Diastereo- and Enantioselective Cyclopropanation with Chromium Fischer Carbene Complexes: Alkenyl Oxazolines as Useful Achiral and Chiral Substrates

José Barluenga,*,† Angel L. Suárez-Sobrino,† Miguel Tomás,† Santiago García-Granda,‡ and Rafael Santiago-García‡

Contribution from the Instituto Universitario de Química Organometálica "Enrique Moles", and Departamento de Química Física y Analítica, Universidad de Oviedo, Avda. Julián Clavería 8, 33071 Oviedo, Spain

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Abstract: The cyclopropanation reaction of chromium Fischer carbene complexes with alkenyl oxazolines has been studied in both racemic and enantioselective fashions. The oxazolinyl group acts as both electron-acceptor substituent and chiral auxiliary. Achiral (4,4-dimethyloxazolin-2-yl)alkenes derived from *trans*-crotonic and *trans*-cinnamic acids **2a,b** undergo the cyclopropanation reaction to give **4a−d,g** with excellent diastereoselectivity (*trans*/*cis* ratio between 93:7 and >97:3), while those derived from acrylic and metacrylic acids **2c,d** give the cyclopropanes **4e,f,h** with much lower selectivity (*trans*/*cis* ratio between 68:32 and 83:17). The homogeneous catalytic hydrogenolysis of **4** leads in a selective manner to **5** or **6**, depending on the nature of the R^3 substituent. The removal of the oxazoline moiety is achieved by carboxybenzylation/hydrolysis and ester reduction, yielding monoprotected 1,4- and 1,3-diols **9** and **11**, respectively. The alkenes derived from enantiopure (*S*)-valinol and (*S*)-*tert*-leucinol **3** led to cyclopropanes *trans*-**12** with high relative and absolute stereocontrol. Using *tert*-leucinol as the auxiliary permits attaining total facial stereoselectivity (>98% ee). Reductive cleavage of the cyclopropane ring and removal of the auxiliary afford the enriched alcohols (3*S*,4*S*)-**9** and (*S*)-**11**. The stereochemical outcome of the cyclopropanation reaction is rationalized by a *trans* approach of the *s-cis* conformer of the alkenyl oxazoline to the carbene complex involving the less hindered face of the oxazoline auxiliary and the *re*-face of the carbene complex.

Introduction

The cyclopropanation reaction of electron-poor alkenes represents one of the first synthetically useful reactions of group 6 Fischer carbene complexes since their discovery by E. O. Fischer.[1] This reaction has been thoroughly studied not only for theoretical purposes, but more importantly also as a powerful method to access donor−acceptor cyclopropanes,[2] compounds that have gained attention because of their high potential to serve as versatile intermediates.[3] The cyclopropanation reaction was first reported for electron-poor[1,4] and, to a much lesser extent, electron-rich alkenes,[5] and later it was extended to electron-poor,[4f,6] electron-rich,[7] and unfunctionalized 1,3-dienes.[8] Significantly, studies carried out recently in our laboratory[9] showed for the first time that simple alkenes are capable of undergoing efficiently the intermolecular cyclopropanation reaction.[10,11]

After 30 years since its discovery, it is well recognized that the stereochemical control is the major limitation of the cyclopropanation reaction using Fischer-type carbene complexes. Thus, the *cis/trans* diastereoselectivity is generally low−

* Corresponding author. Telephone and fax: (34) 98 5103450. E-mail: barluenga@sauron.quimica.uniovi.es.

† Instituto Universitario de Química Organometálica "Enrique Moles".

‡ Departamento de Química Física y Analítica (X-ray service).

(1) (a) Fischer, E. O.; Dötz, K. H. *Chem. Ber.* **1970**, *103*, 1273. (b) Dötz, K. H.; Fischer, E. O. *Chem. Ber.* **1972**, *105*, 1356.

(2) Reviews: (a) Brookhart, M.; Studebaker, W. B. *Chem. Rev.* **1987**, *87*, 7, 411. (b) Reissig H.-U. In *Organometallics in Organic Synthesis;* Werner, H.; Erker, G., Eds.; Springer: Berlin, 1989; Vol. 2, pp 311−322. (c) Doyle, M. P. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds; Pergamon: Oxford, 1995; Vol. 12, pp 387−420. (d) Harvey, D. F.; Sigano, D. M. *Chem. Rev.* **1996**, *96*, 271.

(3) (a) Reissig, H.-U. *Top. Curr. Chem.* **1988**, *144*, 73. (b) Ullman, A.; Gruner, M.; Reissig, H.-U. *Chem. Eur. J.* **1999**, *5*, 187.

(4) (a) Wienand, A.; Reissig, H.-U. *Tetrahedron Lett.* **1988**, *29*, 2315. (b) Herndon, J. W.; Tumer, S. U. *Tetrahedron Lett.* **1989**, *30*, 4771. (c) Wienand, A.; Reissig, H.-U. *Organometallics* **1990**, *9*, 3133. (d) Harvey, D. F.; Brown, M. F. *Tetrahedron Lett.* **1990**, *31*, 2529. (e) Wienand, A.; Reissig, H.-U. *Chem. Ber.* **1991**, *124*, 957. (f) Herndon, J. W.; Tumer, S. U. *J. Org. Chem.* **1991**, *56*, 286.

(5) (a) Fischer, E. O.; Dötz, K. H. *Chem. Ber.* **1972**, *105*, 3966. (b) Dorrer, B.; Fischer, E. O.; Kalbfus, W. *J. Organomet. Chem.* **1974**, *81*, C20. (c) Murray, C. K.;. Yang, D. C.; Wulff, W. D. *J. Am. Chem. Soc.* **1990**, *112*, 5660. (d) Review: Wulff, W. D.; Yang, D. C.; Murray, C. K. *Pure Appl. Chem.* **1988**, *60*, 137.

(6) (a) Buchert, M.; Reissig, H.-U. *Tetrahedron Lett.* **1988**, *29*, 2319. (b) Buchert, M.; Reissig, H.-U. *Chem. Ber.* **1992**, *125*, 2723. (c) Buchert, M.; Hoffmann, M.; Reissig, H.-U. *Chem. Ber.* **1995**, *128*, 605. (d) Barluenga, J.; Tomás, M.; Suárez-Sobrino A. L. *Synthesis* **2000**, 935.

(7) Wulff, W. D.; Yang, D. C.; Murray, C. K. *J. Am. Chem. Soc.* **1988**, *110*, 2653.

(8) (a) Harvey, D. F.; Lund, K. P. *J. Am. Chem. Soc.* **1991**, *113*, 8916. (b) Merlic, C. A.; Bendorf, H. D. *Tetrahedron Lett.* **1994**, *35*, 9529.

(9) (a) Barluenga, J.; Fernández-Acebes, A.; Trabanco, A. A.; Flórez, J. *J. Am. Chem. Soc.* **1997**, *119*, 7591. (b) Barluenga, J.; López, S.; Trabanco, A. A.; Fernández-Acebes, A.; Flórez, J. *J. Am. Chem. Soc.* **2000**, *122*, 8145.

(10) Selected intramolecular cyclopropanations: (a) Barluenga, J.; Montserrat, J. M.; Flórez, J. *J. Chem. Soc., Chem. Commun.* **1993**, 1068. (b) Söderberg, B. C.; Hegedus, L. S. *Organometallics* **1990**, *9*, 3113.

(11) Selected cyclopropanation reactions with non-heteroatom-stabilized group 6 carbene complexes: (a) Casey, C. P.; Albin, L. D.; Burkhardt, T. J. *J. Am. Chem. Soc.* **1977**, *99*, 2533. (b) Harvey, D. F.; Brown, M. F. *J. Am. Chem. Soc.* **1990**, *112*, 7806. (c) Rudler, H.; Audouin, M.; Parlier, A.; Martin-Vaca, B.; Goumont, R.; Durand-Réville, T.; Vaissermann, J. *J. Am. Chem. Soc.* **1996**, *118*, 12045.

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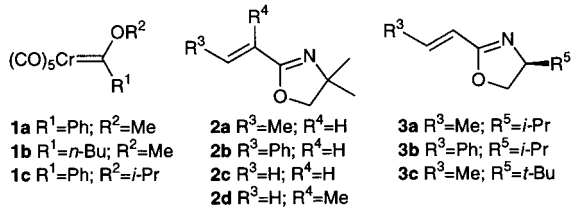


Figure 1. Structures of carbene complexes and alkenyl oxazolines used.

frequently close to 1:1—except when either alkenyl carbene complexes or 1,3-diene based substrates are employed. As an isolated example, we reported excellent diastereoselection in the cyclopropanation of alkenylimines (1-azadienes) by pentacarbonyl[phenyl(methoxy)]carbenechromium complex, in which the nitrogen functionality must exert some influence on the stereochemical course.[12] Significantly, no enantioselective cyclopropanation reactions using Fischer-type carbene complexes have been hitherto described,[13,14] although E. O. Fischer reported in 1973 the use of a chiral phosphine ligand-containing chromium carbene complex to demonstrate that no free carbene species were involved in the cyclopropanation reaction.[15] The use of chiral-at-metal complexes in enantioselective cyclopropanation reactions has been reported by Brookhart et al. for non-heteroatom-stabilized electrophilic iron carbene complexes.[16]

Our observation that alkenes with an imine functionality are cyclopropanated with high stereochemical control (see above)[12] along with the fact that readily accessible, chiral oxazolines are well-known as efficient auxiliaries in enantioselective synthesis[17,18] prompted us to investigate the reaction of simple chromium carbene complexes with various achiral and enantiopure alkenyl oxazolines. We describe herein the results of this study which allows for the effective cyclopropanation with Fischer carbene complexes of chromium in a diastereo and enantioselective fashion. The selective hydrogenolysis of the resulting cyclopropane ring and the subsequent removal of the chiral auxiliary are also reported.

The present study has been undertaken using (i) pentacarbonyl[phenyl(alkoxy)]- and pentacarbonyl[butyl(alkoxy)]carbene chromium complexes **1a**−**c**, (ii) achiral oxazolines **2a**−**d**, derived from 2-amino-2-methyl-1-propanol and *(E)*-2-butenoic (**2a**), *(E)*-3-phenylpropenoic (**2b**), propenoic (**2c**), and 2-methylpropenoic (**2d**) acids, and (iii) enantiopure oxazolines **3a**−**c** derived from (*S*)-valinol (R^5 = *i*-Pr) and *(E)*-2-butenoic (**3a**) and *(E)*-3-phenylpropenoic (**3b**) acids and from (*S*)-*tert*-leucinol and *(E)*-2-butenoic acid (**3c**) (Figure 1).

