Asymmetric Nucleophilic Substitution of Acetals

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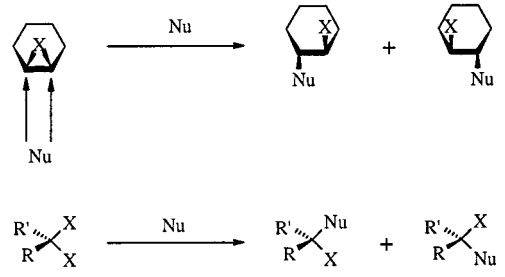
Benzaldehyde dimethylacetal (**1**) and 2-aryl-1,3-dioxolanes **5** react with organolithium reagents **2** in the presence of chiral ligands such as sparteine (**3**), 1-alkoxy-2-aminoethanes, or 1,2-dialkoxyethanes and BF_3 to afford monosubstitution products in high yields and in up to 81% enantiomeric excess. The enantioselectivity is strongly influenced by steric effects in the acetal and in the reagent. The highest *ee* was achieved with 2-(2-isopropyl)-1,3-dioxolane (**5c**) on treatment with 2-ethylphenyllithium (**2i**) in the presence of sparteine. The approach was applied to the synthesis of enantioenriched (*S*)-(–)-neobenodine (**17**) with 49% *ee*.

Introduction

Asymmetric nucleophilic substitutions traditionally involve desymmetrization of *meso* compounds possessing two enantiotopic centers, such as epoxides,[1–5] aziridines,[6–9] oxetanes,[10] or cyclopropanes.[11] With these compounds, the rate of the first substitution step is much greater than that of the second one, owing to the release of ring strain, so that double substitution does not occur. In principle, such reactions may also be accomplished by enantioselective displacement of one out of two enantiotopic leaving groups bound to a prochiral, sp^3-hybridized carbon atom. Acetals are suitable candidates for the study of these latter reactions. They are quite reactive in the presence of electrophiles, and monosubstitution may be controlled through the stabilization of the developing partial positive charge by the alkoxy substituent oxygen atom not displaced in the first step. The Lewis acid catalyzed diastereoselective cleavage of chiral cyclic acetals, permitting asymmetric C–C bond formation, is well established.[12–14] More recently, Harada et al. have described the enantioselective ring opening of 2-substituted 1,3-dioxolanes catalyzed by enantiopure arylboron complexes.[15,16]



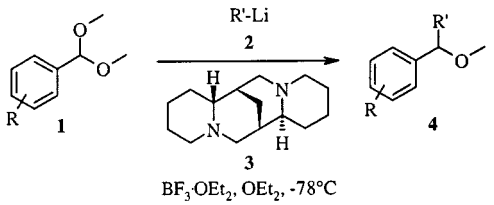
Scheme 1

We have recently reported the desymmetrization of *N*-sulfonated *meso*-aziridines by Grignard or organolithium reagents in the presence of chiral Cu catalysts.[17,18] It appeared feasible that similar conditions might also be applicable to acetal cleavage. While such reactions did indeed proceed in the presence of BF_3, the products were invariably racemic. Extensive screening of reaction conditions was subsequently carried out in order to find an appropriate reagent combination for enantioselective acetal cleavage. Some of the results of this investigation have been reported in preliminary form.[19] This paper gives a complete account of the work and includes additional organometallic reagents and chiral ligands.

Results and Discussion

1. Substitution of Benzaldehyde Dimethylacetal (1a)

Preliminary experiments were carried out with benzaldehyde dimethylacetal (**1a**) and nucleophiles such as trimethylsilyl cyanide, allyltrimethylsilane, or diethylzinc, in conjunction with chiral Lewis acid catalysts based on Sn^{II}, Zn^{II}, Ti^{IV}, Y^{III} and chiral ligands such as BINOL, TADDOL, bis(oxazolines) or pybox. Although monosubstitution could be achieved under certain reaction conditions, only racemic products were formed.[20] In view of these negative results, it was decided to incorporate the chiral feature of the reaction into the attacking nucleophile rather than the electrophile. After much trial and error, we turned our attention to a combination of an organolithium reagent with sparteine (**3**) and BF_3, as successfully applied by Alexakis et al. to the desymmetrization of epoxides (Scheme 2).[21] Indeed, treatment of **1a** with MeLi in the



Scheme 2

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presence of sparteine afforded the substitution product **4a** with significant, although low, enantioselectivity of 11%. The various parameters of the reaction were subsequently varied so as to optimize yield and enantioselectivity.

The reactions were carried out at −78°, by dropwise addition of $BF_3{\cdot}OEt_2$ (3.0 equiv.) to a solution of the acetal **1a** (1.0 equiv.), the organolithium compound **2** (4.0 equiv.), and sparteine (**3**, 4.0 equiv.) in ether. Representative results are summarized in Table 1, and additional examples are reported in refs.[19,20] Although the inductions observed in some of the runs were clearly significant and established the feasibility of the approach, no clear trend emerged from the data. Simple alkyllithium compounds gave moderate enantioselectivity − in the 20−25% range − with **1a**, while aryllithium compounds were somewhat less satisfactory. The introduction of Me or MeO substituents in the *p*-positions of the acetals resulted in decreased enantioselectivity, while *o*-substituents on the aryllithium reagents had only a minor effect. The best result, with a 40% *ee*, was obtained with the *o*-isopropyl-substituted acetal **1d** and *o*-ethylphenyllithium (**2i**) (Entry 17), suggesting that some control over stereoselectivity could be achieved as a result of steric crowding near the reacting center.

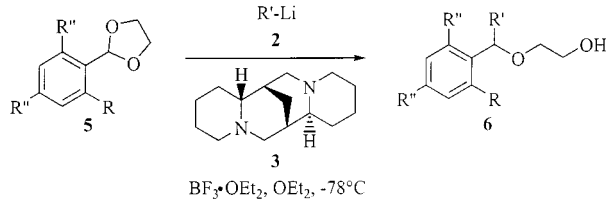
Table 1. Treatment of benzaldehyde dimethylacetal (**1**) with organolithium reagents **2** in the presence of sparteine (**3**)

Run[a]	Acetal (**1**) No.	R =	Reagent (**2**) No.	R′ =	Product (**4**) No.	Yield (%)	*ee* (%)
1	**a**	H	**a**	Me	**a**	50	11
2	**a**	H	**b**	*n*Bu	**b**	90	25
3	**a**	H	**c**	4-MeC_6H_4	**c**	85	23
4	**a**	H	**d**	2-MeC_6H_4	**d**	89	9
5	**a**	H	**e**	1-Naphthyl	**e**	86	5
6	**b**	4-Me	**a**	Me	**f**	53	1
7	**b**	4-Me	**b**	*n*Bu	**g**	85	11
8	**b**	4-Me	**f**	4-$MeOC_6H_4$	**h**	92	12
9	**b**	4-Me	**e**	1-Naphthyl	**i**	89	13
10	**c**	4-MeO	**a**	Me	**k**	89	0
11	**c**	4-MeO	**b**	*n*Bu	**l**	91	0
12	**c**	4-MeO	**c**	4-MeC_6H_4	**h**	91	5
13	**c**	4-MeO	**d**	2-MeC_6H_4	**m**	95	7
14	**c**	4-MeO	**g**	2-$MeOC_6H_4$	**n**	81	13
15	**c**	4-MeO	**h**	Phenyl	**o**	69	6
16	**c**	4-MeO	**e**	1-Naphthyl	**p**	88	4
17	**d**	2-*i*Pr[b]	**i**	2-EtC_6H_4	**q**	92	40

[a] Conditions: see text and Exp. Sect. − [b] With 2 equiv. of sparteine (**3**) and 3 equiv. of $BF_3{\cdot}OEt_2$.

2. Substitution of 2-Aryl-1,3-dioxolanes (5)

In view of the disappointing results with **1a**, we turned our attention to 2-aryl-1,3-dioxolanes **5** in the expectation that the restricted conformational mobility of the cyclic system should result in enhanced selectivity. This was indeed the case. Table 2 summarizes the more representative results; for additional data, the reader is referred to refs.[19,20] In the cyclic system the effect of *o*-substituents in the acetal and in the reagent is more pronounced. Thus, with the unsubstituted acetal **5a**, the *ee* increased from 12 to 34 and 46% on going from 4-methyl- to 2-methyl- and 2-isopropylphenyllithium (Entries 3, 4, and 6). With the sterically more demanding 2-*tert*-butyl (Entry 7) or 2-phenyl[19] groups in the reagent, however, no enantioselectivity was observed. Variation of the bulk of the 2-substituent in the acetal **5** with 2-ethylphenyllithium (**2i**) showed optimum selectivity with an isopropyl group (Entry 9), while bulkier substituents were less favorable. The mesityl derivative **5g** exhibited only poor enantioselectivity with **2i** and 1-naphthyllithium (**2e**) (Entries 15, 20). Treatment with 1-naphthyllithium was generally less satisfactory than with **2i**. The conditions for treatment of **5c** with **2i** were further optimized, and it was found that reduction of the excess of sparteine to 1.5 equiv. resulted in an increase in enantioselectivity from 75 to 81% (Entry 10). However, the *ee* dropped when a still lower amount of sparteine was used.[19] Among the various solvents tried, Et_2O was found to be the most efficient, followed by Bu_2O. Apolar solvents such as pentane and toluene were inappropriate and so was trifluorotoluene. No enantioselectivity was observed with THF as solvent,[19] suggesting complexation of the organolithium reagent by the solvent in competition with complexation by sparteine.



Scheme 3

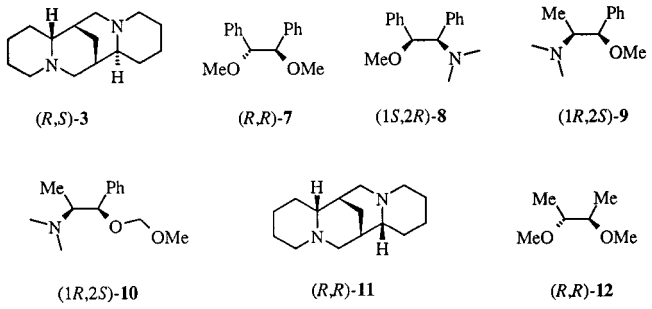


Figure 1. Ligands for asymmetric substitution

Sparteine is a particularly effective chiral ligand for organolithium compounds, with which it forms tight ion pairs.[22] Other ligands have been used for desymmetrization of epoxides with organolithium compounds in the presence of BF_3,[23] and some of these were also examined with **5c** and 2-ethylphenyllithium (**2i**). Isosparteine (**11**) exhibited positive, although moderate induction (38% *ee*), while the other ligands tried were ineffective. Surprisingly, however, treatment of phenyllithium (**2h**) with **5c** in the presence of the dimethyl ether **7** afforded **6f** in 82% *ee* (entry 28), while **10** (in toluene) provided practically no enantioselectivity for the same reaction.

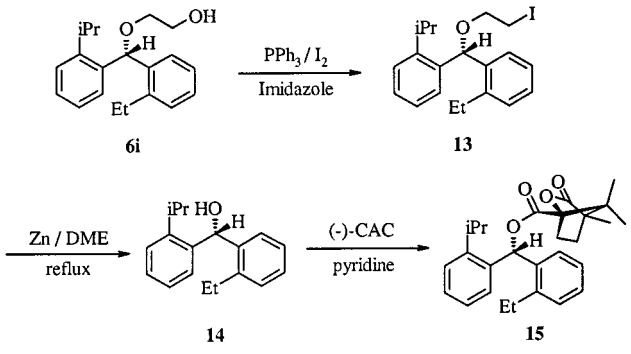
Table 2. Treatment of 2-aryl-1,3-dioxolanes **5** with organolithium reagents **2**

Run	Acetal **5** No.	R	R′	Reagent **2** No.	R′′	Ligand	Product **6** No.	Yield	*ee*
1	**a**	H	H	**a**	Me	**3**	**a**	61	03
2	**a**	H	H	**b**	*n*Bu	**3**	**b**	94	15
3	**a**	H	H	**c**	4-MeC_6H_4	**3**	**c**	89	12
4	**a**	H	H	**d**	2-MeC_6H_4	**3**	**d**	91	34
5	**a**	H	H	**i**	2-EtC_6H_4	**3**	**e**	90	30
6	**a**	H	H	**k**	2-*i*PrC_6H_4	**3**	**f**	94	46
7	**a**	H	H	**l**	2-*t*BuC_6H_4	**3**	**g**	92	04
8	**b**	Me	H	**i**	2-EtC_6H_4	**3**	**h**	76	52
9	**c**	*i*Pr	H	**i**	2-EtC_6H_4	**3**	**i**	85	75
10	**c**	*i*Pr	H	**i**	2-EtC_6H_4	**3**[a]	**i**	88	81
11	**d**	*t*Bu	H	**i**	2-EtC_6H_4	**3**	**k**	87	60
12	**e**	Ph	H	**i**	2-EtC_6H_4	**3**	**l**	77	69
13	**f**	2,3-Benzo	H	**i**	2-EtC_6H_4	**3**	**m**	60	27
14	**g**	Me_3Si	H	**i**	2-EtC_6H_4	**3**	**n**	59	31
15	**h**	Me	Me	**i**	2-EtC_6H_4	**3**	**o**	70	12
16	**b**	Me	H	**e**	1-Naphthyl	**3**	**p**	76	40
17	**c**	*i*Pr	H	**e**	1-Naphthyl	**3**	**q**	84	62
18	**e**	Phenyl	H	**e**	1-Naphthyl	**3**	**r**	57	56
19	**g**	Me_3Si	H	**e**	1-Naphthyl	**3**	**s**	30	31
20	**h**	Me	Me	**e**	1-Naphthyl	**3**	**t**	66	15
21	**c**	*i*Pr	H	**i**	2-EtC_6H_4	**7**	**i**	77	13
22	**c**	*i*Pr	H	**i**	2-EtC_6H_4	**8**	**i**	65	10
23	**c**	*i*Pr	H	**i**	2-EtC_6H_4	**9**	**i**	85	01
24	**c**	*i*Pr	H	**i**	2-EtC_6H_4	**10**	**i**	79	00
25	**c**	*i*Pr	H	**i**	2-EtC_6H_4	**11**	**i**	91	38
26	**c**	*i*Pr	H	**i**	2-EtC_6H_4	**12**	**i**	57	07
27	**c**	*i*Pr	H	**h**	Ph	**3**	**f**	92	65
28	**c**	*i*Pr	H	**h**	Ph	**7**	**f**	73	82
9	**c**	*i*Pr	H	**h**	Ph	**10**	**k**	82	06[b]

[a] With 2.0 equiv. of sparteine. – [b] In toluene.

