Diastereoselectivity in the O–H Insertion Reactions of Rhodium Carbenoids Derived from Phenyldiazoacetates of Chiral Alcohols. Preparation of α-Hydroxy and α-Alkoxy Esters

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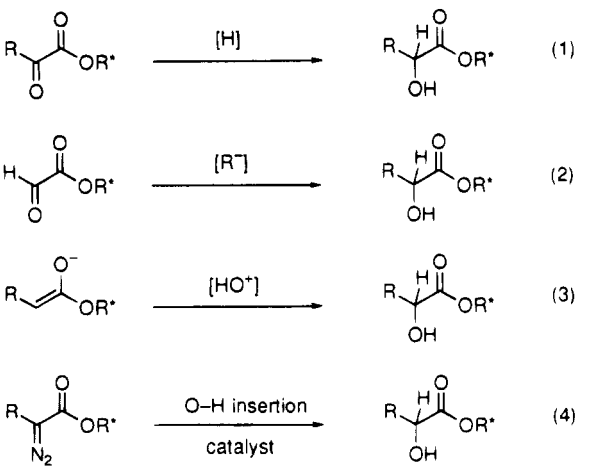
A series of phenyldiazoacetates **3** derived from enantiomerically pure alcohols ((−)-borneol, (+)-menthol, (−)-menthol, (−)-8-phenylmenthol, (−)-*trans*-2-phenylcyclohexanol, (+)-*trans*-2-phenylcyclohexanol, and (−)-10-(dicyclohexylsulfamoyl)-D-isoborneol) were prepared from the corresponding α-keto esters **1** by way of the tosylhydrazones **2**. Rhodium(II)-catalyzed decomposition of the diazoacetates **3** in the presence of water or alcohols resulted in carbenoid O–H insertion reactions to give the corresponding 2-hydroxy- or 2-alkoxyphenylacetates in good yield, but with varying degrees of diastereoselectivity. A range of rhodium(II) and other metal catalysts were investigated, with rhodium(II) acetate and rhodium(II) acetamide giving the best results. The stereochemistry of the major diastereomer was proved in most cases by independent synthesis from a mandelic acid derivative of known configuration. Possible mechanisms are discussed.

Introduction

The synthesis of α-hydroxy and α-alkoxy carboxylic acid derivatives is of considerable importance since such compounds are useful synthetic intermediates for the construction of natural products and other biologically active molecules. Not surprisingly, in recent years much attention has focused on the preparation of this structural unit in enantiomerically pure form, and considerable progress has been achieved in the asymmetric synthesis of α-hydroxy acids and esters using chiral reagents,[1] chiral catalysts,[2] or chiral auxiliaries.[3] Although the use of chiral catalysts may be more efficient, the chiral auxiliary approach is still widely used in the synthesis of α-hydroxy carboxylic acid derivatives.[3] Among the auxiliary-based methods available, those involving diastereoselective reaction at an sp^2-center have been particularly successful. Thus reduction of α-keto esters of chiral alcohols, R*OH, (eq 1) using hydride reagents[4] or catalytic hydrogenation[5] gives the corresponding α-hydroxy esters with good diastereoselectivity. Likewise, addition of carbon nucleophiles to glyoxylate esters of chiral alcohols (eq 2) has proved an equally successful approach; the nucleophiles employed include Grignard reagents,[4a,6] alkenes (with Lewis acids in the ene reaction),[7] and anions of nitroalkanes.[8]

The direct hydroxylation (or acetoxylation) of enolates containing chiral auxiliaries represents an alternative approach (eq 3), although in this case auxiliaries incorporating the amide function such as the Evans oxazolidinone have proved more useful than simple chiral esters.[9]



We have been interested in developing a somewhat different approach to α-hydroxy carboxylic acid derivatives based on the diastereoselective O–H insertion reaction of rhodium carbenoids derived from diazocarbonyl compounds containing chiral auxiliaries (eq 4), and we now report our results in detail.[10]

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(1) For some recent examples, see: Davis, F. A.; Kumar, A.; Chen, B. *Tetrahedron Lett.* **1991**, *32*, 867. Davis, F. A.; Kumar, A. *J. Org. Chem.* **1992**, *57*, 3337. Davis, F. A.; Chen, B.-C. *Chem. Rev.* **1992**, *92*, 919. Rawson, D.; Meyers, A. I. *J. Chem. Soc., Chem. Commun.* **1992**, 494.

(2) For some recent examples, see: Mikami, K.; Terada, M.; Narisawa, S.; Nakai, T. *Synlett* **1992**, 255. Jian-Xin, G.; Zu-Yi, L.; Guo-Qiang, L. *Tetrahedron* **1993**, *49*, 5805.

(3) For relevant reviews on chiral auxiliaries, see: Oppolzer, W. *Tetrahedron* **1987**, *43*, 1969. Whitesell, J. K. *Chem. Rev.* **1992**, *92*, 953.

(4) (a) Whitesell, J. K.; Deyo, D.; Bhattacharya, A. *J. Chem. Soc., Chem. Commun.* **1983**, 803. (b) Solladié-Cavallo, A.; Bencheqroun, M. *Tetrahedron: Asymmetry* **1991**, *2*, 1165. (c) Akiyama, T.; Nishimoto, H.; Ozaki, S. *Tetrahedron Lett.* **1991**, *32*, 1335. (d) Hamon, D. P. G.; Holman, J. W.; Massy-Westropp, R. A. *Tetrahedron: Asymmetry* **1992**, *3*, 1533. (e) Xiang, Y. B.; Snow, K.; Belley, M. *J. Org. Chem.* **1993**, *58*, 993. (f) Monnet, M.-O.; Prévost, P.; Dupas, G.; Bourguignon, J.; Quéguiner, G. *Tetrahedron* **1993**, *49*, 5831. (g) Comins, D. L.; Guerra-Weltzien, L.; Salvador, J. M. *Synlett* **1994**, 972.

(5) Ojima, I.; Kogure, T.; Achiwa, K. *J. Chem. Soc., Chem. Commun.* **1977**, 428.

(6) (a) Whitesell, J. K.; Bhattacharya, A.; Henke, K. *J. Chem. Soc., Chem. Commun.* **1982**, 988. (b) Whitesell, J. K.; Buchanan, C. M. *J. Org. Chem.* **1986**, *51*, 5443.

(7) (a) Whitesell, J. K.; Bhattacharya, A.; Aguilar, D. A.; Henke, K. *J. Chem. Soc., Chem. Commun.* **1982**, 989. (b) Whitesell, J. K.; Chen, H.-H.; Lawrence, R. M. *J. Org. Chem.* **1985**, *50*, 4663. (c) Whitesell, J. K.; Bhattacharya, A.; Buchanan, C. M.; Chen, H. H.; Deyo, D.; James, D.; Liu, C.; Minton, M. A. *Tetrahedron* **1986**, *42*, 2993. (d) Whitesell, J. K.; Nabona, K.; Deyo, D. *J. Org. Chem.* **1989**, *54*, 2258.

(8) Solladié-Cavallo, A.; Khiar, N. *Tetrahedron Lett.* **1988**, *29*, 2189.

(9) (a) Oppolzer, W.; Dudfield, P. *Helv. Chim. Acta* **1985**, *68*, 216. (b) Evans, D. A.; Morrissey, M. M.; Dorow, R. L. *J. Am. Chem. Soc.* **1985**, *107*, 4346. (c) Gamboni, R.; Mohr, P.; Waese-Sarcevic, N.; Tamm, C. *Tetrahedron Lett.* **1985**, *26*, 203.

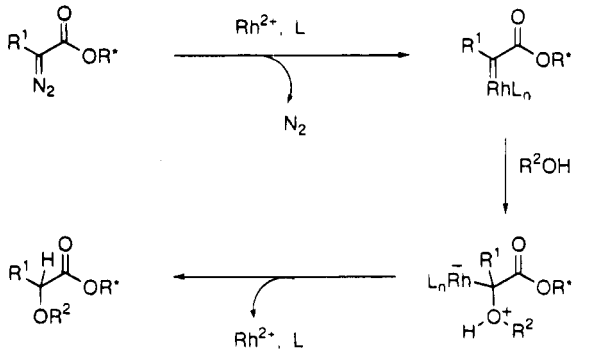
0022-3263/95/1960-4449$09.00/0

Results and Discussion

The ready availability, relative stability, and facile decomposition (under thermal, photochemical, and transition-metal-catalyzed conditions) of diazocarbonyl compounds make them useful intermediates for synthesis. The transition-metal-catalyzed procedure, first discovered almost 90 years ago,[11] is often the method of choice since it takes place under relatively mild conditions. Consequently, synthetic uses of diazocarbonyl compounds have increased dramatically in recent years as a result of the development of new transition-metal catalysts which have supplanted the original catalysts based on copper metal or simple copper(II) salts. Rhodium(II) carboxylates, first introduced by Teyssié and co-workers in the early 1970s,[12] are now widely used since they mediate a wide range of carbenoid transformations such as cyclopropanation, C–H insertion, addition to aromatic rings, and ylide formation.[13] Our own interest in rhodium carbenoid reactivity centers on the so-called X–H insertion process (X = heteroatom; O, N, S, *etc.*), and in particular, O–H insertion,[14] which despite its potential in synthesis has been much less widely studied.[15] Although the rhodium(II)-catalyzed decomposition of diazocarbonyl compounds in the presence of hydroxylic compounds results in the formal insertion of the carbenoid into the O–H bond, it is perhaps better considered as involving initial nucleophilic attack by the alcohol on the highly electrophilic rhodium carbenoid (Scheme 1), although the precise details of the process and, in particular, the stage at which the new metal-free sp^3-center is established remain unknown.[16]

Whatever the mechanism, the utility of the reaction would be significantly enhanced if an "asymmetric version" could be developed, and therefore we were interested in the possibility of using chiral auxiliaries in the ester group (Scheme 1) and/or chiral catalysts to control the stereochemistry of the newly formed tertiary center. Diazocarbonyl compounds containing chiral auxiliaries are known, and, although they have been used in asymmetric cyclopropanations[17] and very recently in Si–H insertion reactions,[18] aside of our own work[10] there is only one report of their use in carbenoid O–H insertion reactions.[18b]

Scheme 1



The diazocarbonyl compounds selected for study were derivatives of phenyldiazoacetic acid, the diazo esters **3a–g** of (−)-borneol, (+)-menthol, (−)-menthol, (−)-8-phenylmenthol, (−)-*trans*-2-phenylcyclohexanol, (+)-*trans*-2-phenylcyclohexanol, and (−)-10-(dicyclohexylsulfamoyl)-D-isoborneol, respectively.

Initial attempts to prepare these diazo esters by diazo-transfer to the corresponding phenylacetates, $PhCH_2CO_2R^*$, using the *in situ* formylation method (NaH, HCO_2Et, MsN_3),[19] resulted in low yields of products. Therefore they were prepared from the corresponding α-keto esters **1** using the Bamford–Stevens reaction.[19] The α-keto esters themselves were obtained either by heating a mixture of phenylglyoxylic acid and the enantiomerically pure alcohol in toluene in the presence of a catalytic amount of TsOH or by treatment of the alcohol with phenylglyoxylyl chloride in the presence of pyridine (for **1d,g**). Reaction of the α-keto esters **1** with tosylhydrazide gave the tosylhydrazones **2** (52%–98%), which were readily converted into the diazo esters **3** (76%–100%) by treatment with triethylamine in dichloromethane at room temperature (Scheme 2).

The phenyldiazoacetyl derivative **4** of Oppolzer's camphorsultam was prepared in a single step by reaction of

(10) Some of the results have appeared in preliminary form: Aller, E.; Cox, G. G.; Miller, D. J.; Moody, C. J. *Tetrahedron Lett.* **1994**, *35*, 5949.

(11) Silberrad, O.; Roy, C. S. *J. Chem. Soc.* **1906**, 179.

(12) Paulissen, R.; Reimlinger, H.; Hayez, E.; Hubert, A. J.; Teyssié, P. *Tetrahedron Lett.* **1973**, 2233. Paulissen, R.; Hayez, E.; Hubert, A. J.; Teyssié, P. *Tetrahedron Lett.* **1974**, 607. Hubert, A. J.; Noels, A. F.; Anciaux, A. J.; Teyssié, P. *Synthesis* **1976**, 600. Noels, A. F.; Demonceau, A.; Petiniot, N.; Hubert, A. J.; Teyssié, P. *Tetrahedron* **1982**, *38*, 2733.

(13) For reviews on inter- and intramolecular reactions of diazo compounds catalyzed by transition metals, see: Burke, S. D.; Grieco, P. A. *Org. React.* **1979**, *26*, 361. Doyle, M. P. *Acc. Chem. Res.* **1986**, *19*, 348. Doyle, M. P. *Chem. Rev.* **1986**, *86*, 919. Maas, G. *Top. Curr. Chem.* **1987**, *137*, 75. Adams, J.; Spero, D. M. *Tetrahedron* **1991**, *47*, 1765. Padwa, A.; Hornbuckle, S. F. *Chem. Rev.* **1991**, *91*, 263. Padwa, A.; Krumpe, K. E. *Tetrahedron* **1992**, *48*, 5385. Shapiro, E. A.; Dyatkin, A. B.; Nefedov, O. M. *Russ. Chem. Rev.* **1993**, *62*, 447. Padwa, A.; Austin, D. J. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1797. Ye, T.; McKervey, M. A. *Chem. Rev.* **1994**, *94*, 1091.

(14) (a) Heslin, J. C.; Moody, C. J. *J. Chem. Soc., Perkin Trans. 1* **1988**, 1417. (b) Moody, C. J.; Taylor, R. J. *J. Chem. Soc., Perkin Trans. 1* **1989**, 721. (c) Davies, M. J.; Heslin, J. C.; Moody, C. J. *J. Chem. Soc., Perkin Trans. 1* **1989**, 2473. (d) Davies, M. J.; Moody, C. J.; Taylor, R. J. *J. Chem. Soc., Perkin Trans. 1* **1991**, 1. (e) Davies, M. J.; Moody, C. J. *J. Chem. Soc., Perkin Trans. 1* **1991**, 9. (f) Moody, C. J.; Sie, E.-R. H. B.; Kulagowski, J. J. *Tetrahedron* **1992**, *48*, 3991. (g) Cox, G. G.; Kulagowski, J. J.; Moody, C. J.; Sie, E.-R. H. B. *Synlett* **1992**, 975. (h) Cox, G. G.; Moody, C. J.; Austin, D. J.; Padwa, A. *Tetrahedron* **1993**, *49*, 5109. (i) Moody, C. J.; Sie, E.-R. H. B.; Kulagowski, J. J. *J. Chem. Soc., Perkin Trans. 1* **1994**, 501. (j) Cox, G. G.; Miller, D. J.; Moody, C. J.; Sie, E.-R. H. B.; Kulagowski, J. J. *Tetrahedron* **1994**, *50*, 3195. (k) Cox, G. G.; Haigh, D.; Hindley, R. M.; Miller, D. J.; Moody, C. J. *Tetrahedron Lett.* **1994**, *35*, 3139.

(15) For other examples of O–H, N–H, and S–H insertions, see: Moyer, M. P.; Feldman, P. L.; Rapoport, H. *J. Org. Chem.* **1985**, *50*, 5223. Brunner, H.; Wutz, K.; Doyle, M. P. *Monatsh. Chem.* **1990**, *121*, 755. Rhodium carbenoid N–H insertion reactions are widely used in the synthesis of thienamycin-type antibiotics; for the early work in this area and two recent examples, see: Cama, L. D.; Christensen, B. G. *Tetrahedron Lett.* **1978**, *44*, 4233. Salzmann, T. N.; Ratcliffe, R. W.; Christensen, B. G.; Bouffard, F. A. *J. Am. Chem. Soc.* **1980**, *102*, 6161. Mastalerz, H.; Menard, M. *J. Org. Chem.* **1994**, *59*, 3223. Bouthillier, G.; Mastalerz, H.; Menard, M. *Tetrahedron Lett.* **1994**, *35*, 4689.

