Zinc bromide as catalyst for the stereoselective construction of quaternary carbon: improved synthesis of diastereomerically enriched spirocyclic diols

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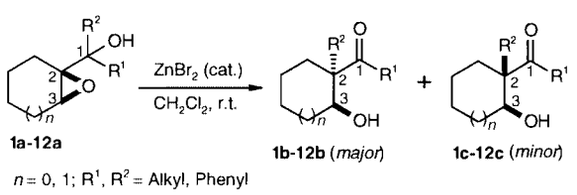
Zinc bromide ($ZnBr_2$) has proved to be a facile and efficient catalyst for the stereoselective semipinacol rearrangement of α-hydroxy epoxides at room temperature. Of note are the presence in the product of two adjacent chiral carbon centers, particularly the creation of a stereoselective quaternary center, and the efficient synthesis of β-hydroxy ketones, including some with naturally occurring spiroalkane skeletons. As an example of its application, important diastereomerically enriched spirocyclic diol ligands have been synthesized conveniently *via* this rearrangement followed by reduction of the spirocyclic β-hydroxy ketones obtained with appropriate hydride reagents.

Introduction

Quaternary carbon has long been an important class of structure, which is difficult to access in the synthesis of natural products. To date, only a few successful procedures for the creation of these centers have been reported,[1,2] and the diastereoselective formation of a quaternary carbon center is even rarer. Among the known procedures the Lewis acid (*e.g.* $TiCl_4$, $Al(i\text{-}PrO)_3$ and $SnCl_4$) promoted semipinacol rearrangement of α-hydroxy epoxides[3–8] has drawn much attention from organic chemists because a chiral quaternary carbon can be obtained if a chiral epoxide is employed. Although a few procedures using this kind of rearrangement have been reported,[2,7,8] they generally started from the hydroxy-protected epoxides (*e.g.* the epoxy silyl ethers) and/or needed an equivalent or excessive amount of Lewis acids. In our recent studies about this subject, we found that a catalytic amount of anhydrous $ZnBr_2$ (2–8 mol%) can promote such a diastereoselective rearrangement using unprotected α-hydroxy epoxides as shown in Scheme 1.



Scheme 1

This finding is of substantial interest because it may offer potential industrial and commercial benefits. Herein we present our experimental results on this subject and its application to the efficient synthesis of diastereomerically enriched spirocyclic diols that are useful intermediates for the preparation of highly effective chiral ligands for hydrogenation catalysts.[9]

Results and discussion

In this study α-hydroxy epoxides with five- or six-membered rings (**1a**–**12a**[10]) were selected for investigation in consideration of their important relationship to natural products and chiral spirocyclic diol ligands of current interest. A typical experimental procedure involved the following steps: (1) The hydroxy epoxide (~1 mmol) was dissolved in dry CH_2Cl_2 (~10 ml), and a catalytic amount of anhydrous $ZnBr_2$ (2–8 mol%) was added to the solution which was stirred at room temperature (15–28 °C) until the reactant disappeared (checked by TLC). (2) The reaction mixture was partitioned with water, the organic phase dried over $MgSO_4$ and purified *via* chromatography on silica gel to afford the β-hydroxy ketones (tabulated in Table 1). All the products contained two diastereoisomerically enriched carbon centers, with one being quaternary. Other Lewis acids have been tested and anhydrous $ZnCl_2$ also proved to be effective to this reaction. However, $AlCl_3$ was found to be too reactive and a complicated mixture was formed.

From Table 1, it can be seen that most of the experiments (entries 1, 3, 5–10 and 12) gave satisfactory results with good yields and fast rates. In particular, entries 1, 3 and 5–8 exhibited excellent stereoselectivity and gave diastereoisomerically pure 2,3-*syn*-β-hydroxy ketones. It appeared that the substrates with a cyclohexene epoxide moiety gave substantially better results than the corresponding substrates containing a cyclopentene epoxide moiety. It is of particular interest to note that the stereoselectivity of this reaction was independent of the C^1-configuration of the substrate. For example, in entries 5–7, the mixed substrates with two C^1-epimers afforded a diastereoisomerically pure β-hydroxy ketone. Furthermore, we have successfully constructed a series of spirane skeletons with various sizes of rings (entries 1–3 and 9–12), some of which are naturally occurring but not easily synthesized. In all examples, we were not able to isolate the bromo-substituted by-products or the competitive rearrangement products (allylic alcohols).[8,11] We believe that the poor results from entries 2, 4 and 11 may be due to the weaker migration ability of the methyl group (entry 4) or due to the unfavorable cycloenlargement from a six-membered-ring to a seven-membered-ring (entries 2 and 11).