Results and Discussion

Synthesis and Ring-Opening of Racemic Cyclopropanes. The reaction of the chromium carbene complexes **1** and achiral alkenyl oxazolines **2** was first studied (Scheme 1, Table 1). We observed that no reaction occurred between the phenyl carbene complex **1a** (R^1=Ph; R^2 = Me) and the alkenyl oxazoline **2a** (R^3 = Me; R^4=H) in THF at room temperature. However, the reaction went to completion upon heating at 60 °C for 14 h affording cleanly the [2 + 1] cycloadduct **4a** after demetalation of the reaction mixture (air, sunlight). The crude product was subjected to column chromatography to furnish pure cyclopropane *trans*-**4a** in 89% yield as the sole diastereoisomer (^{1}H NMR, 300 MHz) (entry 1). Similarly, the oxazoline **2a** gave, on reaction with butyl carbene complex **1b**, the expected cycloadduct *trans*-**4b**, slightly contaminated with *cis*-**4b** (*trans:cis* = 93:7) (entry 2). The cyclopropanation of the styryl oxazoline **2b** with complexes **1a,b** required heating at 100 °C (toluene, 14 h) and yielded the cycloadducts *trans*-**4c,d** with complete diastereoselectivity (entries 3,4). On the contrary, lower selectivity was found when the alkenyl oxazoline lacks a C_β-substituent, as in the reaction of **1a** with alkenyl oxazolines **2c,d** (*trans*/*cis* = 2.1 and 5.0 for **4e** and **4f**, respectively) (entries 5,6). Increasing the bulkiness of the alkoxy substituent of the carbene ligand (**1c**, R^2 = *i*-Pr) results in some improvement of the selectivity. While the reaction of **1c** and crotonyl oxazoline **2a** gave only *trans*-**4g** as expected (entry 7 vs entry 1), the diastereomeric ratio for the acrylic derivative **2c** increased from 2.1 (entry 5) to 2.8 (entry 8). It is noticeable that the reactions were in all cases very clean and the yields very high (ranging from 82 to 92%).

Scheme 1. Cyclopropanation of Achiral Alkenyl Oxazolines with Chromium Carbene Complexes

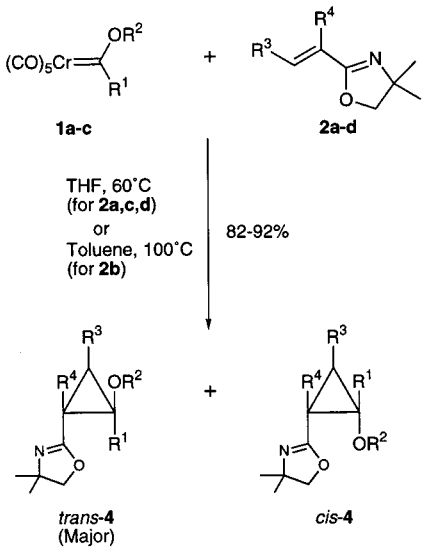


Table 1. Racemic Cyclopropanes **4** Prepared from Carbene Complexes **1** and Oxazolines **2**

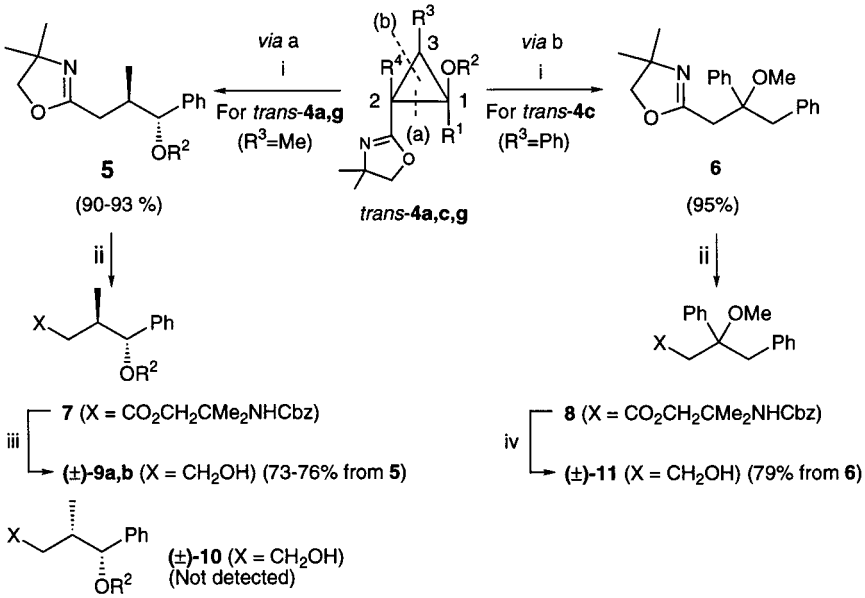
entry	R^1	R^2	R^3	R^4	product	yield (%)[a]	*trans*-**4**/*cis*-**4**[b]
1	Ph	Me	Me	H	**4a**	89	>97:<3
2	*n*-Bu	Me	Me	H	**4b**	85	93:7
3	Ph	Me	Ph	H	**4c**	92	>97:<3
4	*n*-Bu	Me	Ph	H	**4d**	90	>97:<3
5	Ph	Me	H	H	**4e**	84	68:32
6	Ph	Me	H	Me	**4f**	82	83:17
7	Ph	*i*-Pr	Me	H	**4g**	88	>97:<3
8	Ph	*i*-Pr	H	H	**4h**	87	74:26

[a] Isolated yields after column chromatography (silica gel, hexanes/ethyl acetate, 3:1). [b] Determined by ^{1}H NMR.

All attempts to transform the auxiliary oxazoline moiety into carbonyl or carboxylic acid derivatives[17] without affecting the cyclopropane framework were unsuccessful; instead, cleavage of the ring occurred under the reaction conditions tested. This fact is not unexpected, due to the lability of the C1−C2 bond of cyclopropanes having both donor and acceptor substituents.[3] At this point we decided to investigate a two-step alternative

(12) Barluenga, J.; Tomás, M.; López-Pelegrín, J. A.; Rubio, E. *J. Chem. Soc., Chem. Commun.* **1995**, 665.
(13) Wulff, W. D. *Organometallics* **1998**, *17*, 3116.
(14) Enantioselective cyclopropanation with alkyl diazoacetates/metal complexes: (a) Doyle, M. P.; Forbes, D. C. *Chem. Rev.* **1998**, *98*, 911. (b) Davies, H. M. L.; Boebel, T. A. *Tetrahedron Lett.* **2000**, *41*, 8189.
(15) Cooke, M. D.; Fischer, E. O. *J. Organomet. Chem* **1973**, *56*, 279.
(16) Brookhart, M.; Liu, Y.; Goldman, E. W.; Timmers, D. A.; Williams, G. D. *J. Am. Chem. Soc.* **1991**, *113*, 927.
(17) Review: Gant, T. G.; Meyers, A. I. *Tetrahedron* **1994**, *50*, 2297.
(18) We have recently described the [3 + 2] cyclization of achiral alkenyl oxazolines to alkenyl carbene complexes.[6d]

Scheme 2. Hydrogenolysis of Racemic Cyclopropanes **4** and Hydrolysis−Reduction of the Oxazoline Moiety[a]



[a] (i) H_2/Pd (1 atm); Et_3N−THF, 25°C. (ii) Cbz−Cl, Na_2CO_3, CH_2Cl_2, 25° C. (iii) DIBAL-H, toluene, 25°C. (iv) $LiAlH_4$, THF, 25°C.

route, (i) hydrogenolysis of the cyclopropane ring and (ii) hydrolysis−reduction of the oxazoline moiety (Scheme 2). The hydrogenation of cyclopropanes **4a,g** (R^3 = Me) [H_2 (1 atm)/Pd−C/Et_3N−THF] at room temperature resulted in the formation of **5a,g** in 90−93% yield (via a).[19] Interestingly, the hydrogenolysis reaction was found to take place not only in a regioselective manner, as only the C1−C2 bond of the cyclopropane ring suffered cleavage, but also with complete stereoselectivity. Moreover, the stereochemical analysis of **5** (vide infra) reveals that the hydrogenation of C1 takes place with inversion of configuration. This result is of great significance since previous hydrogenolysis reactions of siloxy-methoxycarbonyl-substituted cyclopropanes have been reported by Reissig et al. to take place with low stereoselectivity (diastereoisomeric ratios from 1:1 to 2:1).[4c,19] On the contrary, when a phenyl group is placed on C3, as for **4c** (R^3=Ph), a reversal of the sense of the regiocontrol was observed, leading exclusively to **6** (95% yield) by reductive breaking of the C2−C3 bond (via b). The resulting oxazolines **5** and **6** were treated with benzyl chloroformate in the presence of aqueous sodium carbonate,[20] affording the carbamates **7** and **8**. Without purification, these compounds were reduced with DIBAL-H and LAH, respectively, to produce the corresponding racemic methoxybutanols **9a,b** (73−76% overall yield from **5a,g**) and **11** (79% overall yield from **6**). No traces of the *syn*-diastereoisomer **10** were detected (^{1}H NMR, 300 MHz) in the former case.

