3)
C2-O3-B4	101.8 (135.3)

Figure 1. Computer plot of the MP2/II-optimized structure for $(\text{CO})_5\text{W}=\text{CH}(\text{OBH}_2)$; values in parentheses are obtained at the HF/II level.

changes reveal that the Mo–B interaction should be larger than the W–B interaction, but that both are the same in nature.

We have also attempted to quantify the magnitude of the metal–boron interaction in boroxo Fischer carbene complexes. First, taking our MP2/II-optimized geometries as the starting point, we considered a $(\text{B4}-\text{O3}-\text{C2})(\text{O3}-\text{C2}-\text{M1})$ plane–plane angle of 180.0° instead of 0.0° , and we tried to optimize these at the same level of theory. However, all attempts to minimize these structures led to the previously calculated structures [$(\text{B4}-\text{O3}-\text{C2})(\text{O3}-\text{C2}-\text{M1})$ plane–plane angle of 0.0°], which indicates the strong character of the metal–boron interaction. Therefore, we have included only the MP2/II single-point calculation resulting from our MP2/II-optimized geometries considering a $(\text{B4}-\text{O3}-\text{C2})(\text{O3}-\text{C2}-\text{M1})$ plane–plane angle of 180.0° . Table 2 shows the calculated total and relative energies at the MP2/II/MP2/II and MP2/IIID//MP2/II levels. From the MP2/II level, we derive that this interaction should be 18.5 and 19.8 kcal/mol for W and Mo, respectively. These results indicate that, in boroxo Fischer carbene complexes, the intramolecular Mo–B interaction should be stronger than the W–B interaction by 1.3 kcal/mol at the MP2/II/MP2/II level. Single-point calculations at the MP2 level using the larger basis set IIID denote a slight increase of the metal–boron interaction for molybdenum (20.1 kcal/mol) but not for tungsten (18.5 kcal/mol), and places the tungsten–boron attraction at a level 1.6 kcal/mol less than that for molybdenum.

Diastereoselective C–H Insertion Reactions. To study the influence of the chiral dialkylborane bearing a tertiary $\text{C}_\beta\text{–H}$ bond on the diastereoselectivity of the reaction, a set of experiments using the commercially available (–)-chlorodiisopinocampheylborane [(–)-Ipc₂BCl] was envisaged. Thus, reaction of acylmetalates **1–3** with (–)-Ipc₂BCl in diethyl ether at



Bond Lengths, Å	
Mo1-B4	2.848
Mo1-C2	2.111
C2-O3	1.302
O3-B4	1.478
Mo1-C8	2.052
Mo1-C12	2.062
Mo1-C16	2.083
Bond Angles, deg	
Mo1-C2-O3	128.6
C2-O3-B4	98.6

Figure 2. Computer plot of the MP2/II-optimized structure for $(\text{CO})_5\text{Mo}=\text{CH}(\text{OBH}_2)$.

Table 2. Calculated Total Energies (Hartrees) and Relative Energies (in Parentheses, kcal/mol) for $(\text{CO})_5\text{M}=\text{CH}(\text{OBH}_2)^a$

M	$(\text{B4}-\text{O3}-\text{C2})$ $(\text{O3}-\text{C2}-\text{M1})$ (deg)		MP2/II	MP2/IIID
	W	0.0		
	180.0 ^b	–772.163876 (18.5)	–772.347386 (18.5)	
Mo	0.0	–771.920267 (0.0)	–772.120254 (0.0)	
	180 ^b	–771.888636 (19.8)	–772.088252 (20.1)	

^a All calculations at the MP2/II-optimized geometries. Atom numbering as in Figures 1 and 2. ^b Single-point calculation considering a $(\text{B4}-\text{O3}-\text{C2})(\text{O3}-\text{C2}-\text{M1})$ plane–plane angle of 180.0° instead 0.0° .