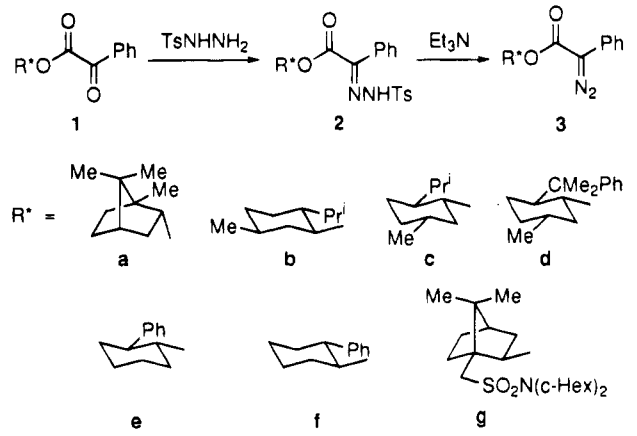
(16) (a) There is no evidence for direct O–H insertion reactions of carbenoids; the more likely mechanisms involve ylide formation or the intermediacy of carbocations. The mechanism of carbene O–H insertion reactions is fully discussed in a recent comprehensive review: Kirmse, W. In *Advances in Carbene Chemistry*; Brinker, U., Ed.; JAI Press: Greenwich, CT, 1994; Vol. 1, p 1. (b) In related work involving the formation (from diazocarbonyl compounds) and subsequent [2,3]-rearrangement of *O*-allyl oxonium ylides, the use of chiral rhodium(II) catalysts results in products with significant enantiomeric excess, perhaps suggesting that the metal is still involved at a late stage in the process: McCarthy, N.; McKervey, M. A.; Ye, T.; McCann, M.; Murphy, E.; Doyle, M. P. *Tetrahedron Lett.* **1992**, *33*, 5983.

(17) Doyle, M. P.; Dorow, R. L.; Terpstra, J. W.; Rodenhouse, R. A. *J. Org. Chem.* **1985**, *50*, 1663. Wilson, S. R.; Venkatesan, A. M.; Augelli-Szafran, C. E.; Yasmin, A. *Tetrahedron Lett.* **1991**, *32*, 2339. Doyle, M. P.; Protopopova, M. N.; Brandes, B. D.; Davies, H. M. L.; Huby, N. J. S.; Whitesell, J. K. *Synlett* **1993**, 151. Davies, H. M. L.; Huby, N. J. S.; Cantrell, W. R.; Olive, J. L. *J. Am. Chem. Soc.* **1993**, *115*, 9468.

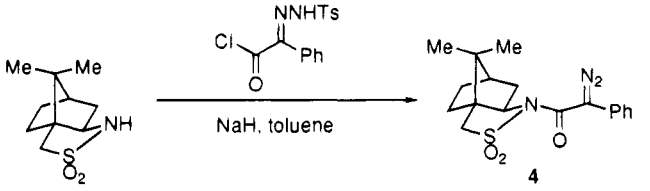
(18) (a) Landais, Y.; Planchenault, D. *Tetrahedron Lett.* **1994**, *35*, 4565. (b) Landais, Y.; Planchenault, D.; Weber, V. *Tetrahedron Lett.* **1994**, *35*, 9549.

(19) Regitz, M.; Maas, G. *Diazo Compounds: Properties and Synthesis*; Academic Press: Orlando, Florida, 1986.

Scheme 2



Scheme 3



the auxiliary with the tosylhydrazone of phenylglyoxylyl chloride (Scheme 3).[20]

The diazo compounds **3g** and **4** were crystalline solids whose structures were confirmed by X-ray crystallography (Figures 1 and 2);[21] for a discussion of the crystal structures, see below.

Rhodium(II) acetate-catalyzed decomposition of the diazo esters **3** in dichloromethane in the presence of the alcohol ROH resulted in rapid evolution of nitrogen and the formation of the carbenoid O−H insertion products **6**−**9** (Table 1). The reactions involving insertion into water were carried out in ether that had been presaturated with water and gave the α-hydroxy esters **5** in good yield.

Decomposition of the diazoamide **4** in the presence of methanol, 2-propanol, or *tert*-butyl alcohol was unsuccessful; no O−H insertion products could be detected in the ^{1}H NMR spectrum of the reaction mixture. Surprisingly a significant amount of the keto sultam **10** was isolated (Scheme 4); indeed in the decompositions of the diazo esters **3**, the starting α-keto ester **1** (which was *not* present in **3**) was a byproduct of the reaction. The origin of these α-keto byproducts is uncertain, but presumably arises by reaction of the carbenoid with oxygen, despite the fact that all reactions were carried out under nitrogen.

In all cases, the insertion products **5**−**9** were formed as mixtures of diastereomers (Table 1), the ratio of which could be determined from the ^{1}H NMR spectrum of the mixture. In the case of the products **5d**−**9d** derived from the 8-phenylmenthyl diazo ester **3d**, the two diastereomers were separable by chromatography; in addition the diastereomers of **6b,c,g** and **8b** were also separable. As well as giving rise to separable diastereomers, the 8-phenylmenthyl diazo ester **3d** generally gave the best

(20) Zimmerman, H. E.; Bunce, R. A. *J. Org. Chem.* **1982**, *47*, 3377.
(21) The authors have deposited atomic coordinates for structures of **3g**, **4**, and **6g** with the Cambridge Crystallographic Data Center. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, U.K.

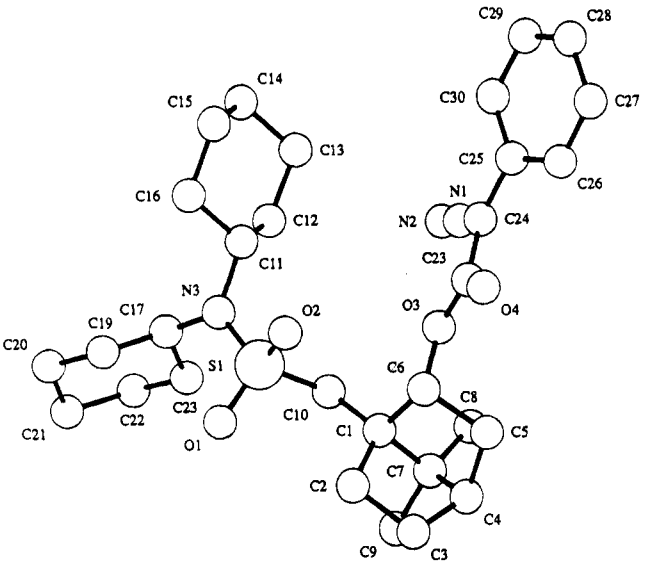


Figure 1. X-ray crystal structure of (−)-10-(dicyclohexylsulfamoyl)-D-isobornyl (2-diazophenyl)acetate, **3g**.

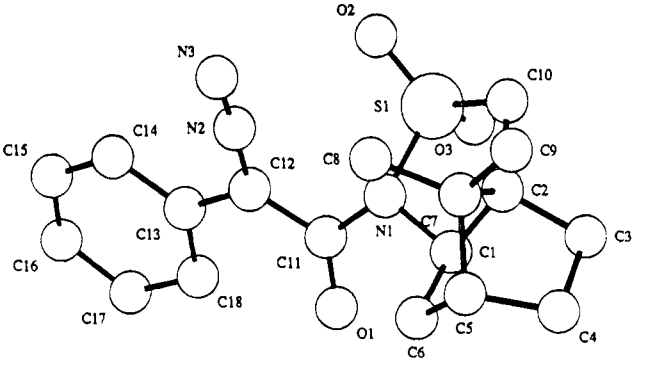


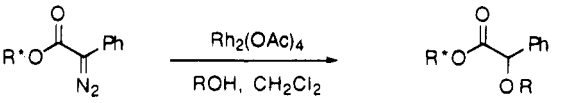
Figure 2. X-ray crystal structure of *N*-(phenyldiazoacetyl)-camphorsultam, **4**.

diastereoeselectivity in its rhodium(II)-catalyzed O−H insertion reactions.

Wherever possible, the stereochemistry of the major diastereomer produced in the O−H insertion reaction was established by an independent and unambiguous synthesis of authentic samples. Thus esterification of (*R*)-mandelic acid with the various chiral alcohols gave the corresponding mandelates thereby confirming the stereochemistry of the major diastereomers formed in the O−H insertion reactions with water. Likewise esterification of commercially available (*S*)-2-methoxy-phenylacetic acid with the various chiral alcohols confirmed the stereochemistry of the major diastereomers **6** formed by insertion into the methanol O−H bond. In the case of 2-isopropoxyphenylacetates **8**, authentic samples of known stereochemistry were prepared by silver(I) oxide-mediated alkylation of the corresponding mandelates with 2-iodopropane. The stereochemistry of the 2-*tert*-butoxyphenylacetates **9** was inferred by comparison of their NMR spectra with the isopropoxy esters **8**.

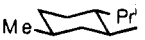
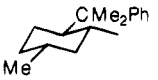
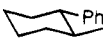
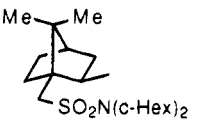
In the case of the major diastereomer **6g** derived from the diazoacetate **3g** of the Oppolzer chiral alcohol, the stereochemistry was proved in two ways. Cleavage of the auxiliary with lithium aluminum hydride gave 2-methoxy-2-phenylethanol in good yield; comparison of its specific rotation with the known value for the (*S*)-enantiomer,[22] proved that the major diastereomer **6g** has (*R*)-stereochemistry. In addition, the minor diastereomer

Table 1. Rhodium(II) Acetate-Catalyzed Decomposition of Diazo Esters 3 in the Presence of Water or Alcohols



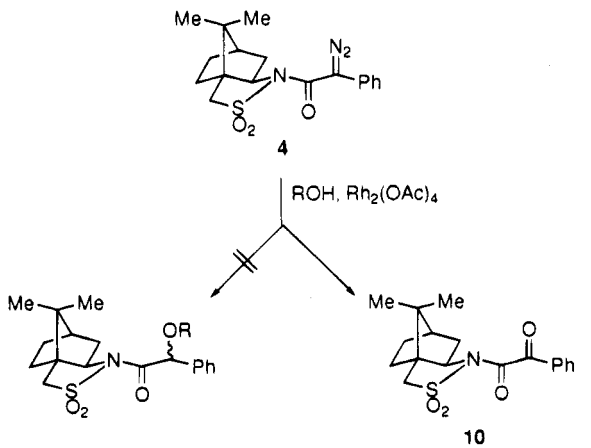
3

5 R = H 8 R = ^{i}Pr
6 R = Me 9 R = ^{t}Bu
7 R = Et

diazo ester	R*	ROH	product	yield (%)	de (%)	major isomer[a]
3a		MeOH	**6a**	95	4	n.d.
		^{i}PrOH	**8a**	95	4	n.d.
		^{t}BuOH	**9a**	70	5	n.d.
3b		H_2O	**5b**	84	1	n.d.
		MeOH	**6b**	75	8	*S*
		^{i}PrOH	**8b**	82	24	*S*
		^{t}BuOH	**9b**	36	14	(*S*)
3c		MeOH	**6c**	83	10	*R*
		^{i}PrOH	**8c**	68	12	*R*
		^{t}BuOH	**9c**	43	14	(*R*)
3d		H_2O	**5d**	79	27	*R*
		MeOH	**6d**	63	44	*R*
		^{i}PrOH	**8d**	85	36	*R*
		^{t}BuOH	**9d**	40	53	(*R*)
3e		H_2O	**5e**	85	50	*S*
		MeOH	**6e**	96	10	*S*
		EtOH	**7e**	95	7	*R*
		^{i}PrOH	**8e**	71	42	*R*
		^{t}BuOH	**9e**	48	16	(*R*)
3f		MeOH	**6f**	68	22	*R*
		^{i}PrOH	**8f**	71	13	*S*
		^{t}BuOH	**9f**	43	17	(*S*)
3g		MeOH	**6g**	98	32	*R*
		^{i}PrOH	**8g**	82	48	(*R*)
		^{t}BuOH	**9g**	37	50	(*R*)

[a] Where the stereochemistry at the α-carbon of the major diastereomer is given in brackets this is inferred by analogy with that resulting from the other nucleophiles used. "n.d.", not determined.

Scheme 4



formed crystals suitable for X-ray crystallography. The structure is shown in Figure 3, and confirms the (*S*)-stereochemistry of the minor diastereomer.[21]

In order to check that the products were configurationally stable under the reaction conditions, the diastereomeric mixture **6e** was resubjected to the reaction conditions, and the diastereomeric ratio remained unchanged within the experimental error of the NMR technique for determining the diastereomeric excess (de).

(22) Otera, J.; Niibo, Y.; Nozaki, H. *Tetrahedron* **1991**, *47*, 7625.

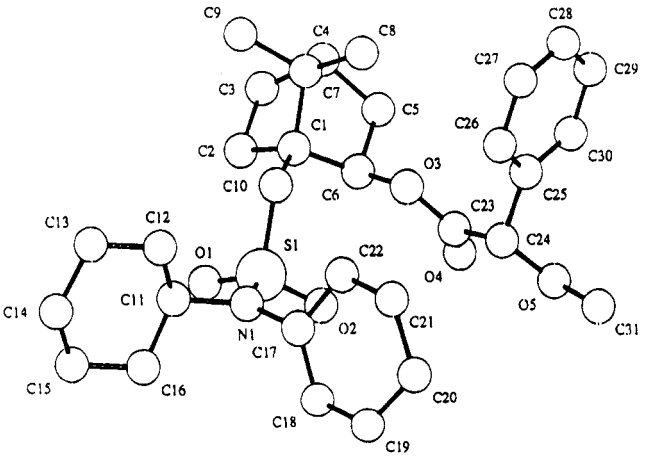
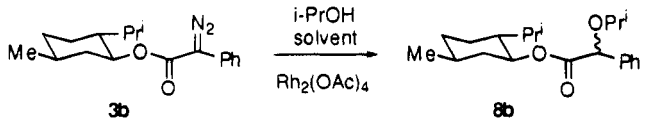


Figure 3. X-ray crystal structure of (−)-10-(dicyclohexylsulfamoyl)-D-isobornyl (*S*)-2-methoxyphenylacetate, **6g**.

The effect of solvent was briefly investigated in the reaction of the diazo ester **3b** with 2-propanol (Table 2). In general, replacing dichloromethane with other solvents led to an increase in side reactions, and no improvement in de was observed. Likewise, lowering the temperature of the reaction (carried out in dichloromethane) to −12 °C resulted in a slight decrease in diastereoselectivity.[23]

The effect of catalyst was also investigated in the reaction of diazo ester **3b** with 2-propanol. A range of

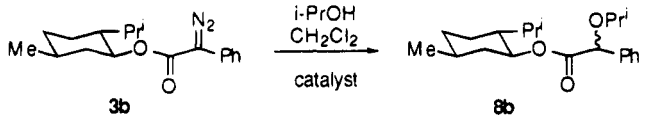
Table 2. Rhodium(II) Acetate-Catalyzed Decomposition of Diazo Ester 3b



3b 8b

solvent	yield (%)	de (%)
CH_2Cl_2	82	24
^iPrOH	56	10
hexane	49	24
THF	43	22
EtOAc	63	16

Table 3. Catalyzed Decomposition of Diazo Ester 3b in Presence of 2-Propanol



3b 8b

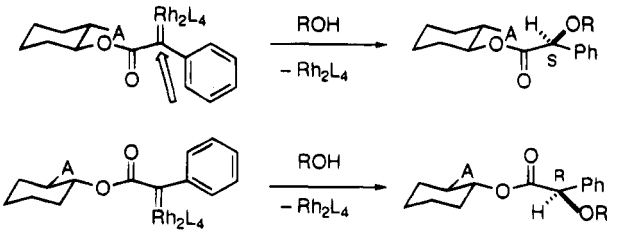
catalyst	yield (%)	de (%)
$Rh_2(OAc)_4$	82	24
$Rh_2(OCOC_{14}H_9)_4$[a]	71	3
$Rh_2(NHAc)_4$	63	24
$Rh_2(NHCOCF_3)_4$	80	22
$Rh_2(NHCOC_3F_7)_4$	57	11
$Cu(OAc)_2$	26	1
$Cu(acac)_2$[b]	45	8
$Cu(hfacac)_2$	45	4
$Cu(OTf)_2$	75	17
CuI·P(OMe)$_3$[b]	54	16
$Ni(acac)_2$[b]	75	17
BF_3·Et_2O	68	17

[a] Dirhodium tetra(9-anthracenecarboxylate). [b] Reaction carried out in 2-propanol at reflux.

rhodium(II) and other catalysts, some of which have been reported to effect O−H insertion reactions, were studied, and the results are summarized in Table 3. None of the alternative conditions proved superior to rhodium(II) acetate; indeed some catalysts proved rather inactive, and the reaction mixture had to be heated before any product formation was observed. Rhodium(III) and rhodium(I) catalysts proved unsatisfactory. Of the other transition metal catalysts tried, those based on copper proved the most satisfactory; dichromium tetraacetate failed to catalyze the reaction, and dimolybdenum tetraacetate gave the expected O−H insertion along with inseparable impurities.