Synthesis and Ring-Opening of Enantiopure Cyclopropanes. The readily accessible (*S*)-isopropyloxazoline derivatives **3a,b** were first selected as the model enantiopure partners for the enantioselective cyclopropanation reaction (Scheme 3; Table 2, entries 1−4). Compared with the case of achiral oxazolines **2**, no noticeable changes when using **3** were observed in terms of reaction conditions (THF/60 °C for oxazolines **3a**; toluene/100 °C for oxazoline **3b**) and yields (86−94%). The four diastereoisomers that might be formed—*trans*-**12** and *cis*-**12**, *trans*-**13** and *cis*-**13**—are shown in Scheme 3. Gratifyingly, very high face selectivity was achieved in the formation of the *trans* cycloadduct (in most cases >90% de in favor of *trans*-**12** was observed). On the contrary, the *cis*/*trans* selectivity of the cyclopropanation was not as high as that found for achiral oxazolines **2** (*trans*-**12**/*cis*-**12** = 1.4−9.0). For instance, the cyclopropanation of alkenyl oxazolines **3a,b** (R^5 = *i*-Pr) with carbene complex **1a** (entries 1,2) took place with acceptable *cis*/*trans* stereoselectivity (*trans*-**12**/*cis*-**12** ≈ 5) and very high facial selectivity (84% de for *trans*-**12a** and >98% de for *trans*-

Scheme 3. Cyclopropanation of Enantiopure Alkenyl Oxazolines with Chromium Carbene Complexes

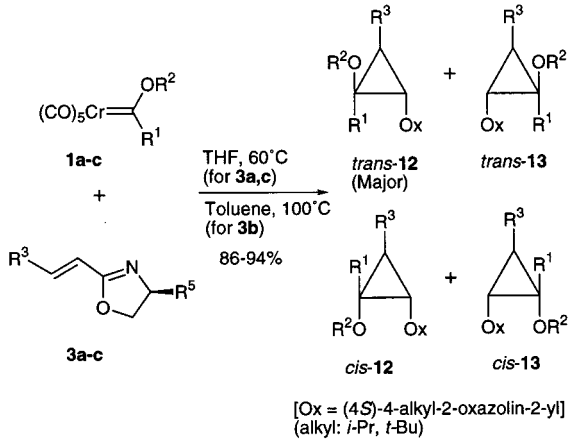


Table 2. Enantiopure Cyclopropanes **12** and **13** from Carbene Complexes **1** and Oxazolines **3**

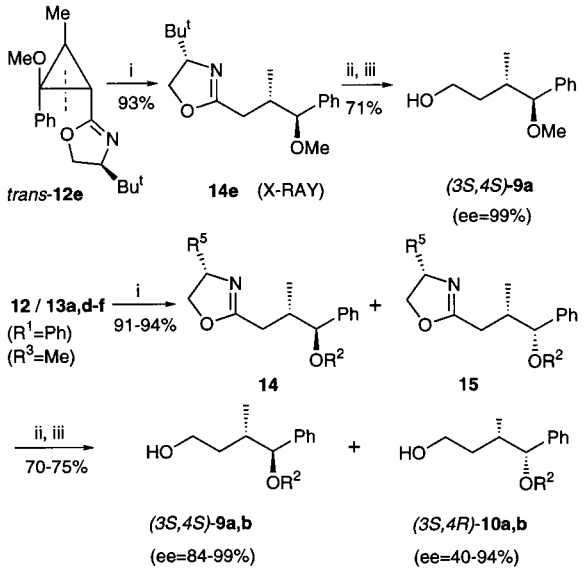
entry	R^1	R^2	R^3	R^5	products	yield (%)[a]	*trans*-**12**/*cis*-**12**[b]	*trans*-**12**/*trans*-**13**[b]
1	Ph	Me	Me	*i*-Pr	**12a**/**13a**	89	83:17	92:8
2	Ph	Me	Ph	*i*-Pr	**12b**/**13b**	94	84:16[c]	>99:<1
3	*n*-Bu	Me	Ph	*i*-Pr	**12c**/**13c**	90	58:42	85:15
4	Ph	*i*-Pr	Me	*i*-Pr	**12d**/**13d**	86	90:10	95:5
5	Ph	Me	Me	*t*-Bu	**12e**/**13e**	87	85:15[c]	>99:<1
6	Ph	*i*-Pr	Me	*t*-Bu	**12f**/**13f**	86	94:6	>99:<1

[a] Isolated yields after column chromatography (silica gel, hexanes/ethyl acetate 3:1). [b] Determined by GC−MS. [c] >99:<1 After crystallization from pentane.

(19) On the basis of the work by Brückner and Reissig for closely related substrates, triethylamine-poisoned catalyst was used to avoid further hydrogenolysis of the benzylic C−O bond. See: Brückner, C.; Reissig, H.-U. *Chem. Ber.* **1987**, *120*, 617.

(20) Kouklovsky, C.; Pouilhès, A.; Langlois, Y. *J. Am. Chem. Soc.* **1990**, *112*, 6672.

Scheme 4. Hydrogenolysis via Cleavage of the C1−C2 Bond of Enantiopure Cyclopropanes and Hydrolysis−Reduction of the Oxazoline Moiety[a]



[a] (i) H_2/Pd (1 atm); Et_3N−THF, 25°C. (ii) Cbz−Cl, Na_2CO_3, CH_2Cl_2. (iii) DIBAL-H, toluene, 25°C.

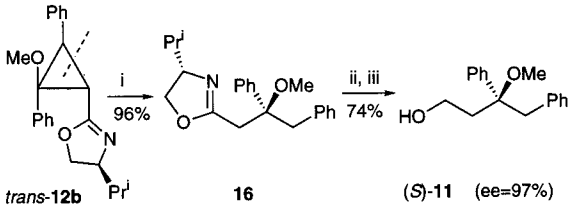
12b). Unfortunately, the selectivity dropped dramatically for the pentacarbonyl[butyl(methoxy)]carbene chromium complex **1b**, as shown in the formation of **12c** (entry 3; *trans*-**12c**/*cis*-**12c** = 1.4; 70% de for *trans*-**12c**). Therefore, further efforts were made to improve the relative and absolute stereocontrol. In this context, slightly superior results were reached when the isopropoxycarbene **1c** (R^2 = *i*-Pr) was employed in place of the methoxy counterpart **1a** (R^2 = Me) (compare entries 1 and 4). At this point, we turned our attention to the alkenyl oxazoline **3c** that contains a bulkier group (R^5 = *t*-Bu; entries 5,6). First, the reaction of **1a** with **3c** took place under the standard reaction conditions and with comparable yield, allowing for almost total absolute stereocontrol, although no significant improvement of the relative stereocontrol could be attained (compare entries 1 and 5). As expected, combining both structural modifications on the carbene and on the oxazoline partners provided the best overall stereoselectivity. This event is illustrated in entry 6, which shows that the carbene complex **1c** and the alkenyl oxazoline **3c** formed the cyclopropane **12f** in good chemical yield (86%) and with excellent relative and absolute stereocontrol (*trans*-**12f**/*cis*-**12f** = 16; >98% de for *trans*-**12f**).

The diastereoisomers *trans*-**12e** (R^3 = Me) and *trans*-**12b** (R^3=Ph) were efficiently isolated as single isomers (*trans*/*cis* = > 99:1) by recrystallization from pentane (>85% recovering material) and afterward used as model cyclopropanes for further elaboration into the chiral, nonracemic alcohols **9** and **11** (Schemes 4 and 5, respectively).

When *trans*-**12e** was subjected to hydrogenolysis [H_2 (1 atm)/Pd−C/Et_3N−THF, 25 °C], regioselective cleavage of the C1−C2 bond occurred to give **14e** (93% yield) as a 93:7 *anti:syn* mixture (Scheme 4). Moreover, the isolation of *anti*-**14e** in pure form was readily achieved by recrystallization from pentane. The final elaboration of pure **14e** into (3*S*,4*S*)-**9a** (99% ee) was accomplished in 71% overall yield by successive treatment with CbzCl/Na_2CO_3 and DIBAL-H.

The reductive cleavage of the C1−C2 bond was also performed on the diastereoisomeric cyclopropane mixtures **12/13a,d,e,f** (R^3 = Me) (Scheme 4, Table 3). First, the hydrogenolysis reaction afforded mixtures consisting of four

Scheme 5. Hydrogenolysis via Cleavage of the C2−C3 Bond of Enantiopure Cyclopropane *trans*-**12b** and Hydrolysis−Reduction of the Oxazoline Moiety[a]



[a] (i) H_2/Pd (1 atm); Et_3N−THF, 25°C. (ii) Cbz−Cl, Na_2CO_3, CH_2Cl_2. (iii) $LiAlH_4$, THF, 25°C.

diastereoisomers wherein compounds **14** and **15**, arising from *trans*-**12** and *cis*-**12**, respectively, were largely predominant. Then, the resulting mixture was subjected to reductive removal of the oxazoline auxiliary to furnish (3*S*,4*S*)-**9** and (3*S*,4*R*)-**10**, as the major stereoisomers. In turn, the minor stereoisomers (3*R*,4*R*)-**9** and (3*R*,4*S*)-**10** (not shown) would originate from *trans*-**13** and *cis*-**13**, respectively. The HPLC analyses revealed that the major isomers (3*S*,4*S*)-**9a,b** had produced with an enantiomeric purity of up to 99% (Table 3) and confirmed the excellent face selectivity for the *trans*-cyclopropane adducts (see also *trans*-**12**/*trans*-**13** ratio in Table 2), particularly for alkenyl oxazolines derived from *tert*-leucinol [see ee's for (3*S*,4*S*)-**9** in Table 3; entries: 3 vs 1 and 4 vs 2]. In Table 3 is also displayed the ee values of the minor isomers (3*S*,4*R*)-**10a,b**, which actually express the face selectivity for the *cis*-cyclopropane adducts. In this case, low enantioselectivity was observed when starting from the (*S*)-valinol oxazoline **3a** (40−46% ee; entries 1,2), while high ee values are reached if the *tert*-leucinol oxazoline **3c** is used (84−94%; entries 3,4). The little discrepancy found in the ratio values for *trans*-**12**/*cis*-**12** (see Table 2) vs (3*S*,4*S*)-**9**/(3*S*,4*R*)-**10** (see Table 3) reflects again that the hydrogenolysis of the cyclopropane ring takes place with very high, but not complete, stereoselectivity. It can be deduced from Tables 2 and 3 that the diastereoselectivity of the hydrogenolysis of cyclopropanes **12** ranges from 85 to 95%. Moreover, the **14**/**15** ratio values (^{1}H NMR, 300 MHz) match well those found for (3*S*,4*S*)-**9**/(3*S*,4*R*)-**10** (HPLC analysis of the carbamates derived from phenylisocyanate).

Finally, hydrogenolysis of the C2−C3 bond of the single cycloadduct *trans*-**12b** was performed under standard conditions leading to the open-chain derivative **16** (96% yield) as a single isomer on the basis of its 300 MHz ^{1}H NMR spectrum (Scheme 5). The conversion of the oxazoline moiety of **16** into the alcohol (*S*)-**11** was efficiently accomplished by formation of the carbamate (CbzCl, Na_2CO_3) and by hydride reduction (LAH). The monoprotected 1,3-butanediol derivative (*S*)-**11** was thus obtained in 74% yield from **16** and 97% ee (HPLC, Chiracel OD-H column, hexane/ethanol, 150:1).