–78 °C led to the corresponding chiral boroxycarbene complexes **14–16**, which were clearly identified by NMR spectroscopy. On heating to room temperature, these complexes evolve to afford the oxaborolane derivatives **17**. Oxidation of **17** gave rise to the 1,3-diols **18** (Scheme 3 and Table 3). To our delight, diastereoselectivities higher than 99% were then reached in the case of **18d** and **18e** (Table 3, entries 6–9). In the same way, starting from (+)-Ipc₂BCl and **2** [$\text{R} = (E)\text{-PhCH}=\text{CH}$], *ent*-**18d** was obtained with diastereoselectivity higher than 99% (Table 3, entry 14). The absolute configuration of the new stereogenic centers in the major and minor diastereoisomers was assigned by NOE experiments of the corresponding acetones **19**, generated by reaction of diols **18** and 2,2-dimethoxypropane in the presence of catalytic amounts of pyridinium *p*-toluenesulfonate (PPTS)³⁴ (Scheme 4). It is interesting to point out that, in all the cases, a quaternary carbon

(34) Luke, G. P.; Morris, J. J. *J. Org. Chem.* **1995**, *60*, 3013.

Scheme 3

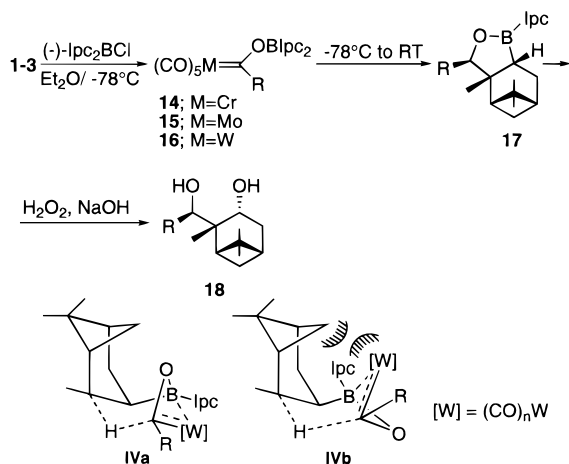
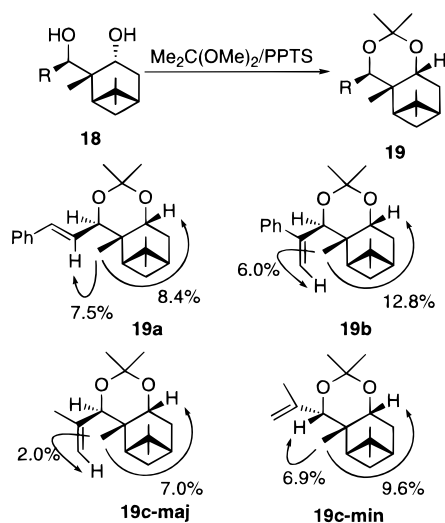


Table 3. Diols **18** from C–H Insertion in the Diisopinocampheylboroxy Fischer Carbene Complexes **14–16^a** and Further Oxidation

entry	carbene complex	R	diol	yield (%) ^b	de (%) ^c
1	14a	Ph	18a	82	50
2	15a	Ph	18a	84	50
3	16a	Ph	18a	87	51
4	15b	4-MeOC ₆ H ₄	18b	78	49
5	16c	2-Naph	18c	85	72
6	14d	(<i>E</i>)-PhCH=CH	18d	80	>99
7	15d	(<i>E</i>)-PhCH=CH	18d	78	>99
8	16d	(<i>E</i>)-PhCH=CH	18d	81	>99
9	16e	CH ₂ =C(Ph)	18e	83	>99
10	16f	Me ₂ C=CH	18f	75	97
11	14g	CH ₂ =C(Me)	18g^d	65	83
12	15g	CH ₂ =C(Me)	18g^d	67	85
13	16g	CH ₂ =C(Me)	18g^d	78	86
14	<i>ent</i> - 15d^e	(<i>E</i>)-PhCH=CH	<i>ent</i> - 18d	82	>99

^a Derived from (–)-Ipc₂BCl. ^b Based on M(CO)₆. ^c Determined by NMR. ^d Both diastereoisomers have been isolated. ^e Derived from (+)-Ipc₂BCl.

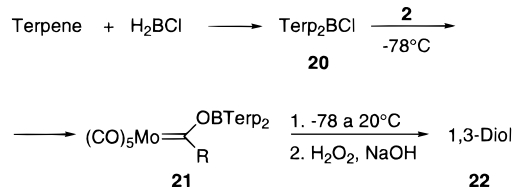
Scheme 4



center has been created in an enantioselective way³⁵ and that the diastereoselectivity depends exclusively on the way that the C–H is approaching the metal–carbon double bond. The high stereoselectivity of the hydride attack leading to oxaborolanes

(35) Nemoto, H.; Tanabe, T.; Fukumoto, K. *J. Org. Chem.* **1995**, *60*, 6785 and references therein.