Therefore we have shown that modest diastereoselectivity can be achieved in the O−H insertion reactions of rhodium carbenoids derived from phenyldiazoacetates of chiral alcohols. Although the mechanism of such processes is unknown, one likely possibility is that, by analogy with the diastereoselective nucleophilic attack on α-keto esters of chiral alcohols,[4] the diastereoselectivity arises from nucleophilic attack by the alcohol on the electrophilic rhodium carbenoid from the face opposite the large group, A, on the auxiliary as shown in Scheme 5, leading to the observed configurations at the α-carbon in the major diastereomer. As expected on this basis, use of the 8-phenylmenthyl auxiliary should (and does) give better results than that derived from menthol itself. The conformation of the carbenoid is, of course, unknown, but we assume that it retains the preferred

Scheme 5



trans-arrangement about the ester O−CO bond and the (*S*)-*trans*-conformation of its diazocarbonyl precursor. This particular arrangement is clearly seen in the X-ray crystal structures of the diazocarbonyl compounds **3g** and **4** although it is not necessarily the only conformation present in solution. On this basis the model predicts that the (+)-menthol-based diazo ester **3b** should have the (*S*)-configuration at the new-formed chiral center, whereas the diazo esters **3c−e** should have the (*R*)-configuration at the newly formed chiral center. The reason why the 2-phenylcyclohexanol-based diazo ester **3e** should give different diastereoselectivities according to the nature of the alcohol is not clear, but presumably reflects the different steric demands of water and the various alcohols used in the O−H insertion reaction.

The above analysis assumes that the stereochemistry of the new C−O bond, established in a face-selective attack on a rhodium carbenoid intermediate is retained in the final product. This is of course far from certain since the mechanistic detail of the process is unknown (*cf.* Scheme 1). An alternative possibility is that the observed stereochemistry is established later in the process, and it is perhaps the stage at which the new metal-free sp^3 center is formed that is under control of the chiral auxiliary. However, the fact that the choice of rhodium ligand does affect the diastereoselectivity of the O−H insertion reaction, is perhaps evidence that the metal is involved at the stage at which the new sp^3-center is established.[16b] Unfortunately the results do not distinguish between the possible mechanisms, and the simultaneous occurrence of metal-bound and metal-free pathways in the stereo-differentiating step must also be considered; additional experiments, in particular, involving the use of chiral catalysts, are in hand.

Experimental Section

All coupling constants are given in hertz. ^1H and ^{13}C NMR spectra were recorded in deuteriochloroform at 250 and 62.9 MHz, respectively, unless otherwise stated. In reporting the NMR data for inseparable mixtures of diastereomers, signals arising from the major and minor isomers are reported separately if possible; the integration of signals is consistent within each isomer, *e.g.*, a methyl group is reported as 3H for both isomers even though the peaks are unequal in area when the ratio of isomers is not 1:1. Optical rotations were recorded at 298 K and are reported as specific rotations. For other general experimental points, see ref 14j.

General Procedure for the Preparation of 2-Oxophenylacetates (1). A solution of the chiral alcohol (1.0 mmol), phenylglyoxylic acid (165 mg, 1.1 mmol, 1.1 equiv with respect to the alcohol), and *p*-TsOH (14 mg, 0.075 mmol) in toluene (25 mL) was heated under reflux with azeotropic removal of water. When the reaction was complete (as judged by TLC), the solvent was removed *in vacuo* before the the crude product was purified.

[(1*S*)-*endo*]-Bornyl 2-Oxophenylacetate (1a). Purified by column chromatography (silica gel, CH_2Cl_2/light petroleum ether, 1:1) (91%), colorless prisms, mp 37−38 °C (from Et_2O/light petroleum ether); $[\alpha]_D$ −24.3° (*c* = 0.012, $CHCl_3$); IR

(23) Similar decreases in diastereoselectivity upon lowering the reaction temperature have been noted previously: Marko, I. E.; Chesney, A.; Hollinshead, D. M. *Tetrahedron: Asymmetry* **1994**, *5*, 569.

(Nujol) 1734 and 1691 cm^{-1}; ^{1}H NMR δ 0.90 (3H, s), 0.93 (3H, s), 0.96 (3H, s), 1.28 (3H, m), 1.76 (2H, m), 1.94 (1H, m), 2.50 (1H, m), 5.23 (1H, m,), 7.51 (2H, t, J = 7.5), 7.66 (1H, t, J = 7.5), and 7.99 (2H, d, J = 7.2); ^{13}C NMR δ 13.5, 18.8, 19.6, 26.9, 27.9, 36.5, 44.8, 48.0, 49.1, 82.5, 128.8, 129.8, 132.5, 134.7, 164.5, and 186.7; MS m/z (EI) 286 (M$^+$, 0.1), 137 (100), 105 (56), and 77 (26); HRMS calcd for $C_{18}H_{22}O_3$, 286.1569, found 286.1566.

(1*S*,2*R*,5*S*)-Menthyl 2-Oxophenylacetate (1b). Purified by column chromatography (silica gel, EtOAc/light petroleum ether, 1:4) (96%), colorless prisms, mp 70−71 °C (from Et_2O/light petroleum ether); $[\alpha]_D$ +50.0° (c = 0.012, $CHCl_3$); IR (Nujol) 1732 and 1685 cm^{-1}; ^{1}H NMR δ 0.85 (3H, d, J = 6.8), 0.89 (1H, m), 0.90 (3H, d, J = 7.0), 0.96 (3H, d, J = 6.5), 1.17 (2H, m), 1.53 (2H, m), 1.73 (2H, m), 1.95 (1H, m), 2.18 (1H, m), 5.01 (1H, dt, J = 10.9 and 4.4), 7.51 (2H, m), 7.66 (1H, m), and 7.98 (2H, m); ^{13}C NMR δ 16.1, 20.6, 21.9, 23.3, 26.1, 31.5, 34.0, 40.5, 46.7, 76.9, 128.8, 129.8, 132.5, 134.7, 163.5, and 186.7; MS m/z (EI) 289 (MH$^+$, 6), 288 (M$^+$, 0.1), 139 (100), 105 (60), 77 (30); HRMS calcd for $C_{18}H_{24}O_3$, 288.1725; found, 288.1720.

(1*R*,2*S*,5*R*)-Menthyl 2-Oxophenylacetate (1c). Purified by column chromatography (silica gel, CH_2Cl_2) (90%), colorless prisms, mp 71−72 °C (from Et_2O/light petroleum ether); $[\alpha]_D$ −51.0° (c = 0.020, $CHCl_3$); IR (Nujol) 1732 and 1685 cm^{-1}; ^{1}H NMR δ 0.85 (3H, d, J = 7.0), 0.90 (3H, d, J = 7.0), 0.91 (1H, m), 0.96 (3H, d, J = 6.5), 1.17 (2H, m), 1.53 (2H, m), 1.73 (2H, m), 1.96 (1H, m), 2.18 (1H, m), 5.01 (1H, dt, J = 10.9 and 4.4), 7.51 (2H, m), 7.65 (1H, m), and 7.98 (2H, m); ^{13}C NMR δ 16.1, 20.6, 21.9, 23.3, 26.1, 31.5, 34.0, 40.5, 46.7, 76.8, 128.8, 129.8, 132.6, 134.7, 163.8, and 186.8; MS m/z (EI) 289 (MH$^+$, 7), 288 (M$^+$, 1), 243 (26), 139 (32), 105 (95), and 77 (40); HRMS calcd for $C_{18}H_{24}O_3$, 288.1725; found, 288.1728.

(1*R*,2*S*,5*R*)-8-Phenylmenthyl 2-Oxophenylacetate (1d). Prepared in 99% yield, mp 91−92 °C (lit.[4b] 89−90 °C); $[\alpha]_D$ −8.5° (c = 0.02, $CHCl_3$) (lit.[4b] $[\alpha]_D$ +0.8° (c = 3, CCl_4); ^{1}H NMR δ 0.91 (3H, d, J = 6.3), 1.06 (3H, m), 1.31 (3H, s), 1.36 (3H, s), 1.58 (3H, m), 2.08 (2H, m), 5.03 (1H, dt, J = 10.7, 4.4), 7.00 (1H, t), 7.11 (2H, t), 7.24 (2H, d), 7.49 (2H, t), 7.64 (1H, t), and 7.96 (2H, d).

(1*R*,2*S*)-*trans*-2-Phenylcyclohexyl 2-Oxophenylacetate (1e). Purified by column chromatography (silica gel, Et_2O/light petroleum ether, 1:1) followed by Kugelrohr distillation (bp 190 °C at 0.8 mmHg) to afford a clear oil (94%). The homogeneous ester crystallized on standing at ambient temperature, mp 84−85 °C; $[\alpha]_D$ −11.3° (c = 0.886, $CHCl_3$); IR (neat) 1755 and 1704 cm^{-1}; ^{1}H NMR δ (400 MHz) 1.24−1.43 (1H, m), 1.48−1.68 (2H, m), 1.74−1.87 (1H, m), 1.80−2.23 (2H, m), 2.23−2.27 (2H, m), 2.75 (1H, ddd, J = 12.4, 10.8 and 3.8), 5.39 (1H, dt, J = 4.35 and 10.7), 7.20−7.47 (9H, m), and 7.49 (1H, m); ^{13}C NMR δ (100 MHz) 24.6, 25.5, 32.0, 34.0, 49.7, 78.3, 126.7, 127.7, 128.5, 128.6, 129.6, 131.9, 134.3, 142.6, 163.7, and 187.1; MS m/z (CI) 327 (M + NH_4, 22), 326 (100), 105 (7), and 91 (3); HRMS calcd for $C_{20}H_{20}O_3 + NH_4$, 326.1756; found, 326.1756. Anal. Calcd for $C_{20}H_{20}O_3$: C, 77.9; H, 6.55. Found: C, 77.85; H, 6.45.

(1*S*,2*R*)-*trans*-2-Phenylcyclohexyl 2-Oxophenylacetate (1f). Purified by column chromatography (silica gel, light petroleum/Et_2O, 1:1) followed by Kugelrohr distillation (bp 190 °C at 0.8 mmHg) to give a colorless oil (83%). The homogeneous ester crystallized on standing at ambient temperature, mp 86−87 °C; $[\alpha]_D$ + 11.8° (c = 0.119, MeOH); IR (neat) 1733 and 1689 cm^{-1}; ^{1}H NMR δ 1.41−2.28 (8H, m), 2.77 (1H, dt, J = 12.0 and 3.8), 5.41 (1H, m), and 7.20−7.54 (10H, m); ^{13}C NMR δ 24.5, 25.6, 31.7, 33.6, 49.4, 78.3, 126.7, 127.8, 128.3, 128.6, 128.64, 129.7, 134.4, 142.6, 164.4, and 187.2; MS m/z (EI) 308 (M$^+$, 11), 159 (100), 105 (49), and 77 (15).

(−)-10-(Dicyclohexylsulfamoyl)-D-isobornyl 2-Oxophenylacetate (1g). A mixture of the chiral alcohol (966 mg, 2.43 mmol), phenylglyoxylyl chloride (840 mg, 5 mmol), pyridine (198 mg, 2.5 mmol), DMAP (310 mg, 2.5 mmol), and CH_2Cl_2 (25 mL) was heated under reflux for *ca.* 15 h. The solvent was removed *in vacuo* to afford after purification by column chromatography (silica gel, Et_2O/light petroleum ether, 1:9) the title compound (1.1 g, 86%), which crystallized at room temperature over a period of days, mp 129−132 °C; $[\alpha]_D$ −40.28° (c = 10.08, $CHCl_3$); IR (neat) 1735 and 1687 cm^{-1}; ^{1}H NMR δ (400 MHz) 0.72−0.82 (2H, m), 0.88 (3H, s), 0.90−1.00 (2H, m), 1.04 (3H, m), 1.17−1.27 (7H, m), 1.37−1.40 (9H, m), 1.51−1.74 (2H, m,), 1.75−1.85 (2H, m), 1.90−2.03 (2H, m), 2.06−2.12 (1H, dd, J = 7.96 and 13.88), 2.62 (1H, d, J = 13.32), 3.04−3.11 (2H, m), 3.23 (1H, d, J = 13.32), 5.21 (1H, dd, J = 3.52 and 7.92), 7.44−7.53 (2H, m), 7.57−7.64 (1H, m), and 8.01−8.16 (2H, m); ^{13}C NMR δ (100 MHz) 19.9, 20.2, 24.8, 26.0, 26.1, 26.9, 30.1, 32.3, 32.7, 39.1, 44.4, 49.1, 53.4, 57.2, 80.3, 126.7, 130.3, 132.4, 134.6, 162.2, and 186.1; MS m/z (EI) 529 (M$^+$, 4), 135 (52), 105 (100), 77 (50); HRMS calcd for $C_{30}H_{43}NO_5S$, 529.2862; found, 529.2860.

General Procedure for the Preparation of the Tosylhydrazones (2). A mixture of the α-keto ester **1** (1.57 mmol), tosylhydrazide (307 mg, 1.65 mmol, 1.05 mol equiv with respect to the ester), and toluene (30 mL) was heated under reflux with azeotropic removal of water. When the reaction was complete (absence of the ester by TLC), the solvent was removed *in vacuo* before the hydrazide was purified.

[(1*S*)-*endo*]-Bornyl 2-Oxophenylacetate Tosylhydrazone (2a). Purified by column chromatography (silica gel, CH_2Cl_2) (87%), colorless prisms, mp 161−162 °C (from Et_2O/light petroleum ether); $[\alpha]_D$ −32.5° (c = 0.02, $CHCl_3$); IR (Nujol) 3205 and 1717 cm^{-1}; ^{1}H NMR δ 0.83 (3H, s), 0.86 (3H, s), 0.92 (3H, s), 1.03 (1H, dd, J = 13.9 and 3.4), 1.20 (2H, m), 1.65 (3H, m), 2.40 (3H, s), 2.45 (1H, m), 5.03 (1H, m), 7.33 (5H, m), 7.52 (2H, m), 7.87 (2H, d, J = 8.3), and 11.59 (1H, s); ^{13}C NMR δ 13.5, 18.8, 19.5, 21.5, 27.1, 27.8, 36.8, 44.6, 47.9, 48.8, 83.2, 127.9, 128.5, 129.2, 129.7, 134.0, 135.4, 138.6, 144.3, 162.5, and 186.7; MS m/z (EI) 227 (22), 137 (100), and 91 (38); molecular ion not observed. Anal. Calcd for $C_{25}H_{30}N_2O_4S$: C, 66.05; H, 6.65; N, 6.16. Found: C, 66.00; H, 6.63; N, 6.15.

(1*S*,2*R*,5*S*)-Menthyl 2-Oxophenylacetate Tosylydrazone (2b). Purified by column chromatography (silica gel, CH_2Cl_2/light petroleum ether, 2:1) (92%), colorless prisms, mp 125−126 °C (from Et_2O/light petroleum ether); $[\alpha]_D$ +70.8° (c = 0.012, $CHCl_3$); IR (Nujol) 3207 and 1736 cm^{-1}; ^{1}H NMR δ 0.76 (3H, d, J = 6.8), 0.85 (3H, d, J = 7.0), 0.88 (2H, m), 0.93 (3H, d, J = 6.5), 1.08 (1H, m), 1.45 (2H, m), 1.72 (3H, m), 2.07 (1H, m), 2.41 (3H, s), 4.93 (1H, dt, J = 10.9 and 4.4), 7.35 (5H, m), 7.50 (2H, m), 7.78 (2H, d, J = 8.3), and 11.44 (1H, s); ^{13}C NMR δ 15.9, 20.6, 21.5, 21.9, 23.0, 26.2, 31.4, 33.8, 40.5, 46.6, 77.2, 127.9, 130.0, 128.4, 129.3, 129.7, 134.0, 135.5, 139.0, 144.3, and 161.8; MS m/z (EI) 317 (2), 139 (23), 105 (56), and 83 (100); molecular ion not observed. Anal. Calcd for $C_{25}H_{32}N_2O_4S$: C, 65.76; H, 7.06; N, 6.13. Found: C, 65.88; H, 7.08; N, 6.11.