In view of the low optical purity of the reaction products **6**, their absolute configurations were not determined, except in the case of **6i**. The alcohol was converted into the iodide **13**,[24] which was subjected to elimination with Zn[25] to afford the diarylmethanol **14** (Scheme 4). Treatment of **14** with (–)-camphanoyl chloride afforded the ester **15** (Figure 2). After chromatography and recrystallization, the *de* of **15** was > 98%. X-ray crystallography established the absolute configuration at the chiral center of **14** as (*R*).

Application of the reaction conditions to other acetals has so far not been successful. Thus, 2-benzyl-1,3-dioxolane and 2-phenyl-1-3-dioxane were unreactive under the reaction conditions used for 2-aryl-1,3-dioxolanes, and the 1,3-dioxolane derived from acetophenone afforded only racemic products. Extension of the approach to other acetals is in progress.



Scheme 4

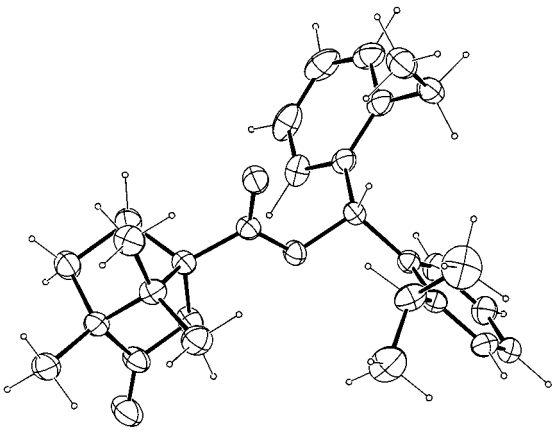
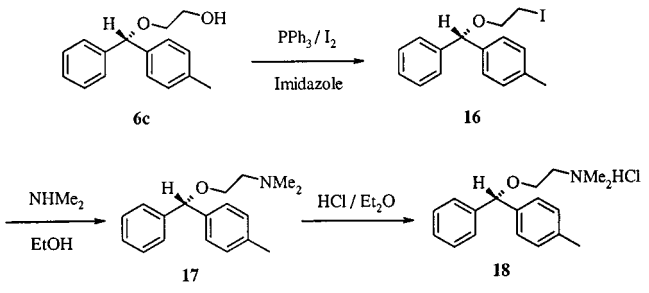


Figure 2. ORTEP view of the crystal structure of **15**

3. Asymmetric Synthesis of (*S*)-Neobenodine

Chiral diarylmethanols are constituents of biologically active compounds such as clemastine,[26] neobenodine,[27] and chloropheniramine.[28–30] Enantioselective syntheses of diarylmethanols use either asymmetric catalytic hydrogenation of diarylketones[31,32] or enantioselective addition of arylzinc reagents to benzaldehydes in the presence of chiral catalysts.[33] Asymmetric monosubstitution of 1,3-dioxolanes provides a simple route to enantioenriched neobenodine (**17**), although the absence of an *o*-substituent in the required acetal precursor **5a** is detrimental to the enantioselectivity of the procedure. Nevertheless, treatment of **5a** with *p*-tolyllithium in the presence of the chiral ligand (*R*,*R*)-**7** afforded **6c** in 82 yield and 49% *ee*. Other ligands such as sparteine (**3**) or **10** were less satisfactory. The alcohol **6c** was converted into the iodide **16** with PPh_3/I_2 in the presence of imidazole and, subsequently, into neobenodine (**17**) by treatment of **16** with dimethylamine (Scheme 5). The absolute configuration of **16** was determined by comparison of its optical rotation ($[\alpha]_D^{21} = -5.07$ for 49% *ee*; $c = 2.07$, EtOH) with that reported in the literature {$[\alpha]_D^{20} = +13.0$ (EtOH) for (+)-(*R*)-neobenodine}. Experiments towards improvement of the enantioselectivity of the substitution step are currently in progress in our laboratory.



Scheme 5

Conclusion

At the present stage of development, the enantioselective substitution at prochiral sp^3-hybridized carbon atoms is far from optimized. The combination of an organolithium compound with a chiral base and an achiral Lewis acid, as presented here, is not yet of general applicability, the enantioselectivity is modest and, above all, the system is not catalytic. However, these problems may eventually be overcome. While the corresponding enantioselective nucleophilic additions to carbonyl compounds are admittedly much more firmly established, these also have limitations in their scope and are essentially restricted to aldehydes,[34] glyoxylates, and pyruvates.[35,36] The enantioselective acetal cleavage could provide an alternative in situations in which carbonyl additions fail. The mechanism of the acetal substitution is not yet established. Although an S_N2-type reaction involving nucleophilic attack of the base-associated organolithium reagent to a BF_3-activated acetal appears plausible, the involvement of chiral ion-pair intermediates cannot be ruled out at present. Further research will deal with the extension of the approach to other prochiral substrates and to the use of chiral electrophiles in place of BF_3.

Experimental Section

General Remarks: See. ref.[18] NMR spectra were recorded with Varian XL 200, Varian Gemini 200, Bruker AMX 400, or Bruker AMX 500 spectrometers. The frequency used is indicated in each case. Chemical shifts are expressed in δ, relative to TMS.

Synthesis of Acetals

1. Substituted Benzaldehyde Dimethylacetals 1: These acetals are either commercially available (**1a**; Fluka) or were synthesized from the commercially available aldehydes according to reported procedures: **1b**,[37] **1c**.[38]

1-Dimethoxymethyl-2-isopropylbenzene (1d): This compound was prepared by transacetalization of the corresponding dioxolane **5c** (see below): Fuming sulfuric acid (4 drops) was added to **5c** (730 mg, 3.80 mmol) and trimethyl orthoformate (0.84 mL, 7.70 mmol) in dry MeOH (10 mL). The mixture was stirred at room temp. for 2 h, whereupon Na_2CO_3 (2.0 g) was added. After stirring for 15 min, the mixture was filtered, and the residue was washed with Et_2O (10 mL). The filtrate was washed with H_2O (10 mL) and dried ($MgSO_4$), and the solvents were evaporated. The residue was purified by distillation (124−126 °C/2 Torr) to give **1d** as a colorless liquid (623 mg, 84%). − IR ($CHCl_3$): $\tilde{\nu}$ = 3010w, 2965s, 2889w, 1713w, 1612w, 1402w, 1101m, 1066s, 1033w, 942m. − ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.25 (d, *J* = 7 Hz, 3 H), 3.34 (s, 6 H), 3.36 (sept, *J* = 7 Hz, 1 H), 5.58 (s, 1 H), 7.17−7.22 (m, 1 H), 7.31−7.37 (m, 2 H), 7.54−7.58 (m, 1 H). − ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 24.0 (q), 28.1 (d), 53.1 (q), 101.4 (d), 125.2 (d), 125.6 (d), 126.6 (d), 128.7 (d), 134.1 (s), 147.2 (s). − MS (EI, 70 eV); *m*/*z*: 163 (1) [$M^+ - CH_3O$], 149 (14), 148 (100), 147 (30), 133 (46), 105 (58), 104 (10), 103 (29), 91 (48), 79 (31), 78 (17), 77 (56), 65 (13), 55 (14), 51 (25).

2. 2-Aryl-[1,3]dioxolanes 5: 2-Phenyl-1,3-dioxolane (**5a**) was purchased from Aldrich. 2-(2-Methylphenyl)-1,3-dioxolane (**5b**) was prepared from *o*-tolualdehyde as described.[39] The other dioxolanes were synthesized according to the procedure given for **5c** (see below).

2-(2-Isopropylphenyl)-1,3-dioxolane (5c): 2-Isopropylbenzaldehyde[40] (1.50 g, 10.5 mmol) and ethylene glycol (1.31 g, 21.1 mmol) were subjected to azeotropic distillation in the presence of *p*-toluenesulfonic acid (100 mg) for 16 h. After addition of Na_2CO_3 (2 g) to the cooled solution, stirring was continued for 15 min, and the solid was filtered and washed with AcOEt (30 mL). The filtrate was washed, dried, and concentrated, and the crude product was purified by distillation (118−120 °C/2 Torr) to give **5c** (1.92 mg, 95%) as a colorless liquid. − IR ($CHCl_3$): $\tilde{\nu}$ = 3009w, 2967s, 2889w, 1710w, 1600w, 1399w, 1100m, 1066s, 1033w, 938m. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.31 (d, *J* = 7 Hz, 6 H), 3.41 (sept, *J* = 7 Hz, 1 H), 4.05−4.13 (m, 2 H), 4.14−4.23 (m, 2 H), 6.12 (s, 1 H), 7.22−7.30 (m, 1 H), 7.36−7.40 (m, 2 H), 7.60−7.64 (m, 1 H). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 24.0 (q), 28.3 (d), 65.2 (t), 101.2 (d), 125.4 (d), 125.6 (d), 125.7 (d), 129.2 (d), 134.0 (s), 147.5 (s). − MS (EI, 70 eV); m/*z*: 193 (12), 192 (91) [M^+], 191 (38), 149 (37), 148 (16), 147 (62), 133 (24), 132 (10), 131 (25), 130 (30), 129 (42), 119 (33), 117 (15), 115 (29), 105 (65), 103 (15), 91 (42), 79 (14), 77 (25), 73 (100),. − HR MS: 192.1145 ($C_{12}H_{16}O_2^+$; calcd. 192.1150).

2-(2-*tert*-Butylphenyl)-1,3-dioxolane (5d): This compound was prepared from 2-*tert*-butylbenzaldehyde.[41] Yield 94%. − IR ($CHCl_3$): $\tilde{\nu}$ = 3023w, 2968s, 2902w, 1713w, 1612w, 1399w, 1111m, 1065s, 1038w, 912m. − ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.49 (s, 9 H), 4.03−4.10 (m, 2 H), 4.22−4.30 (m, 2 H), 6.46 (s, 1 H), 7.27−7.35 (m, 2 H), 7.40−7.44 (m, 1 H). − ^{13}C NMR: ($CDCl_3$, 125 MHz): δ = 32.5 (q), 35.4 (s), 65.5 (t), 100.8 (d), 125.5 (d), 126.2 (d), 128.5 (d), 129.0 (d), 135.9 (s). − MS (EI, 70 eV); *m*/*z*: 206 (10) [M^+], 205 (18), 149 (22), 147 (12), 135 (11), 129 (44), 119 (16), 91 (20), 73 (100). − HR MS: 206.1323 ($C_{13}H_{18}O_2^+$; calcd. 206.1307).

2-(Naphth-1-yl)-1,3-dioxolane (5e): This compound was prepared from 1-naphthaldehyde. Yield 68%, colorless liquid, b.p. 128−130 °C/0.4 Torr. − IR ($CHCl_3$): $\tilde{\nu}$ = 2889m, 1689w, 1512w, 1339w, 1232m, 1171m, 1111s, 1073m, 1034m, 967m, 943w. − ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 4.15−4.21 (m, 2 H), 4.21−4.27 (m, 2 H), 6.53 (s, 1 H), 7.50−7.63 (m, 3 H), 7.83 (d, *J* = 7.1, 1 H), 7.89−7.97 (m, 2 H), 8.28 (dd, *J* = 8.3, 0.5, 1 H). − ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 65.2 (t), 102.2 (d), 123.5 (d), 123.9 (d), 125.0 (d), 125.7 (d), 126.3 (d), 128.5 (d), 129.6 (d), 130.9 (s), 133.0 (s), 133.8 (s). − MS (EI, 70 eV); *m*/*z*: 201 (11), 200 (72) [M^+], 199 (39), 156 (33), 155 (74), 142 (14), 141 36), 140 (15), 139 (27), 129 (23), 128 (100), 127 (56), 126 (12), 77 (19), 51 (15), 45 (38). − HR MS: 200.0840 ($C_{13}H_{12}O_2^+$; calcd. 200.0.837).