Scheme 5



17 may be tentatively accounted for by considering transition states **IVa** and **IVb** (Scheme 3). Assuming that a boron–metal interaction takes place, the chairlike transition state **IVa** would explain the formation of the major diastereoisomer. This stereochemical course should be favored over that involving the boat conformation **IVb**, which exhibits severe hindrance between the metal fragment and the ring moiety. Moreover, the higher diastereoselectivity found for R = alkenyl groups (Table 3, entries 6–13) can be rationalized in terms of coordination of the metal to the carbon–carbon double bond, which would result in increasing the transition state rigidity. Thus, **IVb** is even more disfavored than **IVa**. This coordination has been observed by NMR during the transformation of **16d** as an intermediate species formed at –30 °C. In this intermediate, the olefinic carbon atoms are highly shielded (79.51, 81.17 ppm) related to the starting carbene, and the corresponding protons (5.21, 5.32 ppm) show cross-peaks in the 2D ¹H,¹³C HMBC spectrum, with a carbonyl carbon at 196.91 ppm.

Scope and Limitations. To study the scope of this transformation, and considering that it can be seen as a diastereoselective transformation of a terpene, a set of experiments was carried out with other commercially or easily available terpenes. So, hydroboration of the corresponding terpene with monochloroborane in diethyl ether led to the diterpenylchloroboranes **20**.³⁶ Treatment of these chloroboranes **20** with the acyl molybdates **2** at –78 °C afforded the diterpenylboroxy carbene complexes **21**, which upon warming to room temperature and further oxidation yielded the 1,3-diols **22** with good chemical yields (Scheme 5 and Table 4). It is interesting to note the high diastereoselectivity found in this process. In fact, only one diastereoisomer has been observed for **22a** and **22c–e** (Table 4, entries 1 and 3–5). The absolute configuration of the new stereocenters was also determined by NOE experiments of the representative acetonides **19d,f,g** and by two-dimensional (COSY, HMQC, HMBC, and NOESY) NMR spectral analysis of the acetonide **19e** (Figure 3), generated as described in Scheme 4. According to these results, it can be concluded that, in all cases, the quaternary center has been generated in an enantioselective way and the diastereoselectivity depends only on the way in which the hydride is transferred. On the other hand, the C–H insertion reaction of carbene complex **21g**, derived from 2-carene, bearing two tertiary C_β–H bonds exclusively gave the regioisomer **22g**, and the other possible regioisomer has been not observed (Table 4, entry 7).

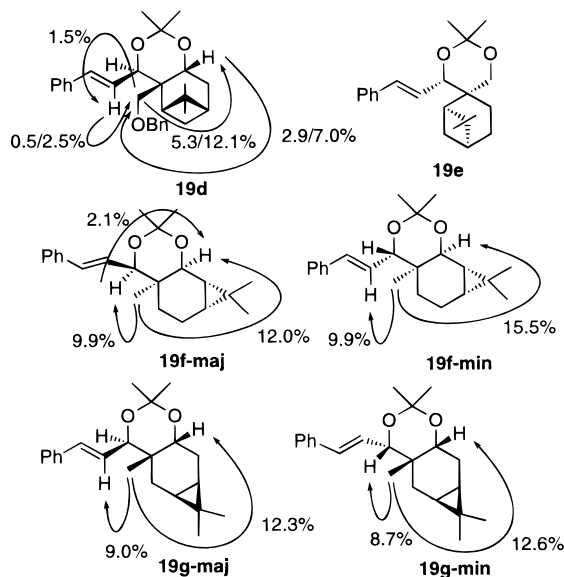
Otherwise, starting from molybdenum carbene complexes **24** and **26**, formed by reaction of acyl molybdate **2** [R = (*E*)-PhCH=CH] and chloroboranes **23**³⁶ derived from (–)-camphene, and **25**,³⁶ derived from (+)-longifolene, respectively, and following the sequence of reactions above-described, the expected 1,3-diols were not observed, and we obtained a mixture of Camph-OH or Long-OH, cinnamic acid, and molybdenum hexacarbonyl (Scheme 6). The reluctance to the formation of 1,3-diols in these cases can be explained by considering that the approach of the carbon–metal double bond to the C–H in

(36) Brown, H. C.; Malhotra, S. V.; Ramchandran, V. *Tetrahedron: Asymmetry* **1996**, *7*, 3527.