(1*R*,2*S*,5*R*)-Menthyl 2-Oxophenylacetate Tosylhydrazone (2c). Purified by column chromatography (silica gel, CH_2Cl_2/light petroleum ether, 2:1) (88%), colorless prisms, mp 124−125 °C (from Et_2O/light petroleum ether); $[\alpha]_D$ −73.4° (c = 0.02, $CHCl_3$); IR (Nujol) 3238 and 1719 cm^{-1}; ^{1}H NMR δ 0.75 (3H, d, J = 7.0), 0.84 (3H, d, J = 7.0), 0.88 (2H, m), 0.92 (3H, d, J = 6.5), 1.06 (1H, m), 1.43 (2H, m), 1.71 (3H, m), 2.05 (1H, m), 2.40 (3H, s), 4.92 (1H, dt, J = 10.9 and 4.4), 7.32 (5H, m), 7.50 (2H, m), 7.87 (2H, d, J = 8.3), and 11.41 (1H, s,); ^{13}C NMR δ 15.9, 20.6, 21.5, 21.9, 23.0, 26.2, 31.4, 33.8, 40.5, 46.6, 77.3, 127.9, 129.9, 128.4, 129.3, 129.6, 133.9, 135.5, 139.1, 144.3, and 161.8; MS m/z (EI) 185 (20), 139 (19), 105 (41), and 83 (100); molecular ion not observed. Anal. Calcd for $C_{25}H_{32}N_2O_4S$: C, 65.76; H, 7.06; N, 6.13. Found: C, 65.88; H, 7.08; N, 6.12.

(1*R*,2*S*,5*R*)-8-Phenylmenthyl 2-Oxophenylacetate Tosylhydrazone (2d). Purified by column chromatography (silica gel, CH_2Cl_2/light petroleum ether, 2:1) (90%), colorless prisms, mp 57−58 °C (from Et_2O/light petroleum ether); $[\alpha]_D$ −88.0° (c = 0.02, $CHCl_3$); IR (Nujol) 3207 and 1685 cm^{-1}; ^{1}H NMR δ 0.90 (3H, d, J = 6.4), 1.00 (3H, m), 1.11 (3H, s), 1.17 (3H, s), 1.57 (5H, m), 2.40 (3H, s), 4.99 (1H, dt, J = 10.7 and 4.4), 6.91 (3H, m), 7.05 (2H, m), 7.28 (7H, m), 7.88 (2H, d, J = 8.3), and 11.42 (1H, s); ^{13}C NMR δ 21.5, 21.7, 24.5, 26.5, 28.4, 31.4, 34.2, 39.4, 41.6, 50.4, 76.7, 124.9, 125.6, 127.5, 127.8, 127.9, 128.6, 128.9, 129.6, 133.9, 135.7, 138.3, 144.2, 150.0, and 161.0; MS m/z (EI) 214 (20), 139 (52), 105 (68), and 91

(100); molecular ion not observed. Anal. Calcd for $C_{31}H_{36}N_2O_4S$: C, 69.90; H, 6.81; N, 5.26. Found: C, 69.76; H, 6.92; N, 5.23.

(1*R*,2*S*)-*trans*-2-Phenylcyclohexyl 2-Oxophenylacetate Tosylhydrazone (2e). Purified by column chromatography (silica gel, light petroleum/Et_2O, 3:1) (75%) as an oil (attempted Kugelrohr distillation led to decomposition); $[\alpha]_D$ +104.0° (*c* = 0.90, $CHCl_3$); IR (neat) 3215 and 1688 cm^{-1}; ^1H NMR δ (400 MHz) 1.25–1.39 (2H, m), 1.42–1.61 (2H, m), 1.76–1.79 (1H, m), 1.87–1.96 (2H, m), 2.17–2.21 (1H, m), 2.39 (3H, s), 2.68 (1H, dt, *J* = 12.12 and 3.72), 5.23 (1H, dt, *J* = 4.40 and 10.72), 6.95–6.98 (2H, m), 7.12–7.15 (5H, m), 7.21–7.29 (5H, m), 7.78–7.80 (2H, m), and 10.97 (1H, br s); ^{13}C NMR δ (100 MHz) 21.5, 24.5, 25.4, 31.8, 34.2, 49.3, 79.0, 126.9, 127.3, 127.8, 127.9, 128.2, 128.7, 129.0, 129.6, 133.5, 135.4, 139.0, 142.5, 144.2, and 161.2; MS *m*/*z* (EI) 477 (MH^+, 2), 310 (45), 174 (100), and 139 (86); HRMS calcd for $C_{27}H_{28}N_2O_4S$ + H, 477.1848; found, 477.1848.

(1*S*,2*R*)-*trans*-2-Phenylcyclohexyl 2-Oxophenylacetate Tosylhydrazone (2f). Purified by column chromatography (silica gel, light petroleum/Et_2O, 3:1) (52%); $[\alpha]_D$ −102.0° (*c* = 1.178, MeOH); IR (neat) 3214 and 1724 cm^{-1}; ^1H NMR δ 1.20–1.59 (4H, m), 1.76–1.91 (3H, m), 2.16–2.21 (1H, m), 2.38 (3H, s), 2.67 (1H, dt, *J* = 12.1 and *J* = 3.6), 5.23–5.28 (1H, m), 6.96–7.31 (14H, m), and 10.97 (1H, br s); ^{13}C NMR δ 21.5, 24.6, 25.5, 31.8, 34.2, 49.3, 79.0, 126.9, 127.3, 127.8 (2C), 127.9, 128.2, 128.6, 129.0, 129.6, 133.5, 139.0, 142.5, 144.2, and 161.2; MS *m*/*z* (EI) 292 (2) and 105 (100); molecular ion not observed.

(−)-10-(Dicyclohexylsulfamoyl)-D-isobornyl 2-Oxophenylacetate Tosylhydrazone (2g). Purified by column chromatography (silica gel, light petroleum/Et_2O, 3:1) (74%), colorless crystals, mp 72–75 °C; $[\alpha]_D$ −39.8° (*c* = 1.056, $CHCl_3$); IR (neat) 3208 and 1727 cm^{-1}; ^1H NMR δ (400 MHz) 0.79, 0.82 (each 3H, s), 0.86–1.05 (2H, m), 1.04–1.24 (6H, m), 1.49–1.79 (18H, m), 1.81–1.96 (1H, m), 1.99–2.05 (1H, m), 2.39 (3H, s), 2.58 (1H, d, *J* = 13.36), 2.95 (1H, d, *J* = 13.36), 3.07–3.15 (2H, m), 5.29 (1H, dd, *J* = 2.92 and 8.52), 7.27–7.34 (5H, m), 7.49–7.52 (2H, m), 7.83–7.86 (2H, m), and 11.39 (1H, br s); ^{13}C NMR δ (100 MHz) 20.1, 20.3, 21.6, 25.1, 26.39, 26.41, 27.0, 31.0, 32.6, 39.4, 44.5, 49.2, 49.9, 54.1, 57.7, 80.3, 127.9, 128.0, 128.5, 129.3, 129.7, 134.3, 135.8, 138.7, 144.2, and 161.2; MS *m*/*z* (CI) 531 (8), 380 (100), and 135 (16).

General Procedure for the Preparation of Diazo Esters (3). Triethylamine (25 mg, 0.25 mmol) was added to a stirred solution of the tosylhydrazone **3** (0.223 mmol) in dry CH_2Cl_2 (25 mL). The reaction time varied depending on the nature of the substrate. When all of the tosylhydrazone had been consumed (TLC), the solvent was removed *in vacuo* and the residue was purified by chromatography.

[(1*S*)-*endo*]-Bornyl 2-Diazophenylacetate (3a). Purified by column chromatography (silica gel, CH_2Cl_2/light petroleum ether, 2:1), orange oil (98%); $[\alpha]_D$ −33.3° (*c* = 0.011, $CHCl_3$); IR (neat) 2084 and 1707 cm^{-1}; ^1H NMR δ 0.85 (6H, s), 0.97 (3H, s), 1.24 (1H, dd, *J* = 13.9 and 3.4), 1.32 (2H, m), 1.81 (3H, m), 2.43 (1H, m), 5.08 (1H, m), 7.16 (1H, t, *J* = 7.5), 7.37 (2H, t, *J* = 7.8), and 7.49 (2H, d, *J* = 8.0); ^{13}C NMR δ 13.5, 18.8, 19.6, 27.0, 28.0, 36.9, 44.9, 47.9, 48.9, 80.8, 123.8, 125.6, 128.8, and 162.5; two quaternary carbons are not observed; MS *m*/*z* (EI) 298 (M^+, 4), 105 (35), and 77 (33); HRMS calcd for $C_{18}H_{22}N_2O_2$, 298.1681; found, 298.1679.

(1*S*,2*R*,5*S*)-Menthyl 2-Diazophenylacetate (3b). Purified by column chromatography (silica gel, CH_2Cl_2/light petroleum ether, 2:1), orange oil (90%); $[\alpha]_D$ +67.2° (*c* = 0.012, $CHCl_3$); IR (neat) 2083 and 1701 cm^{-1}; ^1H NMR δ 0.81 (3H, d, *J* = 6.8), 0.88 (1H, m), 0.91 (3H, d, *J* = 7.1), 0.92 (3H, d, *J* = 6.5), 1.05 (2H, m), 1.50 (2H, m), 1.71 (2H, m), 1.92 (1H, m), 2.12 (1H, m), 4.88 (1H, dt, *J* = 10.9 and 4.4), 7.16 (1H, m), 7.37 (2H, m), and 7.49 (2H, m); ^{13}C NMR δ 16.5, 20.7, 22.0, 23.6, 26.5, 31.4, 34.2, 41.3, 47.1, 75.0, 123.8, 125.56, 125.61, 128.8, and 165.0; one quaternary carbon is not observed; MS *m*/*z* (EI) 300 (M^+, 5), 105 (60), 83 (100), and 77 (40); HRMS calcd for $C_{18}H_{24}N_2O_2$, 300.1838; found, 300.1842.

(1*R*,2*S*,5*R*)-Menthyl 2-Diazophenylacetate (3c). Purified by column chromatography (silica gel, CH_2Cl_2/light petroleum ether, 2:1), orange oil (99%); $[\alpha]_D$ −68.0° (*c* = 0.02, $CHCl_3$); IR (neat) 2083 and 1701 cm^{-1}; ^1H NMR δ 0.81 (3H, d, *J* = 6.9), 0.88 (1H, m), 0.91 (3H, d, *J* = 7.0), 0.92 (3H, d, *J* = 6.4), 1.00 (2H, m), 1.50 (2H, m), 1.71 (2H, m), 1.92 (1H, m), 2.12 (1H, m), 4.88 (1H, dt, *J* = 10.9 and 4.4), 7.16 (1H, m), 7.37 (2H, m), and 7.49 (2H, m); ^{13}C NMR δ 16.6, 20.7, 22.0, 23.7, 26.5, 31.5, 34.2, 41.3, 47.2, 75.0, 123.9, 125.6, 125.8, 128.9, and 164.7; one quaternary carbon is not observed; MS *m*/*z* (EI) 300 (M^+, 3), 272 (4), 105 (46), 83 (100), and 77 (26); HRMS calcd for $C_{18}H_{24}N_2O_2$, 300.1838; found, 300.1832.

(1*R*,2*S*,5*R*)-8-Phenylmenthyl 2-Diazophenylacetate (3d). Purified by column chromatography (silica gel, CH_2Cl_2/light petroleum ether, 1:1), orange oil (97%); $[\alpha]_D$ −120.0° (*c* = 2.01, EtOH); IR (neat) 2087 and 1694 cm^{-1}; ^1H NMR δ 0.89 (3H, d, *J* = 6.5), 1.00 (3H, m), 1.24 (3H, s), 1.35 (3H, s), 1.50 (1H, m), 1.72 (2H, m), 1.93 (1H, m), 2.06 (1H, m), 5.07 (1H, dt, *J* = 10.7 and 4.5), 7.17 (6H, m), and 7.31 (4H, m); ^{13}C NMR δ 21.7, 24.4, 26.6, 28.2, 31.4, 34.4, 39.6, 42.3, 50.9, 74.3, 123.7, 125.0, 125.2, 125.4, 125.9, 127.8, 128.7, 151.3, and 164.9; one quaternary carbon is not observed; MS *m*/*z* (EI) 376 (M^+, 0.6), 119 (100), 105 (32), 91 (48), and 77 (18); HRMS calcd for $C_{24}H_{28}N_2O_2$, 376.2151; found, 376.2148.

(1*R*,2*S*)-*trans*-2-Phenylcyclohexyl 2-Diazophenylacetate (3e). Purified by column chromatography (silica gel, Et_2O/light petroleum ether, 1:40), oil (100%); $[\alpha]_D$ −72.4° (*c* = 0.98, $CHCl_3$); IR (neat) 2085 and 1698 cm^{-1}; ^1H NMR δ (400 MHz) 1.31–1.68 (4H, m), 1.79–2.00 (3H, m), 2.26–2.35 (1H, m), 2.71 (1H, ddd, *J* = 3.76, 10.84, 12.32), 5.15 (1H, dt, *J* = 4.32, 10.52), 7.07–7.13 (1H, m), 7.16–7.22 (3H, m), and 7.25–7.31 (6H, m); ^{13}C NMR δ (100 MHz) 24.6, 25.7, 29.6, 32.6, 33.6, 49.7, 77.3, 123.8, 125.5, 125.6, 126.5, 127.4, 128.3, 128.6, 142.9, and 164.4; MS *m*/*z* (EI) 310 (88) and 152 (100); HRMS calcd for $C_{20}H_{20}N_2O_2$, 320.1525; found, 320.1525.

(1*S*,2*R*)-*trans*-2-Phenylcyclohexyl 2-Diazophenylacetate (3f). Purified by column chromatography (silica gel, Et_2O/light petroleum ether, 1:40), oil (76%); $[\alpha]_D$ +73.8° (*c* = 1.016, MeOH); IR (neat) 2085 and 1700 cm^{-1}; ^1H NMR δ 1.31–2.37 (8H, m), 2.76 (1H, dt, *J* = 2.68, 10.26), 5.11 (1H, m), and 7.13–7.35 (10H, m); ^{13}C NMR δ 24.7, 25.8, 32.7, 33.6, 49.8, 77.3, 123.9, 125.5, 125.6, 126.5, 127.5, 128.3 (2C), 142.9, and 164.5; diazo carbon not observed; MS *m*/*z* (EI) 248 (3), 105 (18), 91 (100), and 77 (16); molecular ion not observed.

(−)-10-(Dicyclohexylsulfamoyl)-D-isobornyl 2-Diazophenylacetate (3g). Purified by column chromatography (silica gel, light petroleum/Et_2O, 9:1), yellow crystals (95%), mp 134–136 °C (decomp) (from EtOH); $[\alpha]_D$ −120.88° (*c* = 1.374, $CHCl_3$); IR (neat) 2081 and 1706 cm^{-1}; ^1H NMR δ (400 MHz) 0.89, 0.99 (each 3H, s), 1.12–1.24 (4H, m), 1.48–1.52 (2H, m), 1.66–1.89 (19H, m), 1.96–2.04 (2H, m), 2.68 (1H, d, *J* = 13.31), 3.16 (1H, d, *J* = 13.31), 3.17–3.25 (2H, m), 5.27 (1H, dd, *J* = 3.13, 8.38), 7.13–7.18 (1H, m), 7.22–7.38 (2H, m), and 7.48–7.51 (2H, m); ^{13}C NMR δ (100 MHz) 19.9, 20.3, 25.0, 26.28, 26.31, 26.9, 30.1, 32.5, 32.7, 39.4, 44.6, 49.1, 49.7, 53.7 (CH_2SO_2), 57.4, 78.5, 123.7, 125.1, 128.8, and 163.4; MS *m*/*z* (CI) 531 (32), 514 (52), 380 (100), and 106 (32); molecular ion not observed.

