Chiral Organometallic Reagents: Part XXII[1]

Discrimination of Enantiotopic Iodine Atoms by an Iodine/Magnesium Exchange Reaction

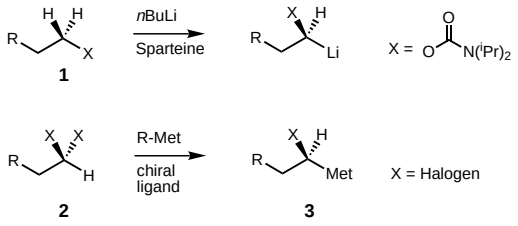
Volker Schulze and Reinhard W. Hoffmann*[a]

Abstract: An enantioselective iodine/magnesium exchange reaction between the diiodoalkane **4** and a chiral Grignard reagent **12** has been realized at $-78\,^{\circ}C$ in THF. The resulting α-iodoalkylmagnesium reagents **13** are configurationally stable under these conditions and during trapping by a benzaldehyde/dimethylaluminium chloride system to furnish the iodohydrins **19** and epoxides **9**.

Keywords: carbenoids · Grignard reagents

Introduction

At present, stereoselective synthesis relies almost exclusively on the differentiation of enantiotopic (or diastereotopic) faces of planar sp^2-hybridized reaction centers.[2] However, the differentiation of enantiotopic groups is increasingly gaining importance, as evidenced by the spectacular enantioselective deprotonation of alkylcarbamates **1** developed by Hoppe (Scheme 1).[3]

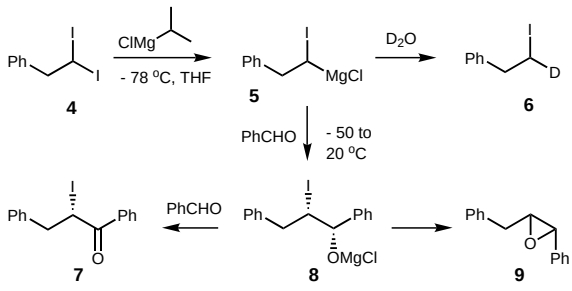


Scheme 1. Enantioselective deprotonation of alkylcarbamates **1** and the halogen/metal exchange reaction of dihaloalkanes **2**.

It occurred to us, that an enantioselective halogen/metal exchange reaction on 1,1-dihaloalkanes **2** should have a similar potential to generate chiral organometallic compounds of the type **3** by a differentiation of enantiotopic halogen atoms. Provided the compounds **3** have sufficient thermal and configurational stability, they would be of considerable interest for stereoselective synthesis. This led us to consider an iodine/magnesium exchange reaction, since α-heterosubstituted alkylmagnesium species have higher thermal[4] and probably also configurational stability[5] than the corresponding lithium compounds.

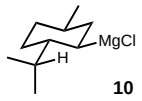
Results and Discussion

We initiated a study of the iodine/magnesium exchange reaction[6] of the 1,1-diiodoalkane **4**, which could be effected with isopropylmagnesium chloride in THF over 2 h at $-78\,^{\circ}C$. The resulting α-iodoalkylmagnesium compound **5** could be quenched with D_2O to furnish **6** in 98% yield (Scheme 2).



Scheme 2. Iodine/magnesium exchange reaction of **4** to give **5** and subsequent reactions to give **6**–**9.**

Trapping of **5** with benzaldehyde generated the magnesium alkoxide **8** which cyclized to form the epoxide **9** (55%) with a *cis*/*trans* selectivity of >98%. This encouraged us to use a chiral Grignard reagent to differentiate between the enantiotopic iodine atoms of **4**. When using[7] the Grignard reagent **10** de-



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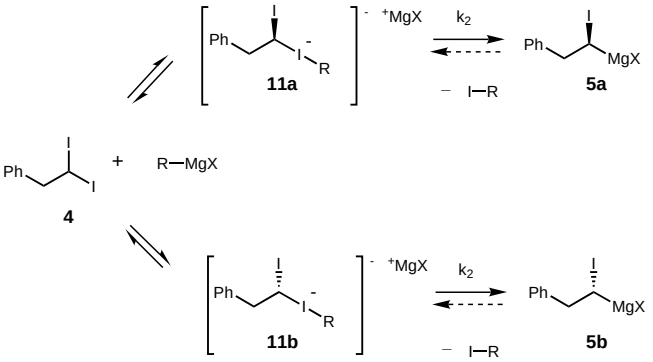
rived from (−)-menthyl chloride,[8] the resulting epoxide **9** (41%) showed little (2%) if any enantiomeric enrichment, according to the ^{1}H NMR spectra recorded in the presence of tris(3-heptafluorobutyryl-D-camphorato)europium.

The low enantiomeric enrichment in **9** could arise either because the organomagnesium species **5** is not configurationally stable on the time scale of the experiment, or, because the enantiotopic differentiation between the two iodine atoms in **4** is too low. We assumed—and later proved—that the α-iodoalkylmagnesium compounds **5** are configurationally stable at −50 °C. Therefore the stereodifferentiating step needed closer attention. The halogen metal exchange reaction is assumed to proceed in a two-step manner,[9] involving halogen ate complexes[10] as intermediates. For the case at hand, it remains open, whether the first or the second step of the following reaction sequence determines the configuration of the final α-iodoalkyl Grignard reagent **5**.

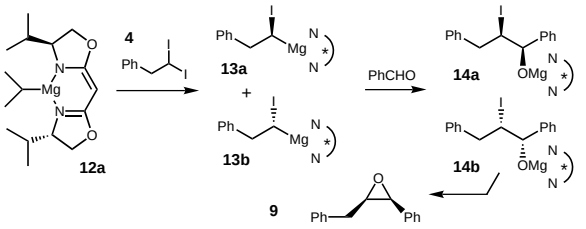
Provided the first step in the reaction between **4** and a Grignard reagent is irreversible, the formation of the ate complexes **11a** and **11b**[11] would be stereodefining (Scheme 3). In this case some level of enantioselection was



Scheme 3. Course of the reaction of **4** to give **5** via the ate complexes **11**.

expected on reaction of the menthyl Grignard reagent. However, if the first step were reversible, the second step, the rate- and stereodetermining conversion of the ate complexes **11** into **5** would involve attack of the magnesium ion at the diiodo-substituted carbon atom of **11**. Attack at this site would be remote from the chirality of the menthyl group due to the interspersed iodine atom and, hence, the attendant enantioselectivity is likely to be small. Enantiodifferentiation in such a situation would rather require a chiral magnesium cation. Combination of the magnesium dication with a chiral anion would bind the chiral information tightly to the magnesium ion by Coulombic attraction. For that reason, we treated one equivalent of diisopropylmagnesium with one equivalent of the bisoxazolidine **15a**[12] to generate what was presumed to be **12a**. Reaction of the resulting solution with the diiodoalkane **4** at −78 °C followed by trapping of the intermediates **13** with benzaldehyde, produced 56% of the product **9** (97% *cis*) with an *ee* value of 49% (scheme 4).

Encouraged by these results we started to investigate this reaction in greater detail. The key question is whether a uniform reagent **12** can be generated. We therefore monitored the reaction between **15** and diisopropylmagnesium (**16**) by



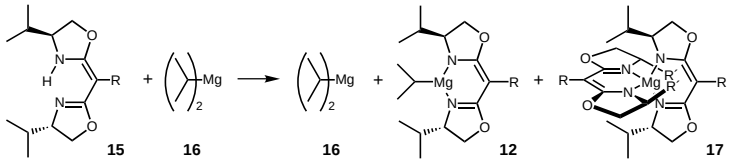
Scheme 4.