Structural Analysis. The assignment of the relative stereochemistry for single racemic and enantiopure cyclopropanes (*trans*-**4** and *trans*-**12b,e**) was based on 2D-NOESY NMR experiments. Crystals of the adduct *anti*-**14e** were growth from pentane and the X-ray analysis was performed (Figure 2),[21] thus allowing for its absolute stereochemistry to be established. The full structure of all compounds is drawn in accordance with these analyses and on the basis that the cyclopropane carbon

(21) Crystal data of compound **14e** $C_{18}H_{27}NO_2$, M_r = 289.41, Monoclinic, space group $P2_1$, a = 7.407(4) Å, b = 12.392(3) Å, c = 9.432(6) Å, β = 102.58(2)°, V = 844.9(7) Å^3, Z = 2, D_x = 1.138 Mg/m^3, Mo Kα radiation (graphite crystal Monochromator, λ = 0.071073 Å), μ = 0.07 mm^{-1}, F(000) = 316, T = 200(2) K. Final conventional R = 0.038, ωR2 = 0.082 and S = 1.033, for 1088 "observed" reflections and 261 variables.

Table 3. Enantiopure Alcohols **9** and **10** from Cyclopropanes **12** and **13**

entry	cyclopropanes	R^2	R^5	products	yield[a,b] (%)	(3*S*,4*S*)−**9**/(3*S*,4*R*)-**10**[c,d]	ee (%) (3*S*,4*S*)−**9**[d]	ee (%) (3*S*,4*R*)−**10**[d]
1	**12a**/**13a**	Me	*i*-Pr	**9a**/**10a**	70	77:23	84	46
2	**12d**/**13d**	*i*-Pr	*i*-Pr	**9b**/**10b**	71	88:12	90	40
3	**12e**/**13e**	Me	*t*-Bu	**9a**/**10a**	71	78:22	99	94
4	**12f**/**13f**	*i*-Pr	*t*-Bu	**9b**/**10b**	75	91:9	98	84

[a] Overall yield from **14**/**15**. [b] Isolated yields after column chromatography (silica gel, hexanes/ethyl acetate, 3:1). [c] Determined for oxazolines **14**/**15** by ^{1}H NMR. [d] Determined by HPLC of the phenylcarbamate derivatives (Chiracel OD-H column hexane/isopropyl alcohol 3:1).

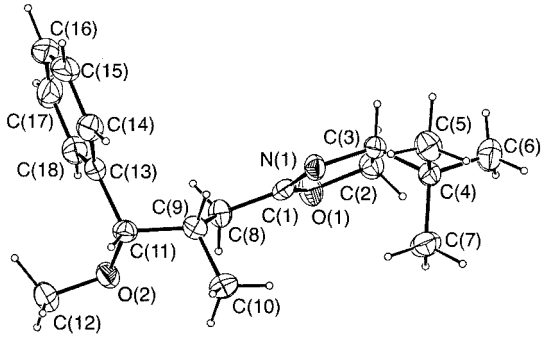


Figure 2. X-Ray crystal structure of compound **14e**.

center not involved in the hydrogenolysis reaction does not epimerize along the successive reactions.

Stereochemical Results. The reaction course outlined in Figure 3 is proposed on the basis of (i) the accepted mechanism for the cyclopropanation reaction of heteroatom-stabilized carbene complexes and electron-withdrawing alkenes[22] and (ii) the relative and absolute stereochemistry of all the cycloadducts. The *s*-*cis* alkenyl oxazoline[23] might approach the *re*-face or the *si*-face of the metal−carbene double bond. Moreover, this approach can take place according to a *cis*- or *trans*-arrangement (in reference to oxazolinyl and alkoxy substituents). Thus, the *trans*-approach of the *s*-*cis* alkenyl oxazoline to the *re*-face of the carbene moiety (pathway *A*) would form the allyl-type *trans*-metallacyclobutane **I**, which would yield, upon reductive elimination, the major cyclopropane *trans*-**12** first and, at the latest stage, the final alcohol (3*S*,4*S*)-**9**. On the other hand, the *cis*-metallacyclobutane species **II**, precursor of *cis*-**12** and (3*S*,4*R*)-**10,** would arise from the *cis*-approach of the alkenyl oxazoline to the *si*-face of the carbene moiety (pathway *B*). The preference for the *trans*-metallacyclobutane species seems to be a consequence of steric interaction between the alkoxy and oxazolinyl groups. Finally, the *trans*-approach of the *s*-*cis* alkenyl oxazoline to the *si*-face of the carbene moiety (pathway *C*) would generate the *trans*-metallacyclobutane species **III**, precursor of *trans*-**13** and (3*R*,4*R*)-**9**. In the same way, the *cis*-approach of the *s*-*cis* alkenyl oxazoline to the *re*-face of the carbene moiety would form the *cis*-metallacyclobutane species **IV** (pathway *D*) which is the precursor of the minor stereoisomers *cis*-**13** and (3*R*,4*S*)-**10**. These latter attacks (pathways *C*, and *D*) appear to be much less favorable due to the steric interaction between the R^5 group of the oxazoline auxiliary and the tetracarbonyl−metal fragment.

Conclusions

The results reported herein demonstrate that alkenyl oxazolines are excellent electron-poor alkene surrogates for the cyclopropanation reaction with group 6 Fischer carbene complexes. Thus, the achiral systems are smoothly cyclopropanated in very good yield and with unusually high diastereoselectivity. The extension of the reaction to chiral nonracemic alkenyl oxazolines allowed us to develop the first enantioselective cyclopropanation with heteroatom-stabilized group 6 Fischer carbene complexes.[24] The asymmetric induction for the major *trans*-diastereoisomer is not only very high, but it can also be increased in general to more than 98% by choosing properly the carbene alkoxy group and the oxazoline substituent. In this case, *cis*/*trans* diastereomeric ratios up to 88% were also reached. The removal of the chiral auxiliary cannot be achieved on the cyclopropane itself, but it can be accomplished if the cyclopropanes are previously subjected to hydrogenation. It is worth noting that the cyclopropanes undergo stereospecific reductive cleavage with inversion of configuration.

Experimental Section

General. All reactions involving air-sensitive compounds were carried out under a N_2 atmosphere (99.99%). All glassware was oven-dried (120 °C), evacuated, and purged with nitrogen. All common reagents and solvents were obtained from commercial suppliers and used without any further purification unless otherwise indicated. Fischer carbene complexes were prepared following described procedures. Solvents were dried by standard methods. Flash column chromatography was carried out on silica gel 60, 230−240 mesh. High-performance liquid chromatography was carried out using a Shimadzu LC-10 and a Waters LC Module I Plus chromatograph, each equipped with a vis−UV Diode-Array detectors; Chiralcel OD-H was employed as chiral column. Enantiomeric excess values were either determined by HPLC of the isolated alcohol or its phenylcarbamate derivative. NMR experiments were carried out on a Bruker AC-300 spectrometer. ^{1}H NMR spectra were recorded in $CDCl_3$ at 300.08 MHz at 20 °C with tetramethylsilane ($\delta = 0.0$) as the internal standard. ^{13}C NMR spectra were recorded in $CDCl_3$ at 75.46 MHz at 20 °C. ^{1}H NMR splitting pattern abbreviations are: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. ^{13}C NMR multiplicities were determined by DEPT, abbreviations are: q, CH_3; t, CH_2; d, CH; s, quaternary carbons. NOESY experiments were carried out on a Bruker AMX-400 spectrometer. Standard pulse sequences were employed for the DEPT experiments. High-resolution mass spectra (HRMS) were obtained with a Finnigan Mat95 Mass Spectrometer, electron impact techniques (70 eV) were employed. Melting points were determined on a Büchi−Tottoli apparatus and are uncorrected. For optical rotations a Perkin-Elmer 241 polarimeter was employed; values were determined using the sodium lamp, and the concentration was reported in g/100 mL. Elemental analyses were carried out with a Perkin-Elmer 240 B microanalyzer.

Synthesis of Cyclopropanes 4, 12, and 13. General Procedure. A mixture of the carbene complex **1** (1.5 mmol) and alkenyl oxazolines **2** or **3** (1.5 mmol) in THF (toluene for **2b** and **3b**) (20 mL) was heated

(22) Casey, C. P.; Cesa, M. *Organometallics* **1982**, *1*, 87.

(23) The requirement of the *s*-*cis* conformation for the alkene is well-documented in the literature. Thus, Wienand and Reissig have demonstrated that α,β-unsaturated lactones that cannot reach a *cis* conformation between the C=C and C=O bonds fail to undergo cyclopropanation with chromium carbene complexes.[4c] In a similar way, only dienes with a readily accessible *s*-*cis* conformation can participate in this reaction, as reported by Harvey and Lund.[8a]

(24) Alkenoic acid esters derived from chiral alcohols are not capable of achieving the enantioselective cyclopropanation. In fact, we have experienced that the carbene complex **1a** does not react with (±)-phenylcyclohexyl acrylate at temperatures up to 120 °C.

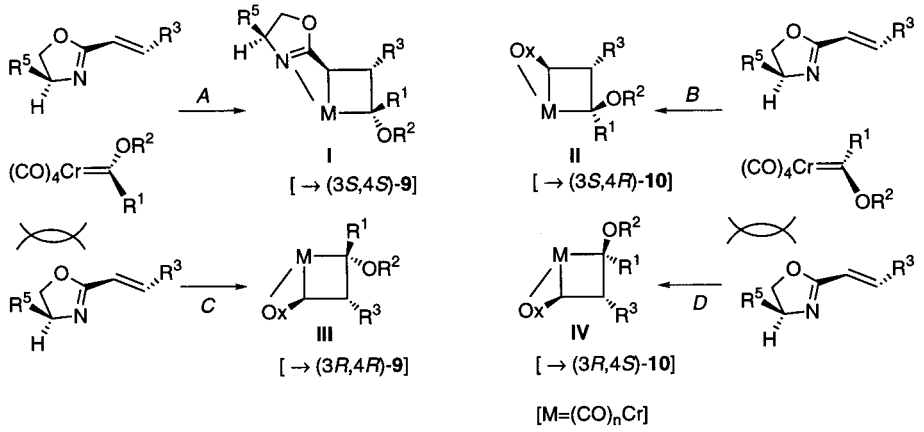


Figure 3. Proposed stereochemical and mechanistic aspects for the reaction course.

at 60 °C (100 °C for **2b** and **3b**) for 14 h. Then the solvent was removed under vacuum, and the crude product was dissolved in a mixture of EtOAc/hexane (1:1) and air-oxidized in an open flask under sunlight or lamp light (10−12 h). The solution was then filtered over Celite, and the filtrate was concentrated under vacuum. The resulting crude product was purified by column chromatography (silica gel, hexanes/EtOAc, 3:1).