***N*-(Phenyldiazoacetyl)camphorsultam (4).** A solution of bornane-10,2-sultam (0.1 g, 0.46 mmol) in toluene (5 mL) was added dropwise at 5 °C to a stirred suspension of NaH (55%–60% dispersion in mineral oil, 46 mg, 1.15 mmol). After 30 min, a solution of the tosylhydrazone of phenylglyoxylic acid chloride (0.156 g, 0.46 mmol) in toluene (4 mL) was added dropwise, and the mixture was stirred at 5 °C for 72 h and then at room temperature for 15 h. Water was added, and the mixture was extracted with EtOAc. The combined organic layers were dried ($MgSO_4$) and evaporated, and the residue was chromatographed (silica gel, CH_2Cl_2/light petroleum ether, 4:1) to give the title compound (0.85 g, 51%), yellow prisms, mp 122–124 °C; $[\alpha]_D$ −401.4° (*c* = 0.012, $CHCl_3$); IR (Nujol) 2095, 1656 cm^{-1}; ^1H NMR δ 0.96 (3H, s), 1.16 (3H, s), 1.47 (2H, m), 1.93 (5H, m), 3.40 (2H, s), 4.12 (1H, m), 7.22 (1H, m), and 7.40 (4H, m); ^{13}C NMR δ 19.8, 20.3, 31.1, 32.4, 36.8, 44.6, 48.0, 48.4, 52.2, 64.2, 124.4, 124.5, 126.6, 128.9, 134.8, and 163.0; MS *m*/*z* (EI) 359 (M^+), 105 (32), and 91 (12); HRMS calcd for $C_{18}H_{21}N_3O_3S$, 359.1303; found, 359.1314.

General Procedure for the Rhodium(II)-Catalyzed Intermolecular O–H Insertion Reactions. Rhodium(II) acetate (2 mol % equiv with respect to the diazo compound)

was added to a stirred solution of the diazo compound (100 mg) and the alcohol (2 mol equiv with respect to the diazo compound) in dry CH_2Cl_2 (2 mL). The mixture was stirred at room temperature until complete (as determined by TLC). The volatiles were removed by evaporation, and the residue was purified by column chromatography. In the case of water as nucleophile, ether presaturated with water was used as solvent.

Water as Nucleophile. (1*S*,2*R*,5*S*)-Menthyl Mandelate (5b). Mixture of diastereomers (1% de); major diastereomer, (*R*)-mandelate. Purified by column chromatography (silica gel, CH_2Cl_2) (84% overall yield), colorless prisms, mp 86–87 °C (from Et_2O/light petroleum ether); IR (Nujol) 3453, 3415, 2926, and 1731 cm^{-1}; ^1H NMR δ 0.39 (3H, d, J = 6.9), 0.58 (3H, d, J = 6.9), 0.78 (3H, d, J = 6.9), 0.82 (3H, d, J = 6.5), 0.90 (3H, d, J = 7.0), 0.91 (3H, d, J = 6.4), 1.22 (16H, m), 1.85 (1H, m), 2.04 (1H, m), 3.64 (1H, d, J = 6.0, major diastereomer), 3.73 (1H, d, J = 5.5, minor diastereomer), 4.65 (1H, dt, J = 10.9 and 4.4, minor diastereomer), 4.77 (1H, dt, J = 10.9 and 4.4, major diastereomer), 5.10 (1H, d, J = 5.5, minor diastereomer), 5.14 (1H, d, J = 6.0, major diastereomer), and 7.34 (10H, m); ^{13}C NMR δ (major diastereomer) 16.3, 20.6, 21.8, 23.3, 26.2, 31.2, 34.0, 40.0, 46.7, 72.8, 76.4, 126.4, 128.2, 128.4, 138.5, and 173.2; (minor diastereomer) 15.5, 20.4, 21.9, 22.9, 25.3, 31.3, 34.0, 40.6, 47.0, 73.1, 76.5, 126.6, 128.3, 138.6, and 173.4; MS m/z (EI) 291 (MH^+, 21), 290 (M^+, 0.1), 139 (100), and 83 (81); HRMS calcd for $C_{18}H_{26}O_3$, 290.1882; found, 290.1886.

(1*R*,2*S*,5*R*)-8-Phenylmenthyl Mandelate (5d). Mixture of diastereomers (27% de); major diastereomer, (*R*)-mandelate. Separated by column chromatography (silica gel, CH_2Cl_2/light petroleum ether, 2:1) (79% overall yield). Major diastereomer: (1*R*,2*S*,5*R*)-8-phenylmenthyl (*R*)-mandelate, colorless prisms, mp 86–87 °C (from Et_2O/light petroleum ether) (lit.[4b] 83–84 °C); $[\alpha]_D$ −54.2° (c = 0.0065, $CHCl_3$) (lit.[4b] $[\alpha]_D$ −57.6° (c = 5.7, CCl_4)); IR (neat) 3560, 3504, and 1725 cm^{-1}; ^1H NMR δ 0.84 (3H, d, J = 6.5), 0.92 (3H, m), 0.93 (3H, s), 1.05 (3H, s), 1.46 (3H, m), 1.59 (1H, m), 1.92 (1H, m), 2.54 (1H, d, J = 4.0), 4.84 (1H, dt, J = 10.7 and 4.4), 4.84 (1H, d, J = 4.0), and 7.25 (10H, m); ^{13}C NMR δ 21.7, 26.2, 26.4, 26.8, 31.3, 34.3, 39.7, 41.4, 50.2, 73.8, 76.9, 125.4, 125.5, 125.7, 127.0, 127.9, 128.4, 137.7, 150.9, and 171.8; MS m/z (EI) 366 (M^+, 0.1), 119 (100), 105 (65), and 91 (51); HRMS calcd for $C_{24}H_{30}O_3$, 366.2195; found, 366.2188. Minor diastereomer: (1*R*,2*S*,5*R*)-8-phenylmenthyl (*S*)-mandelate, colorless prisms, mp 62–63 °C (from Et_2O/light petroleum ether); $[\alpha]_D$ +33.3° (c = 0.0039, $CHCl_3$); IR (neat) 3513 and 1712 cm^{-1}; ^1H NMR δ 0.63 (1H, m), 0.77 (3H, d, J = 6.3), 0.85 (1H, m), 1.20 (3H, s), 1.33 (3H, s), 1.35 (3H, m), 1.65 (1H, m), 1.86 (1H, m), 2.05 (1H, m), 3.20 (1H, br s), 4.04 (1H, s), 4.85 (1H, dt, J = 10.7 and 4.3), 7.05 (2H, m), 7.22 (4H, m), and 7.34 (4H, m); ^{13}C NMR δ 21.6, 22.6, 26.1, 29.7, 31.1, 34.3, 39.3, 40.6, 50.2, 72.0, 76.0, 125.2, 125.3, 126.3, 127.9, 128.0, 128.1, 138.4, 151.9, and 172.9; MS m/z (EI) 366 (M^+, 0.3), 119 (100), 105 (64), and 91 (22); HRMS calcd for $C_{24}H_{30}O_3$, 366.2195; found, 366.2203.

(1*R*,2*S*)-*trans*-2-Phenylcyclohexyl Mandelate (5e). Mixture of diastereomers (50% de); major diastereomer (*S*)-mandelate. Purified by column chromatography (silica gel, Et_2O) (85% overall yield), bp 160 °C at 2.0 mmHg; $[\alpha]_D$ −23.1° (c = 0.736, MeOH); IR (neat) 3502 and 1729 cm^{-1}; ^1H NMR δ 1.23–1.95 (16H, m), 2.60–2.70 (2H, m), 3.21 (2H, br s), 4.78, 4.92 (each 1H, s), 4.98–5.06 (2H, m), and 6.87–7.29 (20H, m); ^{13}C NMR δ 24.5, 24.6, 25.5, 25.6, 31.6, 32.2, 33.6, 34.0, 49.4, 72.8, 72.8, 78.2, 78.2, 126.1, 126.3, 126.5, 126.6, 127.1, 127.4, 127.7, 128.1, 128.2, 128.4, 128.4, 138.4, 142.2, 142.5, and 172.8; MS m/z 310 (M^+, 1), 204 (22), 91 (100), and 77 (32); HRMS calcd for $C_{20}H_{22}O_3 + NH_4$, 328.1913; found, 328.1913.

Methanol as Nucleophile. [(1*S*)-*endo*]-Bornyl 2-Methoxyphenylacetate (6a). Mixture of diastereomers (4% de); major diastereomer not determined. Purified by column chromatography (silica gel, CH_2Cl_2/light petroleum ether, 2:1) (95), colorless oil, IR (neat) 1748 cm^{-1}; ^1H NMR δ 0.57 (3H, s), 0.64 (1H, dd, J = 13.8 and 3.3), 0.82 (6H, s), 0.84 (3H, s), 0.85 (3H, s), 0.86 (3H, s), 0.97 (1H, m), 1.19 (4H, m), 1.70 (6H, m), 2.28 (2H, m), 3.43 (3H, s), 3.44 (3H, s), 4.77 (1H, s), 4.78 (1H, s), 4.91 (2H, m), 7.35 (6H, m), and 7.45 (4H, m); ^{13}C NMR δ 13.1, 13.4, 18.8, 19.6, 26.8, 27.0, 27.7, 27.9, 36.3, 36.4, 44.6, 44.8, 47.8, 48.7, 48.9, 57.3, 80.5, 80.7, 82.6, 82.7, 127.0, 127.1, 128.5, 128.5, 136.5, 136.7, 170.8, and 170.9; MS m/z (EI) 303 (MH^+, 7), 302 (M^+, 0.5), 137 (71), 121 (100), and 77 (18); HRMS calcd for $C_{19}H_{26}O_3$, 302.1882; found, 302.1873.

(1*S*,2*R*,5*S*)-Menthyl 2-Methoxyphenylacetate (6b). Mixture of diastereomers (8% de); major diastereomer, (*S*)-2-methoxyphenylacetate. Separated by column chromatography (silica gel, CH_2Cl_2/light petroleum ether, 4:1) (75% overall yield). Major diastereomer: (1*S*,2*R*,5*S*)-menthyl (*S*)-2-methoxyphenylacetate, colorless oil, $[\alpha]_D$ +118.8° (c = 0.0064, $CHCl_3$); IR (neat) 1745 cm^{-1}; ^1H NMR δ 0.42 (3H, d, J = 6.9), 0.63 (3H, d, J = 6.9), 0.90 (3H, d, J = 7.2), 0.97 (2H, m), 1.20 (2H, m), 1.46 (1H, m), 1.56 (3H, m), 2.01 (1H, m), 3.41 (3H, s), 4.65 (1H, dt, J = 10.9 and 4.4), 4.71 (1H, s), 7.34 (3H, m), and 7.42 (2H, m); ^{13}C NMR δ 15.5, 20.5, 21.9, 22.9, 25.4, 31.3, 34.1, 40.7, 47.0, 57.2, 75.2, 82.7, 127.2, 128.4, 128.6, 136.3, and 170.2; MS m/z (EI) 305 (MH^+, 10), 304 (M^+, 0.2), 121 (100), and 77 (13); HRMS calcd for $C_{19}H_{28}O_3$, 304.2038; found, 304.2043. Minor diastereomer: (1*S*,2*R*,5*S*)-menthyl (*R*)-2-methoxyphenylacetate, colorless oil, $[\alpha]_D$ +22.8° (c = 0.0057; $CHCl_3$); IR (neat) 1745 cm^{-1}; ^1H NMR δ 0.70 (3H, d, J = 7.0), 0.83 (3H, d, J = 6.9), 0.86 (3H, d, J = 6.9), 0.91 (3H, m), 1.38 (2H, m), 1.64 (2H, m), 1.77 (2H, m), 3.42 (3H, s), 4.74 (1H, dt, J = 10.9 and 4.4), 4.75 (1H, s), 7.34 (3H, m), and 7.44 (2H, m); ^{13}C NMR δ 16.0, 20.6, 21.8, 23.2, 26.1, 31.2, 34.0, 40.1, 46.8, 57.2, 75.0, 82.7, 126.9, 128.4, 128.5, 136.3, and 170.3; MS m/z (EI) 305 (MH^+, 27), 304 (M^+, 0.2), 121 (100); HRMS calcd for $C_{19}H_{28}O_3$, 304.2038; found, 304.2041.

(1*R*,2*S*,5*R*)-Menthyl 2-Methoxyphenylacetate (6c). Mixture of diastereomers (10% de); major diastereomer, (*R*)-2-methoxyphenylacetate. Separated by column chromatography (silica gel, CH_2Cl_2/light petroleum ether, 1:1) (83% overall yield). Major diastereomer: (1*R*,2*S*,5*R*)-menthyl (*R*)-2-methoxyphenylacetate, colorless oil, $[\alpha]_D$ +117.6° (c = 0.0017, $CHCl_3$); IR (neat) 1745 cm^{-1}; ^1H NMR δ 0.43 (3H, d, J = 7.0), 0.64 (3H, d, J = 7.0), 0.89 (3H, d, J = 6.5), 0.92 (2H, m), 1.25 (2H, m), 1.51 (4H, m), 2.00 (1H, m), 3.41 (3H, s), 4.66 (1H, dt, J = 10.9 and 4.4), 4.71 (1H, s), 7.34 (3H, m), and 7.42 (2H, m); ^{13}C NMR δ 15.5, 20.5, 21.9, 22.9, 25.4, 31.3, 34.1, 40.7, 47.0, 57.2, 75.2, 82.7, 127.3, 128.4, 128.5, 136.3, and 170.2; MS m/z (EI) 305 (MH^+, 14), 304 (M^+, 0.2), 167 (34), 139 (39), 121 (100), 83 (46), and 77 (20); HRMS calcd for $C_{19}H_{28}O_3$, 304.2038; found, 304.2040. Minor diastereomer: (1*R*,2*S*,5*R*)-menthyl (*S*)-2-methoxyphenylacetate, colorless oil, $[\alpha]_D$ −21.7° (c = 0.0055, $CHCl_3$); IR (neat) 1745 cm^{-1}; ^1H NMR δ 0.70 (3H, d, J = 7.0), 0.83 (3H, d, J = 6.5), 0.85 (3H, d, J = 6.9), 0.91 (3H, m), 1.38 (2H, m), 1.65 (2H, m), 1.78 (2H, m), 3.42 (3H, s), 4.74 (1H, dt, J = 10.9 and 4.4), 4.75 (1H, s), 7.35 (3H, m), and 7.43 (2H, m); ^{13}C NMR δ 16.0, 20.6, 21.8, 23.2, 26.1, 31.2, 34.1, 40.2, 46.8, 57.2, 75.0, 82.7, 126.9, 128.4, 128.4, 136.3, and 170.3; MS m/z (EI) 305 (MH^+, 14), 304 (M^+, 0.2), 121 (100); HRMS calcd for $C_{19}H_{28}O_3$, 304.2038; found, 304.2041.

(1*R*,2*S*,5*R*)-8-Phenylmenthyl 2-Methoxyphenylacetate (6d). Mixture of diastereomers (44% de); major diastereomer, (*R*)-2-methoxyphenylacetate. Separated by column chromatography (silica gel, EtOAc/light petroleum ether, 1:12) (63% overall yield). Major diastereomer: (1*R*,2*S*,5*R*)-8-phenylmenthyl 2-(*R*)-methoxyphenylacetate, colorless oil, $[\alpha]_D$ −63.6° (c = 0.008, $CHCl_3$); IR (neat) 1741 cm^{-1}; ^1H NMR δ 0.83 (3H, d, J = 6.3), 0.85 (3H, m), 0.91 (3H, s), 1.05 (3H, s), 1.39 (3H, m), 1.84 (1H, m), 1.99 (1H, m), 3.33 (3H, s), 4.53 (1H, s), 4.80 (1H, dt, J = 10.7 and 4.4), 7.11 (3H, m), 7.20 (2H, m), and 7.38 (5H, m); ^{13}C NMR δ 21.8, 23.9, 27.3, 29.5, 31.4, 34.5, 40.1, 41.8, 50.5, 57.2, 73.0, 83.2, 125.3, 125.8, 127.9, 128.1, 128.6, 128.9, 135.8, 150.2, and 169.8; MS m/z (EI) 380 (M^+, 0.6), 121 (100), 105 (80), and 91 (13); HRMS calcd for $C_{25}H_{32}O_3$, 380.2351; found, 380.2356. Minor diastereomer: (1*R*,2*S*,5*R*)-8-phenylmenthyl 2-(*S*)-methoxyphenylacetate, colorless oil, $[\alpha]_D$ +43.1° (c = 0.0052, $CHCl_3$); IR (neat) 1741 cm^{-1}; ^1H NMR δ 0.57 (1H, m), 0.74 (3H, d, J = 6.5), 1.08 (1H, m), 1.13 (1H, m), 1.18 (3H, s), 1.31 (3H, s), 1.49 (3H, m), 1.78 (1H, m), 2.01 (1H, m), 3.27 (3H, s), 3.67 (1H, s), 4.81 (1H, dt, J = 10.7 and 4.4), 7.12 (2H, m), 7.22 (4H, m), and 7.36 (4H, m); ^{13}C NMR δ 21.7, 23.8, 27.2, 29.3, 31.2, 34.3, 40.0, 41.6, 50.3, 57.1, 76.4, 83.1, 125.2, 125.6, 127.8, 127.9, 128.5, 128.8, 135.7, 150.1, and 169.7; MS m/z

(EI) 380 (M^+, 0.4), 121 (100), 105 (80), 91 (45), and 77 (24); HRMS calcd for $C_{25}H_{32}O_3$, 380.2351; found, 380.2356.