^{13}C NMR spectroscopy. Addition of one equivalent of **15a** to a solution of **16** in THF at 0 °C was found to result in a 1:2:1 statistical mixture of products **16**, **12a,** and **17a** (Scheme 5).

Evidently, such a reagent mixture is not desirable for enantioselective halogen/metal exchange reactions, since the remaining diisopropylmagnesium (**16**) will react with the diiodo compound **4** to generate a racemic α-iodoalkylisopropylmagnesium species.[13] Hence, the results obtained above suggest, that pure **12** should show a substantially higher enantioselection on reaction with the diiodoalkane **4**. We therefore intensified our efforts to generate uniform **12**. On addition of two equivalents of **15a** to diisopropylmagnesium (**16**) all of the material could be converted into **17a**. Addition of further diisopropylmagnesium (**16**) at this stage, however, did not lead to a comproportionation to give **12a**.

It appears that **12a** has a basicity similar to that of diisopropylmagnesium (**16**) in deprotonating **15a**. In search of a ligand, the anion of which is less basic than that of **15a**, we turned to the arylthio-substituted ligands **15b** and **15c**. Using those, ^{13}C NMR spectroscopy indicated the selective generation of the desired reagents **12b** and **12c**. For further ligands tested see reference [14]. Armed with this knowledge, the chiral magnesium reagent **12c** was treated with the diiodo compound **4** to give the α-iodoalkylmagnesium compounds **13** which could be trapped by the addition of D_2O to give a 94% yield of **6**.

Trapping of the derived α-iodoalkylmagnesium compounds **5** or **13** by benzaldehyde needed also improvement. As discussed above, trapping of **5** with benzaldehyde furnished the epoxide **9** in yields, which did not exceed 55%, but were



a	1 equiv	1 equiv	0.25 equiv	0.5 equiv	0.25 equiv
b	1 equiv	1 equiv	trace	0.95 equiv	trace

Scheme 5. Reaction of **15** with **16**. **a**: R = H, **b**: R = S-C_6H_5, **c**: S-C_6H_4Cl. R′ = $CH(CH_3)_2$.

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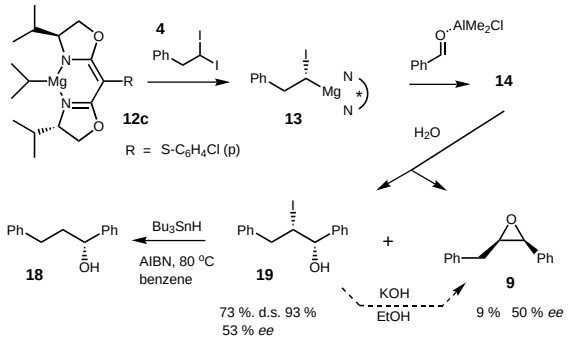
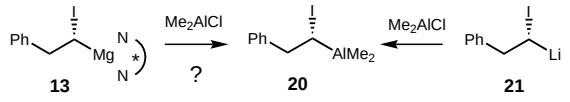
frequently lower. This is a consequence of a side reaction, in which the magnesium alkoxides **8** were oxidized by excess of benzaldehyde to the α-iodoketone **7**. Aside from the fact that this lowers the yield of **9**, oxidation of **8** by benzaldehyde could be diastereomer-discriminating and could therefore influence the *cis*/*trans* ratio of the product **9**. In the case of **14** any differentiation in the oxidation of the diastereomers **14** and **14b** would alter the enantiomeric purity of the product **9** ultimately obtained. It was therefore mandatory to develop a high-yield trapping procedure for **13**. This goal was achieved by using a combination of benzaldehyde and dimethylaluminum chloride as trapping reagent. In this way, the α-iodo alcohols **19** plus some of the epoxide **9** could be obtained in good yield (Scheme 6).

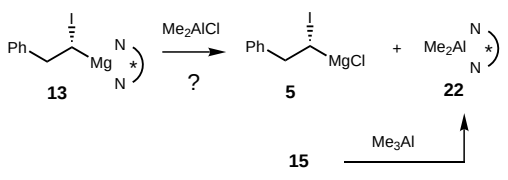


Scheme 6. Reaction of **12c** with **4**.

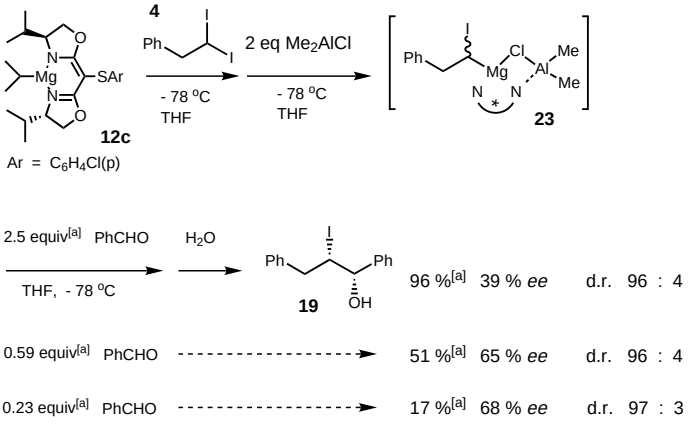
The enantiomeric excess of the iodohydrins **19** was determined to be 53% after conversion into the epoxide **9**. For the determination of the absolute configuration of the iodohydrin **19**, a sample that gave epoxide **9** of 29% *ee* was reduced with tributyltin hydride to give the dextrorotatory alcohol **18** (25% optical purity) which is known[15] to have the (*R*)-configuration. While the introduction of dimethylaluminum chloride into the system led to acceptable yields in trapping of **13**, it created at the same time potential complications, that required further control experiments. For example, is there a transmetalation from magnesium in **13** to the aluminum compound **20**?



In order to assess the reactivity of **20**, we generated it from the lithium compound **21** at $-105\,^{\circ}C$. Adding benzaldehyde and warming the mixture to $-78\,^{\circ}C$ led to only negligible amounts of **19** or **9**. Apparently, the reactivity of **20** is much lower than that of **13**, and, hence, the transmetalation of **13** to give **20** is not considered to interfere in the reactions and trapping of **13**. A second complication could be a ligand exchange reaction of **13** to give **5**.



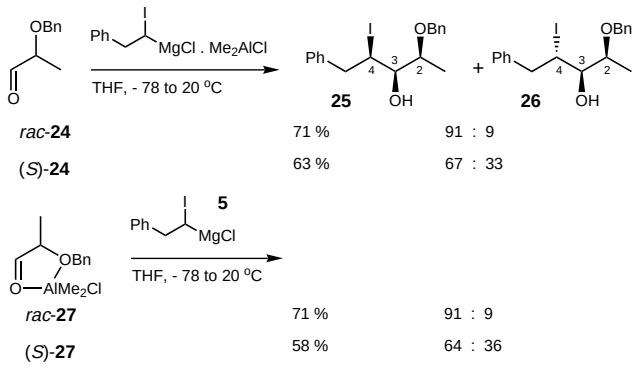
To address this possibility, **22** was generated from the bisoxazolidine **15c** and trimethylaluminum. When **22** was added to racemic **5** at $-78\,^{\circ}C$ followed by addition of benzaldehyde the reaction produced a 28% yield of the epoxide **9** (*cis* only) and a 22% yield of the iodohydrins **19** (*syn*/*anti* = 7:3). The much lower enantiomer enrichment of **9** (7%), *syn*-**19** (14%) and of *anti*-**19** (1%) formed in this experiment suggests that the formation of **5** is not a serious complication in the trapping of the chiral Grignard reagent **13** with dimethylaluminum chloride and benzaldehyde, a reaction which led to products with a much higher *ee* value. In fact, addition of dimethylaluminum chloride to **13** first, followed by benzaldehyde, or, trapping of **13** with benzaldehyde precomplexed to dimethylaluminum chloride made little difference in the course of the reaction. However, the enantiomeric enrichment of the resulting iodohydrins **19** was somehow variable. This was eventually traced to a kinetic resolution during the reaction of the diastereomeric α-iodoalkyl Grignard reagents **13** with benzaldehyde. The set of experiments shown in Scheme 7, in which the relative amount of benzaldehyde was varied, illustrates this point.