Table 4. Diols **22** from Terpenes via C–H Insertion in the Diterpenylboroxymolybdenum Fischer Carbene Complexes **21** and Further Oxidation

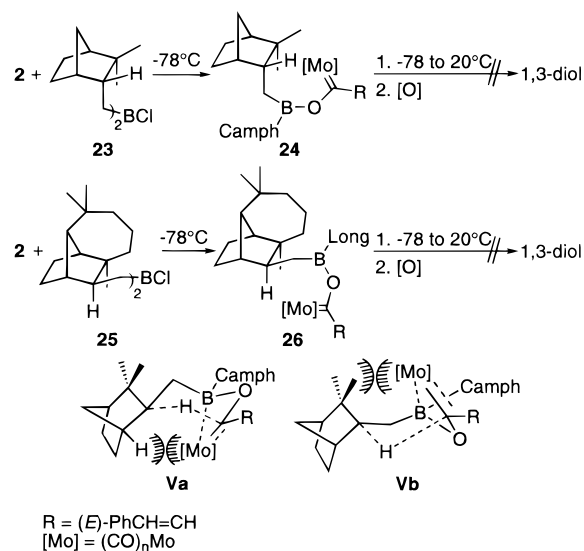
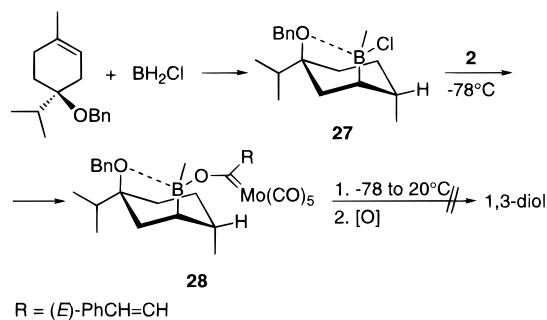
Entry	Terpene	Diterp. borane	Terp	Carbene complex	R	Diol	Yield (%) ^a	de (%) ^b
1		20a		21a	(<i>E</i>)-PhCH=CH		61	>99
2		20a		21b	CH ₂ =C(Ph)		72	88
3		20b		21c	(<i>E</i>)-PhCH=CH		71	>99
4		20c		21d	(<i>E</i>)-PhCH=CH		62	>99
5		20d		21e	(<i>E</i>)-PhCH=CH		76	>99
6		20d		21f	CH ₂ =C(Ph)		62	70
7		20e		21g	(<i>E</i>)-PhCH=CH		68	20
8		20f		21h	(<i>E</i>)-PhCH=CH		71	40

^a Based on Mo(CO)₆. ^b Determined by NMR. ^c Both diastereoisomers have been isolated (the major diastereoisomer has been represented).

**Figure 3.**

the corresponding carbene complexes **24** and **26** would be sterically hindered by both faces, as depicted in transition states **Va** and **Vb** for the hydride transfer to the carbene carbon in complex **24** (Scheme 6).

Finally, the influence of a dialkylborane bearing a heteroatom on the outcome of the C–H insertion reaction was studied. In this sense, synthesis of several chloroboranes was first carried out. Thus, hydroboration of *O*-benzylterpinen-4-ol with monochloroborane led to the chloroborane **27** as a single diastereoisomer (Scheme 7). The relative stereochemistry was assigned by NMR studies carried out with the 5-benzyloxy-5-isopropyl-2-methylcyclohexanol, obtained after oxidative workup (3 N NaOH, 30% H₂O₂) of **27**. The exclusive formation of one diastereoisomer can be accounted for by a coordination of the ether