(1*R*,2*S*)-*trans*-2-Phenylcyclohexyl 2-Methoxyphenylacetate (6e). Mixture of diastereomers (10% de); major diastereomer, (*S*)-2-methoxyphenylacetate. Purified by column chromatography (silica gel, Et_2O/light petroleum ether, 1:3) (96% overall yield), bp 205 °C at 0.8 mmHg; $[\alpha]_D$ −27.9° (c = 1.72, $CHCl_3$); IR (neat) 1748 cm^{-1}; ^1H NMR δ (400 MHz) 1.25−2.15 (16H, m), 2.67 (2H, m), 3.08 (3H, s), 3.11 (3H, s), 4.42 and 4.51 (each 1H, s), 5.07 (2H, dq, J = 4.44 and 11.20), and 7.00−7.27 (20H, m); ^{13}C NMR δ (100 MHz) 24.5, 24.6, 25.59, 25.63, 31.8, 32.1, 33.8, 34.2, 49.5, 49.6, 56.9, 57.0, 76.7, 77.1, 82.4, 82.5, 126.2, 126.3, 126.5, 126.9, 127.2, 127.5, 128.0, 128.1, 128.2, 128.3, 135.9, 136.1, 142.5, 142.7,169.9, and 170.1; MS m/z (CI) 342 (M + NH_4, 31), 325 (MH^+, 328), and 121 (100); HRMS calcd for $C_{21}H_{24}O_3$ + H, 325.1804; found, 325.1804. Anal. Calcd for $C_{21}H_{24}O_3$: C, 77.75; H, 7.45. Found: C, 77.75; H, 7.5.

(1*S*,2*R*)-*trans*-2-Phenylcyclohexyl 2-Methoxyphenylacetate (6f). Mixture of diastereomers (22% de); major diastereomer, (*R*)-2-methoxyphenylacetate. Purified by column chromatography (silica gel, Et_2O/light petroleum ether, 1:3) (68% overall yield), bp 170 °C at 1.0 mmHg; $[\alpha]_D$ +24.5° (c = 0.858, MeOH); IR (neat) 1731 cm^{-1}; ^1H NMR δ 1.28−1.99 (16H, m), 2.71 (2H, m), 3.10 (3H, s), 3.14 (3H, s), 4.45, 4.54 (each 1H, s), 5.10 (2H, m), and 7.04−7.26 (20H, m); ^{13}C NMR δ 24.5, 24.6, 25.6, 25.7, 31.8, 32.2, 33.9, 34.3, 49.5, 49.6, 57.0, 57.1, 76.7, 76.8, 82.8, 82.5, 126.2, 126.4, 126.6, 126.9, 127.2, 127.5, 127.5, 128.0, 128.2, 128.28, 128.35, 142.6, 142.8, and 170.0; MS m/z 325 (MH^+, 1), 324 (M^+, 1), 121 (100), 91 (93), and 77 (46).

(−)-10-(Dicyclohexylsulfamoyl)-D-isobornyl 2-Methoxyphenylacetate (6g). Mixture of diastereomers (32% de); major diastereomer, (*R*)-2-methoxyphenylacetate. Separated by column chromatography (silica gel, Et_2O/light petroleum ether, 1:3) (98% overall yield). Major diastereomer: mp 145−146 °C, $[\alpha]_D$ −27.9° (c = 0.68, $CHCl_3$); IR (neat) 1731 cm^{-1}; ^1H NMR δ 0.46, 0.77 (each 3H, s), 0.79−0.92 (1H, m), 1.07−1.17 (14H, m), 1.30−1.37 (3H, m), 1.56−1.69 (5H, m), 1.73−1.92 (4H, m), 2.62 (1H, d, J = 13.24), 3.18 (1H, d, J = 13.24), 3.30 (2H, m), 3.45 (3H, s), 4.67 (1H, s), 4.96 (1H, dd, J = 3.36 and 7.80), and 7.29−7.36 (5H, m); ^{13}C NMR δ (100 MHz) 19.3, 20.2, 25.1, 26.5, 26.8, 29.6, 30.1, 32.7, 38.9, 44.2, 48.9, 49.2, 53.8, 57.5, 57.6, 77.1, 79.1, 82.3, 127.2, 128.5, 136.5, 142.0, and 168.8; MS m/z (EI) 563 [M + NH_4^+], 546 [MH^+], 380 (100), and 121 (37); HRMS calcd for $C_{31}H_{47}NO_5S$ + NH_4, 563.3519; found, 563.3520. Minor diastereomer: $[\alpha]_D$ −25.0° (c = 0.64, $CHCl_3$); IR (neat) 1736 cm^{-1}; ^1H NMR δ 0.43, 0.74 (each 3H, s), 0.76−0.85 (1H, m), 1.07−1.13 (2H, m), 1.25−1.33 (6H, m), 1.52−1.66 (6H, m), 1.69−1.87 (12H, m), 2.58 (1H, d, J = 13.24), 3.15 (1H, d, J = 13.24), 3.19−3.29 (2H, m), 3.41 (3H, s), 4.63 (1H, s), 4.93 (1H, dd, J = 3.36 and 7.84), and 7.21−7.47 (5H, m); ^{13}C NMR δ (100 MHz) 19.2, 20.2, 25.1, 26.5, 26.8, 29.6, 30.1, 32.8, 39.0, 44.1, 48.9, 49.2, 53.9, 57.5, 77.2, 79.1, 82.3, 127.3, 128.5, 136.5, and 168.8; MS m/z (CI) 563 [M + NH_4^+], 546 [MH^+], 380 (100), and 121 (43); HRMS calcd for $C_{31}H_{47}NO_5S$ + NH_4, 563.3519; found, 563.3520.

Preparation of (*R*)-(−)-2-Methoxy-2-phenylethanol from 6g. To a stirred solution of the major diastereomer of (−)-10-(dicyclohexylsulfamoyl)-D-isobornyl 2-methoxyphenylacetate (**6g**) (545 mg, 1 mmol) in freshly distilled dry THF (10 mL) was added lithium aluminum hydride (47 mg, 1.25 mmol, 1.25 mol equiv) in one portion. The mixture was stirred rapidly overnight before being quenched the addition of water. The products were extracted into Et_2O which was washed sequentially with water (3 × 25 mL) and brine (2 × 25 mL) before being dried over $MgSO_4$. The solvent was removed before the mixture was separated by column chromatography (SiO_2, Et_2O) to afford the chiral alcohol (321 mg, 81%) and the title compound (99 mg, 65%), $[\alpha]_D$ −117.3° (c = 1.006, EtOH) [lit.[22] for (*S*)-enantiomer, $[\alpha]_D$ +116.9° (c = 2.70, EtOH)]; IR (neat) 3430 (br) cm^{-1}; ^1H NMR δ 2.61 (1H, br s), 3.32 (3H, s) 3.62−3.68 (2H, m), 4.29−4.34 (1H, m), and 7.26−7.43 (5H, m); ^{13}C NMR δ 56.8, 67.3, 84.9, 126.8, 128.1, 128.5, and 138.2.

Ethanol as Nucleophile. (1*R*,2*S*)-*trans*-2-Phenylcyclohexyl 2-Ethoxyphenylacetate (7e). Mixture of diastereomers (7% de); major diastereomer, (*R*)-2-ethoxyphenylacetate. Purified by column chromatography (silica gel, Et_2O/light petroleum ether, 1:3) (95% overall yield), bp 165 °C at 0.5 mmHg; $[\alpha]_D$ −19.2° (c = 1.04, MeOH); IR (neat) 1737 cm^{-1}; ^1H NMR δ 1.12 (6H, t, J = 6.98), 1.45−1.97 (16H, m), 2.17 (2H, m), 2.68−2.74 (4H, m), 4.56, 4.65 (each 1H, s), 5.10 (2H, m), and 7.05−7.29 (20H, m); ^{13}C NMR δ 14.9, 15.0, 24.5, 24.6, 25.6, 25.7, 31.8, 32.1, 33.8, 34.4, 49.5, 49.7, 64.9, 65.1, 76.5, 76.7, 80.7, 81.0, 126.2, 126.4, 126.6, 126.9, 127.2, 127.5, 127.9, 128.1, 128.2, 128.3, 136.6, 136.4, 142.7, 142.8, 170.4, and 170.5; MS m/z (EI) 338 (M^+, 13), 159 (100), and 158 (68); HRMS calcd for $C_{22}H_{26}O_3$ + H, 339.1960; found, 339.1960.

Isopropyl Alcohol as Nucleophile. [(1*S*)-*endo*]-Bornyl 2-Isopropoxyphenylacetate (8a). Mixture of diastereomers (4% de); major diastereomer not determined. Purified by column chromatography (silica gel, CH_2Cl_2/light petroleum ether, 2:1) (95% overall yield), colorless oil, IR (neat) 1749 cm^{-1}; ^1H NMR δ 0.61 (3H, s), 0.68 (1H, dd, J = 13.8 and 3.4), 0.82 (3H, s), 0.84 (3H, s), 0.86 (3H, s), 0.90 (6H, s), 0.93 (1H, dd, J = 13.8 and 3.4), 1.19 (4H, m), 1.21 (3H, d, J = 6.1), 1.22 (3H, d, J = 6.1), 1.27 (3H, d, J = 6.1), 1.28 (3H, d, J = 6.1), 1.69 (6H, m), 2.29 (2H, m), 3.72 (2H, m), 4.90 (2H, m), 4.98 (1H, s), 4.99 (1H, s), 7.32 (6H, m), and 7.47 (4H, m); ^{13}C NMR δ 13.2, 13.5, 18.8, 19.7, 22.0, 22.3, 26.9, 27.1, 27.9, 28.0, 36.5, 44.8, 44.9, 47.9, 48.8, 49.0, 70.8, 70.9, 78.7, 78.8, 80.4, 80.7, 127.1, 127.2, 128.30, 128.34, 128.4, 137.6, 136.8, 171.8, and 171.9; MS m/z (EI) 330 (M^+, 0.4), 149 (100), 95 (11), and 77 (13); HRMS calcd for $C_{21}H_{30}O_3$, 330.2195; found, 330.2194.

(1*S*,2*R*,5*S*)-Menthyl 2-Isopropoxyphenylacetate (8b). Mixture of diastereomers (24% de); major diastereomer, (*S*)-2-isopropoxyphenylacetate. Separated by column chromatography (silica gel, CH_2Cl_2/light petroleum ether, 1:1) (82% overall yield). Major diastereomer: (1*S*,2*R*,5*S*)-menthyl (*S*)-2-isopropoxyphenylacetate, colorless oil, $[\alpha]_D$ +107.5° (c = 0.004, $CHCl_3$); IR (neat) 1748 cm^{-1}; ^1H NMR δ 0.44 (3H, d, J = 6.8), 0.65 (3H, d, J = 6.8), 0.89 (3H, d, J = 6.5), 0.96 (2H, m), 1.20 (3H, d, J = 6.1), 1.26 (3H, d, J = 6.1), 1.27 (2H, m), 1.45 (1H, m), 1.61 (3H, m), 2.00 (1H, m), 3.69 (1H, m), 4.64 (1H, dt, J = 10.9 and 4.4), 4.93 (1H, s), 7.32 (3H, m), and 7.44 (2H, m); ^{13}C NMR δ 15.6, 20.6, 22.0, 22.1, 22.9, 25.4, 31.4, 34.2, 40.8, 47.1, 70.7, 75.0, 78.6, 127.2, 128.3 (2C), 137.5, and 171.1; MS m/z (EI) 333 (MH^+, 3), 332 (M^+, 0.2), 195 (22), 149 (100), and 77 (12); HRMS calcd for $C_{21}H_{32}O_3$, 332.2351; found, 332.2350. Minor diastereomer: (1*S*,2*R*,5*S*)-menthyl (*R*)-2-isopropoxyphenylacetate, colorless oil, $[\alpha]_D$ +36.4° (c = 0.003; $CHCl_3$); IR (neat) 1748 cm^{-1}; ^1H NMR δ 0.68 (3H, d, J = 7.0), 0.84 (6H, d, J = 6.8), 0.99 (2H, m), 1.21 (3H, d, J = 6.1), 1.26 (3H, d, J = 6.1), 1.39 (2H, m), 1.69 (5H, m), 3.70 (1H, m), 4.71 (1H, dt, J = 10.9 and 4.4), 4.96 (1H, s,), 7.32 (3H, m), and 7.45 (2H, m); ^{13}C NMR δ 16.0, 20.6, 21.9, 22.2, 23.2, 26.0, 31.2, 34.1, 40.2, 46.9, 71.1, 74.9, 78.7, 126.8, 128.1, 128.3, 137.3, and 171.2; MS m/z (EI) 333 (MH^+, 31), 332 (M^+, 0.2), 195 (75), and 149 (100); HRMS calcd for $C_{21}H_{32}O_3$, 332.2351; found, 332.2353.

(1*R*,2*S*,5*R*)-Menthyl 2-Isopropoxyphenylacetate (8c). Mixture of diastereomers (12% de); major diastereomer, (*R*)-2-isopropoxyphenylacetate. Purified by column chromatography (silica gel, CH_2Cl_2/light petroleum ether, 1:1) (68%), colorless oil, IR (neat) 1748 cm^{-1}; ^1H NMR δ 0.45 (3H, d, J = 6.8), 0.65 (3H, d, J = 7.0), 0.68 (3H, d, J = 7.0), 0.84 (6H, d, J = 6.8), 0.88 (3H, d, J = 6.5), 0.90 (2H, m), 1.23 (12H, m), 1.45 (13H, m), 2.00 (1H, m), 3.70 (2H, m), 4.66 (2H, m), 4.93 (1H, s), 4.96 (1H, s), 7.28 (6H, m), and 7.44 (2H, m); ^{13}C NMR δ (major diastereomer) 15.5, 20.5, 21.9, 22.1, 22.9, 25.4, 29.6, 31.3, 40.2, 46.9, 70.7, 74.9, 78.6, 126.8, 127.9, 128.3, 137.3, and 171.1; (minor diastereomer) 16.1, 20.6, 21.9, 22.2, 23.3, 26.0, 31.2, 34.1, 40.7, 47.1, 71.0, 74.9, 78.7, 127.2, 128.1, 128.4, 137.5, and 171.2; MS m/z (EI) 333 (MH^+, 2), 332 (M^+, 0.2), 195 (25), 149 (100), and 77 (16); HRMS calcd for $C_{21}H_{32}O_3$, 332.2351; found, 332.2355.