2-(2-Biphenyl)-1,3-dioxolane (5f): This compound was prepared from 2-phenylbenzaldehyde.[42] Yield 90%, b.p. 170−180 °C/0.4 Torr. − IR ($CHCl_3$): $\tilde{\nu}$ = 3026m, 2889m, 1599w, 1481m, 1397m, 1219s, 1120m, 1074s, 946m. − 1H NMR ($CDCl_3$, 400 MHz): δ = δ = 3.92−4.01(m, 2 H), 4.15−4.24 (m, 2 H), 5.71 (s, 1 H), 7.31−7.35 (m, 1 H), 7.39−7.51 (m, 7 H), 7.75−7.79 (m, 1 H). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 65.4 (t), 101.2 (d), 126.6 (d), 127.1 (d), 127.5 (s), 127.9 (d), 128.9 (d), 129.6 (d), 130.0 (d), 134.5 (s), 139.9 (s), 142.1 (s). − MS (EI, 70 eV); *m*/*z*: 227 (15), 226 (94) [M^+], 225 (91), 198 (19), 197 (15), 182 (17), 181 (100), 166 (15), 165 (52), 154 (50), 153 (47), 152 (63), 151 (18), 148 (50), 104 (11), 77 (11), 76 (14), 73 (58). − HR MS: 226.0974 ($C_{15}H_{14}O_2^+$; 226.0994).

2-(2-Trimethylsilanylphenyl)-1,3-dioxolane (5g): This compound was prepared from 2-(trimethylsilanyl)benzaldehyde.[43] Yield 88%, b.p. 110−112 °C/4 Torr. − IR ($CHCl_3$): $\tilde{\nu}$ = 2956m, 2893m, 1391m, 1251s, 1202m, 1127m, 1094s, 1061m, 944m, 842s. − ^{1}H NMR

($CDCl_3$, 500 MHz): δ = 0.38 (s, 9 H), 4.03−4.07 (m, 2 H), 4.15−4.19 (m, 2 H), 6.01 (s, 1 H), 7.33−7.38 (m, 1 H), 7.40−7.45 (m, 1 H), 7.56 (d, *J* = 7.3, 1 H), 7.67 (d, *J* = 7.6, 1 H). − ^{13}C NMR: ($CDCl_3$, 125 MHz): δ = 0.00 (q), 64.6 (t), 102.3 (d), 125.7 (d), 127.7 (d), 128.6 (d), 133.7 (d), 138.1 (s), 142.2 (s). − MS (EI, 70 eV); *m*/*z*: 222 (1) [M^+], 207 (27), 165 (15), 163 (100), 149 (31), 105 (16), 77 (11), 75 (15), 45 (12). − HR MS: 222.1029 ($C_{12}H_{18}O_2Si^+$; calcd. 222.1076).

2-(2,4,6-Trimethylphenyl)-1,3-dioxolane (5h): This compound was prepared from mesitaldehyde in 79% yield. Colorless crystals, m.p. 65−67 °C. − IR ($CHCl_3$): ṽ = 3029m, 2928m, 1734m, 1680s, 1608s, 1379w, 1208s, 1149m, 1077m, 1032m, 854w, 758s. − ^1H NMR ($CDCl_3$, 500 MHz): δ = 2.27 (s, 3 H), 2.41 (s, 6 H), 4.01−4.04 (m, 2 H), 4.18−4.22 (m, 2 H), 6.08 (s, 1 H), 6.83 (s, 2 H). − ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 19.9 (q), 20.9 (q), 65.0 (t), 102.2 (d), 128.3 (s), 130.0 (d), 138.0 (s), 138.6 (s). − MS (EI, 70eV); *m*/*z*: 192 (9) [M^+], 148 (74), 147 (100),120 (100), 120 (11), 119 (48), 105 (14), 91 (18), 77 (14), 62 (11). − HR MS; 192.1145 ($C_{12}H_{16}O_2^+$; 192.1151).

Chiral Ligands

Sparteine (3): (−)-Sparteine·H_2SO_4·$5H_2O$ (Fluka) was treated with aq. NaOH, the mixture extracted with Et_2O, the extract distilled, and the product stored under Ar at −78°. (*R*,*R*)-1,2-Diphenyl-1,2-dimethoxyethane (**7**) and (*R*,*R*)-2,3-dimethoxybutane (**12**) were prepared from the appropriate diols according to Kündig et al.,[44] (1*R*,2*S*)-2-dimethylamino-1-methoxy-1,2-diphenylethane (**8**) from (−)-(1*R*,2*S*)-2-amino-1,2-diphenylethanol according to ref.[45] and (1*R*,2*S*)-2-dimethylamino-1-methoxy-1-phenylpropane (**9**) from (−)-(1*R*,2*S*)-*N*-methylephedrine according to ref.[46]

(−)-(1*R*,2*S*)-2-Dimethylamino-1-methoxymethoxy-1-phenylpropane (10): (−)-(1*R*,2*S*)-*N*-methylephedrine (3.00 g, 16.7 mmol) and NaH (80%; 747 mg, 25.1 mmol) in anhydrous DMF (50 mL) were stirred at room temp. for 1.5 h. $MeOCH_2Cl$ (MOMCl, 1.72 mg, 21.4 mmol) in DMF (15 mL) was added at 0 °C and the mixture was stirred for 1.5 h at room temp. The solution was poured into ice/water (80 mL) and extracted with EtOAc (2 × 150 mL). The organic layers were washed with satd. NaCl (100 mL) and dried (Na_2SO_4), and the solvents were evaporated. The residue was purified by distillation (150−155 °C/0.3 Torr) to afford **10** (2.95 g, 79%) as a colorless oil. − $[\alpha]_D^{21}$ = −107.3 (*c* = 1.0, $CHCl_3$). − IR ($CHCl_3$): ṽ = 3020w, 1890w, 1670m, 1410w, 1170m, 1080w, 980m. − ^1H NMR ($CDCl_3$, 500 MHz): δ = 1.14 (d, *J* = 6. 6, 3 H), 2.33 (s, 6 H), 2.82 (dq, *J* = 6.6, 5.6, 1 H), 3.43 (s, 3 H), 4.59 (q, *J* = 6.6, 2 H), 4.81 (d, *J* = 5.6, 1 H), 7.28−7.39 (m, 5 H). − ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 8.6 (q), 41.4 (q), 56.0 (d), 64.4 (d), 79.3 (q), 94.5 (t), 127.2 (d), 128.0 (d), 141.1 (s). − MS (EI, 70 eV); *m*/*z*: 162 (9), 147 (5), 117 (7), 105 (13), 91 (7), 77 (11), 73 (12), 72 (100), 56 (7), 51 (6), 45 (55).

(*R*,*R*)-Isosparteine (11): This compound was prepared by isomerization of sparteine (**3**) with $AlCl_3$.[47] − M.p. 101−103 °C. − $[\alpha]_D^{21}$ = −29.1 (*c* = 1.0, EtOH). − IR ($CHCl_3$): ṽ = 2936w, 1203w, 786m, 738s. − ^1H NMR ($CDCl_3$, 500 MHz): δ = 1.25−1.40 (m, 2 H), 1.53−1.62 (m, 2 H), 1.65−1.85 (m, 4 H), 1.86−2.00 (m, 1 H), 2.10−2.30 (m, 1 H), 2.83−2.96 (m, 1 H), 3.00−3.10 (m, 1 H), 3.46 (s, large, 1 H). − ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 24.6 (t), 25.1 (t), 29.8 (t), 35.1 (d), 56.0 (t), 57.1 (t), 66.4 (d).

Substitution of Acetals 1 and Dioxolanes 5. − General Procedure: BuLi (1.0 mL, 1.6 M) was slowly added at −30° to the appropriate bromide or iodide (1.60 mmol) and sparteine (**3**; 375 mg, 1.60 mmol) in Et_2O (2.0 mL). After stirring for 1 h, the mixture was cooled to −78° and the acetal (0.40 mmol) was added, followed by slow addition of BF_3·OEt_2 (0.16 mL, 1.2 mmol) in Et_2O (1.0 mL). After the addition, stirring was continued at −78°. The reaction mixture was hydrolyzed with saturated NH_4Cl (5.0 mL) and extracted with Et_2O (3 × 10 mL). The combined organic layers were dried (Na_2SO_4), the solvent was evaporated, and the crude product was purified by flash chromatography (SiO_2; pentane/AcOEt) to afford the pure product. For yields: see Tables 1 and 2.

Substitution of Acetals 1

(1-Methoxyethyl)benzene (4a): B.p. 172−174 °C (ref.[48] 71−72 °C/23 Torr). 11% *ee* (Lipodex E, 40 °C, T_1 = 17.3, T_2 = 20.8 min). − IR ($CHCl_3$): ṽ = 2935w, 2824w, 1698w, 1452w, 1372w, 1111s, 992w. − ^1H NMR ($CDCl_3$, 500 MHz): δ = 1.37 (d, *J* = 6.3, 3 H), 3.15 (s, 3 H), 4.22 (q, *J* = 6.3, 1 H), 7.18−7.25 (m, 5 H). − ^{13}C NMR ($CDCl_3$, 125 MHz): δ = δ = 23.9 (q), 56.4 (q), 79.6 (d), 125.1 (d), 126.4 (d), 127.4 (d), 143.5 (s).

(1-Methoxypentyl)benzene (4b): B.p. 144−145 °C (ref.[49] 145−150 °C). − $[\alpha]_D^{21}$ = +10.3 (*c* = 1.01, EtOH) for 25% *ee* (Lipodex E, 45 °C, T_1 = 95.6, T_2 = 100.9 min). − IR ($CHCl_3$): ṽ = 3619w, 3032s, 2933w, 2399s, 1521s, 1424m, 1228s, 1202s, 1091m, 1045m, 928m, 802s, 703s. − ^1H NMR ($CDCl_3$, 500 MHz): δ = 0.88 (t, *J* = 7.1, 3 H), 1.19−1.43 (m, 4 H), 1.60−1.68 (m, 1 H), 1.79−1.88 (m, 1 H), 3.22 (s, 3 H), 4.09 (dd, *J* = 6.3, 7.1, 1 H), 7.27−7.31 (m, 3 H), 7.34−7.38 (m, 2 H). − ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 14.0 (q), 22.6 (t), 28.0 (t), 37.9 (t), 56.6 (q), 84.1 (d), 126.7 (d), 127.4 (d), 128.3 (d), 142.5 (s). − MS (EI, 70 eV); *m*/*z*: 178 (1) [$M^{+\cdot}$], 122 (9), 121 (100), 105 (4), 91 (12), 77 (10), 51 (3). − HR MS: 178.13258 ($C_{12}H_{18}O^{+\cdot}$; calcd. 178.13577).

1-[Methoxy(phenyl)methyl]-4-methylbenzene (4c): B.p. 286−288 °C (ref.[50] 160−162 °C/10 Torr.). − $[\alpha]_D^{21}$ = +7.5 (*c* = 2.10, EtOH) for 23% *ee* (HPLC, Chiracel OD-H, hexane/2-propanol, 25:1, 0.5 mL/min, T_1 = 14.2 min, T_2 = 15.2 min. − IR ($CHCl_3$): ṽ = 3001s, 2928w, 2359w, 1513w, 1453w, 1208s, 1088s, 738s. − ^1H NMR ($CDCl_3$, 400 MHz): δ = 2.36 (s, 3 H), 3.41 (s, 3 H), 5.25 (s, 1 H), 7.15−7.20 (m, 2 H), 7.25−7.30 (m, 3 H), 7.33−7.40 (m, 4 H). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 21.0 (q), 56.9 (q), 85.2 (d), 126.7 (d), 126.8 (d), 127.3 (d), 128.3 (d), 129.0 (d), 137.0 (s), 139.0 (s). − SM (EI, 70 eV, *m*/*z*): 212 (32) [$M^{+\cdot}$], 213 (6), 211 (8), 197 (10), 182 (9), 181 (49), 178 (8), 166 (12), 165 (14), 136 (5), 135 (42), 122 (6), 121 (67), 119 (15), 105 (21), 91 (20), 89 (6), 88 (6), 86 (38), 84 (60), 77 (18), 65 (7), 51 (41), 50 (7), 49 (100), 48 (8), 47 (15). − HR MS: 212.12322 ($C_{15}H_{16}O^{+\cdot}$; calcd. 212.12012).

1-[Methoxy(phenyl)methyl]-2-methylbenzene (4d): B.p. 298−300 °C (ref.[51] 94−97 °C/0.1 Torr). 9% *ee* (HPLC, Chiracel OJ, *n*-hexane/2-propanol, 99:1, T_1 = 12.6, T_2 = 14.5 min). − IR ($CHCl_3$): ṽ = 3010s, 1620m, 1513m, 1250w, 1205s, 1180w, 1081m, 1042w. − ^1H NMR ($CDCl_3$, 500 MHz): δ = 2.30 (s, 3 H), 3.41 (s, 3 H), 5.55 (s, 1 H), 7.04−7.19 (m, 4 H), 7.21−7.25 (m, 4 H), 7.34 (dd, *J* = 7.6, 1.3, 1 H). − ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 19.4 (q), 57.0 (q), 82.6 (d), 126.0 (d), 126.8 (d), 127.4 (d), 127.45 (d), 127.5 (d), 128.3 (d), 130.5 (s), 135.9 (s), 139.5 (s), 140.9 (s).