***trans,trans*-2-(4,4-Dimethyl-2-oxazolin-2-yl)-1-methoxy-3-methyl-1-phenylcyclopropane (*trans*-4a):** obtained as a single diastereoisomer; oil; yield = 89%; ^{1}H NMR: δ = 7.4−7.2 (m, 5 H), 3.6 (d, J = 7.9 Hz, 1H), 3.5 (d, J = 7.9 Hz, 1H), 3.1 (s, 3H), 2.1 (m, 1H), 1.7 (d, J = 7.0 Hz, 1H), 1.4 (d, J = 8.4 Hz, 3H), 1.1 (s, 3H), 0.6 (s, 3H); ^{13}C NMR: δ = 162.9 (s), 136.0 (s), 129.5 (d, 2C), 127.7 (d, 3C), 78.6 (t), 72.0 (s), 66.2 (s), 55.0 (q), 29.5(d), 28.0 (q), 27.6 (q), 23.0 (d), 11.2 (q); HRMS *m*/*z* calcd for $C_{15}H_{18}NO_2$ [M − CH_3]$^+$ 244.1337; found 244.1338. Anal. Calcd for $C_{16}H_{21}NO_2$: C 74.10, H 8.16, N 5.40. Found: C 74.29, H 8.05, N 5.59.

***trans,trans*-1-Butyl-2-(4,4-dimethyl-2-oxazolin-2-yl)-1-methoxy-3-methylclopropane(*trans*-4b):** obtained as a mixture of diastereoisomers (*trans*-**4b**/*cis*-**4b**, 93:7); oil; yield = 85%; ^{1}H NMR: δ = 3.9 (d, J = 7.8 Hz, 1H), 3.8 (d, J = 7.8 Hz, 1H), 3.1 (s, 3H), 2.0 (m, 2H), 1.4−1.1 (m, 6H), 1.2 (s, 3H), 1.1 (s, 3H), 1.0 (d, J = 5.9 Hz, 3H), 0.9 (t, J = 7.0 Hz, 3H); ^{13}C NMR: δ = 163.9 (s), 78.9 (t), 70.2 (s), 66.3 (s), 53.9 (q), 28.8 (d), 28.7 (t), 28.1 (q), 27.9 (q), 27.3 (t), 24.9 (d), 22.5 (t), 13.8 (q), 13.0 (q); HRMS *m*/*z* calcd for $C_{13}H_{22}NO_2$ [M − CH_3]$^+$ 224.1650; found 224.1648. Anal. Calcd for $C_{14}H_{25}NO_2$: C 70.25, H 10.53, N 5.85. Found: C 70.39, H 10.36, N 5.72.

***trans,trans*-2-(4,4-Dimethyl-2-oxazolin-2-yl)-1-methoxy-1,3-diphenylcyclopropane (*trans*-4c):** obtained as a single diastereoisomer, white solid, mp 81−83 °C; yield = 92%; ^{1}H NMR: δ = 7.6−7.2 (m, 10 H), 3.7 (d, J = 7.9 Hz, 1H), 3.6 (d, J = 7.9 Hz, 1H), 3.3 (d, J = 8.4 Hz, 1H), 2.8 (s, 3H), 2.7 (d, J = 8.4 Hz, 1H), 1.2 (s, 3H), 0.8 (s, 3H); ^{13}C NMR: δ = 162.0 (s), 135.6 (s), 135.1 (s), 129.6 (d), 128,2 (d), 128.0 (d), 127.9 (d), 127.8 (d), 126.3 (d), 78.9 (t), 73.1 (s), 66.5 (s), 54.6 (q), 33.0 (d), 29,1 (d), 28.0 (q), 27.6 (q); HRMS *m*/*z* calcd for $C_{21}H_{23}NO_2$ 321.1729; found 321.1728. Anal. Calcd for $C_{21}H_{23}NO_2$: C 78.47, H 7.21, N 4.36. Found: C 78.61, H 7.14, N 4.25.

***trans,trans*-1-Butyl-2-(4,4-dimethyl-2-oxazolin-2-yl)-1-methoxy-3-phenylclopropane (*trans*-4d):** obtained as a single diastereoisomer; oil; yield = 90%; ^{1}H NMR: δ = 7.5−7.1 (m, 5 H), 4.0 (d, J = 8.1 Hz, 1H), 3.9 (d, J = 8.1 Hz, 1H), 3.3 (s, 3H), 3.1 (d, J = 7.2 Hz, 1H), 2.1 (d, J = 7.2 Hz, 1H), 1.4 (s, 3H), 1.3 (s, 3H), 1.5−1.1 (m, 6H), 0.7 (t, J = 6.5 Hz, 3H); ^{13}C NMR: δ = 162.7 (s), 135.9 (s), 128.6 (d, 4C), 126.2(d), 79.0 (t), 71.2 (s), 66.7 (s), 54.4 (q), 35.0 (d), 28.5 (t), 28.3 (q), 28.1 (q), 26.7 (t), 26.6 (d), 22.2 (t), 13.6 (q); HRMS *m*/*z* calcd for $C_{19}H_{27}NO_2$ 301.2042; found 301.2039. Anal. Calcd for $C_{19}H_{27}NO_2$: C 75.71, H 9.03, N 4.65. Found: C 75.49, H 9.14, N 4.55.

***trans*-2-(4,4-Dimethyl-2-oxazolin-2-yl)-1-methoxy-1-phenylcyclopropane (*trans*-4e):** obtained as a mixture of diastereoisomers (*trans*-**4e**/*cis*-**4e**, 68:32); oil; yield = 84%; ^{1}H NMR: δ = 7.5−7.2 (m, 5 H), 3.6 (d, J = 8.4 Hz, 1H), 3.5 (d, J = 8.4 Hz, 1H), 3.1 (s, 3H), 2.2 (dd, J = 10.0, 7.0 Hz, 1H), 1.7 (dd, J = 7.0, 6.3 Hz, 1H), 1.5 (dd, J = 10.0, 6.3 Hz, 1H), 1.1 (s, 3H), 0.7 (s, 3H); ^{13}C NMR: δ = 162.5 (s), 139.0 (s), 129.1(d, 2C), 127.5 (d), 127.3 (d, 2C), 78.8 (t), 69.0(s), 66.3-(s), 54.5 (q), 27.9 (q), 27.6 (q), 24.0 (d), 15.0 (t); HRMS *m*/*z* calcd for $C_{15}H_{19}NO_2$ 245.1416; found 246.1417. Anal. Calcd for $C_{15}H_{19}NO_2$: C 73.44, H 7.81, N 5.71. Found: C 73.23, H 7.93, N 5.59.

***trans*-2-(4,4-Dimethyl-2-oxazolin-2-yl)-1-methoxy-2-methyl-1-phenylcyclopropane (*trans*-4f):** obtained as a mixture of diastereoisomers (*trans*-**4f**/*cis*-**4f**, 83:17); oil; yield = 82%; ^{1}H NMR: δ = 7.4−7.1 (m, 5 H), 3.5 (s, 2H), 3.1 (s, 3H), 2.0 (d, J = 6.1 Hz, 1H), 1.6 (s, 3H), 1.1 (s, 3H), 1.0 (d, J = 6.1 Hz, 1H), 0.6 (s, 3H); ^{13}C NMR: δ = 165.0 (s), 135.9 (s), 128.7 (d, 2C), 127.0 (d, 3C), 78.3 (t), 70.1 (s), 65.7 (s), 54.3 (q), 27.5 (q), 27.4 (s), 27.0 (q), 20.3 (t), 14.9 (q); HRMS *m*/*z* calcd for $C_{16}H_{21}NO_2$ 259.1572; found 259.1582. Anal. Calcd for $C_{16}H_{21}NO_2$: C 74.10, H 8.16, N 5.40. Found: C 74.23, H 8.01, N 5.56.

***trans,trans*-2-(4,4-Dimethyl-2-oxazolin-2-yl)-1-isopropoxy-3-methyl-1-phenylcyclopropane (*trans*-4g):** obtained as a single diastereoisomer; oil; yield = 88%; ^{1}H NMR: δ = 7.4−7.1 (m, 5 H), 3.7 (m, 1H), 3.6 (d, J = 7.0 Hz, 1H), 3.4 (d, J = 7.0 Hz, 1H), 2.0 (m, 1H), 1.7 (d, J = 7.0 Hz, 1H), 1.4 (d, J = 6.4 Hz, 3H), 1.1 (s, 3H), 1.0 (d, J = 6.1 Hz, 6H), 0.7 (s, 3H); ^{13}C NMR: δ = 163.2 (s), 137.7(s), 129.5 (d, 2C), 127.4 (d, 3C), 78.4 (t), 70.5 (s), 69.4 (d), 66.0 (s), 29.1 (d), 27.9 (q), 27.4 (q), 23.2 (q), 22.9 (q), 22.5 (d), 12.0 (q); HRMS *m*/*z* calcd for $C_{15}H_{18}NO_2$ [M−C_3H_7]$^+$ 244.1337; found 244.1337; Anal. Calcd for $C_{18}H_{25}NO_2$: C 75.22, H 8.77, N 4.87. Found: C 75.20, H 8.70, N 4.95**.**

***trans-trans*-2-(4,4-Dimethyl-2-oxazolin-2-yl)-1-isopropoxy-1-phenylcyclopropane (*trans*-4h):** obtained as a mixture of diastereoisomers (*trans*-**4h**/*cis*-**4h**, 74:26); oil; yield = 87%; ^{1}H NMR: δ = 7.5−7.1 (m, 5 H), 3.7 (m, 1H), 3.5 (d, J = 8.3 Hz, 1H), 3.4 (d, J = 8.3 Hz, 1H), 2.1 (dd, J = 10.0, 7.0 Hz, 1H), 1.8 (dd, J = 7.0, 6.1 Hz, 1H), 1.4 (dd, J = 10.0, 6.1 Hz, 1H), 1.1 (s, 6H), 1.0 (d, J = 6.1 Hz, 3H), 0.9 (d, J = 6.1 Hz, 3H); ^{13}C NMR: δ = 162.8 (s), 136.5 (s), 129.3 (d, 2C), 127.0 (d, 3C), 78.7 (t), 69.5 (d), 66.1 (s), 65.9 (s), 28.5 (q), 28.1 (q), 23.2 (d), 23.0 (q), 22.5 (q), 16.7 (t); HRMS *m*/*z* calcd for $C_{17}H_{23}NO_2$ 273.1729; found 273.1725. Anal. Calcd for $C_{17}H_{23}NO_2$: C 74.69, H 8.48, N 5.12. Found: C 74.81, H 8.55, N 5.20.