(1*R*,2*S*,5*R*)-8-Phenylmenthyl 2-Isopropoxyphenylacetate (8d). Mixture of diastereomers (36% de); major diastereomer, (*R*)-2-isopropoxyphenylacetate. Separated by column chromatography (silica gel, CH_2Cl_2/light petroleum ether, 1:1) (86% overall yield). Major diastereomer: (1*R*,2*S*,5*R*)-8-phenylmenthyl 2-(*R*)-isopropoxyphenylacetate, colorless oil, $[\alpha]_D$

−55.6° (c = 0.0072, $CHCl_3$); IR (neat) 1743 cm^{-1}; ^1H NMR δ 0.82 (3H, d, J = 6.4), 0.87 (3H, m), 0.97 (3H, s), 1.08 (3H, s), 1.14 (3H, d, J = 6.1), 1.22 (3H, d, J = 6.1), 1.38 (3H, m), 1.82 (1H, m), 1.97 (1H, m), 3.63 (1H, m), 4.74 (1H, s,), 4.74 (1H, dt, J = 10.7 and 4.3), 7.22 (8H, m), and 7.45 (2H, m); ^{13}C NMR δ 21.7, 21.9, 22.2, 23.8, 27.2, 29.6, 31.2, 34.4, 40.1, 41.5, 50.5, 70.5, 76.2, 78.9, 125.2, 125.7, 127.8, 128.3, 128.4, 136.8, 150.1, and 170.4; MS m/z (EI) 408 (M^+, 0.1), 149 (93), 107 (100), 91 (30), and 77 (14); HRMS calcd for $C_{27}H_{36}O_3$, 408.2658; found, 408.2664. Minor diastereomer: (1*R*,2*S*,5*R*)-8-phenylmenthyl 2-(*S*)-isopropoxyphenylacetate, colorless oil, $[\alpha]_D$ +32.5° (c = 0.0031; $CHCl_3$); IR (neat) 1744 cm^{-1}; ^1H NMR δ 0.57 (1H, m), 0.73 (3H, d, J = 6.5), 1.11 (3H, m), 1.12 (3H, d, J = 6.1), 1.18 (3H, s), 1.21 (3H, d, J = 6.1), 1.30 (3H, s), 1.56 (2H, m), 1.72 (1H, m), 1.98 (1H, m), 3.50 (1H, m), 4.05 (1H, s), 4.75 (1H, dt, J = 10.7 and 4.3), 7.14 (2H, m), 7.21 (4H, m), and 7.34 (4H, m); ^{13}C NMR δ 21.6, 22.1, 22.2, 24.0, 26.3, 28.7, 31.1, 34.5, 39.5, 40.4, 50.1, 70.3, 74.9, 77.7, 125.0, 125.4, 127.1, 127.9, 128.0, 128.1, 137.4, 152.1, and 170.3; MS m/z (EI) 409 (MH^+, 8), 408 (M^+, 0.6), 215 (42), and 149 (100); HRMS calcd for $C_{27}H_{36}O_3$, 408.2658; found, 408.2656.

(1*R*,2*S*)-*trans*-2-Phenylcyclohexyl 2-Isopropoxyphenylacetate (8e). Mixture of diastereomers (42% de); major diastereomer, (*R*)-2-isopropoxyphenylacetate. Purified by column chromatography (silica gel, Et_2O/light petroleum ether, 1:9) (71% overall), $[\alpha]_D$ −22.0° (c = 1.56, $CHCl_3$); IR (neat) 1748 cm^{-1}; ^1H NMR δ (400 MHz) 0.98 and 1.02 (each 3H, d, J = 6.08), 1.03 and 1.05 (each 6H, d, J = 6.08), 1.24−2.26 (20H, m, 2.68 (1H, m), 2.74 (1H, m), 3.17 (1H, m, J = 6.1), 3.30 (1H, m, J = 6.12), 4.63 (1H, s), 4.74 (1H, s), 5.07 (2H, m), 7.01−7.34 (19H, m), and 7.43−7.52 (1H, m); ^{13}C NMR δ (100 MHz) 21.3, 21.4, 22.18, 22.22, 24.5, 24.55, 24.6, 25.5, 25.6, 25.7, 31.8, 32.0, 33.8, 34.0, 34.5, 49.8, 49.7, 70.7, 70.8, 76.38, 76.41, 78.2, 78.3, 126.2, 126.3, 126.4, 126.44, 127.1, 127.5, 127.67, 127.72, 128.1, 128.2, 128.2, 128.5, 136.9, 137.0, 142.7, 142.8, 170.8, and 171.0; MS m/z (EI) 353 (MH^+, 30), 326 (29), 212 (100); HRMS calcd for $C_{23}H_{28}O_3$ + H, 353.2117; found, 353.2117.

(1*S*,2*R*)-*trans*-2-Phenylcyclohexyl 2-Isopropoxyphenylacetate (8f). Mixture of diastereomers (13% de); major diastereomer, (*S*)-2-isopropoxyphenylacetate. Purified by column chromatography (silica gel, Et_2O/light petroleum ether, 1:9) (71% overall), $[\alpha]_D$ +20.0° (c = 0.998, MeOH); IR (neat) 1748 cm^{-1}; ^1H NMR δ 1.00−1.10 (12H, m), 1.28−2.15 (16H, m), 2.70 (2H, m), 3.20 (1H, sept, J = 6.9), 3.36 (1H, sept, J = 6.1), 4.67 (1H, s), 4.78 (1H, s), 5.10 (2H, dt, J = 4.2 and 10.7), and 7.06−7.27 (20H, m); ^{13}C NMR δ 21.3, 21.5, 22.2, 22.3, 24.58, 24.62, 24.7, 25.67, 25.73, 31.9, 32.1, 33.9, 34.6, 49.5, 49.8, 70.7, 70.9, 76.4, 76.5, 78.3, 126.2, 126.3, 126.5, 126.9, 127.2, 127.6, 127.7, 127.8, 128.0, 128.2, 128.25, 128.6, 128.6, 129.6, 134.6, 137.1, 143.1, 170.8, and 171.0; MS m/z (EI) 353 (MH^+, 18), 352 (M^+, 1), 195 (24), 107 (100), and 91 (78).

(−)-10-(Dicyclohexylsulfamoyl)-D-isobornyl 2-Isopropoxyphenylacetate (8g). Mixture of diastereomers (48% de); major diastereomer not determined. Purified by column chromatography (silica gel, Et_2O/light petroleum ether, 1:3) (82% overall); $[\alpha]_D$ −15.5° (c = 1.676, $CHCl_3$); IR (neat) 1751 cm^{-1}; ^1H NMR δ (C_6D_6) 0.55 and 0.59 (each 3H, s), 0.73 and 0.92 (each 3H, s), 0.98−1.47 (26H, m), 1.15 (6H, d, J = 6.06), 1.27 (6H, d, J = 6.06), 1.64−2.22 (28H, m), 2.69, 2.77 (each 1H, d, J = 13.16 and 13.40), 3.27−3.44 (6H, m), 3.86 (1H, septet, J = 6.06), 4.01 (1H, septet, J = 6.04), 5.15 (1H, s), 5.17 (1H, s), 5.26 (2H, 2 × d, J = 3.31 and 3.29), 7.07−7.24 (6H, m), and 7.60−7.63 (4H, m); ^1H NMR δ (400 MHz) 0.41 and 0.76 (each 3H, s), 0.88 and 0.91 (each 3H, s), 1.02−1.15 (9H, m), 1.17 (6H, d, J = 6.09), 1.23 (6H, d, J = 6.16), 1.52−1.67 (10H, m), 1.71−2.07 (23H, m), 2.59 (1H, d, J = 13.20), 2.67 (1H, d, J = 13.55), 3.18 (2H, m), 3.21−3.35 (4H, m), 3.72−3.79 (2H, m), 4.89−4.95 (4H, m), 7.25−7.36 (6H, m), and 7.40−7.49 (4H, m); ^{13}C NMR δ (100 MHz) 19.3, 19.9, 20.4, 20.6, 22.1, 22.2, 25.18, 25.23, 26.46, 26.5, 26.58, 26.6, 26.9, 27.0, 29.7, 30.2, 30.3, 32.6, 32.86, 32.94, 33.0, 39.2, 39.7, 44.3, 44.5, 49.0, 49.1, 49.3, 49.6, 53.9, 53.8, 57.6, 57.8, 71.0, 71.1, 78.7, 78.4, 79.4, 79.7, 127.1, 127.5, 128.1, 128.3, 128.5, 137.5, 170.0, and 170.1; MS m/z (EI) 380 (5), 226 (100); HRMS calcd for $C_{33}H_{51}O_5S$ + NH_4, 591.3832; found, 591.3830.

***tert*-Butyl Alcohol as Nucleophile. [(1*S*)-*endo*]-Bornyl 2-*tert*-Butoxyphenylacetate (9a).** Mixture of diastereomers (5% de); major diastereomer not determined. Purified by column chromatography (silica gel, CH_2Cl_2/light petroleum ether, 2:1) (70%), colorless oil; IR (neat) 1754 cm^{-1}; ^1H NMR δ 0.68 (3H, s), 0.80 (3H, s), 0.83 (3H, s), 0.85 (3H, s), 0.86 (6H, s), 1.01 (6H, m), 1.27 (18H, s), 1.66 (4H, m), 1.91 (2H, m), 2.31 (2H, m), 4.87 (2H, m), 5.04 (1H, s), 5.06 (1H, s), 7.29 (6H, m), and 7.46 (4H, m); ^{13}C NMR δ 13.3, 13.4, 18.7, 19.6, 26.9, 27.0, 27.8, 27.9, 28.0, 36.3, 36.4, 44.7, 44.8, 47.8, 48.78, 48.83, 73.8, 74.0, 75.4, 80.2, 80.5, 126.5, 126.63, 127.7, 127.8, 128.2, 138.9, 139.0, 172.9, and 173.0; MS m/z (EI) 345 (MH^+, 10), 344 (M^+, 0.3), 289 (29), 107 (100); HRMS calcd for $C_{22}H_{32}O_3$, 344.2351; found, 344.2354.

(1*S*,2*R*,5*S*)-Menthyl 2-*tert*-Butoxyphenylacetate (9b). Mixture of diastereomers (14% de); major diastereomer not determined. Purified by column chromatography (silica gel, CH_2Cl_2/light petroleum ether, 1:1) (35% overall), colorless oil; IR (neat) 1751 cm^{-1}; ^1H NMR δ 0.49 (3H, d, J = 7.0), 0.66 (3H, d, J = 6.9), 0.70 (3H, d, J = 6.9), 0.82 (3H, d, J = 6.6), 0.85 (3H, d, J = 6.6), 0.88 (3H, d, J = 6.6), 1.26 (9H, s), 1.27 (9H, s), 0.70−2.00 (18H, m), 4.63 (1H, dt, J = 10.8 and 4.3), 4.71 (1H, dt, J = 10.8 and 4.3), 5.00 (1H, s), 5.05 (1H, s), 7.30 (6H, m), and 7.45 (4H, m); ^{13}C NMR δ (major diastereomer) 15.7, 20.6, 22.0, 23.0, 25.5, 28.0, 31.4, 34.2, 40.2, 47.1, 74.1, 74.8, 75.5, 126.8, 127.9, 128.2, 138.9, and 172.3; (minor diastereomer) 15.9, 20.7, 22.0, 23.2, 25.9, 27.9, 31.3, 34.2, 40.5, 47.0, 73.9, 74.7, 75.5, 126.4, 127.8, 128.2, 138.8, and 172.4; MS m/z (EI) 346 (M^+, 0.2), 163 (55), 121 (21), 107 (100); HRMS calcd for $C_{22}H_{34}O_3$, 346.2508; found, 346.2507.

(1*R*,2*S*,5*R*)-Menthyl 2-*tert*-Butoxyphenylacetate (9c). Mixture of diastereomers (14% de); major diastereomer not determined. Purified by column chromatography (silica gel, CH_2Cl_2/light petroleum ether, 1:1) (43% overall), colorless oil; IR (neat) 1748 cm^{-1}; ^1H NMR δ 0.49 (3H, d, J = 7.0), 0.66 (3H, d, J = 6.9), 0.70 (3H, d, J = 6.9), 0.82 (3H, d, J = 6.6), 0.85 (3H, d, J = 6.6), 0.88 (3H, d, J = 6.6), 1.26 (9H, s), 1.27 (9H, s), 1.50 (17H, m), 1.97 (1H, m), 4.63 (1H, dt, J = 10.8 and 4.3), 4.71 (1H, dt, J = 10.8 and 4.3), 5.01 (1H, s), 5.05 (1H, s), 7.31 (6H, m), and 7.45 (4H, m); ^{13}C NMR δ (major diastereomer) 15.6, 20.6, 22.0, 23.0, 25.5, 28.0, 31.3, 34.2, 40.2, 47.1, 74.1, 74.8, 75.5, 126.8, 127.9, 128.2, 138.9, and 172.3; (minor diastereomer) 15.9, 20.7, 21.9, 23.1, 25.8, 27.9, 31.3, 34.2, 40.5, 47.0, 73.8, 74.7, 75.5, 126.4, 127.8, 128.2, 139.0, and 172.4; MS m/z (EI) 346 (M^+, 0.4), 163 (58), 121 (27), 107 (100); HRMS calcd for $C_{22}H_{34}O_3$, 346.2508; found, 346.2506.

(1*R*,2*S*,5*R*)-8-Phenylmenthyl 2-*tert*-Butoxyphenylacetate (9d). Mixture of diastereomers (53% de); major diastereomer, (*R*)-2-*tert*-butoxyphenylacetate. Separated by column chromatography (silica gel, CH_2Cl_2/light petroleum ether, 1:1) (40% overall yield). Major diastereomer: (1*R*,2*S*,5*R*)-8-phenylmenthyl 2-(*R*)-*tert*-butoxyphenylacetate, colorless oil, $[\alpha]_D$ −27.8° (c = 0.0071, $CHCl_3$); IR (neat) 1746 cm^{-1}; ^1H NMR δ 0.82 (3H, d, J = 6.3), 0.86 (3H, m), 1.06 (3H, s), 1.12 (3H, s), 1.22 (9H, s), 1.32 (3H, m), 1.85 (2H, m), 4.73 (1H, dt, J = 10.6 and 4.3), 4.82 (1H, s), 7.23 (8H, m), and 7.46 (2H, m); ^{13}C NMR δ 21.7, 23.7, 27.2, 28.1, 29.7, 31.2, 34.4, 40.1, 41.1, 50.5, 74.5, 75.6, 75.9, 125.1, 125.7, 127.4, 127.8, 128.0, 128.2, 138.5, 150.3, and 171.3; MS m/z (EI) 422 (M^+, 0.8), 215 (53), 107 (100), 91 (38); HRMS calcd for $C_{28}H_{38}O_3$, 422.2821; found, 422.2828. Minor diastereomer: (1*R*,2*S*,5*R*)-8-phenylmenthyl 2-(*S*)-*tert*-butoxyphenylacetate, colorless oil, IR (neat) 1746 cm^{-1}; ^1H NMR δ 0.60 (1H, m), 0.74 (1H, d, J = 6.5), 0.96 (2H, m), 1.17 (3H, s), 1.20 (9H, s), 1.28 (3H, s), 1.46 (6H, m), 1.99 (1H, m), 4.41 (1H, s), 4.70 (1H, dt, J = 10.7 and 4.2), 7.21 (6H, m), and 7.31 (4H, m); ^{13}C NMR δ 21.7, 25.5, 26.7, 27.6, 28.1, 31.1, 34.6, 39.7, 40.4, 50.1, 73.3, 75.3, 75.7, 125.1, 125.5, 126.8, 127.5, 127.96, 127.99, 139.1, 152.0, and 171.4; MS m/z (EI) 422 (M^+, 0.2), 215 (26), 119 (100), and 91 (30); HRMS calcd for $C_{28}H_{38}O_3$, 422.2821; found, 422.2816.

(1*R*,2*S*)-*trans*-2-Phenylcyclohexyl 2-*tert*-Butoxyphenylacetate (9e). Mixture of diastereomers (20% de); major diastereomer not determined. Purified by column chromatography (silica gel, Et_2O/light petroleum ether, 1:9) (48% overall); IR (neat) 1751 cm^{-1}; ^1H NMR δ (400 MHz) 0.97 and 1.08 (each 9H, s), 1.27−2.14 (16H, m), 2.73 (2H, m), 4.72, 4.81 (each 1H,

s), 5.07 (2H, m), and 6.94–7.49 (20H, m); ^{13}C NMR δ (100 MHz) 24.5, 25.6, 27.5, 27.5, 31.8, 31.8, 34.1, 34.5, 49.4, 49.6, 73.3, 73.5, 75.3, 76.5, 76.6, 125.9, 126.3, 126.4, 127.2, 127.3, 127.5, 127.5, 128.0, 128.1, 128.2, 128.3, 138.0, 138.3, 142.9, 143.0, 171.9, and 172.2; MS *m/z* (CI) 367 (MH^+, 32) and 328 (100); HRMS calcd for $C_{24}H_{30}O_3$ + NH_4, 384.2539; found, 384.2539.