To assign the main stereochemistry of this $ZnBr_2$-catalyzed rearrangement and thus support a possible reaction mechanism, we examined the ^1H NMR of the exclusive or predominant products incorporating a cyclohexanol moiety (entries 1–8). All of them displayed a singlet for H-3, suggesting the direction of axial C^3-OH and thus equatorial C^2-acetyl because it was

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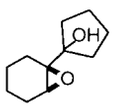
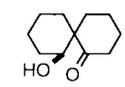
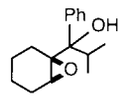
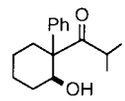
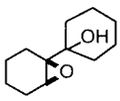
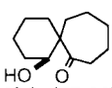
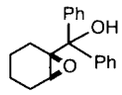
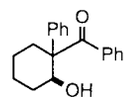
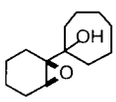
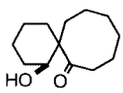
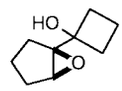
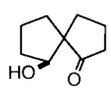
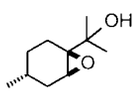
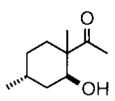
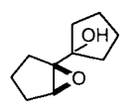
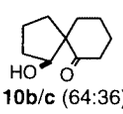
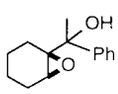
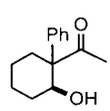
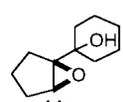
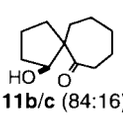
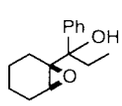
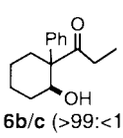
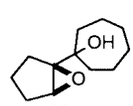
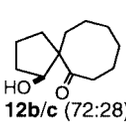
Table 1 $ZnBr_2$-Catalyzed rearrangement of α-hydroxy epoxides[a]

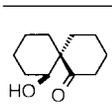
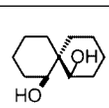
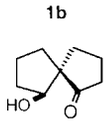
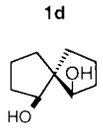
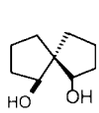
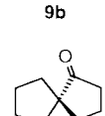
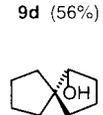
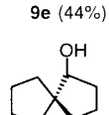
Entry	Substrate *syn*:*anti*	Product	Reaction time/h	Total yield (%)	Entry	Substrate *syn*:*anti*	Product	Reaction time/h	Total yield (%)
1	 **1a**	 **1b/c** (>99:<1)	8	91	7	 **7a** (87:13)	 **7b/c** (>99:<1)	4	95
2	 **2a**	 **2b/c** (77:23)	14	41	8	 **8a**	 **8b/c** (>99:<1)	0.5	90
3	 **3a**	 **3b/c** (>99:<1)	5	83	9	 **9a**	 **9b/c** (57:43)	1.5	94
4	 **4a**	 **4b/c** (78:22)	95	64	10	 **10a**	 **10b/c** (64:36)	7	60
5	 **5a** (70:30)	 **5b/c** (>99:<1)	1	94	11	 **11a**	 **11b/c** (84:16)	240	55
6	 **6a** (61:39)	 **6b/c** (>99:<1)	0.5	89	12	 **12a**	 **12b/c** (72:28)	3	68

[a] The sturctures of all products were determined on the basis of NMR and MS, and the ratios of diastereoisomers were established by ^1H NMR and/or GC-MS analysis.

unlikely that two sterically hindering substituents were located at two adjacent axial directions. We concluded that the main β-hydroxy ketone products of this reaction possessed the 2,3-*syn*-configuration. The elucidation of the stereochemistry is consistent with other reported Lewis acid-promoted rearrangements.[3,7,8] This is confirmed by the fact that the treatment of product **1b** with DIBAL-H, gave diol **1d** which is identical to the 3,2-*syn* compound previously reported.[8] Based on these observations, we propose an *anti*-1,2-migration process which involves the activation of the C^2–O bond to be cleaved by the coordination of $ZnBr_2$ to the oxygen of the epoxide, accompanied by a 1,2-migration of R^2. In entries 2, 4 and 9–12, the formation of the minor 3,2-*anti*-products (**2c**, **4c** and **9c**–**12c**) may be due to a faster C^2–O bond cleavage than the 1,2-migration of R^2 and the existence of a carbocation transition state which permits a *syn*-1,2-migration of R^2.