1-[Methoxy(4-methylphenyl)methyl]naphthalene (4e): Colorless oil, 4% *ee* (HPLC, Chiracel OD-H, hexane/2-propanol, 25:1, 0.5 mL/min, T_1 = 16.8, T_2 = 18.4 min). − IR ($CHCl_3$): ṽ = 3023w, 2359m, 1230m, 1202m, 1090m, 802m, 747m. − ^1H NMR ($CDCl_3$, 500 MHz): δ = 3.49 (s, 3 H), 5.96 (s, 1 H), 7.25−7.30 (m, 1 H), 7.32−7.37 (m, 2 H), 7.41−7.54 (m, 5 H), 7.62 (d, *J* = 6.9, 1 H), 7.84 (d, *J* = 8.2, 1 H), 7.88−7.91 (m, 1 H), 8.07−8.12 (m, 1 H). − ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 57.3 (q), 83.2 (d), 124.1 (d), 125.2 (d), 125.4 (d), 125.5 (d), 126.0 (d), 127.3 (d), 127.5 (d), 128.3 (d), 128.4 (d), 128.7 (d), 131.1 (s), 134.0 (s), 136.8 (s), 141.3 (s).

(1-Methoxyethyl)]-4-methylbenzene (4f): Colorless liquid, b.p. 198−200 °C (ref.[52] 71−74 °C/10 Torr. 1% *ee* (Lipodex E, 40 °C, T_1 = 15.2, T_2 = 17.6 min). − IR ($CHCl_3$): $\tilde{\nu}$ = 2929w, 2826w, 1703w, 1455w, 1367w, 1117s, 994w, 883w. − ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.41 (d, *J* = 6.4, 3 H), 3.18 (s, 3 H), 3.63 (s, 3 H), 4.22 (q, *J* = 6.3, 1 H), 7.16 (d, *J* = 7.9, 2 H), 7.35 (d, *J* = 7.9, 2 H). − ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 21.2 (q), 23.9 (q), 52.6 (q), 79.6 (d), 125.1 (d), 126.4 (d), 127.4 (d), 138.1 (s), 143.5 (s).

4-(1-Methoxypentyl)-1-methylbenzene (4g): B.p. 256−258 °C (ref.:[53] 125 °C/10 Torr). 11% *ee* (HPLC. Chiracel OJ, hexane/2-propanol, 25:1, 1 mL/min; T_1 = 3.5, T_2 = 4.1 min). − IR ($CHCl_3$): $\tilde{\nu}$ = 3629w, 3012s, 2935w, 2399s, 1525s, 1434m, 1228s, 1202s, 1093m, 1044m, 928m, 802s. − ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 0.89 (t, *J* = 7.2, 3 H), 1.21−1.41 (m, 4 H), 1.59−1.67 (m, 1 H), 1.77−1.89 (m, 1 H), 3.26 (s, 3 H), 4.13 (dd, *J* = 6.5, 7.2, 1 H), 7.17 (d, *J* = 7.8, 2 H), 7.36 (d, *J* = 7.8, 2 H). − ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 14.0 (q), 21.2 (q), 22.5 (t), 28.2 (t), 37.8 (t), 56.7 (q), 84.1 (d), 126.8 (d), 127.5 (d), 128.2 (d), 142.5 (s). − MS: (EI, 70 eV); *m*/*z*: 192 (1) [$M^{+\cdot}$], 136 (25), 135 (100), 119 (15), 105 (14), 91 (28), 65 (7). − HR MS: 192.15104 ($C_{13}H_{20}O^{+\cdot}$; calcd.: 192.15141).

1-[Methoxy(phenyl)methyl]-4-methylbenzene (4h): Colorless oil. 12% *ee* (HPLC, Chiracel OJ, hexane/2-propanol, 25:1, 0.5 mL/min, T_1 = 23.3, T_2 = 27.2 min). − IR ($CHCl_3$): $\tilde{\nu}$ = 3001m, 2929w, 2363w, 1501w, 1455w, 1201s, 1101s, 725s. − ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 2.34 (s, 3 H), 3.38 (s, 3 H), 3.80 (s, 3 H), 5.15 (s, 1 H), 6.87 (d, *J* = 8.8, 2 H), 7.15 (d, *J* = 7.9, 2 H), 7.24 (d, *J* = 7.9, 2 H), 7.27 (d, *J* = 8.8, 2 H). − ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 21.1 (q), 55.2 (q), 56.8 (q), 84.7 (d), 113.7 (d), 126.7 (d), 128.1 (d), 129.0 (d), 134.5 (s), 136.9 (s), 139.3 (s), 158.8 (s). SM (EI, 70 eV); *m*/*z*: 243 (11), 242 [$M^{+\cdot}$, 41), 243 (16), 212 (31), 211 (100), 155 (22), 152 (19), 151 (31), 135 (42), 119 (14), 92 (18). − HR MS: 242.13102 ($C_{16}H_{18}O_2^{+\cdot}$; calcd. 242.13143).

1-[Methoxy(4-methylphenyl)methyl]naphthalene (4i): Colorless oil. 13% *ee* (HPLC, Chiracel OD-H, hexane/2-propanol, 25:1, 0.5 mL/min, T_1 = 10.0, T_2 = 10.7 min). − IR ($CHCl_3$): $\tilde{\nu}$ = 3010s, 2932w, 2361w, 1515w, 1453w, 1208s, 1089s, 741m. − ^{1}H NMR ($CDCl_3$, 500 MHz): δ = δ = 2.35 (s, 3 H), 3.50 (s, 3 H), 5.94 (s, 1 H), 7.15 (d, *J* = 7.9, 2 H), 7.32 (d, *J* = 7.9, 2 H), 7.45−7.62 (m, 4 H), 7.80−7.91 (m, 2 H), 8.10−8.16 (m, 1 H). − ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 21.1 (q), 57.2 (q), 83.0 (d), 124.1 (d), 125.1 (d), 125.3 (d), 125.4 (d), 125.9 (d), 127.3 (d), 128.3 (d), 128.7 (d), 129.0 (d), 131.1 (s), 132.1 (s), 133.9 (s), 136.9 (s), 137.1 (s), 137.4 (s), 138.3 (d). − MS (EI, 70 eV); *m*/*z*: 263 (20), 262 (96) [$M^{+\cdot}$], 261 (10), 255 (8), 254 (79), 247 (13), 232 (23), 231 (100), 230 (6), 229 (11), 217 (6), 216 (28), 215 (36), 202 (8), 172 (5), 171 (36), 156 (9), 155 (38), 136 (5), 135 (50), 129 (7), 128 (60), 127 (75), 126 (15), 120 (6), 119 (56), 115 (7), 114 (7), 108 (18), 101 (14), 91 (18), 77 (10), 76 (5), 75 (9), 74 (8), 65 (13), 63 (9), 51 (10). 50 (7). − SM-HR: 262.13833 ($C_{19}H_{18}O^{+\cdot}$; calcd. 262.13577).

4-Methoxy-(1-methoxyethyl)benzene (4k): B.p. 182−184 °C (ref.[54] 72 °C/10 Torr). 0% *ee* (γ-Dex, 80 °C, T_1 = 60.8, T_2 = 61.4 min). − IR ($CHCl_3$): $\tilde{\nu}$ = 3619w, 3025s, 2399s, 1611w, 1513s, 1475w, 1244s, 1202s, 1103w, 1082w, 1035s, 928m, 803s, 708s. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.45 (d, *J* = 6.5, 3 H), 3.22 (s, 3 H), 3.83 (s, 3 H), 4.27 (q, *J* = 6.5, 1 H), 6.91 (d, *J* = 8.5, 2 H), 7.26 (d, *J* = 8.5, 2 H). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 23.7 (q), 55.2 (q), 56.1 (q), 79.0 (d), 113.7 (d), 127.3 (d), 127.4 (d), 135.4 (s), 158.9 (s).

1-Methoxy-4-(1-methoxypentyl)benzene (4l): Colorless liquid, b.p. 262−263 °C (ref.[53] 95 °C/1 Torr). 0% *ee* (γ-Dex, 80 °C, 60 min, rate 1 °C/min to 120 °C, T_1 = 95.1, T_2 = 95.5 min. − IR ($CHCl_3$): $\tilde{\nu}$ = 3620w, 3022s, 2960m, 2400m, 1611w, 1511s, 1423m, 1231s, 1202s, 1035m, 928m, 802s, 708s. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.88 (t, *J* = 7, 3 H), 1.15−1.25 (m, 1 H), 1.25−1.41 (m, 3 H), 1.58−1.68 (m, 1 H), 1.78−1.88 (m, 1 H), 3.19 (s, 3 H), 3.83 (s, 3 H), 4.05 (t, *J* = 6.9, 1 H), 6.91 (d, *J* = 8.3, 2 H), 7.23 (d, *J* = 8.3, 2 H). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 13.9 (q), 22.5 (t), 37.7 (t), 55.1 (q), 56.2 (q), 83.6 (d), 113.7 (d), 127.8 (d), 134.4 (s), 158.9 (s).

1-[Methoxy(4-methoxyphenyl)methyl]-2-methylbenzene (4m): Colorless oil. 7% *ee* (HPLC, Chiracel OD-H, hexane/2-propanol, 25:1, 0.5 mL/min, T_1 = 15.7, T_2 = 16.4 min). − IR ($CHCl_3$): $\tilde{\nu}$ = 3010s, 1610w, 1511m, 1250m, 1205s, 1172w, 1082m, 1031w. − ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 2.26 (s, 3 H), 3.39 (s, 3 H), 3.80 (s, 3 H), 5.38 (s, 1 H), 6.87 (d, *J* = 8.5, 2 H), 7.15 (d, *J* = 7.3, 2 H), 7.19−7.26 (m, 2 H), 7.23 (d, *J* = 8.5, 2 H), 7.48 (dd, *J* = 7.3, 1.3, 1 H). − ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 19.3 (q), 55.2 (q), 56.9 (q), 82.1 (d), 113.6 (d), 125.9 (d), 126.4 (d), 127.2 (d), 129.1 (d), 130.4 (d), 132.9 (s), 135.7 (s), 139.7 (s), 158.9 (s). − MS (EI, 70 eV); *m*/*z*: 242 (23) [$M^{+\cdot}$], 243 (6), 212 (21), 211 (100), 155 (12), 152 (9), 150 (31), 135 (32), 119 (16), 92 (14). − HR MS: 242.13003 ($C_{16}H_{18}O_2^{+\cdot}$; calcd. 242.13069).

4-Methoxy-1-[methoxy(2-methoxyphenyl)methyl]benzene (4n): Colorless oil. 13% *ee* (Chiracel OB-H, hexane/2-propanol, 9:1, 0.5 mL/min, T_1 = 28.6, T_2 = 32.9 min). − IR ($CHCl_3$): $\tilde{\nu}$ = 2998s, 1601w, 1512s, 1251m, 1210s, 1181m, 1081w, 1032w. − ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 3.38 (s, 3 H), 3.78 (s, 3 H), 3.80 (s, 3 H), 5.65 (s, 1 H), 6.82−6.87 (m, 3 H), 6.99 (ddd, *J* = 8.2, 7.3, 0.7, 1 H), 7.23 (ddd, *J* = 9.1, 7.9, 1.6, 1 H), 7.30 (d, *J* = 8.5, 2 H), 7.49 (dd, *J* = 7.9, 1.6, 1 H). − ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 55.2 (q), 55.4 (q), 55.9 (q), 78.4 (d), 110.5 (d), 113.5 (d), 120.7 (d), 126.5 (d), 128.2 (d), 130.7 (s), 134.2 (s), 156.5 (s), 158.7 (s). − MS (EI, 70 eV); *m*/*z*: 259 (10), 258 (54) [$M^{+\cdot}$], 257 (10), 243 (16), 228 (14), 227 (74), 226 (35), 225 (6), 211 (16), 197 (5), 195 (7), 181 (7), 168 (5), 153 (6), 152 (15), 151 (69), 141 (5), 139 (5), 136 (6), 135 (48), 122 (9), 121 (100), 115 (8), 92 (8), 91 (8), 78 (6), 77 (15), 76 (5), 65 (6), 65 (11), 63 (8), 51 (7), 50 (5), 45 (14). − HR MS: 258.12370 ($C_{16}H_{18}O_3^{+\cdot}$; calcd. 258.12558).