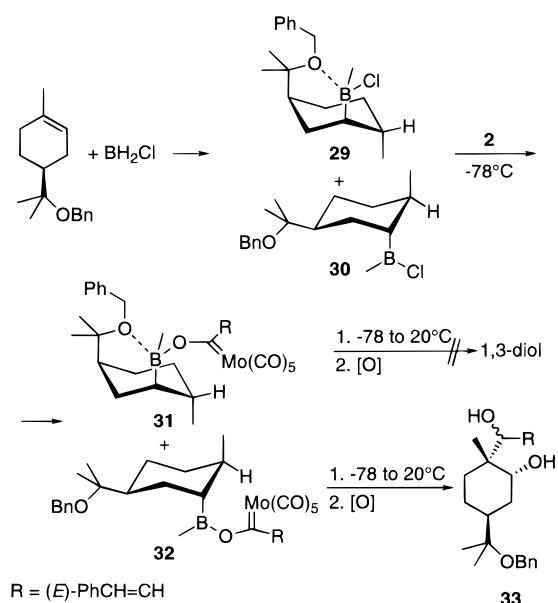
Scheme 6**Scheme 7**

oxygen to the borane previous to the hydroboration reaction. This result constitutes one of the few examples of a heteroatom-directed asymmetric hydroboration.³⁷ Reaction of acyl molybdate **2** [R = (*E*)-PhCH=CH] with the chloroborane **27** at –78 °C gave rise to the boroxymolybdenum carbene complex **28**. Warming of the reaction mixture to room temperature followed by oxidative workup also did not lead to the corresponding 1,3-diol (Scheme 7). The failure to generate the expected diol in this case could be explained in terms of an intramolecular coordination of the ether oxygen to the boron atom, which could, on one hand, prevent the coordination between the boron atom and the metal, assumed for the reaction take to place, and, on the other hand, could hinder the approach of the carbon–metal double bond to the C_β–H by steric effects.

Finally, *O*-benzyl- α -terpineol was tested in this type of process. First, hydroboration of this terpene led to a nearly equimolar mixture of diastereoisomer chloroboranes **29** and **30**. In this case, an oxygen-directed hydroboration has not been observed, presumably because the director group is not close enough to the double bond to induce a diastereoselective reaction (Scheme 8). Treatment of **2** [R = (*E*)-PhCH=CH] with the mixture of chloroboranes **29** and **30** at –78 °C afforded a mixture of carbene complexes **31** and **32**, which under the workup conditions described above generated exclusively the 1,3-diol **33** as a 5.3:1 mixture of diastereoisomers in 34% yield [based on the Mo(CO)₆], derived from a C–H insertion reaction of carbene complex **32** (Scheme 8). The lack of evolution of **31** to the corresponding 1,3-diol could be understood in the same

(37) (a) Hoveyda, A. H.; Evans, D. A.; Fu, G. C. *Chem. Rev.* **1993**, *93*, 1307. (b) Hodgson, D. M.; Thomson, A. J.; Wadman, S. *Tetrahedron Lett.* **1998**, *39*, 3357. (c) Garret, C. E.; Fu, G. C. *J. Org. Chem.* **1998**, *63*, 1370.

Scheme 8



sense explained for the carbene complex **28**. Thus, the intramolecular oxygen–boron coordination would make difficult the insertion reaction by steric or/and electronic effects. On the contrary, for carbene complex **32**, the intramolecular oxygen–boron coordination is not possible, and then the C–H insertion reaction occurs.

Conclusions

We have described an efficient and diastereoselective conversion of boroxycarbene complexes to oxaborolane, oxazaborolidine, 1,3-diol, and 1,2-amino alcohol derivatives. This methodology permits the regio- and diastereoselective modification of terpenes, in which a quaternary center has been formed in an enantioselective way. In addition, an intermediate of this reaction has been characterized by NMR spectroscopy, and theoretical calculations have shown the presence of a boron–metal interaction. On the other hand, a heteroatom-directed hydroboration has been described. Formation of other difunctional compounds, of potential interest as ligands, from terpenes and modification of other natural products by using this novel transformation are underway.

Acknowledgment. This work was supported by DGICYT (Grants PB92-1005 and PB94-0483) and the European Community (Human Capital and Mobility Network Contract No. ERBCHRXCT940501). J.V. and M.B. thank European Community and Ministerio de Educación y Ciencia, respectively, for fellowships.

Supporting Information Available: Experimental procedures and spectral data for all compounds (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>. JA991161+