(1*S*,2*S*,3*S*)-2-[(4*S*)-4-Isopropyl-2-oxazolin-2-yl]-1-methoxy-3-methyl-1-phenylcyclopropane (*trans*-12a): obtained as a mixture of diastereoisomers (*trans*-**12a**/*cis*-**12a**, 83:17 and *trans*-**12a**/*trans*-**13a**, 92:8); oil; yield = 89%; ^{1}H NMR: δ = 7.5−7.2 (m, 5 H), 3.9 (dd, J = 9.4, 7.9 Hz, 1H), 3.6 (m, 1H), 3.3 (dd, J = 8.5, 7.9 Hz, 1H), 3.1 (s, 3H), 2.1 (m, 1H), 1.9 (d, J = 6.8 Hz, 1H), 1.6 (m, 1H), 1.4 (d, J = 6.1 Hz, 3H), 0.8 (d, J = 6.8 Hz, 3H), 0.7 (d, J = 6.8 Hz, 3H); ^{13}C NMR: δ = 164.4 (s), 136.1 (s), 129.5 (d, 2C), 127.7 (d, 3C), 77.5 (s), 71.6 (d), 69.1 (t), 54.8 (q), 31.9 (d), 29.8 (d), 23.8 (d), 18.8 (q), 17.7 (q), 11.4 (q); HRMS *m*/*z* calcd for $C_{17}H_{23}NO_2$ 273.1729; found 273.1724. Anal. Calcd for $C_{17}H_{23}NO_2$: C 74.69, H 8.48, N 5.12. Found: C 74.73, H 8.44, N 5.23.

(1*S*,2*S*,3*S*)-2-[(4*S*)-4-Isopropyl-2-oxazolin-2-yl]-1-methoxy-1,3-diphenylcyclopropane (*trans*-12b): obtained as a mixture of diastereoisomers (*trans*-**12b**/*cis*-**12b**, 84:16); yield = 94%; obtained as a single product after recrystallization from pentane; white solid; mp

86−88 °C; $[\alpha]^{20}_D = -59.4$ ($c = 0.55$ in $CHCl_3$); ^{1}H NMR: $\delta = 7.5-7.2$ (m, 10 H), 4.0 (dd, $J = 8.5$, 7.9 Hz, 1H), 3.7 (m, 1H), 3.4 (dd, $J = 8.5$, 8.2 Hz, 1H), 3.3 (d, $J = 7.3$ Hz, 1H), 2.9 (s, 3H), 2.8 (d, $J = 7.3$ Hz, 1H), 1.6 (m, 1H), 0.9 (d, $J = 6.9$ Hz, 3H), 0.8 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR: $\delta = 165.6$ (s), 137.8 (s), 137.2 (s), 131.6 (d, 2C), 130.1 (d, 2C), 129.9 (d, 3C), 128.4 (d, 3C), 74.8 (s), 73.9 (d), 71.5 (t), 56.6 (q), 35.8 (d), 34.1 (d), 31.5 (d), 20.8 (q), 19.9 (q); HRMS *m*/*z* calcd for $C_{22}H_{25}NO_2$ 335.1885; found 335.1880. Anal. Calcd for $C_{22}H_{25}NO_2$: C 78.77, H 7.51, N 4.18. Found: C 78.61, H 7.39, N 4.21.

(1*S*,2*S*,3*S*)-1-Butyl-2-[(4*S*)-4-isopropyl-2-oxazolin-2-yl]-1-methoxy-3-phenylcyclopropane (*trans*-12c): obtained as a mixture of diastereoisomers (*trans*-**12c**/*cis*-**12c**, 58:42 and *trans*-**12c**/*trans*-**13c**, 85:15); oil; yield = 90%; ^{1}H NMR: $\delta = 7.3-7.0$ (m, 5H), 4.2 (m, 1H), 3.9 (m, 2H), 3.3 (s, 3H), 3.1 (d, $J = 7.0$ Hz, 1H), 2.1 (d, $J = 7.0$ Hz, 1H), 1.7 (m, 1H), 1.4−1.0 (m, 6H), 0.9 (d, $J = 6.8$ Hz, 3H); 0.8 (d, $J = 6.8$ Hz, 3H), 0.7 (t, $J = 7.1$ Hz, 3H); ^{13}C NMR: $\delta = 164.0$ (s), 135.9 (s), 128.0 (d, 4C), 126.1 (d), 71.7 (d), 71.0 (s), 69.9 (t), 54.3 (q), 34.6 (d), 32.3 (d), 28.5 (t), 26.8 (d), 26.7 (t), 22.1 (t), 18.5 (q), 17.7 (q), 13.6 (q); HRMS *m*/*z* calcd for $C_{20}H_{29}NO_2$ 315.2198; found 315.2194. Anal. Calcd for $C_{20}H_{29}NO_2$: C 76.15, H 9.27, N 4.44. Found: C 76.34, H 9.35, N 4.31.

(1*S*,2*S*,3*S*)-1-Isopropoxy-2-[(4*S*)-4-isopropyl-2-oxazolin-2-yl]-3-methyl-1-phenylcyclopropane (*trans*-12d): obtained as a mixture of diastereoisomers (*trans*-**12d**/*cis*-**12d**, 90:10 and *trans*-**12d**/*trans*-**13d**, 95:5); oil; yield = 86%; ^{1}H NMR: $\delta = 7.5-7.1$ (m, 5 H), 3.9 (dd, $J = 9.5$, 8.2 Hz, 1H), 3.7 (m, 2H), 3.4 (dd, $J = 9.5$, 9.0 Hz, 1H), 2.0 (m, 1H), 1.8 (d, $J = 7.0$ Hz, 1H), 1.6 (m, 1H), 1.3 (d, $J = 6.1$ Hz, 3H), 1.0 (d, $J = 6.1$ Hz, 3H), 0.95 (d, $J = 6.1$ Hz, 3H), 0.9 (d, $J = 6.7$ Hz, 3H), 0.8 (d, $J = 6.7$ Hz, 3H); ^{13}C NMR: $\delta = 164.8$ (s), 138.1 (s), 129.6 (d, 2C), 127.6 (d, 3C), 71.7 (d), 70.4 (s), 69.5 (d), 69.2 (t), 32.6 (d), 29.7 (d), 24.1 (d), 23.0 (q), 22.8 (q), 18.7 (q), 17.9 (q), 12.2 (q); HRMS *m*/*z* calcd for $C_{16}H_{20}NO_2$ $[M-C_3H_7]^+$ 258.1494; found 258.1492. Anal. Calcd for $C_{19}H_{27}NO_2$: C 75.71, H 9.03, N 4.65. Found: C 75.58, H 9.09, N 4.72.

(1*S*,2*S*,3*S*)-2-[(4*S*)-4-*tert*Butyl-2-oxazolin-2-yl]-1-methoxy-3-methyl-1-phenylcyclopropane (*trans*-12e): obtained as a mixture of diastereoisomers (*trans*-**12e**/*cis*-**12e**, 85:15), yield = 87%; obtained as a single diastereoisomer after recrystallization from pentane; white solid; mp 82−84 °C; $[\alpha]^{20}_D = -61.7$ ($c = 0.53$ in $CHCl_3$); ^{1}H NMR: $\delta = 7.5-7.2$ (m, 5 H), 3.9 (dd, $J = 9.7$, 8.0 Hz, 1H), 3.7 (dd, $J = 9.7$, 9.0 Hz, 1H), 3.3 (dd, $J = 9.0$, 8.0 Hz, 1H), 3.2 (s, 3H), 2.1 (m, 1H), 1.9 (d, $J = 7.0$ Hz, 1H), 1.4 (d, $J = 6.1$ Hz, 3H), 0.8 (s, 9H); ^{13}C NMR: $\delta = 164.2$ (s), 136.1 (s), 129.4 (d, 2C), 127.6 (d, 3C), 75.4 (d), 71.7 (s), 67.7 (t), 54.7 (q), 32.9 (s), 30.0 (d), 25.8 (q, 3C), 23.8 (d), 11.4 (q); HRMS *m*/*z* calcd for $C_{18}H_{25}NO_2$ 287.1885; found 287.1882. Anal. Calcd for $C_{18}H_{25}NO_2$: C 75.22, H 8.77, N 4.87. Found: C 75.09, H 8.86, N 4.75.

(1*S*,2*S*,3*S*)-2-[(4*S*)-4-*tert*Butyl-2-oxazolin-2-yl]-1-isopropoxy-3-methyl-1-phenylcyclopropane (*trans*-12f): obtained as a mixture of diastereoisomers (*trans*-**12f**/*cis*-**12f**, 94:6); oil; yield = 86%; ^{1}H NMR: $\delta = 7.4-7.1$ (m, 5 H), 3.8 (dd, $J = 9.5$, 8.1 Hz, 1H), 3.6 (m, 2H), 3.3 (dd, $J = 9.0$, 8.1 Hz, 1H), 2.0 (m, 1H), 1.3 (d, $J = 6.1$ Hz, 3H), 1.0 (d, $J = 7.9$ Hz, 3H), 0.9 (d, $J = 7.9$ Hz, 3H), 0.8 (s, 9H); ^{13}C NMR: $\delta = 164.8$ (s), 138.1 (s), 129.7 (d, 2C), 127.7 (d), 127.6 (d, 2C), 75.5 (d), 70.5 (s), 69.5 (d), 67.8 (t), 33.1 (s), 30.0 (d), 25.9 (q, 3C), 24.2 (d), 23.0 (q), 22.8 (q), 12.3 (q); HRMS *m*/*z* calcd for $C_{20}H_{29}NO_2$ 315.2198; found 315.2201. Anal. Calcd for $C_{20}H_{29}NO_2$: C 76.15, H 9.27, N 4.44. Found: C 75.97, H 9.49, N 4.31.

Hydrogenolysis of Cyclopropanes 4, 12, and 13. General Procedure. A suspension of Pd/C (10%, 106 mg, 0.1 mmol) in 20 mL of THF was saturated with hydrogen. Then, triethylamine (0.1 mL, 0.7 mmol) and the corresponding cyclopropane **4a,c,g** (1 mmol) were added, and the mixture was treated with hydrogen at atmospheric presure. After vigorous stirring for 12 h, the mixture was filtered over Celite, the solvent was removed, and the crude product was purified by column chromatography (silica gel, hexanes/AcOEt, 1:1).