4-Methoxy-1-[methoxy(phenyl)methyl]benzene (4o): Colorless solid, m.p. 61−63 °C (ref.[55] 64−66 °C), b.p. > 300 °C (ref.[56] 135 °C/1 Torr). 6% *ee* (Chiracel OJ, hexane/2-propanol, 99:1, 1 mL/min, T_1 = 60.7, T_2 = 69.8 min). − IR ($CHCl_3$): $\tilde{\nu}$ = 3619w, 3026s, 2399m, 1511m, 1423w, 1228s, 1202s, 1032w, 928m, 802s, 710s. − ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 3.38 (s, 3 H), 3.80 (s, 3 H), 5.23 (s, 1 H), 6.88 (d, *J* = 8.8, 2 H), 7.27 (d, *J* = 8.8, 2 H), 7.34−7.36 (m, 5 H). − ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 55.2 (q), 56.9 (q), 84.9 (d), 113.7 (d), 126.7 (d), 127.3 (d), 128.2 (d), 128.3 (d), 134.2 (s), 142.3 (s), 159.0 (s).

1-[Methoxy(4-methoxyphenyl)methyl]naphthalene (4p): M.p. 46−48 °C (ref.[57] 50 °C). 4% *ee* (HPLC, Chiracel OD-H, hexane/2-propanol, 25:1, 0.5 mL/min, T_1 = 21.2, T_2 = 22.7 min). − IR ($CHCl_3$): $\tilde{\nu}$ = 3023m, 2365m, 1235s, 1205m, 1100s, 805m. − ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 3.47 (s, 3 H), 3.78 (s, 3 H), 5.91 (s, 1 H), 6.86 (d, *J* = 8.8, 2 H), 7.32 (d, *J* = 8.8, 2 H), 7.36−7.55 (m, 3 H), 7.63 (d, *J* = 6.9, 1 H), 7.82 (d, *J* = 8.2, 1 H), 7.80−7.98 (m, 1 H), 8.05−8.11 (m, 1 H). − ^{13}C NMR ($CDCl_3$,125 MHz): δ = 55.2 (q), 57.2 (q), 82.7 (d), 113.7 (d), 124.3 (d), 125.2 (d), 125.3 (d), 125.5 (d), 126.1 (d), 127.2 (d), 127.6 (d), 128.2 (d), 128.4 (d), 128.6 (d), 131.2 (s), 134.2 (s), 136.5 (s), 141.4 (s), 158.9 (s).

1-Ethyl-2-[(2-isopropylphenyl)(methoxy)methyl]benzene (4q): Colorless oil, $[\alpha]_D^{21}$ = 6.5 (*c* = 1.08, EtOH) for 40% *ee* (HPLC, Chiracel OJ, hexane/2-propanol, 99:1, 0.5 mL/min, T_1 = 7.8, T_2 = 9.9 min). − IR ($CHCl_3$): $\tilde{\nu}$ = 3005s, 2934w, 2359w, 1511w, 1453w, 1203s,

1088s, 744s. − ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.10 (d, *J* = 7, 3 H), 1.21 (t, *J* = 7, 3 H), 1.30 (d, *J* = 7, 3 H), 2.58−2.74 (m, 2 H), 3.12 (sept, *J* = 7, 1 H), 3.43 (s, 3 H), 5.78 (s, 1 H), 7.14−7.20 (m, 4 H), 7.24−7.31 (m, 3 H), 7.35 (dd, *J* = 7.6, 1.3, 1 H). − ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 14.9 (q), 23.5 (q), 24.2 (q), 25.2 (t), 28.5 (d), 57.5 (q), 78.5 (d), 125.5 (d), 125.6 (d), 125.7 (d), 127.4 (d), 127.5 (d), 127.7 (d), 127.9 (d), 128.6 (d), 137.1 (s), 138.2 (s), 142.4 (s), 147.5 (s). − MS (EI, 70 eV); *m/z*: 268 (1) [$M^{+\cdot}$], 237 (6), 236 (24), 225 (6), 222 (5), 221 (27), 208 (19), 207 (100), 194 (12), 193 (65), 192 (23), 191 (5), 182 (5), 179 (11), 178 (19), 165 (7), 163 (14), 149 (39), 147 (5), 133 (8), 132 (8), 131 (59), 130 (5), 129 (11), 119 (8), 117 (21), 116 (8), 115 (13), 105 (7), 103 (10), 91 (28), 89 (8), 77 (10), 51 (5). 237.1653 ($C_{18}H_{21}^+$; calcd. 237.1638).

Substitution of 2-Aryl-1,3-dioxolanes 5

2-(1-Phenylethoxy)ethanol (6a): Colorless liquid, b.p. 145−147 °C (ref.[58] 64−65 °C/16 Torr). 3% *ee* (HPLC, Chiralcel OD-H, hexane/2-propanol, 9:1, 0.5 mL/min, T_1 = 12.6, T_2 = 13.9 min). − IR ($CHCl_3$): ṽ = 3430brs, 3014s, 1231w, 1205s, 801m, 783s, 745w. − ^{1}H NMR ($CDCl_3$, 500 MHz,):1.47 (d, *J* = 6.5, 3 H), 1.85 (s large, 1 H), 3.41−3.46 (m, 2 H), 3.70−3.74 (m, 2 H), 4.46 (q, *J* = 6.5, 1 H), 7.26−7.38 (m, 5 H). − ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 24.0 (q), 62.0 (t), 69.6 (t), 78.5 (d), 126.1 (d), 127.6 (d), 128.5 (d), 143.5 (s).

2-[(1-Phenylpentyl)oxy]ethanol (6b): Colorless oil, 15% *ee* (HPLC, Chiracel OB-H, hexane/2-propanol, 9:1, 0.5 mL/min, T_1 = 10.4, T_2 = 11.8 min). − IR ($CHCl_3$): ṽ = 3443sbr, 3007w, 2933m, 2862w, 2341s, 1453w, 1203s, 1102m, 1050m, 889w. − ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 0.88 (t, *J* = 7, 3 H), 1.19−1.45 (m, 4 H), 1.61−1.70 (m, 1 H), 1.79−1.90 (m, 1 H), 2.07 (s, 1 H), 3.38−3.45 (m, 2 H), 3.68−3.72 (m, 2 H), 4.24 (dd, *J* = 7.2, 6.6, 1 H), 7.28−7.31 (m, 3 H), 7.35−7.39 (m, 2 H). − ^{13}C NMR: ($CDCl_3$, 125 MHz): δ = 14.1 (q), 22.7 (t), 28.0 (t), 37.9 (t), 62.0 (t), 69.9 (t), 82.9 (d), 126.5 (d), 127.6 (d), 128.6 (d), 142.5 (s). − MS (EI, 70 eV); *m/z*: 208 (1) [$M^{+\cdot}$], 152 (16), 151 (100), 147 (8), 108 (11), 107 (93), 105 (9), 104 (8), 92 (7), 91 (71), 79 (33), 78 (5), 77 (14), 51 (6), 45 (32). − HR MS: 208.14475 ($C_{13}H_{20}O_2^{+\cdot}$; calcd. 208.14633).

2-[(4-Methylphenyl)(phenyl)methoxy]ethanol (6c): Colorless oil, 12% *ee* (HPLC, Chiracel OD-H, hexane/2-propanol, 9:1, 0.5 mL/min, T_1 = 16.5, T_2 = 24.4 min). − IR ($CHCl_3$): ṽ = 3610brw, 2932w, 2360m, 1481w, 1451w, 1091s, 1032s, 1029w, 912w. − ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 2.02 (s large, 1 H), 2.34 (s, 3 H), 3.60(dd, *J* = 4.8, 4.4, 2 H), 3.79 (dd, *J* = 4.8, 4.4, 2 H), 5.39 (s, 1 H), 7.14−7.17 (m, 2 H), 7.24−7.29 (m, 3 H), 7.31−7.38 (m, 4 H). − ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 21.1 (q), 62.0 (t), 70.2 (t), 83.9 (d), 126.8 (d), 126.9 (d), 127.4 (d), 128.4 (d), 129.1 (d), 137.3 (s), 138.9 (s), 142.0 (s). − MS (EI, 70 ev); *m/z*: 242 (19) [$M^{+\cdot}$], 198 (5), 197 (28), 182 (17), 181 (100), 180 (16), 179 (6), 167 (5), 166 (19), 165 (31), 152 (5), 121 (13), 119 (15), 107 (7), 105 (17), 91 (9), 89 (6), 77 (12), 51 (5), 45 (7). − HR MS: 242.13003 ($C_{16}H_{18}O_2^{+\cdot}$; calcd. 248.13068).

2-[(2-Methylphenyl)(phenyl)methoxy]ethanol (6d): Colorless oil, $[\alpha]_D^{21}$ = +3.60 (*c* = 1.25, EtOH), for 34% *ee* (HPLC, hexane/2-propanol, 9:1, 0.5 mL/min, T_1 = 16.5, T_2 = 24.4 min). − IR ($CHCl_3$): ṽ = 3600brw, 2930w, 2359w, 1493w, 1452w, 1094s, 1035s, 1029w, 899w. − ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.80 (s large, 1 H), 2.28 (s, 3 H), 3.60−3.62 (m, 2 H), 3.79−3.81 (m, 2 H), 5.59 (s, 1 H), 7.15−7.17 (m, 2 H), 7.19−7.31 (m, 3 H), 7.31−7.35 (m, 4 H), 7.42−7.45 (m, 1 H). − ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 19.4 (q), 62.1 (t), 70.4 (t), 81.3 (d), 126.0 (d), 126.9 (d), 127.55 (d), 127.57 (d), 127.59 (d), 128.4 (d), 130.6 (d), 135.9 (s), 139.4 (s), 140.7 (s). − MS (EI, 70 eV); *m/z*: 242(34) [$M^{+\cdot}$], 197 (24), 182 (19), 181 (100), 180 (65), 179 (38), 178 (13), 166 (31), 165 (46), 151 (14), 121 (16), 119 (12), 107 (21), 105 (16), 91 (14), 77 (18), 45 (14). HR MS: 242.1310 ($C_{16}H_{18}O_2^+$; calcd. 242.1307).

2-[(2-Ethylphenyl)(phenyl)methoxy]ethanol (6e): Colorless oil, $[\alpha]_D^{21}$ = −5.90 (*c* = 0.96, EtOH). 30% *ee* (HPLC, Chiracel AD; hexane/2-propanol, 99:1; 1 mL/min, T_1 = 13.7, T_2 = 16.3 min). − IR ($CHCl_3$): ṽ = 3620m, 2975m, 2894w, 1390w, 1240w, 1048s, 877m. − ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.16 (t, *J* = 7.6, 3 H), 2.01 (s large, 1 H), 2.58−2.67 (m, 1 H), 2.67−2.76 (m, 1 H), 3.60−3.64 (m, 2 H), 3.79 (dd, *J* = 6, 4.5, 2 H), 5.67 (s, 1 H), 7.21−7.30 (m, 4 H), 7.31−7.36 (m, 4 H), 7.44 (dd, *J* = 7.3, 1.3, 1 H). − ^{13}CNMR ($CDCl_3$, 125 MHz): δ = 15.1 (q), 25.1 (t), 63.6 (t), 70.5 (t), 80.9 (d), 126.0 (d), 127.2 (d), 127.51 (d), 127.55 (d), 127.8 (d), 128.3 (d), 128.6 (d), 138.5 (s), 141.2 (s), 141.9 (s). − MS (EI, 70 eV); *m/z*: 256 (6) [$M^{+\cdot}$], 195 (45), 194 (60), 180 (20), 179 (100), 178 (14), 165 (14), 151 (11), 135 (10), 117 (57), 115 (12), 107 (21), 105 (17), 91 (23), 89 (12), 79 (18), 77 (18), 45 (15). − HR MS: 256.14676 ($C_{17}H_{20}O_2^{+\cdot}$; calcd. 256.14633).

2-[(2-Isopropylphenyl)(phenyl)methoxy]ethanol (6f): Colorless solid, m.p. 40−42 °C, $[\alpha]_D^{21}$ = +1.50 (c = 1.36, EtOH) for 46% *ee* (HPLC, Chiracel OD-H, hexane/2-propanol, 25:1, 0.5 mL/min, T_1 = 19.8, T_2 = 20.9 min). − IR ($CHCl_3$): ṽ = 3620m, 2973m, 2891w, 1402w, 1242w, 1054s, 867m. − ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.08 (d, *J* = 6.7, 3 H), 1.21 (d, *J* = 6.7, 3 H), 2.01 (s large, 1 H), 3.24 (sept, *J* = 6.7, 1 H), 3.62−3.66 (m, 2 H), 3.80−3.85 (m, 2 H), 5.74 (s, 1 H), 7.21−7.44 (m, 9 H). − ^{13}C NMR (125 MHz, $CDCl_3$): 23.7 (q), 24.1 (q), 28.4 (d), 62.1 (t), 70.5 (t), 90.0 (d), 125.7 (d), 125.80 (d), 127.4 (d), 127.5 (d), 128.0 (d), 128.3 (d), 137.6 (s), 141.6 (s), 146.9 (s). − MS (EI, 70 eV); *m/z*: 270 (3) [$M^{+\cdot}$], 209 (20), 208 (49), 194 (18), 193 (100), 179 (15), 178 (15), 165 (8), 151 (10), 132 (7), 131 (62), 129 (6), 117 (5), 116 (5), 115 (8), 107 (18), 105 (11), 91 (30), 89 (6), 79 (8), 77 (10), 51 (5), 45 (11). − HR MS: 270.16205 ($C_{18}H_{22}O_2^{+\cdot}$; calcd. 270.16199).