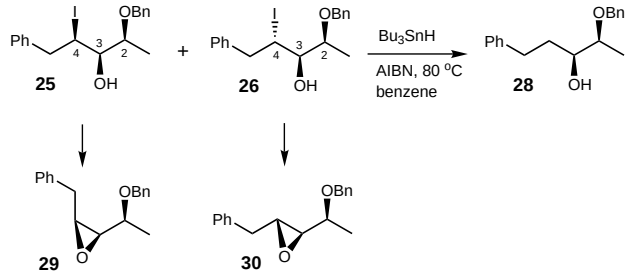
[a] referring to the amount of **23** generated

Scheme 7. Influence of the relative amount of benzaldehyde on the *ee* value and diastereomeric ratio.

In addition, these observations prove the important fact that any diastereoisomerization of the magnesium compounds **13** or **23** is slower than their rate of reaction with the complexed benzaldehyde. That the α-iodoalkylmagnesium compounds **13** do not racemize in the presence of dimethylaluminum chloride more rapidly than they are trapped by aldehydes has also been assessed by another test[16] based on kinetic resolution (Scheme 8). To this end, a mixture of the Grignard reagents **5** with dimethylaluminum chloride is added to 2-benzyloxypropionaldehyde **24** to give the two diastereomeric adducts **25** and **26**. These products should have the same configuration at C-2 and C-3 and be epimeric at C-4. In line with this notion, reduction of a mixture of **25** and **26** with tributyltin hydride furnished a single isomer of **28**. Treatment of the isomers **25** and **26** separately with potassium hydroxide led specifically to a *cis*-epoxide **29** and a *trans*-epoxide **30** (Scheme 9).



Scheme 8. Formation of **25** and **26**.

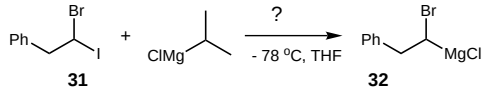


Scheme 9. Reactions of **25** and **26**.

The differences in the product ratio of **25** and **26** obtained on reaction of **5** with either racemic or enantiomerically pure aldehyde **24** indicate that the Grignard reagent **5** is trapped more rapidly than it racemizes. Further experiments delineated that the same result applies irrespective of whether dimethylaluminum chloride is first added to the Grignard reagent and then benzaldehyde, or whether the aldehyde is precomplexed with dimethylaluminum chloride first, that is by using **27** as trapping reagent.

This statement of configurational stability of **5** relates to the time scale of trapping of **5** by the dimethylaluminum chloride/benzaldehyde system. But this leaves the possibility that the two diastereomeric complexes **13** have equilibrated prior to the addition of the trapping reagent. To exclude this possibility the configurational stability of **5** and of the diastereomeric complexes **13** had to be established on a macroscopic time scale at $-78\,^{\circ}C$.

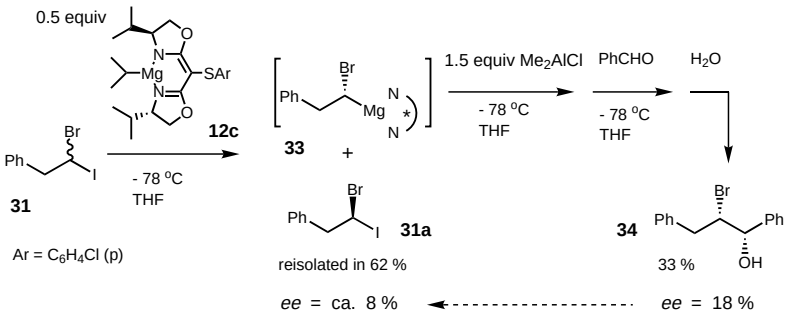
For this we envisaged the α-bromoalkyl Grignard reagent **32** to be generated from an enantiomerically enriched iodobromo compound **31** by a chemoselective iodine/magnesium exchange reaction (cf. the preferential exchange of iodine over bromine for lithium.[17]



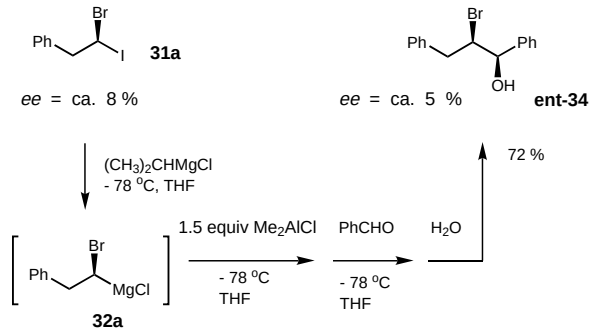
Since we had established above that the chiral Grignard reagent **12c** is able to differentiate the enantiotopic iodine atoms of **4**, it should also be in a position to discriminate the enantiomers of the racemic bromoiodo compound **31**, and, hence, should allow a kinetic resolution of **31**. When racemic **31** was treated with 0.5 equivalents of the chiral Grignard reagent **12c**, followed by trapping with dimethylaluminum chloride/benzaldehyde, the resulting bromohydrin **34** was obtained in 33 % yield and 18 % *ee* (Scheme 10).

This indicated[18] that the remaining bromoiodoalkane **31a**, reisolated in 62 % yield, should have an *ee* of about 8 %. This material was then subjected to an iodine–magnesium exchange reaction with achiral isopropylmagnesium chloride. After two hours at $-78\,^{\circ}C$, the resulting **32a** was trapped with dimethylaluminum chloride and benzaldehyde to furnish 72 % of the bromohydrin *ent*-**34** of about 5 % *ee* (Scheme 11). The latter had the opposite configuration to the bromohydrin **34** obtained above. The fact that the resulting *ent*-**34** has an *ee* value similar to that of the starting material demonstrates that the generation of **32a** from **31a** and trapping of **32a** by dimethylaluminum chloride/benzaldehyde is not subject to significant racemization.

Therefore, the α-bromoalkylmagnesium compound **32** and, by inference, the α-iodoalkylmagnesium compound **5** are



Scheme 10. Kinetic resolution of **31**.



Scheme 11. Formation of *ent*-**34**.

configurationally stable on a macroscopic time scale at $-78\,^{\circ}C$. With this information in hand, the following statements can be made: The chiral Grignard reagent **12** is in a position to differentiate the enantiotopic iodine atoms of **4** and generates in a kinetically controlled iodine/magnesium exchange reaction a mixture of two diastereomeric complexes **13a** and **13b**. These may be trapped in good yield by a reagent

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combination of dimethylaluminum chloride and benzaldehyde to give the iodohydrins **19**. The enantiomeric purity of these iodohydrins is influenced by a kinetic resolution during trapping of the diastereomeric complexes **13a** and **13b**.