(1*S*,2*S*)/(1*R*,2*R*)-3-(4,4-Dimethyl-2-oxazolin-2-yl)-1-methoxy-2-methyl-1-phenylpropane (5a): obtained as a single diastereoisomer; oil; yield = 93%; ^{1}H NMR: $\delta = 7.4-7.2$ (m, 5 H), 3.8 (s, 2H), 3.7 (d, $J = 7.4$ Hz, 1H), 3.1 (s, 3H), 2.6 (dd, $J = 13.6$, 3.8 Hz, 1H), 2.2 (m, 2H), 1.2 (s, 6H), 0.7 (d, $J = 6.7$ Hz, 3H); ^{13}C NMR: $\delta = 165.4$ (s), 140.0 (s), 128.0 (d, 2C), 127.4 (d), 127.3 (d, 2C), 87.6 (d), 78.6 (t), 66.6 (s), 56.7 (q), 37.3 (d), 31.5 (t), 28.3 (q), 28.2 (q), 15.8 (q); HRMS *m*/*z* calcd for $C_{15}H_{20}NO_2$ $[M-CH_3]^+$ 246.1494; found 246.1496. Anal. Calcd for $C_{16}H_{23}NO_2$: C 73.53, H 8.87, N 5.36. Found: C 73.76, H 8.72, N 5.30.

(1*S*,2*S*)/(1*R*,2*R*)-3-(4,4-Dimethyl-2-oxazolin-2-yl)-1-isopropoxy-2-methyl-1-phenylpropane (5g): obtained as a single diastereoisomer; oil; yield = 90%; ^{1}H NMR: $\delta = 7.3-7.2$ (m, 5 H), 4.1 (d, $J = 6.9$ Hz, 1H), 3.8 (s, 2H), 3.4 (m, 1H), 2.7 (dd, $J = 10.8$, 2.8 Hz, 1H), 2.1(m, 2H), 1.2 (s, 6H), 1.1 (d, $J = 6.2$ Hz, 3H), 1.0 (d, $J = 6.2$ Hz, 3H), 0.8 (d, $J = 6.4$ Hz, 3H); ^{13}C NMR: $\delta = 165.3$ (s), 141.6 (s), 127.7 (d, 2C), 127.2 (d, 2C), 127.0 (d), 87.6 (d), 78.5 (t), 68.6 (d), 66.6 (s), 37.5 (d), 31.1 (t), 28.3 (q), 28.2 (q), 23.2 (q), 20.8 (q), 15.8 (q); HRMS *m*/*z* calcd for $C_{15}H_{20}NO_2$ $[M-C_3H_7]^+$ 246.1494; found 246.1491. Anal. Calcd for $C_{18}H_{27}NO_2$: C 74.70, H 9.40, N 4.84. Found: C 74.88, H 9.36, N 4.91.

(2*S*)/(2*R*)-3-(4,4-Dimethyl-2-oxazolin-2-yl)-2-methoxy-1,2-diphenylpropane (6): obtained as a single diastereoisomer; oil; yield = 95%; ^{1}H NMR: $\delta = 7.4-7.1$ (m, 8 H), 6.9 (m, 2H), 4.0 (s, 2H), 3.5 (d, $J = 13.2$ Hz, 1H), 3.3 (s, 3H), 3.2 (d, $J = 13.2$ Hz, 1H), 2.9 (s, 2H), 1.3 (s, 3H), 1.2 (s, 3H); ^{13}C NMR: $\delta = 162.7$ (s), 142.0 (s), 136.7 (s), 130.8 (d, 2C), 127.8 (d, 2C), 127.4 (d, 2C), 127.1 (d), 126.8 (d, 2C), 126.1 (d), 81.1 (t), 79.0 (s), 66.5 (s), 50.9 (q), 44.7 (t), 33.2 (t), 28.1 (q, 2C); HRMS *m*/*z* calcd for $C_{20}H_{22}NO_2$ $[M-CH_3]^+$ 308.1650; found 308.1646. Anal. Calcd for $C_{21}H_{25}NO_2$: C 77.98, H 7.79, N 4.33. Found: C 77.79, H 7.71, N 4.31.

(1*S*,2*S*)-3-[(4*S*)-4-Isopropyl-2-oxazolin-2-yl]-1-methoxy-2-methyl-1-phenylpropane (14a): obtained as a mixture of diastereoisomers (**14a**/**15a**, 77:23); oil; yield = 92%; ^{1}H NMR: $\delta = 7.4-7.2$ (m, 5 H), 4.2 (m, 1H), 3.9 (m, 3H), 3.1 (s, 3H), 2.7 (m, 1H), 2.2 (m, 2H), 1.7 (m, 1H), 1.0 (d, $J = 6.4$ Hz, 3H), 0.9 (d, $J = 6.8$ Hz, 3H), 0.7 (d, $J = 6.4$ Hz, 3H); ^{13}C NMR: $\delta = 166.5$ (s), 140.1 (s), 128.0 (d, 2C), 127.4 (d, 3C), 87.6 (d), 71.8 (d), 69.5 (t), 56.7 (q), 37.3 (d), 32.5 (d), 31.4 (t), 18.7 (q), 18.0 (q), 15.9 (q); HRMS *m*/*z* calcd for $C_{16}H_{22}NO_2$ $[M-CH_3]^+$ 260.1650; found 260.1648. Anal. Calcd for $C_{17}H_{25}NO_2$: C 74.14, H 9.15, N 5.09. Found: C 74.35, H 9.11, N 5.13.

(1*S*,2*S*)-1-Isopropoxy-3-[(4*S*)-4-isopropyl-2-oxazolin-2-yl]-2-methyl-1-phenylpropane (14d): obtained as a mixture of diastereoisomers (**14d**/**15d**, 88:12); oil; yield = 94%; ^{1}H NMR: $\delta = 7.4-7.1$ (m, 5 H), 4.1 (m, 1H), 4.0 (d, $J = 7.0$ Hz, 1H), 3.9 (m, 2H), 3.4 (m, 1H), 2.7 (d, $J = 11.7$ Hz, 1H), 2.1 (m, 2H), 1.7 (m, 1H), 1.1 (d, $J = 7.0$ Hz, 3H), 1.0 (d, $J = 6.2$ Hz, 3H), 0.9 (d, $J = 6.2$ Hz, 3H), 0.8 (d, $J = 6.2$ Hz, 3H), 0.7 (d, $J = 6.5$ Hz, 3H); ^{13}C NMR: $\delta = 166.8$ (s), 141.7 (s), 127.8 (d, 2C) 127.0 (d, 3C), 82.6 (d), 71.8 (d), 69.5 (t), 68.7 (d), 37.6 (d), 32.5 (d), 31.1 (t), 20.9 (q), 18.7 (q), 18.0 (q), 16.0 (q), 14.4 (q); HRMS *m*/*z* calcd for $C_{19}H_{29}NO_2$ 303.2198; found 303.2195. Anal. Calcd for $C_{19}H_{29}NO_2$: C 75.21, H 9.63, N 4.62. Found: C 74.19, H 9.49, N 4.69.

(1*S*,2*S*)-3-[(4*S*)-4-*tert*Butyl-2-oxazolin-2-yl]-1-methoxy-2-methyl-1-phenylpropane (14e): obtained as a mixture of diastereoisomers (**14e**/**15e**, 78:22); yield = 93%; obtained as well from pure **12e** as a mixture of diastereoisomers (**14e**/**15e**, 93:7); obtained as a single diastereoisomer after recrystallization from pentane; white solid; mp 72−74 °C; $[\alpha]^{20}_D = -102.0$ ($c = 1.02$ in $CHCl_3$); ^{1}H NMR: $\delta = 7.4-7.2$ (m, 5 H), 4.1 (m, 2H), 3.8 (m, 2H), 3.2 (s, 3H), 2.7 (dd, $J = 13.6$, 2.3 Hz, 1H), 2.2 (m, 2H), 0.9 (s, 9H), 0.8 (d, $J = 6.4$ Hz, 3H); ^{13}C NMR: $\delta = 166.5$ (s), 140.6 (s), 128.0 (d, 2C), 127.4 (d, 3C), 87.5 (d), 75.6 (d), 68.1 (t), 56.7 (q), 37.4 (d), 33.5 (s), 31.3 (t), 25.7 (q, 3C), 15.8 (q); HRMS *m*/*z* calcd for $C_{18}H_{27}NO_2$ 289.2042; found 289.2037. Anal. Calcd for $C_{18}H_{27}NO_2$: C 74.70, H 9.40, N 4.84. Found: C 74.86, H 9.36, N 4.78.

(1*S*,2*S*)-3-[(4*S*)-4-*tert*Butyl-2-oxazolin-2-yl]-1-isopropoxy-2-methyl-1-phenylpropane (14f): obtained as a mixture of diastereoisomers (**14f**/**15f**, 91:9); oil; yield = 91%; ^{1}H NMR: $\delta = 7.4-7.2$ (m, 5 H), 4.1 (m, 3H), 3.9 (m, 1H), 3.4 (m, 1H), 2.7 (m, 1H), 2.1 (m, 2H), 1.2 (d, $J = 6.2$ Hz, 3H), 1.1 (d, $J = 6.2$ Hz, 3H), 0.9 (s, 9H), 0.8 (d, $J = 6.2$ Hz, 3H); ^{13}C NMR: $\delta = 166.7$ (s), 141.5 (s), 127.8 (d, 2C), 127.2 (d, 2C), 127.1 (d), 82.5 (d), 75.4 (d), 68.6 (d), 68.0 (t), 37.6 (d), 33.4 (s), 30.9 (t), 25.6 (q, 3C), 23.2 (q), 20.9 (q), 15.8 (q); HRMS *m*/*z* calcd for $C_{17}H_{24}NO_2$ $[M-C_3H_7]^+$ 274.1807; found 274.1804. Anal. Calcd for $C_{20}H_{31}NO_2$: C 75.67, H 9.84, N 4.41. Found: C 75.59, H 9.90, N 4.49.