2-[(2-*tert*-Butylphenyl)(phenyl)methoxy]ethanol (6g): 4% *ee* (HPLC, Chiracel OD-H, hexane/2-propanol, 25:1, 0.5 mL/min, T_1 = 23.7, T_2 = 31.2 min). − IR ($CHCl_3$): ṽ = 3630m, 2965m, 2891w, 1400w, 1250w, 1049s, 857m. − ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.35(s, 9 H), 1.93 (s large, 1 H), 3.46−3.51 (m, 1 H), 3.63−3.72 (m, 3 H), 6.17 (s, 1 H), 7.14−7.26 (m, 7 H), 7.37−7.43 (m, 2 H). − ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 32.4 (q), 35.6 (s), 62.2 (t), 70.2 (t), 79.6 (d), 125.9 (d), 126.4 (d), 127.4 (d), 127.7 (d), 128.1 (d), 128.2 (d), 130.3 (d), 139.1 (s), 142.3 (s), 148.2 (s). − MS (EI, 70 eV); *m/z*: 285 (9), 284 (42) [$M^{+\cdot}$], 239 (17), 224 (11), 223 (50), 222 (7), 208 (13), 207 (66), 193 (10), 181 (6), 179 (10), 178 (16), 167 (14), 166 (5), 165 (14), 163 (8), 161 (11), 152 (14), 151 (100), 146 (8), 145 (61), 131 (7), 130 (6) 129 (20), 128 (7), 117 (10), 115 (11), 108 (5), 107 (68), 105 (24), 104 (5), 103 (7), 91 (52), 89 (12), 79 (16), 77 (18), 76 (5), 57 (30), 51 (8), 45 (23). − HR MS: 284.17813 ($C_{19}H_{24}O_2^{+\cdot}$; calcd. 284.17764).

2-[(2-Ethylphenyl)(2-methylphenyl)methoxy]ethanol (6h): Colorless oil, $[\alpha]_D^{21}$ = +2.51 (*c* = 0.93, EtOH) for 52% *ee* (HPLC, Chiracel OD-H, hexane/2-propanol, 25:1, 0.5 mL/min, T_1 = 21.4, T_2 = 23.2 min). − IR ($CHCl_3$): ṽ = 3619m, 2956m, 2887w, 1447w, 1391w, 1248w, 1049s, 877m. − ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.21 (t, *J* = 7.6, 3 H), 2.09 (s large, 1 H), 2.34 (s, 3 H), 2.58−2.73 (m, 2 H), 3.65 (dd, *J* = 4.8, 4.4, 2 H), 3.80 (dd, *J* = 4.4, 5.1, 3 H), 5.83 (s, 1 H), 7.18−7.31 (m, 8 H). − ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 14.9 (q), 19.3 (q), 25.1 (t), 62.1 (t), 71.1 (t), 77.9 (d), 125.8 (d), 125.9 (d), 127.4 (d), 127.7 (d), 127.9 (d), 128.6 (d), 130.5 (d), 136.6 (s), 137.4 (s), 138.6 (s), 142.5 (s). − MS (EI, 70 eV); *m/z*: 270 (1) [$M^{+\cdot}$], 210 (7), 209 (40), 208 (50), 194 (19), 193 (100), 181 (7), 180 (10),

179 (48), 178 (20), 166 (5), 165 (24), 135 (13), 133 (12), 131 (5), 121 (18), 119 (14), 118 (6), 117 (43), 115 (10), 105 (12), 103 (5), 96 (8), 93 (7), 91 (20), 89 (9), 79 (9), 77 (11), 65 (6), 51 (5), 45 (14). − HR MS: 270.16372 ($C_{18}H_{22}O_2^{+\cdot}$; calcd. 270.16199).

2-[(2-Ethylphenyl)(2-isopropylphenyl)methoxy]ethanol (6i): Colorless oil, $[\alpha]_D^{21}$ = 10.0 (*c* = 1.33, EtOH) for 75% *ee* (HPLC, Chiracel OD-H, hexane/2-propanol, 25:1, 0.5 mL/min, T_1 = 14.0, T_2 = 14.9 min). − IR ($CHCl_3$): $\tilde{\nu}$ = 3623m, 2956m, 2892w, 1447w, 1394w, 1245w, 1052s, 877m. − ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.11 (d, *J* = 7, 3 H), 1.15 (t, *J* = 7.6, 3 H), 1.31 (d, *J* = 7, 3 H), 1.89 (s large, 1 H), 2.57−2.72 (m, 2 H), 3.15 (sept, *J* = 7, 1 H), 3.63−3.67 (m, 2 H), 3.78−3.82 (m, 2 H), 5.95 (s, 1 H), 7.12−7.39 (m, 8 H). − ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 14.9 (q), 23.7 (q), 24.3 (q), 25.2 (t), 28.5 (d), 62.2 (t), 71.1 (t), 77.2 (d), 125.68 (d), 125.7 (d), 125.9 (d), 126.6 (d), 126.7 (d), 127.9 (d), 128.2 (d), 128.7 (d), 136.9 (s), 137.9 (s), 142.4 (s), 147.5 (s). − MS (EI, 70 eV); *m*/*z*: 237 (8) [$M^{+\cdot}$ − $C_2H_6O_2$] 236 (17), 222 (5), 221 (25), 208 (18), 207 (100), 195 (8), 194 (14), 193 (78), 192 (17), 179 (22), 178 (19), 165 (6), 135 (13), 133 (10), 132 (10), 131 (65), 129 (8), 119 (5), 117 (14), 116 (6), 115 (9), 105 (9), 103 (7), 91 (25), 89 (5), 79 (10), 77 (8), 45 (13). − HR MS: 236.1574 ($C_{18}H_{20}^+$, calcd. 236.1565). − $C_{20}H_{26}O_2$: calcd. C 80.49, H 8.78; found C 80.19, H 8.86.

2-[(2-*tert*-Butylphenyl)(2-ethylphenyl)methoxy]ethanol (6k): Colorless oil, $[\alpha]_D^{21}$ = −15.3 (*c* = 0.85, EtOH) for 60% *ee* (HPLC, Chiracel OD-H, hexane/2-propanol, 25:1, 0.5 mL/min, T_1 = 10.6 min, T_2 = 13.2 min). − IR ($CHCl_3$): $\tilde{\nu}$ = 3620m, 2959m, 2921w, 1448w, 1398w, 1239w, 1064s, 887m. − ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.35 (s, 9 H), 1.93 (s br, 1 H), 3.46−3.51 (m, 1 H), 3.63−3.72 (m, 3 H), 6.17 (s, 1 H), 7.14−7.26 (m, 7 H), 7.37−7.43 (m, 2 H). − ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 32.4 (q), 35.6 (s), 62.2 (t), 70.2 (t), 79.6 (d), 125.9 (d), 126.4 (d), 127.4 (d), 127.7 (d), 128.1 (d), 128.2 (d), 130.3 (d), 139.1 (s), 142.3 (s), 148.2 (s). − MS (EI, 70 eV); *m*/*z*: 285 (6), 286 (42) [$M^{+\cdot}$], 239 (17), 224 (11), 223 (50), 222 (7), 208 (13), 207 (66), 193 (10), 181 (6), 179 (10), 178 (16), 167 (14), 166 (5), 165 (14), 163 (8), 161 (11), 152 (14), 151 (100), 146 (8), 145 (61), 131 (7), 130 (6), 129 (20), 128 (7), 117 (10), 115 (11), 108 (5), 107 (68), 105 (24), 104 (5),103 (7), 91 (52), 89 (12), 79 (16), 77 (18), 76 (5), 57 (30), 51 (8), 45 (23). − HR MS: 284.1711 ($C_{19}H_{24}O_2^{+\cdot}$; calcd. 284.1776).

2-[(1,1′-Biphenyl-2-yl)(2-ethylphenyl)methoxy]ethanol (6l): Colorless oil. − $[\alpha]_D^{21}$ = +28.4 (*c* = 0.94, EtOH) for 69% *ee* (HPLC, Chiracel OD-H, hexane/2-propanol, 9:1, 0.5 mL/min, T_1 = 9.7, T_2 = 10.6 min). − IR ($CHCl_3$): $\tilde{\nu}$ = 3610w, 3503w, 2983w, 1609w, 1227s, 1047m, 757w. − ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 0.89 (t, *J* = 7.6, 3 H), 1.87 (s large, 1 H), 2.18−2.36 (m, 2 H), 3.28−3.34 (m, 1 H), 3.46−3.51 (m, 1 H), 3.65−3.76 (m, 2 H), 5.63 (s, 1 H), 7.14−7.48 (m, 13 H). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 14.5 (q), 24.9 (t), 62.0 (t), 70.4 (t), 77.4 (d), 125.7 (d), 127.0 (d), 127.2 (d), 127.4 (d), 127.5 (d), 127.6 (d), 128.1 (d), 128.2 (d), 128.7 (d), 129.0 (d), 130.0 (d), 137.95 (s), 137.97 (s), 141.0 (s), 142.3 (s), 142.5 (s). − MS (EI, 70 eV); *m*/*z*: 332 (7) [$M^{+\cdot}$], 287 (17), 271 (19), 270 (73), 269 (5), 256 (11), 255 (47), 254 (5), 253 (6), 252 (5), 242 (5), 241 (17), 239 (6), 181 (14), 179 (10), 178 (5), 166 (15), 165 (100), 153 (5), 152 (7), 135 (11), 133 (7), 128 (6), 126 (5), 117 (7), 115 (6), 105 (7), 91 (9), 79 (6), 77 (6), 45 (8). − HR MS: 332.17765 ($C_{23}H_{24}O_2^{+\cdot}$; calcd. 332.17764).

2-[(2-Ethylphenyl)(1-naphthyl)methoxy]ethanol (6m): Colorless oil, $[\alpha]_D^{21}$ = +2.41 (*c* = 1.08, EtOH) for 27% *ee* (HPLC, Chiracel OD-H, hexane/2-propanol, 9:1, 0.5 mL/min, T_1 = 17.2, T_2 = 20.5 min). − IR ($CHCl_3$): $\tilde{\nu}$ = 3611w, 3503w, 2975m, 1601w, 1232s, 1045m, 764w. − ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.24 (t, *J* = 7.6, 3 H), 2.14 (s large, 1 H), 2.58−2.80 (m, 2 H), 3.65−3.85 (m, 4 H), 6.42 (s, 1 H), 7.20−7.48 (m, 6 H), 7.50−7.61 (m, 2 H), 7.85 (d, *J* = 8.1, 1 H), 7.93 (dd, *J* = 8.4, 1.8, 1 H), 8.08 (d, *J* = 8.1, 1 H). − ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 14.9 (q), 25.0 (t), 62.1 (t), 71.2 (t), 77.8 (d), 123.5 (d), 125.2 (d), 125.6 (d), 125.7 (d), 126.3 (d), 127.6 (d), 128.0 (d), 128.6 (d), 128.8 (d), 131.8 (s), 133.9 (s), 136.1 (s), 137.4 (s), 142.5 (s). − MS (EI, 70 eV); *m*/*z*: 307 (11), 306 (50) [$M^{+\cdot}$], 246 (16), 245 (61), 244 (21), 230 (23), 229 (100), 228 (14), 217 (17), 216 (23), 215 (31), 202 (10), 201 (26), 179 (10), 157 (21), 155 (11), 135 (11), 133 (58), 129 (18), 128 (11), 127 (12), 118 (10), 117 (40), 115 (38), 114 (15), 91 (10), 45 (14). − HR MS: 306.16316 ($C_{21}H_{22}O_2^{+\cdot}$; calcd. 306.16199).

2-[(2-Ethylphenyl)(2-trimethylsilanylphenyl)methoxy]ethanol (6n): Colorless oil. − $[\alpha]_D^{21}$ = −4.90 (*c* = 2.17, EtOH) for 31% *ee* (HPLC, Chiracel OD-H, hexane/2-propanol, 9:1, 0.5 mL/min, T_1 = 8.6, T_2 = 9.5 min). − IR ($CHCl_3$): $\tilde{\nu}$ = 3682w, 3603w, 3028m, 2965w, 2360w, 1601w, 1228s, 1048m, 839m, 795m, 676m. − ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 0.22 (s, 9 H), 1.34 (t, *J* = 7.6, 3 H), 2.06 (s large, 1 H), 2.75−2.90 (m, 2 H), 3.57−3.67 (m, 2 H), 3.75−3.79 (m, 2 H), 5.94 (s, 1 H), 6.80 (dd, *J* = 7.9, 1, 1 H), 7.07 (ddd, *J* = 8.8, 7.6, 1.3, 1 H), 7.24−7.29 (m, 1 H), 7.30−7.33 (m, 1 H), 7.35 (ddd, *J* = 8.8, 7.6, 1.3, 1 H), 7.46 (ddd, *J* = 8.8, 7.6, 1.3, 1 H), 7.55 (dd, *J* = 7.6, 1, 1 H), 7.61 (dd, *J* = 7.6, 1.3, 1 H). − ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 0.47 (q), 14.9 (q), 24.8 (t), 62.1 (t), 70.2 (t), 80.1 (d), 125.4 (d), 127.1 (d), 128.0 (d), 128.1 (d), 128.3 (d), 128.5 (d), 129.3 (d), 134.9 (d), 138.6 (s), 139.2 (s), 142.3 (s), 145.2 (s). − MS (EI, 70 eV); *m*/*z*: 328 (1) [$M^{+\cdot}$], 267 (8), 266 (6), 255 (5), 254 (14), 253 (56), 251 (8), 223 (9), 195 (15), 194 (17), 193 (27), 192 (34), 180 (8), 179 (51), 178 (15), 167 (8), 165 (11), 163 (10), 135 (11), 119 (9), 117 (8), 105 (5), 77 (6), 75 (54), 74 (12), 73 (100), 59 (11), 45 (15). − HR MS: 328.18961 ($C_{20}H_{28}SiO_2^{+\cdot}$; calcd. 328.18630).