Acknowledgements

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Experimental Section

All temperatures quoted are not corrected. Low temperatures were determined with a GTH 215 precision digital thermometer from Greisinger, Regenstauf, Germany. Reactions with organometallic compounds were carried out in dried solvents under nitrogen or argon. ^{1}H NMR, ^{13}C NMR: Bruker AC 300, AMX 500. Boiling range of petroleum ether: 40–60 °C. pH7 buffer: $NaH_2PO_4 \cdot 2H_2O$ (56.2 g) + $Na_2HPO_4 \cdot 2H_2O$ (213.2 g) in water (1.0 L). Column chromatography: silica gel 60: 63–200 μm or aluminium oxide 90, neutral, activity I (63–200 μm), E. Merck AG, Darmstadt. Flash chromatography: silica gel 60 (40–63 μm), E. Merck AG, Darmstadt. MPLC: siliga gel 60 (15–25 μm), E. Merck AG, Darmstadt.

Preparation of starting materials

1,1-Dibromo-2-phenylethane: To a mixture of THF (80 mL), diethyl ether (80 mL), and diisopropylamine (17.5 g, 162 mmol) was added at −30 °C a solution of *n*-butyllithium in hexane (1.55 M, 162 mmol). After stirring for 0.5 h at −30 °C and 0.5 h at 0 °C the solution was cooled to −105 °C. A solution of dibromomethane (28.16 g, 162 mmol) in THF (50 mL) was added dropwise. After stirring for 0.5 h at −105 °C a solution of benzyl bromide (27.71 g, 162 mmol) in THF (30 mL) was added dropwise. Stirring was continued for 0.5 h at −105 °C. After the mixture had been allowed to warm to room temperature overnight, saturated aqueous NH_4Cl solution (100 mL), aqueous 20% $Na_2S_2O_3$ solution (20 mL) and petroleum ether (50 mL) were added. The phases were separated and the aqueous phase was extracted with petroleum ether (3 × 50 mL). The combined organic phases were washed with brine (30 mL), dried (Na_2SO_4), and concentrated. Distillation at 85 °C/10^{-2} Torr furnished the product (17.50 g, 41%) as a colorless liquid. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 3.62$ (d, $J = 6.8$ Hz, 2H), 5.67 (t, $J = 6.8$ Hz, 1H), 7.15–7.30 (m, 5 H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 45.1$, 51.4, 127.7, 128.6, 129.4, 136.7; elemental analysis calcd for $C_8H_8Br_2$ (264.0): C 36.40, H 3.05; found C 36.61, H 3.00.

1,1-Diiodo-2-phenylethane (**4**): *n*-Butyllithium in hexane (1.84 M, 190 mmol) was added dropwise to a solution of hexamethyldisilazane (50 g, 0.31 mol) in THF (50 mL) at −30 °C. The solution was stirred for 0.5 h at −30 °C and 0.5 h at 0 °C. A solution of diiodomethane (53.6 g, 0.2 mol) in THF (100 mL) was cooled to −105 °C. The freshly prepared solution of lithium h examethyldisilazide was added dropwise over 1 h.[19] Stirring was continued for 0.5 h at −105 °C. A solution of benzyl bromide (42.7 g, 250 mmol) in THF (30 mL) was added dropwise. After stirring for 1.5 h at −105 °C the solution was allowed warm to room temperature. Saturated aqueous NH_4Cl solution (90 mL), 20% $Na_2S_2O_3$ solution (20 mL) and petroleum ether (50 mL) were added. The phases were separated and the aqueous phase was extracted with petroleum ether (3 × 50 mL). The combined organic phases were washed with brine (30 mL), dried (Na_2SO_4) and concentrated. The residue was taken up in a mixture of petroleum ether (68 mL) and dichloromethane (7 mL), and the solution was stored at −25 °C. The next day the crystalline product (32 g) could be collected. The mother liquor was concentrated and the residue was crystallized from petroleum ether/dichloromethane to furnish further 5.7 g of **4**. Total yield: 37.7 g (55%). For analysis a sample was recrystallized as above to give crystals (with a pink touch) of m.p. 37 °C. ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 3.74$ (d, $J = 7.4$ Hz, 2H), 5.08 (t, $J = 7.4$ Hz, 1H), 7.20–7.24 (m, 2H), 7.29–7.36 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = -25.8$, 54.4, 127.6, 128.7, 128.9, 139.8; elemental analysis calcd for $C_8H_8I_2$ (358.0): C 26.84, H 2.25; found C 26.66, H 2.28.

1-Bromo-1-iodo-2-phenylethane (**31**): A solution of 1,1-dibromo-2-phenylethane (5.28 g, 20 mmol) in THF (6 mL) was added dropwise at −78 °C to a mixture of *n*-butyllithium in hexane (1.55 M, 24.0 mmol), THF (40 mL), and diethyl ether (20 mL). After stirring for 0.5 h at −105 °C a solution of iodine (7.61 g, 30.0 mmol) in THF (20 mL) was continuously added over a period of 1.5 h . After stirring for 1 h at −105 °C the solution was allowed to warm to −70 °C over 3 h. Saturated aqueous NH_4Cl solution (30 mL), 20% $Na_2S_2O_3$ solution (20 mL), and petroleum ether (30 mL) were added. The phases were separated and the aqueous phase was extracted with petroleum ether (3 × 30 mL). The combined organic phases were washed with brine (20 mL), dried (Na_2SO_4), and concentrated. The residue was chromatographed over silica gel with petroleum ether to furnish **31** as a colorless oil (4.71 g, 76%). For analysis a sample was purified further by low-temperature crystallization from petroleum ether/dichloromethane at −78 °C; ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 3.61$ (dd, $J = 14.5$ and 7.2 Hz, 1H), 3.70 (dd, $J = 14.6$ and 7.0 Hz, 1H), 5.47 (t, $J = 7.1$ Hz, 1H), 7.12–7.30 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 11.6$, 53.2, 127.7, 128.6, 129.2, 138.2; elemental analysis calcd for C_8H_8BrI (311.0): C 30.90, H 2.59; found C 30.97, H 2.52.

Phenylthio-[2-((4*S*)-4,5-dihydro-4-isopropyl-oxazolyl)]-[2-((4*S*)-4,5-dihydro-4-isopropyl-oxazolidinylidene)]methane (**15b**): *n*-Butyllithium in hexane (1.44 M, 22.0 mmol) and TMEDA (3.30 mL, 22 mmol) were added to a solution of bisoxazolidine **15a**[12] (4.77 g, 20.0 mmol) in THF (75 mL) at −78 °C. After stirring for 1.5 h at −78 °C and 0.5 h at 0 °C the solution was cooled to −78 °C again. A solution of diphenyldisulfide (10.92 g, 50 mmol) in THF (20 mL) was added dropwise. After stirring for 1.5 h at −78 °C and 2 h at 0 °C water (50 mL) and *tert*-butyl methyl ether (50 mL) were added. The phases were separated and the aqueous phase was extracted with *tert*-butyl methyl ether (3 × 50 mL). The combined organic phases were washed with semisaturated aqueous $NaHCO_3$ solution (50 mL), water (30 mL), and brine (30 mL), dried (Na_2SO_4) and concentrated. The residue was chromatographed over basic alumina (500 g) with petroleum ether/ethyl acetate = 9:1 to 3:1 to give **15b** (4.60 g, 66%) as a colorless solid of m.p. 84–86 °C. For analysis a sample was recrystallized from petroleumether/*tert*-butyl methyl ether = 1:1. $[\alpha]_D^{25} = +36.9$ ($c = 1.105$, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.89$ (d, $J = 6.7$ Hz, 6H), 0.99 (d, $J = 6.7$ Hz, 6H), 1.71 (pseudo-octet, $J = 6.7$ Hz, 2H), 3.86 (dt, $J = 8.6$ and 7.1 Hz, 2H), 4.02 (dd, $J = 8.4$ and 7.3 Hz, 2H), 4.36 (dd, $J = 8.6$ and 8.6 Hz, 2H), 6.93–7.21 (m, 5H), 9.00–10.50 (br, 1H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 18.3$, 18.6, 32.9, 57.9, 67.2, 71.2, 124.0, 124.3, 128.3, 141.1, 168.5; elemental analysis calcd for $C_{19}H_{26}N_2O_2S$ (346.5): C 65.86, H 7.56, N 8.09; found C 65.83, H 7.52, N 7.97.