As one of the applications of this $ZnBr_2$-catalysed procedure for constructing quaternary carbon diastereoisoselectively, we have successfully developed an improved synthetic method for preparation of diastereoisomerically enriched spirocyclic diols (**1d** and **9d**–**f**). Recently, these kinds of diols have proved to be useful ligands for the preparation of highly effective chiral phosphinite ligands, which showed high enantioselectivity in the Rh-catalyzed asymmetric hydrogenation of enamides.[9] Although other synthetic methods for these kinds of diols have been reported,[8,12–14] they generally involve many steps or are restricted to the synthesis of one or two diastereoisomers. Our target is to develop a convenient procedure that is based on the diastereoselective reduction of the quaternary-carbon-containing spirocyclic β-hydroxy ketone thus obtained. As a result (listed in Table 2), the *cis*,*trans*-spiro[5.5]undecane-1,7-diols (**1d**) were successfully synthesized in nearly 100% de *via* the reduction of **1b** with DIBAL-H. Similarly, two mixtures, the *cis*,*trans* and *cis*,*cis* (**9d** and **9e**), and *cis*,*trans* and *trans*,*trans* (**9d** and **9f**)-spiro[4.4]nonane-1,6-diols were obtained from the reaction of **9b** and **9c** with $NaBH_4$ and DIBAL-H, respectively. From these racemic spirocyclic diols (**1d**, **9d**–**f**), the optically

Table 2 Reduction of β-hydroxy ketones with hydride reagents[a]

Substrates	Spirocyclic diols		Reductive reagents	Yield (%)
 **1b**	 **1d**		DIBAL-H	83
 **9b**	 **9d** (56%)	 **9e** (44%)	$NaBH_4$	92
 **9c**	 **9d** (56%)	 **9f** (44%)	DIBAL-H	81

[a] The DIBAL-H reduction was carried out with two equivalents of DIBAL-H at −78 °C in dry CH_2Cl_2 and the $NaBH_4$ reduction was carried out with 4 equivalents of $NaBH_4$ at 0 °C using MeOH as solvent.

pure spirocyclic diol ligands can be readily obtained, if the established chiral resolution procedures are put in use.[12,14]

In conclusion, we have developed a facile and efficient method for the construction of chiral quaternary carbon through the $ZnBr_2$-catalyzed semipinacol rearrangement of α-hydroxy epoxides. This method is expected to find more applications in organic synthesis.

Experimental

The ^1H NMR and ^{13}C NMR data in $CDCl_3$ solution were recorded on a Bruker AM-400 MHz spectrometer. The chemical shifts are reported in ppm relative to TMS. *J* Values are given in Hz. The GC-MS, MS and HRMS data were obtained with EI (70 eV). Column chromatographies were generally performed on silica gel (200–300 meshes) eluting with petroleum ether–EtOAc (20 : 1→50 : 1). Unless otherwise noted, TLC inspections on silica gel F_{254} plates were performed with petroleum ether–EtOAc (10 : 2.5). All starting α-hydroxy epoxides were prepared by literature procedures[12] and were characterized by NMR and mass spectroscopy.

General procedure for rearrangement reaction

To a solution of α-hydroxy epoxide (~1 mmol) in dry CH_2Cl_2 (~10 ml) was added $ZnBr_2$ (2–8 mol%) under argon. The mixture was stirred at rt and monitored with TLC until the starting material disappeared. The reaction mixture was partitioned with water, the organic phase dried over $MgSO_4$ and concentrated *in vacuo*. The residue was purified by column chromatography on silica gel to give the β-hydroxy ketone.

1-Hydroxyspiro[5,5]undecan-7-one 1b. Following the typical procedure above (rt, 8 h), the epoxide **1a** (200 mg, 1.10 mmol) was treated with $ZnBr_2$ (9.9 mg, 0.044 mmol) to afford the product **1b** (182 mg) in 91% yield. δ_H 1.19 (m, 1H), 1.25–1.37 (m, 2H), 1.47 (m, 1H), 1.61–1.83 (m, 7H), 1.92–1.98 (m, 2H), 2.16–2.21 (m, 2H), 2.52 (m, 1H), 3.22 (br, 1H), 3.39 (br s, 1H); δ_C 20.2, 21.1, 22.4, 28.1, 29.9, 30.8, 36.0, 39.3, 53.5, 74.1, 219.0; *m*/*z* (GC-MS) 182 (M^+, 14%), 164 (41), 135 (18), 111 (100), 98 (44), 81 (32), 67 (33), 55 (48); HRMS (EI): found 182.1307; calc. for $C_{11}H_{18}O_2$: 182.1306.