(2*S*)-1-[(4*S*)-4-Isopropyl-2-oxazolin-2-yl]-2-methoxy-2,3-diphenylpropane (16): obtained as a single diastereoisomer, oil; yield = 96%; $[\alpha]^{20}_D = -59.7$ ($c = 0.64$ in $CHCl_3$); ^{1}H NMR: $\delta = 7.4-6.9$ (m, 10 H), 4.3 (m, 1H), 4.0 (m, 2H), 3.5 (d, $J = 13.1$ Hz, 1H), 3.3 (s, 3H), 3.2 (d, $J = 13.1$ Hz, 1H), 3.0 (s, 2H), 1.8 (m, 1H), 1.0 (d, $J = 6.5$ Hz, 3H), 0.9 (d, $J = 6.5$ Hz, 3H); ^{13}C NMR: $\delta = 163.9$ (s), 141.9 (s), 136.7 (s), 130.8 (d, 2C), 127.8 (d, 2C), 127.3 (d, 2C), 127.1 (d), 126.7 (d, 2C), 126.0 (d), 80.1 (s), 71.8 (d), 69.7 (t), 50.8 (q), 44.8 (t), 32.6 (t), 32.5 (d), 18.7 (q), 18.0 (q); HRMS *m*/*z* calcd for $C_{22}H_{27}NO_2$ 337.2042; found 337.2034. Anal. Calcd for $C_{22}H_{27}NO_2$: C 78.30, H 8.06, N 4.15. Found: C 78.39, H 7.98, N 4.21.

Elaboration of the Oxazoline Moiety. Synthesis of Alcohols 9 and 11. To a solution of compounds **5**, **6**, **14**, or **16** (1 mmol) in CH_2Cl_2 (10 mL), 5% aqueous Na_2CO_3 (10 mL) and CBzCl (1.5 mmol) was added. The mixture was stirred overnight and, after addition of water (50 mL), extracted with CH_2Cl_2. The combined organic phases were washed first with 5% aqueous Na_2CO_3, second with water, and then dried. The solvent was removed and the residue dissolved in toluene (20 mL) and treated with DIBAL-H (1 M toluene, 1.5 mL, 1.5 mmol) at −78 °C (compounds **5** and **14**) or in THF and treated with $LiAlH_4$ (1.5 mmol) (compounds **6** and **16**) at 0 °C. The mixture was allowed to warm and, after stirring for 2 h at room temperature, quenched with H_2O and extracted with Et_2O. The combined organic phases were washed with H_2O and dried. The solvent was removed and the crude purified by column chromatography (silica gel, hexanes/EtOAc 3:1).

(3*S*,4*S*)-4-Methoxy-3-methyl-4-phenylbutan-1-ol (9a): obtained as a single diastereoisomer from crystallized oxazoline **14e**; oil; yield = 71%; $[\alpha]^{20}_D = -113.8$ ($c = 0.65$ in $CHCl_3$); ^{1}H NMR: $\delta = 7.4-7.2$ (m, 5 H), 3.9 (d, $J = 7.9$ Hz, 1H), 3.7 (m, 2H), 3.2 (s, 3H), 2.3 (brs, 1H), 1.9 (m, 2H), 1.6 (m, 1H), 0.7 (d, $J = 6.7$ Hz, 3H); ^{13}C NMR: $\delta = 142.5$ (s), 130.1 (d, 2C), 129.5 (d), 129.4 (d, 2C), 91.0 (d), 60.1 (t), 58.7 (q), 39.3 (d), 38.7 (t), 19.2 (q); HRMS *m*/*z* calcd for $C_{12}H_{18}O_2$ 194.1307; found 194.1316. Anal. Calcd for $C_{12}H_{18}O_2$: C 74.19, H 9.34. Found: C 74.31, H 9.23. HPLC (phenylcarbamate derivative): Chiracel OD-H, hexane/2-propanol, 3:1, flow rate 0.8 mL/min, $t_R = 36.8$ (3*S*,4*S*), $t_R = 48.7$ (3*R*,4*R*).

(3*S*,4*S*)-4-Isopropoxy-3-methyl-4-phenylbutan-1-ol (9b): obtained from **14f**/**15f** as a mixture of diastereoisomers (**9b**/**10b**, 91:9), oil; yield = 75%; ^{1}H NMR: $\delta = 7.4-7.2$ (m, 5 H), 4.1 (d, $J = 7.4$ Hz, 1H), 3.7 (m, 2H), 3.5 (m, 1H), 3.2 (brs, 1H), 1.9 (m, 2H), 1.6 (m, 1H), 1.2 (d, $J = 6.1$ Hz, 3H), 1.1 (d, $J = 6.1$ Hz, 3H), 0.7 (d, $J = 7.9$ Hz, 3H); ^{13}C NMR: $\delta = 141.9$ (s), 128.0 (d, 2C), 127.3 (d, 3C), 83.9 (d), 68.9 (d), 61.1 (t), 38.1 (d), 36.5 (t), 23.2 (q), 20.6 (q), 17.7 (q); HRMS *m*/*z* calcd for $C_{14}H_{22}O_2$ 222.1620; found 222.1620. Anal. Calcd for $C_{14}H_{22}O_2$: C 75.63, H 9.97. Found: C 75.69, H 10.06. HPLC (phenylcarbamate derivative): Chiracel OD-H, hexane/2-propanol, 3:1, flow rate 0.8 mL/min, $t_R = 24.7$ (3*S*,4*S*), $t_R = 48.4$ (3*R*,4*R*).

(3*S*)-3-Methoxy-3-phenyl-4-phenylbutan-1-ol (11): Oil; yield = 74% from **16**; $[\alpha]^{20}_D = -32.9$ ($c = 0.45$ in $CHCl_3$); ^{1}H NMR: $\delta = 7.4-7.1$ (m, 8 H), 6.8 (m, 2H), 3.8 (t, $J = 5.1$ Hz. 2H), 3.3 (s, 3H), 3.2 (s, 2H), 2.5 (brs, 1H), 2.2 (m, 2H); ^{13}C NMR: $\delta = 142.6$ (s), 136.4 (s), 130.2 (d, 2C), 127.9 (d, 2C), 127.6 (d, 2C), 127.0 (d), 126.5 (d, 2C), 126.1 (d), 81.8 (s), 58.7 (t), 50.2 (q), 44.3 (t), 36.0 (t); HRMS *m*/*z* calcd for $C_{15}H_{15}O$ $[M-C_2H_5O]^+$ 211.1123; found 211.1121. Anal. Calcd for $C_{17}H_{20}O_2$: C 79.65, H 7.86. Found: C 79.73, H 7.83. HPLC: Chiracel OD-H, hexane/ethanol, 150:1, flow rate 0.85 mL/min, $t_R = 57.8$ (*S*), $t_R = 63.2$ (*R*).

X-ray Crystal Structure Determination. Data for **14e** were collected on a Nonius CAD4 single-crystal diffractometer. The intensities were measured using the $\omega-2\theta$ scan technique with a scan angle of 1.5° and a variable scan rate with a maximum scan time of 60 s per reflection. The intensity of the primary beam was checked throughout the collection by monitoring three standard reflections every 60 min. On all reflections, profile analysis was performed.[25] Symmetry-equivalent reflections were averaged, and Lorentz and polarization corrections were applied. The structure was solved by direct methods using SHELXS97.[26] Isotropic least-squares refinement on F^2 using SHELXL97.[27] During the final stages of the refinements, all positional parameters and the anisotropic temperature factors of all the non-H atoms were refined. The H-atoms were located by Fourier defference synthesis and refined free or riding with common isotropic thermal parameters. The function minimized was $([\Sigma w F_o^2 - F_c^2)/\Sigma w(F_o^2)]^{1/2}$ where $w = 1/[\sigma^2(F_o^2) + (0.0510P)^2]$ with $\sigma(F_o^2)$ from counting statistics and $P = (\mathrm{Max}(F_o^2, o) + 2^* F_c^2)/3$. Atomic scattering factors were taken from *International Tables for X-ray Crystallography*.[28] Plots were made with the EUCLID package.[29] Geometrical calculations were made with PARST.[30] All calculations were made at the Scientific Computer Centre of the University of Oviedo and on the X-ray group computers.

Table 4. Crystal Data and Structure Refinement for **14e**

identification code	**14e**
empirical formula	$C_{18}H_{27}NO_2$
formula weight	289.41
temperature	200(2) K
wavelength	0.71073 A
crystal system, space group	monoclinic, $P2_1$
unit cell dimensions	$a = 7.407(4)$ Å $b = 12.392(3)$ Å $\beta = 102.58(2)°$ $c = 9.432(6)$ Å
volume	844.9(7) Å^3
Z, calculated density	2, 1.138 Mg/m^3
absorption coefficient	0.073 mm^{-1}
F(000)	316
crystal size	0.30 mm × 0.16 mm × 0.13 mm
θ range for data collection	2.21−25.97°
index ranges	$0 \le h \le 9$, $0 \le k \le 15$, $-11 \le l \le 11$
reflections collected/unique	1871/1736 [*R*(int) = 0.0321]
completeness to $2\theta = 25.97$	100.0%
absorption correction	none
refinement method	full-matrix least-squares on F^2
data/restraints/parameters	1736/1/261
goodness-of-fit on F^2	1.033
final *R* indices [$I > 2\sigma(I)$]	$R_1 = 0.0380$, $wR_2 = 0.0820$
R indices (all data)	$R_1 = 0.1009$, $wR_2 = 0.1015$
largest diff. peak and hole	0.195 and −0.212 e·Å^{-3}

The most relevant crystal and refinement data are collected in Table 4. The unit-cell dimensions were determined from the angular settings of 25 reflections in the range $10 \le \theta \le 15°$. The space group was inferred to be $P2_1$ from systematic absences and structure determination. Absolute configuration was assumed based on the knowledge of configuration of C(3).

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Supporting Information Available: Details and tables for X-ray crystal structures of **14e** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(25) (a) Lehman, M. S.; Larsem, F. K. *Acta Crystallogr. A* **1974**, *30*, 580. (b) Grant, D. F.; Gabe, E.F. *J. Appl. Crystallogr.* **1978**, *11*, 114.

(26) Sheldrick, G. M. *SHELXS-97, Program for the Solution of Crystal Structures*; University of Göttingen, Germany, 1997.

(27) Sheldrick, G. M., *SHELXS-97, Program for the Refinement of Crystal Structures*; University of Göttingen, Germany, 1997.

(28) *International Tables for X-ray Crystallography*; Birmingham: Kynoch Press, 1974; Vol. IV (Present distributor: Kluwer Academic Publishers: Dordrecht).

(29) Spex, A. L. In *Computational Crystallography*; Sayre, D., Ed.; Clarendon Press: Oxford, 1983; p 95.

(30) Nardelli, A. *Comput. Chem.* **1983**, *7*, 95.