***p*-Chlorophenylthio-[2-((4*S*)-4,5-dihydro-4-isopropyloxazolyl)]-[2-((4*S*)-4,5-dihydro-4-isopropyl-oxazolidinylidene)]methane** (**15c**): The bis-oxazolidine **15a**[12] (7.15 g, 30.0 mmol) and 4,4′-dichlorodiphenyldisulfide (12.9 g, 44.9 mmol) were allowed to react as described for **15b**. The crude product was purified by chromatography over silica gel with petroleum ether/ethyl acetate = 10:1 to *tert*-butyl methyl ether/petroleum ether = 1:1 to *tert*-butyl methyl ether/petroleum ether = 3:1 to give **15c** (9.59 g, 84%) as a colorless solid of m.p. 98–100 °C. For analysis a sample was recrystallized from *tert*-butyl methyl ether/petroleum ether = 1:1. $[\alpha]_D^{25} = +27.1$ ($c = 1.045$, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.89$ (d, $J = 6.7$ Hz, 6H), 0.98 (d, $J = 6.7$ Hz, 6H), 1.71 (pseudo-octet, $J = 6.7$ Hz, 2H), 3.87 (dt, $J = 8.6$ and 7.1 Hz, 2H), 4.03 (dd, $J = 8.5$ and 7.3 Hz, 2H), 4.36 (dd, $J = 8.6$ and 8.6 Hz, 2H), 7.00–7.08 (m, 2H), 7.10–7.18 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 18.4$, 18.7, 33.0, 57.8, 67.3, 71.3, 125.7, 128.5, 129.7, 139.9, 168.4; elemental analysis calcd for $C_{19}H_{25}N_2O_2SCl$ (380.9): C 59.91, H 6.62, N 7.35; found C 59.95, H 6.54, N 7.25.

Generation of the chiral magnesium reagent 12: THF (0.1 mL), C_6D_6 (0.07 mL), and a solution of diisopropylmagnesium (**16**) in THF (0.59 M, 0.20 mmol) were placed in a dry NMR tube which was closed with a septum. A solution of the bisoxazolidine (**15a**) in THF (1.00 M, 0.200 mmol) was added to the NMR tube at 0 °C and ^{13}C NMR (125 MHz) spectra were recorded at 25 °C and at −78 °C. Another 0.2 mmol of **15a** were added and spectra were recorded again. Finally a solution of diisopropylmagnesium (**16**) in THF (0.59 M, 0.20 mmol) was added, and a third ^{13}C NMR spectrum was recorded. The following chracteristic signals were observed at −78 °C: **12a**: $\delta = 9.01$, 14.7, 19.0, 25.9, 26.0, 33.1, 35.2, 66.2, 67.8, 172.4; **17a**: 16.1, 19.2, 33.8, 54.1, 67.6, 68.3, 173.0. In a similar manner the data for **12b** (−30 °C): $\delta = 9.56$, 15.5, 15.6, 19.5, 19.7, 26.3, 26.4, 33.7, 33.8, 55.1, 67.3, 67.5, 69.6, 69.8, 123.5, 124.1, 128.9, 145.7, 174.3, 174.5 and **12c** (25 °C): $\delta = 9.0$,

15.3, 18.9, 25.3, 25.5, 32.9, 55.4, 67.1, 69.4, 125.5, 125.6, 128.6, 144.3, 174.0 were recorded.

Reactions of magnesium carbenoids

Generation and trapping of 1-iodo-2-phenyl-ethylmagnesium chloride (5): THF (4 mL), diethyl ether (2 mL), petroleum ether (2 mL), and a solution of isopropylmagnesium chloride in diethyl ether (1.34 M, 1.60 mmol) were cooled to $-78\,^{\circ}C$. A solution of 1,1-diiodo-2-phenylethane (**4**) (2.88 M, 1.00 mmol) in diethyl ether was added dropwise resulting in the formation of an intensive yellow color.[11] After stirring for 2 h at $-78\,^{\circ}C$ the color had faded and water (5 mL) was added dropwise. After the reaction mixture had reached room temperature, saturated aqueous NH_4Cl solution (20 mL), 20% $Na_2S_2O_3$ solution (3 mL) and *tert*-butyl methyl ether (20 mL) were added. The phases were separated and the aqueous phase was extracted with *tert*-butyl methyl ether (3×20 mL). The combined organic extracts were washed with brine (10 mL), dried (Na_2SO_4) and concentrated. Flash chromatography with petroleum ether/ethyl acetate = 20:1 furnished 1-iodo-2-phenylethane (227 mg, 98%) as a colorless oil; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 3.19$ (t, $J = 7.6$ Hz, 2H), 3.36 (dt, $J = 7.8$ and 0.9 Hz, 2H), 7.18–7.37 (m, 5H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 5.45$, 40.3, 126.8, 128.3, 128.6, 140.6; elemental analysis calcd for C_8H_9I (232.1): C 41.41, H 3.91; found C 41.33, H 3.84. The reaction proceeded in the same manner in pure THF solvent. Quenching with D_2O resulted in the formation of **6**.

2-Benzyl-3-phenyloxirane (9): The carbenoid **5** was generated as described above from **4** (358 mg, 1.00 mmol) and isopropylmagnesium chloride (1.50 M in diethyl ether, 1.3 mmol) in THF solution. The carbenoid **5** was trapped by addition of benzaldehyde (0.25 mL, 2.50 mmol). After workup as described for **5**, ^{13}C NMR analysis of the crude product revealed the presence of **9** and **19** in a 5:1 ratio. The crude product was purified by flash chromatography with petroleum ether/ethyl acetate = 30:1 changing to 15:1 to give *cis*-2-benzyl-3-phenyloxirane (**9**) (116 mg, 55%) as a colorless oil; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 2.50$ (dd, $J = 14.6$ and 6.6 Hz, 1H), 2.72 (dd, $J = 14.6$ and 5.9 Hz, 1H), 3.38 (ddd, $J = 6.3$, 6.3, and 4.2 Hz, 1H), 4.10 (d, $J = 4.1$ Hz, 1H), 6.98–7.01 (m, 2H), 7.10–7.38 (m, 8H); cf. the data in ref. [20]; ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 32.2$, 57.5, 59.6, 126.5, 126.6, 127.7, 128.1, 128.5, 128.8, 135.4, 137.4.

The enantiomeric purity of **9** was determined using tris(3-heptafluorobutyryl-D-camphorato)europium as a shift reagent in $CDCl_3$. Especially the signal at $\delta = 4.10$ was shifted downfield to, for example, $\delta = 5.1$ and 5.3. It was shown that the lowfield signal at $\delta = 5.3$ corresponds to (3*R*)-(+)-**9**.

After a similar experiment the reaction mixture was allowed to warm to room temperature very slowly over a period of 15 h. GC analysis of the crude product revealed the presence of **9** (21%), *trans*-**9** (4%), and the iodoketone (**7**). After flash chromatography 47% of **7** was obtained as a colorless oil; ^1H NMR (300 MHz, $CDCl_3$): $\delta = 3.40$ (dd, $J = 14.3$ and 6.7 Hz, 1H), 3.68 (dd, $J = 14.3$ and 8.1 Hz, 1H), 5.53 (dd, $J = 8.1$ and 6.8 Hz, 1H), 7.20–7.80 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 25.5$, 40.9, 127.0, 128.5, 128.6, 128.7, 129.1, 133.5, 134.0, 139.1, 194.1; characteristic ^1H NMR data of *trans*-**9** (300 MHz, $CDCl_3$): $\delta = 2.97$ (d, $J = 5.7$ Hz, 2H), 3.15 (dt, $J =$ 2.0 and 5.5 Hz, 1H), 3.65 (d, $J = 2.0$ Hz, 1H).