1-Hydroxyspiro[5,6]dodecan-7-one 2b/c. Following the typical procedure above (rt, 14 h), the epoxide **2a** (200 mg, 1.02 mmol) was treated with $ZnBr_2$ (11.5 mg, 0.05 mmol) to afford the product **2b/c** (82 mg, 77 : 23) in 41% total yield. δ_H 1.14–2.61 (m, 16H), 3.59 (t, *J* 4.9, 1H), 3.92 (dd, *J* 4.1, 11.3, 1H); δ_C 20.5, 21.5, 21.5, 24.1, 24.7, 25.5, 26.4, 26.5, 27.3, 29.4, 30.1, 30.1, 30.2, 30.7, 33.0, 34.6, 39.9, 41.2, 55.0, 55.6, 73.2, 74.6, 219.0, 219.4; *m*/*z* (GC-MS) **2b**: 196 (M^+, 7%), 178 (15), 149 (11), 125 (89), 111 (53), 81 (72), 67 (52), 55 (100); **2c**: 196 (M^+, 8%), 178 (22), 149 (15), 125 (87), 111 (59), 81 (44), 67 (47), 55 (100); HRMS (EI): found 196.1469; calc. for $C_{12}H_{20}O_2$: 196.1463.

1-Hydroxyspiro[5.7]tridecan-7-one 3b. Following the typical procedure above (rt, 5 h), the epoxide **3a** (200 mg, 0.95 mmol) was treated with $ZnBr_2$ (10.7 mg, 0.048 mmol) to afford the product **3b** (166 mg) in 83% yield. δ_H 1.18–2.04 (m, 18H), 2.32 (m, 1H), 2.49 (m, 1H), 3.27 (br, 1H), 3.74 (dd, *J* 3.4, 5.6, 1H); δ_C 20.9, 21.0, 24.1, 24.7, 26.0, 28.1, 29.6, 29.7, 30.9, 37.0, 53.6, 72.2, 222.9; *m*/*z* (GC-MS) 210 (M^+, 35%), 182 (8), 149 (14), 139 (45), 111 (78), 98 (72), 81 (100), 55 (88); HRMS (EI): found 210.1624; calc. for $C_{13}H_{22}O_2$: 210.1620.

(1*S*,5*R*)-2-Acetyl-2,5-dimethylcyclohexan-1-ol 4b/c. Following the typical procedure above (rt, 95 h), the epoxide **4a** (200 mg, 1.18 mmol) was treated with $ZnBr_2$ (21.2 mg, 0.094 mmol) to afford the product **4b/c** (128 mg, 78 : 22) in 64% total yield. δ_H 0.84 (d, *J* 6.6, 3H), 0.90 (d, *J* 6.6, 3H), 1.03 (s, 3H), 1.04 (s, 3H), 1.05–2.08 (m, 12H), 2.45–2.46 (m, 1H), 2.67–2.75 (m, 1H), 3.73 (d, *J* 7.6, 1H), 3.93 (br s, 1H); δ_C 19.6, 21.7, 22.2, 22.7, 24.0, 25.1, 25.5, 27.6, 28.1, 29.4, 32.3, 36.9, 40.1, 40.3, 51.0, 52.1, 71.4, 74.2, 215.7, 215.7; *m*/*z* (GC-MS) **4b**: 170 (M^+, 5%), 152 (5), 109 (68), 95 (49), 85 (97), 68 (51), 43 (100); **4c**: 170 (M^+, 10%), 152 (2), 123 (11), 109 (13), 84 (52), 68 (88), 43 (100); HRMS (EI): found 170.1326; calc. for $C_{10}H_{18}O_2$: 170.1307.