2-[(2-Ethylphenyl)(2,4,6-trimethylphenyl)methoxy]ethanol (6o): Colorless oil, 12% *ee*, (HPLC, Chiracel OD-H, hexane/2-propanol, 9:1, 0.5 mL/min, T_1 = 9.3, T_2 = 10.1 min). − IR ($CHCl_3$): $\tilde{\nu}$ = 3688w, 3607w, 2965w,1224m, 1208w, 794s, 743s, 717w. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.33 (t, *J* = 7.6, 3 H), 2.08 (s large, 1 H), 2.30 (s, 6 H), 2.34 (s, 3 H), 2.84 (d*q*, *J* = 7.6, 2.8, 2 H), 3.51−3.64 (m, 2 H), 3.76−3.82 (m, 2 H), 6.01 (s, 1 H), 6.92 (s, 2 H), 6.97 (d, *J* = 7.6, 1 H), 7.07 (ddd, *J* = 9.1, 7.8, 1.5, 1 H), 7.25−7.34 (m, 2 H). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 15.2 (q), 20.8 (q), 20.9 (q), 25.2 (t), 62.2 (t), 70.4 (t), 78.8 (d), 125.3 (d), 127.8 (d), 128.0 (d), 128.8 (d), 130.1 (d), 132.2 (s), 136.6 (s), 136.9 (s), 137.4 (s), 143.9 (s). − MS (EI, 70 eV); *m*/*z*: 298 (2) [$M^{+\cdot}$], 238 (6), 237 (33), 236 (42), 222 (18), 221 (90), 209 (5), 208 (20), 207 (100), 206 (15), 205 (8), 194 (8), 193 (47), 192 (20), 191 (8), 179 (22), 178 (25), 149 (30), 147 (25), 135 (16), 134 (6), 133 (35), 121 (6), 119 (11), 118 (10), 117 (44), 115 (13), 105 (21), 103 (12), 91 (15), 79 (12), 77 (11), 45 (25). − HR MS: 298.19079 ($C_{20}H_{26}O_2^{+\cdot}$; calcd. 298.19327).

2-[(2-Methylphenyl)(1-naphthyl)methoxy]ethanol (6p): Colorless oil. − $[\alpha]_D^{21}$ = −1.1 (*c* = 1.24, EtOH) for 40% *ee* (HPLC, Chiracel OD-H, hexane/2-propanol, 9:1, 0.5 mL/min, T_1 = 23.7, T_2 = 26.3 min). − IR ($CHCl_3$): $\tilde{\nu}$ = 3611w, 3499w, 2975m, 1601w, 1227s, 1049m, 756w. − ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.96 (s large, 1 H), 2.34 (s, 3 H), 3.75−7.85 (m, 4 H), 6.32 (s, 1 H), 7.17−7.33 (m, 5 H), 7.43 (dd, *J* = 7.55, 7.6, 1 H), 7.49−7.56 (m, 2 H), 7.83 (d, *J* = 8.2, 1 H), 7.89−7.92 (m, 1 H), 8.02 (d, *J* = 7.9, 1 H). − ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 19.3 (q), 62.2 (t), 71.6 (t), 78.5 (d), 123.5 (d), 125.3 (d), 125.6 (d), 125.62 (d), 126.1 (d), 126.3 (d), 127.4 (d), 127.8 (d), 128.7 (d), 128.9 (d), 130.7 (d), 131.8 (s), 133.9 (s), 135.7 (s), 136.6 (s), 138.3 (s). − MS (EI, 70 eV); *m*/*z*: 293 (14), 292 (65) [$M^{+\cdot}$], 232 (24), 231 (100), 230 (36), 229 (26), 228 (10), 216 (34),

215 (43), 202 (11), 201 (23), 165 (12), 157 (17), 155 (11), 129 (16), 127 (12), 121 (14), 119 (65), 115 (14), 114 (11), 108 (27), 91 (16), 45 (13). − HR MS: 292.14628 ($C_{20}H_{20}O_2^{+\cdot}$; calcd. 292.14633).

2-[2-Isopropylphenyl)(1-naphthyl)methoxy]ethanol (6q): Colorless oil. − $[\alpha]_D^{21}$ = +3.5 (*c* =1.1, EtOH) for 62% *ee* (HPLC: Chiracel OD-H, hexane/2-propanol, 25:1, 0.5 mL/min, T_1 = 23.7, T_2 = 31.2 min). − IR ($CHCl_3$): $\tilde{\nu}$ = 3625m, 2958m, 2901w, 1441w, 1398w, 1242w, 1052s, 875m. − ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.10 (d, *J* = 7, 3 H), 1.32 (d, *J* = 7, 3 H), 2.08 (s large, 1 H), 3.14 (sept, *J* = 7, 1 H), 3.75−3.81 (m, 2 H), 3.81−3.86 (m, 2 H), 6.46 (s, 1 H), 7.20 (ddd, *J* = 7.6, 7.6, 1.3, 1 H), 7.25 (d, *J* = 7.6, 1 H), 7.31−7.38 (m, 2 H), 7.39−7.45 (m, 2 H), 7.48−7.58 (m, 2 H), 7.83 (d, *J* = 8.2, 1 H), 7.92 (dd, *J* = 7.6, 1.6, 1 H), 8.07 (d, *J* = 8.2, 1 H). − ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 23.5 (q), 24.5 (q), 28.5 (q), 62.2 (t), 71.2 (t), 77.8 (d), 123.6 (d), 125.2 (d), 125.6 (d), 125.8 (d), 125.9 (d), 126.4 (d), 127.6 (d), 128.2 (d), 128.7 (d), 128.9 (d), 131.8 (s), 133.9 (s), 136.3 (s), 136.4 (s), 147.5 (s). − MS (EI, 70 eV); *m*/*z*: 321 (7), 320 (27) [$M^{+\cdot}$], 259 (14), 258 (14), 244 (22), 243 (100), 229 (11), 228 (16), 217 (9), 216 (6), 215 (16), 202 (7), 201 (18), 193 (5), 157 (15), 155 (7), 147 (22), 141 (8), 132 (12), 131 (82), 130 (11), 129 (30), 128 (14), 127 (11), 122 (5), 117 (5), 116 (8), 115 (21), 114 (11), 105 (5), 91 (22), 77 (6), 45 (11). − HR MS: 320.17574 ($C_{22}H_{24}O_2^{+\cdot}$; calcd. 320.17764).

2-[(1,1′-Biphenyl-2-yl)(1-naphthyl)methoxy]ethanol (6r): Colorless oil. − $[\alpha]_D^{21}$ = +14.3 (*c* = 1.01, EtOH) for 56% *ee* (HPLC, Chiracel OD-H, hexane/2-propanol, 9:1, 0.5 mL/min; T_1 = 12.6, T_2 = 17.4 min). − IR ($CHCl_3$): $\tilde{\nu}$ = 3620w, 3504w, 2986m, 1609w, 1227s, 1048m, 765w. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.63 (s large, 1 H), 3.36−3.42 (m, 1 H), 3.56−3.62 (m, 1 H), 3.71−3.78 (m, 2 H), 5.32 (s, 1 H), 7.33−7.53 (m, 12 H), 7.57−7.63 (m, 2 H), 7.82 (d, *J* = 8.3, 1 H), 7.85 (d, *J* = 7.8, 1 H). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 62.1 (t), 70.5 (t), 77.9 (d), 123.5 (d), 125.0 (d), 125.1 (d), 125.4 (d), 125.9 (d), 127.2 (d), 127.5 (d), 127.7 (d), 128.2 (d), 128.3 (d), 128.6 (d), 129.1 (d), 130.2 (d), 131.2 (s), 133.8 (s), 136.3 (s), 137.8 (s), 141.0 (s), 142.3 (s). − MS (EI, 70 eV); *m*/*z*: 355 (12), (45) 354 [$M^{+\cdot}$], 309 (12), 294 (6), 293 (14), 292 (49), 291 (27), 290 (9), 289 (12), 276 (5), 201 (7), 181 (27), 166 (16), 165 (100), 157 (6), 155 (6), 153 (6), 152 (6), 145 (10), 128 (7), 127 (8). − HR MS: 354.16245 ($C_{25}H_{22}O_2^{+\cdot}$; calcd. 354.16244).

2-[(1-Naphthyl)(2-trimethylsilanylphenyl)methoxy]ethanol (6s): Colorless oil. − $[\alpha]_D^{21}$ = −33.8 (*c* = 1.01, EtOH) for 31% *ee* (HPLC, Chiracel OD-H, hexane/2-propanol, 9:1, 0.5 mL/min, T_1 = 10.1, T_2 = 18.2 min). − IR ($CHCl_3$): $\tilde{\nu}$ = 3682w, 3604w, 3032m, 2965w, 2360w, 1623w, 1224s, 1054m, 839m, 791m. − ^{1}H NMR ($CDCl_3$, 500 MHz,): 0.13 (s, 9 H), 1.95 (s large, 1 H), 3.70−3.86 (m, 4 H), 6.43 (s, 1 H), 6.83 (d, *J* = 7.3, 1 H), 7.28 (dd, *J* = 7.9, 7.3, 1 H), 7.40 (ddd, *J* = 8.9, 7.6, 1.3, 1 H), 7.51−7.56 (m, 2 H), 7.61−7.66 (m, 2 H), 7.70 (d, *J* = 7.3, 1 H), 7.79 (d, *J* = 8.2, 1 H), 7.90 (d, *J* = 7.9, 1 H), 8.19 (d, *J* = 8.2, 1 H). − ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 0.41 (q), 62.2 (t), 70.7 (t), 80.3 (d), 123.8 (d), 124.9 (d), 125.7 (d), 126.6 (d), 126.8 (d), 127.3 (d), 127.9 (d), 128.8 (d), 128.9 (d), 129.4 (d), 132.2 (s), 134.0 (s), 134.9 (s), 137.3 (s), 139.2 (s), 144.7 (s). − MS (EI, 70 eV); *m*/*z*: 350 (10) [$M^{+\cdot}$], 289 (12), 275 (17), 218 (6), 217 (33), 216 (39), 215 (52), 201 (15), 177 (12), 129 (17), 119 (15), 75 (60), 73 (100), 45 (10). − HR MS 350.16926 ($C_{22}H_{26}SiO_2^{+\cdot}$; calcd. 350.17020).

2-[(1-Naphthyl)(2,4,6-trimethylphenyl)methoxy]ethanol (6t): Colorless oil, 15% *ee* (HPLC, Chiracel OD-H, hexane/2-propanol, 9:1, 0.5 mL/min, T_1 = 10.7, T_2 = 15.7 min). − IR ($CHCl_3$): $\tilde{\nu}$ = 3689w, 3610w, 2965w,1224m, 1208w, 795s, 753s, 733m, 717w cm^{-1}. − ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.17 (s large, 1 H), 2.31 (s, 6 H), 2.38 (s, 3 H), 3.61−3.68 (m, 1 H), 3.76−3.87 (m, 3 H), 6.52 (s, 1 H), 6.97 (s, 2 H), 7.05−7.08 (m, 1 H), 7.33 (dd, *J* = 8.1, 7.4, 1 H), 7.53−7.58 (m, 1 H), 7.61−7.66 (m, 1 H), 7.82 (d, *J* = 8.1, 1 H), 7.92 (d, *J* = 8.1, 1 H), 8.25 (d, *J* = 8.3, 1 H). − ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 20.8 (q), 20.9 (q), 62.3 (t), 70.5 (t), 78.8 (d), 124.3 (d), 124.9 (d), 125.5 (d), 125.6 (d), 126.3 (d), 128.8 (d), 128.9 (d), 130.1 (d), 131.7 (s), 132.4 (s), 134.2 (s), 134.6 (s), 137.1 (s), 137.6 (s). − MS (EI, 70 eV); *m*/*z*: 231 (15), 320 (63) [$M^{+\cdot}$], 260 (13), 259 (45), 258 (34), 257 (16), 244 (21), 243 (62), 242 (10), 230 (9), 229 (28), 228 (13), 215 (8), 208 (6), 202 (7), 201 (19), 193 (21), 157 (19), 156 (6), 155 (25), 149 (25), 148 (13), 147 (100), 132 (5), 129 (26), 128 (15), 127 (19), 122 (22), 121 (20), 120 (7), 119 (17), 115 (24), 114 (18), 113 (6), 108 (14), 105 (7), 101 (7), 91 (10), 86 (9), 84 (11), 73 (6), 57 (7), 55 (5), 45 (17). − HR MS: 320.17970 ($C_{22}H_{24}O_2^{+\cdot}$; calcd. 320.17764).