Generation of 13 and trapping with D_2O: A solution of **15c** (0.82 M in THF, 1.19 mmol) was added slowly to a solution of diisopropylmagnesium (1.59 M in diethyl ether, 1.05 mmol) at $0\,^{\circ}C$, and the mixture was stirred for 1 h at room temperature. After cooling to $-78\,^{\circ}C$ a solution of the diiodoalkane **4** (1.10 M in THF, 0.70 mmol) was added, leading to the slow generation of an intensive yellow color.[11] The color had faded after the mixture had been stirred for 1.5 h at $-78\,^{\circ}C$. A CH_3OD/D_2O mixture (2:1, 1.0 mL) was added. Stirring was continued for 0.5 h at this temperature. After allowing the mixture to warm to room temperature, saturated aqueous NH_4Cl solution (20 mL) and *tert*-butyl methyl ether (20 mL) were added. The phases were separated and the aqueous phase was extracted with *tert*-butyl methyl ether (3×20 mL). The combined organic extracts were washed with brine (10 mL), dried (Na_2SO_4), and concentrated. Flash chromatography with petroleum ether/ethyl acetate = 15:1 changing to 1:1 to *tert*-butyl methyl ether furnished the iodo compound **6** (153 mg, 94%) as a colorless oil and the recovered **15c** (371 mg, 81%).

1-Hydroxy-2-iodo-1,3-diphenylpropane (19): A solution of **15c** (0.79 M in THF, 1.20 mmol) at $0\,^{\circ}C$ was added dropwise to a solution of diisopropylmagnesium (**16**) (0.90 M in diethyl ether, 1.05 mmol). After stirring for 1 h at room temperature the solution was cooled to $-78\,^{\circ}C$ and a solution of the diiodoalkane (0.97 M in THF, 0.70 mmol) was added, resulting in the slow formation of an intensive yellow color.[11] The color had faded after the mixture had been stirred for 1.5 h at $-78\,^{\circ}C$. A solution of benzaldehyde (0.18 mL, 1.75 mmol) in THF (5 mL at $-78\,^{\circ}C$) was prepared to which was added a solution of dimethylaluminum chloride (1.00 M in hexane, 1.4 mmol) at $-78\,^{\circ}C$. The latter solution was transferred by canula into the former carbenoid solution at $-78\,^{\circ}C$. After stirring for 2 h, the solution was allowed to warm to room temperature overnight. pH7 Buffer solution (20 mL) and *tert*-butyl methyl ether (20 mL) were added, and the suspension was sonicated for 15 min in a cleaning bath. The phases were separated and the aqueous phase was extracted with *tert*-butyl methyl ether (3×20 mL). The combined organic phases were washed with brine (10 mL), dried (Na_2SO_4), and concentrated. Flash chromatography of the residue with petroleum ether/ethyl acetate = 11:1 to 7:1 *tert*-butyl methyl ether/petroleum ether = 1:1 furnished **9** (14 mg, 9%), **19** (172 mg, 73%) and residual ligand **15c** (285 mg, 62%). The diastereomeric purity of **9** was determined from the ^1H NMR spectrum to be >97% *cis*. **19**: ^1H NMR (300 MHz, $CDCl_3$): $\delta = 2.51$ (d, $J = 6.4$ Hz, 1H), 3.26 (dd, $J = 14.4$ and 8.3 Hz, 1H), 3.30 (dd, $J = 14.4$ and 7.1 Hz, 1H), 4.32 (dd, $J = 5.4$ and 5.4 Hz, 1H), 4.55 (ddd, $J = 8.2$, 7.2, and 4.6 Hz, 1H), 7.17–7.40 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 43.9$, 48.9, 75.1, 125.8, 126.9, 128.0, 128.4, 128.6, 128.9, 139.5, 141.6; for comparison, the data for the *anti*-diastereomer are: ^1H NMR (300 MHz, $CDCl_3$): $\delta = 2.60$ (d, $J = 1.4$ Hz, 1H), 3.02 (dd, $J = 15.0$ and 9.6 Hz, 1H), 3.09 (dd, $J = 15.1$ and 4.6 Hz, 1H), 4.59 (ddd, $J = 8.9$, 4.8, and 4.8 Hz, 1H), 5.10 (d, $J = 3.8$ Hz, 1H), 7.03–7.48 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 39.2$, 46.3, 78.0, 126.5, 126.7, 128.1, 128.3, 128.5, 128.9, 139.6, 140.2; elemental analysis calcd for $C_{15}H_{15}IO$ (338.2): C 53.27, H 4.47; found C 53.41, H 4.22.

The iodohydrin **19** (110 mg, 0.32 mmol, 50% *ee*) was dissolved in ethanol (15 mL) to which was added KOH (1.80 M in ethanol, 0.59 mmol) at $0\,^{\circ}C$. After stirring the mixture for 2 h at $0\,^{\circ}C$ and overnight at room temperature, NH_4Cl (ca. 150 mg) was added. The solution was concentrated in vacuo and the residue was partitioned between saturated aqueous NH_4Cl solution (20 mL) and *tert*-butyl methyl ether (20 mL). The phases were separated and the aqueous phase was extracted with *tert*-butyl methyl ether (3×20 mL). The combined organic phases were washed with brine (10 mL), dried (Na_2SO_4), and concentrated. Flash chromatography with petroleum ether/ethyl acetate = 12:1 resulted in **9** (51 mg, 75%) as a colorless oil. The ^1H NMR spectra showed a *cis*/*trans* ratio of 93:7. The enantiomeric purity was determined as for **9** to be 53%.

The experiments have also been carried out in the manner that a solution of dimethylaluminum chloride in hexane was added first immediately followed by the addition of benzaldehyde. This involved for instance addition of 2.5, 0.59, or 0.23 equivalents of benzaldehyde resulting in different enantiomeric enrichments of the iodohydrin **19** obtained.

(*R*)-(+)-1,3-Diphenyl-1-propanol (18): The iodohydrin **19** (70 mg, 0.21 mmol) was dissolved in benzene (15 mL) to which was added tributyltin hydride (0.20 mL, 0.76 mmol) and AIBN (ca. 200 mg). The mixture was refluxed for 2 h, further AIBN was added, and refluxing was continued for 2 h. Saturated aqueous NH_4Cl solution (15 mL) and *tert*-butyl methyl ether (20 mL) were added, the phases were separated, and the aqueous phase was extracted with *tert*-butyl methyl ether (3×20 mL). The combined organic phases were washed with brine (10 mL), dried (Na_2SO_4), and concentrated. Flash chromatography of the residue with petroleum ether/ethyl acetate = 10:1 furnished the alcohol **18** (43 mg, 95%) as a colorless oil. $[\alpha]_D^{25} = +3.9$ ($c = 3.60$, ethanol); ^1H NMR (300 MHz, $CDCl_3$): $\delta = 1.90–2.08$ (m, 3H), 2.52–2.69 (m, 2H), 4.58 (dd, $J = 7.7$ and 4.4 Hz, 1H), 7.06–7.31 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 32.0$, 40.4, 73.8, 125.8, 125.9, 127.6, 128.3, 128.4, 128.6, 141.8, 144.6, cf. the data in ref. [15].