(1*S*,2*R*)-*trans*-2-Phenylcyclohexyl 2-*tert*-Butoxyphenylacetate (9f). Mixture of diastereomers (17% de); major diastereomer not determined. Purified by column chromatograph (silica gel, Et_2O/light petroleum ether, 1:9) (43% overall); IR (neat) 1751 cm^{-1}; ^{1}H NMR δ 0.90 and 1.00 (each 9H, s), 1.19–2.89 (16H, m), 2.57–2.68 (2H, m), 4.65, 4.75 (each 1H, s), 4.95–5.01 (2H, m), and 6.91–7.17 (20H, m); ^{13}C NMR δ 24.6, 24.7, 25.5, 25.7, 27.5, 27.6, 31.8, 32.1, 34.0, 34.5, 49.5, 49.6, 73.4, 73.5, 76.2, 76.4, 126.1, 126.5, 126.6, 126.8, 126.9, 127.4, 127.5, 127.6, 127.7, 127.9, 128.2, 128.3, 138.2, 138.5, 143.1, 143.2, 172.1, and 172.4; MS *m/z* (EI) 366 (M^+, 2), 163 (78), and 107 (100).

(−)-10-(Dicyclohexylsulfamoyl)-D-isobornyl 2-*tert*-Butoxyphenylacetate (9g). Mixture of diastereomers (50% de); major diastereomer not determined. Purified by column chromatography (silica gel, Et_2O/light petroleum ether, 1:3) (37% overall); $[\alpha]_D$ −12.5° (*c* = 0.48, $CHCl_3$); IR (neat) 1734 cm^{-1}; ^{1}H NMR δ 0.77, 0.84 (each 3H, s), 0.89, 0.90 (each 3H, s), 1.06–1.24 (28H, m), 1.25 (14H, s), 1.59–1.83 (32H, m), 2.51–2.59 (2H, m), 3.05–3.33 (6H, m), 4.96–4.99 (2H, m), 4.98 (1H, s), 5.03 (1H, s), and 7.26–7.48 (10H, m); ^{13}C NMR δ (100 MHz) 19.2, 19.9, 20.3, 20.5, 25.0, 25.1, 26.0, 26.3, 26.4, 26.5, 28.0, 28.2, 29.2, 30.1, 30.6, 32.2, 32.4, 32.7, 53.7, 58.3, 57.5, 57.6, 73.9, 79.4, 80.0, 125.9, 126.7, 127.2, 128.0, 128.1, 128.5, 128.7, 129.7, 142.0, and 172.0; MS *m/z* (CI) 605 (M + NH_4, 12), 533 (8), and 380 (100); HRMS calcd for $C_{34}H_{53}NO_5S$ + NH_4, 605.3988; found, 605.3990.

Independent Synthesis of (*R*)-Mandelates (5). A solution of the chiral alcohol (1.0 mmol), (*R*)-mandelic acid (165 mg, 1.1 mmol, 1.1 equiv with respect to the alcohol), and *p*-TsOH (14 mg, 0.075 mmol) in toluene (25 mL) was heated under reflux with azeotropic removal of water. When the reaction was complete (absence of the alcohol, according to TLC), the solvent was removed *in vacuo* before the the crude product was purified.

(1*S*,2*R*,5*S*)-Menthyl (*R*)-Mandelate (5b). Purified by column chromatography (silica gel, CH_2Cl_2) (89%), colorless prisms, mp 99–100 °C (from Et_2O/light petroleum ether); $[\alpha]_D$ −2.5° (*c* = 0.02, $CHCl_3$); IR (Nujol) 3466, 3433, and 1729 cm^{-1}; ^{1}H NMR δ 0.78 (3H, d, *J* = 6.9), 0.80 (1H, m), 0.82 (3H, d, *J* = 6.5), 0.90 (3H, d, *J* = 7.0), 1.04 (2H, m), 1.38 (2H, m), 1.69 (3H, m), 1.85 (1H, m), 3.58 (1H, d, *J* = 6.0), 4.77 (1H, dt, *J* = 10.9 and 4.4), 5.13 (1H, d, *J* = 6.0), and 7.34 (5H, m); ^{13}C NMR δ 16.3, 20.6, 21.8, 23.4, 26.3, 31.2, 34.0, 40.0, 46.8, 72.8, 76.4, 126.4, 128.2, 128.4, 138.5, and 173.2; MS *m/z* (EI) 291 (MH^+, 16), 290 (M^+, 0.1), 139 (100), and 77 (36); HRMS calcd for $C_{18}H_{26}O_3$, 290.1882; found, 290.1873.

(1*R*,2*S*,5*R*)-8-Phenylmenthyl (*R*)-Mandelate (5d). Purified by column chromatography (silica gel, Et_2O/light petroleum ether, 2:1) (48%), colorless prisms, mp 86–87 °C (lit.[4b] 83–84 °C); $[\alpha]_D$ −54.2° (*c* = 0.024, $CHCl_3$) (lit.[4b] $[\alpha]_D$ −57.6° (*c* = 5.7, CCl_4)). All the spectroscopic data are coincident with those of the sample prepared by the O–H insertion reaction described above.

(1*R*,2*S*)-*trans*-2-Phenylcyclohexyl (*R*)-Mandelate (5e). Purified by column chromatography (silica gel, Et_2O/light petroleum ether, 1:1) (76%), colorless prisms, mp 94–95 °C; $[\alpha]_D$ −67.9° (*c* = 1.002, MeOH); IR (neat) 3438 and 1713 cm^{-1}; ^{1}H NMR δ 1.36–2.32 (8H, m), 2.60 (1H, ddd, *J* = 3.6 and 11.6), 3.20 (1H, br s), 4.96 (1H, s), 5.11 (1H, dt, *J* = 4.50 and 11.60), and 6.90–7.12 (10H, m); ^{13}C NMR δ 24.6, 25.6, 32.2, 34.0, 49.4, 72.8, 78.2, 126.1, 126.3, 127.1, 129.7, 128.2 (2C), 138.0, 142.2, and 173.7; MS *m/z* (CI) 328 (M + NH_4^+, 100), 311 (MH^+, 20), and 159 (70); HRMS calcd for $C_{20}H_{22}O_3$ + NH_4, 328.1913; found, 328.1913.

Independent Synthesis of (*S*)-2-Methoxyphenylacetates (6). A solution of the chiral alcohol (1.0 mmol), an authentic sample of (*S*)-2-methoxyphenylacetic acid (165 mg, 1.1 mmol, 1.1 equiv with respect to the alcohol) (or the *R*-enantiomer or the racemate), and *p*-TsOH (14 mg, 0.075 mmol) in toluene (25 mL) was heated under reflux with azeotropic removal of water. When the reaction was complete (absence of the alcohol, according to TLC), the solvent was removed *in vacuo* before the crude product was purified.

(1*S*,2*R*,5*S*)-Menthyl 2(*S*)-Methoxyphenylacetate (6b). Purified by column chromatography (silica gel, CH_2Cl_2) (91), colorless oil; $[\alpha]_D$ +124.3° (*c* = 0.017, $CHCl_3$). All the spectroscopic data are coincident with those of the sample prepared by the O–H insertion reaction described above.

(1*R*,2*S*,5*R*)-8-Phenylmenthyl 2(*S*)-Methoxyphenylacetate (6d). Purified by column chromatography (silica gel, CH_2Cl_2/light petroleum ether, 1:1) (81%), colorless oil; $[\alpha]_D$ +45.8° (*c* = 0.017, $CHCl_3$). All the spectroscopic data are coincident with those of the sample prepared by the O–H insertion reaction described above.

(1*R*,2*S*)-*trans*-2-Phenylcyclohexyl 2(*R*/*S*)-Methoxyphenylacetate (6e). Purification and characterization as described above with the exception of the diastereomeric ratio and the optical rotation; $[\alpha]_D$ −29.8° (*c* = 1.006, $CHCl_3$); diastereomeric ratio 19% with bias toward the (*S*)-enantiomer.

(1*R*,2*S*)-*trans*-2-Phenylcyclohexyl 2(*S*)-Methoxyphenylacetate (6e). Purified by column chromatography (silica gel, Et_2O/light petroleum ether, 1:3) (98%), colorless oil, bp 220 °C at 2.5 mmHg; $[\alpha]_D$ −5.9° (*c* = 1.008, $CHCl_3$); IR (neat) 1747 cm^{-1}; ^{1}H NMR δ (400 MHz) 1.25–1.59, 1.73–1.81, 1.89–1.98 (8H, m), 2.78 (1H, ddd, *J* = 3.8, 10.9 and 15.4), 3.08 (3H, s), 4.43 (1H, s), 5.09 (1H, dt, *J* = 4.20 and 10.90), and 7.13–7.27 (10H, m); ^{13}C NMR δ (100 MHz) 24.5, 25.6, 31.8, 33.8, 49.6, 57.0, 76.6, 82.4, 126.3, 126.9, 127.5, 128.2 (2C), 128.3, 136.1, 142.8, and 169.9; MS *m/z* (CI) 325 (MH^+, 18), 184 (27), and 121 (100); HRMS calcd for $C_{21}H_{24}O_3$ + H, 325.1804; found, 325.1804. Anal. Calcd for $C_{21}H_{24}O_3$: C, 77.75; H, 7.45. Found: C, 77.75; H, 7.5.

(1*R*,2*S*)-*trans*-2-Phenylcyclohexyl 2(*R*)-Methoxyphenylacetate (6e). Purified by column chromatography (silica gel, Et_2O/light petroleum ether, 1:3) (92%), bp 210 °C at 2.0 mmHg; $[\alpha]_D$ −58.9° (*c* = 1.002, $CHCl_3$); IR (neat) 1748 cm^{-1}; ^{1}H NMR δ (400 MHz) 1.25–1.55, 1.73–1.91, 2.09–2.15 (8H, m), 2.65 (1H, ddd, *J* = 3.7, 11.0 and 12.3), 3.12 (3H, s), 4.51 (1H, s), 5.06 (1H, dt, *J* = 4.48 and 11.00), and 6.99–7.25 (10H, m); ^{13}C NMR δ (100 MHz) 24.6, 25.6, 32.1, 34.2, 49.5, 57.0, 77.1, 82.5, 126.2, 126.5, 127.2, 128.0, 128.1, 128.2, 135.9, 142.5, and 170.1; MS *m/z* (CI) 342 (M + NH_4, 25), 325 (MH^+, 18), and 121 (100); HRMS calcd for $C_{21}H_{24}O_3$ + H, 325.1804; found, 325.1804. Anal. Calcd for $C_{21}H_{24}O_3$: C, 77.75; H, 7.45. Found: C, 77.60; H, 7.45.

Independent Synthesis of (*R*)-2-Isopropoxyphenylacetates (8). The appropriate (*R*)-mandelate **5** (0.86 mmol), prepared by esterification of authentic sample of (*R*)-mandelic acid with the corresponding chiral alcohol, was dissolved in 2-iodopropane (1.17 g, 6.88 mmol), and the resulting solution was treated with silver(I) oxide (0.4 g, 1.72 mmol). The mixture was heated under reflux for about 30 h, after which it was filtered, the filtrate was evaporated, and the crude product was purified by chromatography.

(1*S*,2*R*,5*S*)-Menthyl 2(*R*)-Isopropoxyphenylacetate (8c). Purified by column chromatography (silica gel, CH_2Cl_2) (45%), colorless oil; $[\alpha]_D$ +35.5° (*c* = 0.0214, $CHCl_3$). All the spectroscopic data are coincident with those of the sample prepared by the O–H insertion reaction described above.

(1*R*,2*S*,5*R*)-8-Phenylmenthyl 2(*R*)-Isopropoxyphenylacetate (8d). Purified by column chromatography (silica gel, CH_2Cl_2) (58%), colorless oil; $[\alpha]_D$ −53.6° (*c* = 0.0112, $CHCl_3$). All the spectroscopic data are coincident with those of the sample prepared by the O–H insertion reaction described above.

(1*R*,2*S*)-*trans*-2-Phenylcyclohexyl 2(*R*)-Isopropoxyphenylacetate (8e). Purified by column chromatography (silica gel, Et_2O/light petroleum ether, 1:3) (48%), colorless oil, bp 200 °C at 4.0 mmHg; $[\alpha]_D$ −44.4° (*c* = 1.172, MeOH); IR (neat) 1749 cm^{-1}; ^{1}H NMR δ 1.04 (6H, m), 1.12–2.15 (8H, m), 2.69 (1H, dt, *J* = 3.21 and 10.63), 3.30 (1H, m), 4.74 (1H, s), 5.07 (1H, dt, *J* = 4.41 and 10.63), and 7.03–7.24 (10H, m); ^{13}C NMR δ 21.5, 22.2, 24.6, 25.7, 32.1, 34.6, 49.5, 70.7, 76.5, 78.3, 126.2, 126.5, 127.2, 127.7, 128.2, 128.2, 137.0, 142.8, and 171.0; MS

m/z (CI) 370 ($M + NH_4^+$, 31), 353 (MH^+, 12), 212 (100), and 149 (32); HRMS calcd for $C_{23}H_{28}O_3$ + H, 353.2117; found, 353.2117.

(1*S*,2*R*)-*trans*-2-Phenylcyclohexyl (*R*)-Mandelate (5f). Prepared as described above for its isomer, and purified by column chromatography (silica gel, Et_2O/light petroleum ether, 1:1) (69%), bp 190 °C at 0.5 mmHg, mp 94–95 °C; $[\alpha]_D$ +4.9° (c = 1.024, MeOH); IR (neat) 3502 (br), 3498, and 1731 cm^{-1}; ^1H NMR δ 1.27–1.99 (8H, m), 2.71 (1H, dt, J = 1.0 and 8.3), 3.22 (1H, br s), 4.81 (1H, s), 5.04 (1H, dt, J = 4.4 and 8.3), and 7.20–7.36 (10H, m); ^{13}C NMR δ 24.5, 25.5, 31.6, 33.6, 49.4, 72.7, 78.2, 126.5, 126.6, 127.4, 128.1, 128.36, 128.41, 138.4, 142.6, and 172.6; MS m/z (EI) 311 (MH^+, 64), 310 (M^+), 91 (100), and 77 (27).

(1*S*,2*R*)-*trans*-2-Phenylcyclohexyl 2(*R*)-Isopropoxyphenylacetate (8f). Purified by column chromatography (silica gel, Et_2O/light petroleum ether, 1:3) (73%), bp 190 °C at 1.0 mmHg; $[\alpha]_D$ +10.2° (c = 0.492, MeOH); IR (neat) 1749 cm^{-1}; ^1H NMR δ 0.99–1.07 (6H, m), 1.23–2.00 (8H, m), 2.71 (1H, m), 3.20 (1H, septet, J = 6.07), 4.67 (1H, m), 5.10 (1H, m), and 7.18–7.29 (10H, m); ^{13}C NMR δ 21.4, 22.3, 24.6, 25.7, 31.9, 33.9, 49.8, 70.9, 76.5, 78.3, 126.4, 126.9, 127.6, 128.0, 128.2 (2C), 137.2, 142.9, and 172.0; MS m/z (EI) 353 (MH^+, 5), 352 (M^+, 2), 195 (24), 107 (100), and 91 (78).

(1*R*,2*S*)-*trans*-2-Phenylcyclohexyl 2(*R*)-Ethoxyphenylacetate (7e). Prepared as above but using iodoethane; purified by column chromatography (silica gel, Et_2O/light petroleum ether, 1:3) (83%), bp 170 °C at 0.1 mmHg; $[\alpha]_D$ −48.8° (c = 1.292, MeOH); IR (neat) 1748 cm^{-1}; ^1H NMR δ 1.06 (3H, t, J = 6.76), 1.26–2.14 (8H, m), 2.66 (1H, dt, J = 8.04 and 10.53), 3.18 (2H, m), 4.62 (1H, s), 5.07 (1H, m), and 7.02–7.23 (10H, m); ^{13}C NMR δ 15.1, 24.6, 25.7, 32.1, 34.4, 49.6, 65.1, 76.7, 81.0, 126.6, 127.2, 127.9, 128.2 (2C), 128.5, 137.2, 142.7, and 170.7; MS m/z (CI) 356 ($M + NH_4^+$, 82), 339 (MH^+, 12), 198 (55), and 135 (100); HRMS calcd for $C_{22}H_{26}O_3$ + H, 339.1960; found, 339.1960.

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Supporting Information Available: Full listing of all the spectroscopic data and copies of ^1H and/or ^{13}C NMR spectra of **1a**,**b**,**g**, **2a**,**b**,**d**,**e**,**g**, **3a**,**c**–**e**, **5b**,**d**,**e**, **6a**,**b**,**d**, **7e**, **8a**,**b**,**d**,**e**,**g**, and **9a**,**b**,**d**,**e**,**g** (58 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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