Absolute Configuration of 2-[(2-Ethylphenyl)(2-isopropylphenyl)-methoxy]ethanol (6i)

2-Ethyl-1-[(2-iodoethoxy)(2-isopropylphenyl)methyl]benzene (13): PPh_3 (1.526 g, 5.82 mmol), imidazole (396 mg, 5.82 mmol), and I_2 (1.107 g, 4.36 mmol) were stirred in dry Et_2O (5.0 mL) and MeCN (2.0 mL) at room temp. for 30 min. Compound **6i** (434 mg, 1.45 mmol) in Et_2O (2.0 mL) was added dropwise. The mixture was stirred at room temp. for 3 h, and was then diluted with petroleum ether (25 mL). The precipitate was removed by filtration, the filtrate was concentrated to 75% and filtered again, and the solvents were evaporated. The residue was purified by column chromatography (SiO_2; pentane/EtOAc, 25:1) to give **13** (525 mg, 89%). − IR ($CHCl_3$): $\tilde{\nu}$ = 3602m, 1602m, 1479w, 1227s, 908w, 740s. − ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.10 (d, *J* = 6.9, 3 H), 1.19 (t, *J* = 7.4, 3 H), 1.31 (d, *J* = 6.9, 3 H), 2.56−2.73 (m, 2 H), 3.15 (sept, *J* = 6.9, 1 H), 3.31 (t, *J* = 7.1, 2 H), 3.75−3.83 (m, 2 H), 5.97 (s, 1 H), 7.12−7.22 (m, 3 H), 7.23−7.32 (m, 4 H), 7.34−7.37 (m, 1 H). − ^{13}C NMR: ($CDCl_3$, 125 MHz): δ = 2.3 (t), 14.8 (q), 23.6 (q), 24.3 (q), 25.2 (t), 28.5 (d), 70.7 (t), 77.3 (d), 125.62 (d), 125.65 (d), 125.8 (d), 127.71 (d), 127.77 (d), 127.9 (d), 128.2 (d), 128.6 (d), 136.7 (s), 137.8 (s), 142.3 (s), 147.5 (s).

(2-Ethylphenyl)(2-isopropylphenyl)methanol (14): A mixture of **13** (450 mg, 1.10 mmol) and Zn (previously dried at 100 °C/0.4 Torr, 401 mg, 6.13 mmol) in dry DME (3.0 mL) was heated to reflux for 12 h. The suspension was filtered, the filtrate concentrated and the residue purified by flash chromatography (SiO_2; pentane/AcOEt, 4:1) to give **14** (273 mg, 98%) as a colorless oil. − $[\alpha]_D^{21}$ = +7.37 (*c* = 0.99, $CHCl_3$) for 79% *ee* (HPLC, Chiracel OD-H, hexane/2-propanol, 9:1, 0.5 mL/min; T_1 = 9.9, T_2 = 11.3 min). − IR ($CHCl_3$): $\tilde{\nu}$ = 3597m, 2967s, 2361w, 1731w, 1602w, 1485m, 1450m, 1230s, 1201s, 1006s. − ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.07 (d, *J* = 6.9, 3 H), 1.19 (t, *J* = 7.6, 3 H), 1.30 (d, *J* = 6.9, 3 H), 1.93 (s large, 1 H), 2.59−2.75 (m, 2 H), 3.23 (sept, *J* = 6.9, 1 H), 6.38 (s, 1 H), 7.15−7.36 (m, 8 H). − ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 14.9 (q), 23.5 (q), 24.3 (q), 25.1 (t), 28.3 (d), 69.2 (d), 125.6 (d), 125.7 (d), 125.8 (d), 126.7 (d), 126.8 (d), 127.8 (d), 128.0 (d), 128.6 (d), 139.6 (s), 140.8 (s), 141.5 (s), 146.7 (s). − MS (EI, 70 eV); *m*/*z*: 253 (1) [$M^{+\cdot}$], 236 (17), 225 (5), 222 (5), 221 (27), 211 (7), 208 (18), 207 (100), 194 (11), 193 (57), 192 (27), 182 (5), 179 (11), 178 (17), 165 (6), 149 (6), 148 (6), 147 (20), 135 (13), 134 (10), 133 (43), 131 (22), 129 (12), 119 (9), 117 (10), 116 (5), 115 (11), 106 (9), 105 (46), 103 (11), 91 (35), 89 (7), 79 (24), 78 (6), 77 (21), 65 (5), 51 (8). − HR MS: 236.1574 ($C_{18}H_{20}^{+}$, calcd. 236.1565).

(1*R*)-(2-Ethylphenyl)(2-isopropylphenyl)methyl (1*S*,4*R*)-4,7,7-Trimethyl-3-oxo-2-oxabicyclo[2.2.1]heptane-1-carboxylate (15): (−)-(1*S*)-Camphanoyl chloride (222 mg, 1.02 mmol) was added at 0 °C to

14 (200 mg, 0.79 mmol) in dry pyridine (6.0 mL). The mixture was stirred at room temp. for 2 h, then 2 M HCl (20 mL) was added, followed by CH_2Cl_2 (40 mL). The organic layer was washed with saturated $NaHCO_3$ (20 mL) and H_2O (20 mL) and then dried (Na_2SO_4), and the solvents were evaporated. The residue was purified by flash chromatography (SiO_2; pentane/AcOEt, 4:1) to afford **15** (321 mg, 93%) as a colorless solid, m.p. 110−114°. − $[\alpha]_D^{21}$ = +7.77 (c = 1.03, $CHCl_3$) for > 98% *de* (HPLC, Chiracel OD-H, hexane/2-propanol, 9:1, 0.5 mL/min; T_1 = 9.2, T_2 = 9.9 min). − IR ($CHCl_3$): $\tilde{\nu}$ = 3021m, 2969m, 1784s, 1727s, 1450w, 1272w, 1226m, 1100m, 1058m, 929w. − ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 0.92 (s, 3 H), 1.04 (s, 3 H), 1.10 (s, 3 H), 1.10 (d, J = 6.7, 3 H), 1.19 (t, J = 7.5, 3 H), 1.29 (d, J = 6.7, 3 H), 1.66−1.73 (m, 1 H), 1.88−1.95 (m, 1 H), 2.03−2.12 (m, 1 H), 2.40−2.47 (m, 1 H), 2.55−2.72 (m, 2 H), 3.12 (sept, J = 6.7, 1 H), 7.12−7.36 (m, 8 H), 7.56 (s, 1 H). − ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 9.6 (q), 14.7 (q), 16.7 (q), 16.8 (q), 23.6 (q), 24.0 (q), 25.3 (t), 28.7 (d), 28.9 (t), 30.9 (t), 54.3 (s), 54.8 (s), 71.9 (d), 90.9 (s), 125.7 (d), 125.8 (d), 125.9 (d), 127.7 (d), 127.8 (d), 128.5 (d), 128.7 (d), 128.7 (d), 135.0 (s), 136.3 (s), 141.8 (s), 146.8 (s), 166.8 (s), 178.3 (s). − MS (EI, 70 eV); *m/z*: 434 (1) [$M^{+\cdot}$], 392 (5), 391 (16), 237 (17), 236 (29), 222 (5), 221 (28), 209 (5), 208 (19), 207 (100), 195 (12), 194 (17), 193 (94), 192 (11), 179 (11), 178 (15), 165 (5), 132 (13), 131 (83), 130 (31), 129 (6), 119 (8), 118 (8), 117 (12), 116 (8), 115 (7), 91 (24), 83 (20), 77 (5), 55 (12). − HR MS: 434.24665 ($C_{28}H_{34}O_4^{+\cdot}$; calcd. 434.24570).

Synthesis of (*S*)-Neobenodine (17)

1-[(2-Iodoethoxy)(phenyl)methyl]-4-methylbenzene (16): This compound was prepared as described for **13**. − IR ($CHCl_3$): $\tilde{\nu}$ = 3620m, 1580w, 1450w, 1213s, 880w, 760s. − ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 2.34 (s, 3 H), 3.32 (dd, J = 6.6, 6.6, 2 H), 3.73 (dd, J = 6.6, 6.6, 2 H), 5.42 (s, 1 H), 7.16 (d, J = 7.9, 2 H), 7.24−7.29 (m, 3 H), 7.32−7.40 (m, 4 H). − ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 3.3 (t), 21.2 (q), 69.5 (t), 83.6 (d), 126.9 (d), 127.0 (d), 128.4 (d), 129.1 (d), 137.3 (s), 138.7 (s), 141.9 (s).

(*S*)-Dimethyl{2-[(4-methylphenyl)(phenyl)methoxy]ethyl}amine (17): The iodide **16** (280 mg, 0.79 mmol) was stirred in Me_2NH (2.0 mL, 40% in H_2O) and EtOH (5.0 mL) for 72 h at room temp. The solvent was evaporated and 5% KOH (10 mL) was added. The mixture was extracted with AcOEt (3 × 50 mL) and washed with H_2O (2 × 20 mL) and satd. NaCl (50 mL). After drying (Na_2SO_4) and solvent removal, crude **17** (201 mg, 94%) was obtained as colorless oil. − IR ($CHCl_3$): $\tilde{\nu}$ = 2905m, 1453w, 1224s, 1102m, 705w. − ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 2.32 (s, 9 H), 2.66 (dd, J = 6.0, 6.0, 2 H), 3.59 (dd, J = 6.0, 6.0, 2 H), 5.34 (s, 1 H), 7.16 (d, J = 7.9, 2 H), 7.22−7.26 (m, 3 H), 7.29−7.36 (m, 4 H). − ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 21.1 (q), 45.8 (q), 58.8 (t), 67.1 (t), 83.9 (d), 126.8 (d), 126.9 (d), 127.2 (d), 128.3 (d), 129.0 (d), 137.0 (s), 139.1 (s), 142.3 (s). − MS (EI, 70 eV); *m/z*: 269 (1) [M^+], 165 (5), 73 (17), 59 (5), 58 (100), 45 (10). − HR MS: 269.1814 ($C_{18}H_{23}ON^+$, calcd. 269.1780).

(*S*)-Dimethyl{2-[(4-methylphenyl)(phenyl)methoxy]ethyl}ammonium Chloride (18): Compound **17** (185 mg, 0.69 mmol) in dry Et_2O (10 mL) was added to 2 M HCl (1.0 mL in Et_2O). The solution was stirred for 15 min at room temp., and the resulting colorless precipitate was collected by filtration, and recrystallized (AcOEt) to yield **18** (202 mg, 96%). − M.p. 146−148 °C (ref.[59] 144−146 °C). − $[\alpha]_D^{20}$ = −5.07 for 49% *ee* (c = 2.07, EtOH) {ref.[59] $[\alpha]^{20}$ = +13.0 for (*R*) isomer}. − ^{1}H NMR ($CDCl_3$, 500 MHz): δ = 1.80 (br. s, 1 H), 2.32 (s, 3 H), 2.86 (d, J = 4.1, 3 H), 2.87 (d, J = 4.1, 3 H), 3.26−3.30 (m, 2 H), 3.90−3.93 (m, 3 H), 5.39 (s, 1 H), 7.14 (d, J = 7.9, 2 H), 7.19 (d, J = 7.9, 2 H), 7.24−7.35 (m, 5 H). − ^{13}C NMR ($CDCl_3$, 125 MHz): δ = 21.1 (q), 43.6 (q), 43.7 (q), 57.0 (t), 63.4 (t), 84.5 (d), 126.7 (d), 126.8 (d), 127.8 (d), 128.6 (d), 129.3 (d), 137.8 (s), 141.0 (s).

X-ray Crystallographic Study of 15: $C_{28}H_{34}O_4$, M_r = 434.6; μ = 0.08mm^{-1}, d_X = 1.147 g·cm^{-3}, orthorhombic, $P2_12_12_1$, Z = 4, a = 9.0595(4), b = 13.7776(8), c = 20.1637(13) Å, V = 2516.8(2) Å^3, colorless prism 0.11 × 0.16 × 0.21 mm. Cell dimensions and intensities were measured at 200 K with a Stoe IPDS diffractometer with graphite-monochromated Mo-K_α radiation (λ = 0.71069 Å). $-11 < h < 11$; $-16 < k < 16$; $-24 < l < 24$; 31768 measured reflections, 4930 unique reflections of which 2435 were observables ($|F_o| > 4\ \sigma\ (F_o)$)]. Full-matrix, least-squares refinement based on F using weighting of $1/[\sigma^2(F_o) + 0.0003(F_o^2)]$ gave final values of R = 0.039, wR = 0.041, and S = 1.90(4) for 289 variables and 2435 contributing reflections. The absolute configuration of the (−)-camphor moiety being known, the Flack parameter was fixed to 0. Hydrogen atoms were placed in calculated positions. The final Δρ showed a maximum of +0.20 and a minimum of −0.70 eÅ^{-3}. Crystallographic data (excluding structure factors) for the structure of **15** reported in this paper have been deposited at the Cambridge Crystallographic Data Centre (deposition no. CCDC-160245). Copies of the data can be obtained free of charge on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

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