Control experiments with (1-iodo-2-phenylethyl)dimethylaluminum (20): A solution of *n*-butyllithium (1.5 M in hexane, 1.5 mmol), THF (8 mL), diethyl ether (4 mL), and petroleum ether (4 mL) were mixed at $-78\,^{\circ}C$ and cooled to $-105\,^{\circ}C$. A solution of the diiodo compound **4** (1.00 M in THF, 1.00 mmol) was added dropwise resulting in an intense yellow coloration. The yellow color faded over 15 min at $-105\,^{\circ}C$. A solution of dimethylaluminum chloride (1.00 M in hexane, 2.00 mmol) was added, resulting in the formation of a second yellowish phase. Benzaldehyde (0.20 mL, 2.00 mmol) was added and the emulsion was stirred vigorously for 1 h at $-105\,^{\circ}C$. The mixture was allowed to warm to $-78\,^{\circ}C$ over 2 h, was stirred for 1 h at this temperature, and was quenched by addition of pH7 buffer (20 mL). 20% $Na_2S_2O_3$ solution (3 mL) and *tert*-butyl methyl-

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ether (20 mL) were added and the mixture was sonicated for 15 min in a cleaning bath. The phases were separated and the aqueous phase was extracted with *tert*-butyl methyl ether (3 × 20 mL). The combined organic phases were washed with brine (10 mL), dried (Na_2SO_4), and concentrated. The residue (225 mg) was essentially pure 1-iodo-2-phenylethane.

Control experiment involving dimethylaluminum bisoxazolidine complex 22: A solution of **15c** (0.785 M in THF, 1.60 mmol) was added at 0 °C to a solution of trimethylaluminum (2.00 M in hexane, 1.50 mmol) and THF (5 mL). The mixture was stirred first at 0 °C, then at room temperature. This solution was added dropwise at −78 °C to a solution of the carbenoid **5** generated from the diiodo compound **4** (1.00 mmol) as described for **5**. After the mixture had been stirred for 1 h at −78 °C, benzaldehyde (0.35 mL, 3.5 mmol) was added dropwise and stirring was continued for 2 h. After the mixture had been allowed to warm to room temperature overnight workup as described for **19** provided **9** (60 mg, 28 %) and **19** (75 mg, 22 %) as colorless oils in addition to recovered **15c** (588 mg). The diastereomer ratio of **9** was determined by ^{1}H NMR spectroscopy to be >97:<3. The enantiomer enrichment of **9** obtained directly, and that of the epoxide formed by subsequent cyclization of the iodohydrin **19** was recorded as described for **9**.

Kinetic resolution of 1-bromo-1-iodo-2-phenylethane: A solution of **15c** (0.75 M in THF, 2.10 mmol) was added dropwise at 0 °C to a solution of diisopropylmagnesium (1.46 M in diethyl ether, 1.80 mmol) in THF (15 mL). After stirring for 30 min the mixture was allowed to warm to room temperature. This solution was added with a motor-driven syringe to a solution of the bromoiodo compound **31** (3.22 M in THF, 3.00 mmol) and THF (15 mL) over a period of 1.5 h at −78 °C. Stirring was continued for another 1.5 h at this temperature. Solutions of dimethylaluminum chloride (1.00 M in hexane, 3.24 mmol) and benzaldehyde (0.33 mL, 3.30 mmol) were added sequentially. After stirring for 2 h at −78 °C, the mixture was allowed to warm to room temperature. A pH7 buffer solution (20 mL) and *tert*-butyl methyl ether (20 mL) were added and the suspension was sonicated for 15 min in a cleaning bath. The phases were separated and the aqueous phase was extracted with *tert*-butyl methyl ether (3 × 20 mL). The combined organic phases were washed with brine (10 mL), dried (Na_2SO_4), and concentrated. Flash chromatography with petroleum ether/ethyl acetate = 15:1 to 7:1 to *tert*-butyl methyl ether/petroleum ether = 1:1 to *tert*-butyl methyl ether furnished the recovered bromoiodo compound **31a** (580 mg, 62 %, $[\alpha]_D^{25} = -0.652$ ($c = 10.5$, CH_2Cl_2)) and the bromohydrin **34** (290 mg, 33%) in addition to the recovered ligand **15c** (747 mg). Bromohydrin **34**: *syn*/*anti* = 97:3; $[\alpha]_D^{25} = -1.27$ ($c = 6.90$, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 2.74$ (d, $J = 5.7$ Hz, 1H), 3.08 (dd, $J = 14.3$ and 8.9 Hz, 1H), 3.22 (dd, $J = 14.3$ and 5.8 Hz, 1H), 4.43 (ddd, $J = 8.9$, 5.5, and 5.5 Hz, 1H), 4.69 (dd, $J = 5.4$ and 5.4 Hz, 1H), 7.13–7.40 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 35.2$, 64.9, 75.3, 126.2, 126.9, 128.2, 128.48, 128.50, 129.1, 138.0, 140.6; elemental analysis calcd for $C_{15}H_{15}BrO$ (291.2): C 61.87, H 5.19; found C 61.73, H 5.26. The bromohydrin **34** obtained was cyclized as described for **19** to (3*R*)-**9**, which showed an enantiomeric excess of 18 %. $[\alpha]_D^{25} = +3.52$ ($c = 2.73$, CH_2Cl_2).

Generation of 1-bromo-2-phenylethylmagnesium chloride from 1-bromo-1-iodo-2-phenylethane (31a): Starting from (S)-(−)-**31a** of about 8 % *ee* (500 mg, 1.6 mmol) the carbenoid **32a** was generated as described for **5** by using isopropylmagnesium chloride (2.00 M in diethyl ether, 2.09 mmol). The carbenoid was quenched with dimethylaluminum chloride (1 M in hexane, 3.70 mmol) followed by benzaldehyde (0.45 mL, 4.50 mmol). Workup as described for **19** provided the bromohydrin *ent*-**34** (336 mg, 72 %) as a colorless oil. According to ^{1}H NMR spectroscopy, the diastereomer ratio was *syn*/*anti* = 94:6. $[\alpha]_D^{25} = +0.347$, ($c = 5.62$, CH_2Cl_2). The bromohydrin *ent*-**34** was converted into (3*S*)-**9** as described for **19** with an *ee* of 5 %; $[\alpha]_D^{25} = -0.965$, ($c = 1.71$, CH_2Cl_2).

Reaction of the carbenoid 5 complexed with dimethylaluminum chloride with 2-benzyloxypropionaldehyde (24): A solution of 1,1-diiodo-2-phenylethane (**4**) (1.00 M in THF, 1.00 mmol) was added at −78 °C to a solution of isopropylmagnesium chloride (2.00 M in diethyl ether, 1.2 mmol) in THF (15 mL). After the mixture had been stirred for 2.5 h at −78 °C, the initial intense yellow color had faded. A solution of dimethylaluminum chloride (1.00 M in hexane, 2.50 mmol) was added and stirring was continued for 5 min. The resulting solution was transferred by canula into a precooled (−78 °C) solution of (2*S*)-benzyloxypropionaldehyde (**24**)[21] (493 mg, 3.0 mmol) in THF (15 mL). After stirring for 2 h at −78 °C the mixture was allowed to warm to room temperature. A pH7 buffer solution (20 mL) and *tert*-butyl methyl ether (20 mL) were added. The resulting mixture was sonicated for 15 min in a cleaning bath and the phases were separated. The aqueous phase was extracted with *tert*-butyl methyl ether (3 × 20 mL). The combined organic phases were washed with brine (10 mL), dried (Na_2SO_4), and concentrated. The residue consisted of excess aldehyde **24** and the iodohydrins **25** and **26**. In order to facilitate separation, the crude product was taken up in THF (15 mL) and cooled to −78 °C. Borane-dimethylsulfide complex (152 mg, 2.0 mmol) was added and the mixture was stirred for 2 h at −78 °C and 5 h at room temperature. Saturated aqueous NH_4Cl solution (20 mL) and *tert*-butyl methyl ether (20 mL) were added. The phases were separated and the aqueous phase was extracted with *tert*-butyl methyl ether (3 × 20 mL). The combined organic phases were washed with brine (10 mL), dried (Na_2SO_4), and concentrated. Flash chromatography of the residue with petroleum ether/ethyl acetate = 10:1 to 7:1 furnished a mixture of **25** and **26** (249 mg, 63 %) as a colorless oil. The diastereomer ratio was determined by ^{13}C NMR spectroscopy to be 67:33. Pure samples of **25** and **26** were obtained by MPLC separation with petroleum ether/ethyl acetate = 7:1. **25**: $[\alpha]_D^{25} = +13.6$ ($c = 2.80$, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 0.99$ (d, $J = 6.2$ Hz, 3H), 2.48 (dd, $J = 7.5$ and ca. 2 Hz, 1H), 2.95 (s, br., 1H), 3.29 (dd, $J = 14.0$ and 7.5 Hz, 1H), 3.36 (dd, $J = 14.0$ and 8.5 Hz, 1H), 3.55 (dq, $J = 7.4$ and 6.2 Hz, 1H), 4.16 (td, $J = 7.9$ and 2.1 Hz, 1H), 4.51 (d, $J = 11.2$ Hz, 1H), 4.55 (d, $J = 11.2$ Hz, 1H), 7.09–7.30 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 14.8$, 38.6, 44.4, 71.3, 74.7, 81.1, 126.8, 127.8, 128.4, 128.5, 129.0, 137.9, 139.5; elemental analysis calcd for $C_{18}H_{21}IO_2$ (396.3): C 54.56, H 5.34; found C 54.74, H 5.50. **26**: $[\alpha]_D^{25} = +25.9$ ($c = 2.02$, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.20$ (d, $J = 6.3$ Hz, 3H), 2.54 (d, $J = 9.1$ Hz, 1H), 3.04 (dd, $J = 14.8$ and 9.6 Hz, 1H), 3.43 (dd, $J = 14.8$ and 3.5 Hz, 1H), 3.52 (ddd, $J = 8.8$, 8.8, and 2.3 Hz, 1H), 4.12 (qd, $J = 6.3$ and 2.4 Hz, 1H), 4.29 (ddd, $J = 9.6$, 8.6, and 3.5 Hz, 1H), 4.39 (d, $J = 11.4$ Hz, 1H), 4.58 (d, $J = 11.3$ Hz, 1H), 7.10–7.32 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 17.0$, 40.1, 41.6, 71.3, 75.2, 78.6, 126.6, 127.9, 128.0, 128.2, 128.5, 129.4, 138.0, 139.5; elemental anlysis calcd for $C_{18}H_{21}IO_2$ (396.3): C 54.56, H 5.34; found C 54.61, H 5.26.

An identical experiment using racemic 2-benzyloxypropionaldehyde (**24**) furnished 71 % of **25** and **26** in a 91:9 diastereomer ratio. Essentially identical experiments were also carried out in which the solution of the carbenoid **5** was introduced by canula into a solution of 2-benzyloxypropionaldehyde precomplexed with dimethylaluminum chloride (cf. **27**).

Structure assignment of 25 and 26: A crude product containing a mixture of **25** and **26** (64:36, 230 mg, 0.58 mmol) and excess aldehyde **24** was taken up in ethanol (15 mL). Carefully powdered $NaBH_4$ (76 mg, 2.0 mmol) was added. The mixture was stirred for 3 h at room temperature and KOH (1.8 M in ethanol, 0.2 mL) was added. After the mixture had been stirred overnight, saturated aqueous NH_4Cl solution (20 mL), hydrochloric acid (3 M, 1 mL) and *tert*-butyl methyl ether (20 mL) were added. After the hydrogen evolution had ceased, the mixture was brought to pH7 by addition of aqueous $NaHCO_3$ solution. The phases were separated, and the aqueous phase was extracted with *tert*-butyl methyl ether (3 × 20 mL). The combined organic phases were washed with brine (10 mL) dried (Na_2SO_4), and concentrated. Flash chromatography with petroleum ether/ethyl acetate = 10:1 furnished a mixture of **29** and **30** (150 mg, 96 %) as a colorless oil. The diastereomer ratio was determined from the ^{13}C NMR spectrum to be 64:36; elemental analysis calcd for $C_{18}H_{20}O_2$ (268.4): C 80.56, H 7.51; found C 80.34, H 7.64.

The diastereomeric epoxides **29** and **30** were separated by MPLC with petroleum ether/ethyl acetate = 7:1. **29**: $[\alpha]_D^{25} = -43.6$ ($c = 2.825$, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.17$ (d, $J = 6.3$ Hz, 3H), 2.70 (dd, $J = 15.6$ and 7.5 Hz, 1H), 2.76 (dd, $J = 15.2$ and 5.1 Hz, 1H), 2.98 (dd, $J = 8.1$ and 4.4 Hz, 1H), 3.10 (ddd, $J = 7.1$, 4.9 and 4.9 Hz, 1H), 3.46 (dq, $J = 8.1$ and 6.5 Hz, 1H), 4.57 (d, $J = 11.8$ Hz, 1H), 4.76 (d, $J = 11.8$ Hz, 1H), 7.11–7.35 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 17.7$, 34.7, 54.7, 60.7, 71.2, 73.7, 126.7, 127.5, 127.8, 128.3, 128.6, 137.7, 138.7. **30**: $[\alpha]_D^{25} = +0.84$ ($c = 0.96$, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.12$ (d, $J = 6.5$ Hz, 3H), 2.70–2.88 (m, 4H), 3.21 (dq, $J = 6.5$ and 6.5 Hz, 1H), 4.48 (d, $J = 11.9$ Hz, 1H), 4.65 (d, $J = 11.9$ Hz, 1H), 7.10–7.29 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 17.4$, 38.2, 54.9, 61.9, 71.2, 75.6, 126.7, 127.5, 127.7, 128.3, 128.6, 128.9, 137.1, 138.6.

A mixture of the iodohydrins **25** and **26** (66 mg, 0.17 mmol) was reduced with tributyltin hydride as described for **18**. Flash chromatography of the crude product with petroleum ether/ethyl acetate = 8:1 furnished the

alcohol **28** (33 mg, 73 %) as a colorless oil; $[\alpha]_D^{25} = +12$ ($c = 0.11$, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.09$ (d, $J = 6.0$ Hz, 3H), 1.61 – 1.72 (m, 2H), 2.1 – 2.7 (br. s, 1H), 2.60 (ddd, $J = 13.7$, 9.3, and 7.3 Hz, 1H), 2.77 (ddd, $J = 14.1$, 8.9, and 5.6 Hz, 1H), 3.28 – 3.40 (m, 2H), 4.34 (d, $J = 11.5$ Hz, 1H), 4.58 (d, $J = 11.5$ Hz, 1H), 7.01 – 7.31 (m, 10H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 15.5$, 31.9, 34.8, 71.0, 74.2, 78.4, 125.7, 127.7, 127.8, 128.3, 128.4, 128.5, 138.3, 142.2; elemental analysis calcd for $C_{18}H_{22}O_2$ (270.4): C 79.96, H 8.20; found C 79.61, H 8.41.

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