2-Acetyl-2-phenylcyclohexan-1-ol 5b. Following the typical procedure above (rt, 1 h), the epoxide **5a** (200 mg, 0.92 mmol) was treated with $ZnBr_2$ (6.2 mg, 0.028 mmol) to afford the product **5b** (188 mg) in 94% yield. δ_H 1.31–1.70 (m, 6H), 1.86 (s, 3H), 2.15–2.19 (m, 2H), 3.22 (br, 1H), 4.20 (br s, 1H), 7.18–7.29 (m, 5H); δ_C 21.4, 21.9, 26.1, 28.2, 29.9, 60.2, 72.7, 127.2, 127.5, 127.5, 128.8, 128.8, 138.8, 212.9; *m*/*z* (GC-MS) 218 (M^+, 4%), 175 (18), 158 (72), 147 (24), 143 (25), 129 (35), 115 (22), 91 (100), 77 (25); HRMS (EI): found 218.1291; calc. for $C_{14}H_{18}O_2$: 218.1307.

2-Propionyl-2-phenylcyclohexan-1-ol 6b. Following the typical procedure above (rt, 0.5 h), the epoxide **6a** (200 mg, 0.86 mmol) was treated with $ZnBr_2$ (5.8 mg, 0.026 mmol) to afford the product **6b** (178 mg) in 89% yield. δ_H 0.80 (t, *J* 7, 3H), 1.29–1.69 (m, 6H), 2.15–2.20 (m, 4H), 3.33 (br, 1H), 4.20 (br s, 1H), 7.15–7.29 (m, 5H); δ_C 8.0, 21.4, 21.9, 28.0, 29.9, 30.9, 60.0, 72.8, 127.0, 127.4, 127.4, 128.6, 128.6, 139.1, 215.6; *m*/*z* (GC-MS) 232 (M^+, 2%), 175 (10), 158 (100), 130 (42), 91 (84), 77 (27), 57 (37); HRMS (EI): 232.1442; calc. for $C_{15}H_{20}O_2$: 232.1463.

2-(2′-Methylpropionyl)-2-phenylcyclohexan-1-ol 7b. Following the typical procedure above (rt, 4 h), the epoxide **7a** (200 mg, 0.81 mmol) was treated with $ZnBr_2$ (5.5 mg, 0.024 mmol) to afford the product **7b** (190 mg) in 95% yield. δ_H 0.61 (d, *J* 6.6, 3H), 0.92 (d, *J* 6.7, 3H), 1.36–1.40 (m, 2H), 1.64–1.76 (m, 5H), 2.25 (m, 1H), 2.37 (m, 1H), 2.73 (m, 1H), 4.54 (br s, 1H), 7.25–7.42 (m, 5H); δ_C 20.2, 20.4, 20.9, 21.6, 25.6, 28.8, 35.5, 60.4, 71.4, 127.2, 128.3, 128.3, 128.7, 128.7, 137.6, 219.4; *m*/*z* (GC-MS) 246 (M^+, <1%), 158 (100), 143 (36), 130 (39), 115 (16), 105 (14), 91 (57), 77 (19); HRMS (EI): found 246.1678; calc. for $C_{16}H_{22}O_2$: 246.1620.

2-Benzoyl-2-phenylcyclohexan-1-ol 8b. Following the typical procedure above (rt, 0.5 h), the epoxide **8a** (200 mg, 0.71 mmol) was treated with $ZnBr_2$ (3.2 mg, 0.014 mmol) to afford the product **8b** (180 mg) in 90% yield. δ_H 1.11 (m, 1H), 1.31 (m, 1H), 1.48 (m, 1H), 1.71 (m, 1H), 1.77–1.82 (m, 2H), 2.08 (m, 1H), 2.33 (m, 1H), 3.52 (br, 1H), 3.64 (br s, 1H), 7.09–7.41 (m, 10H); δ_C 22.2, 23.5, 31.5, 32.1, 59.4, 76.8, 127.2, 127.7, 127.7, 127.8, 127.8, 128.6, 128.6, 128.8, 128.8, 131.6, 137.7, 140.0, 207.3; *m*/*z* (GC-MS) 280 (M^+, 2%), 262 (1), 158 (56), 130 (19), 115 (9), 105 (100), 91 (38), 77 (54); HRMS (EI): found 280.1447; calc. for $C_{19}H_{20}O_2$: 280.1463.

1-Hydroxyspiro[4.4]nonan-6-one 9b/c. Following the typical procedure above (rt, 1.5 h), the epoxide **9a** (200 mg, 1.30 mmol) was treated with $ZnBr_2$ (14.6 mg, 0.062 mmol) to afford the product **9b** (107 mg) and **9c** (81 mg) in 94% total yield. δ_H **9b**: 1.48–1.96 (10H), 2.25 (t, *J* 7.1, 2H), 3.52 (s, 1H), 3.94 (br s, 1H); **9c**: 1.49–2.24 (m, 12H), 4.14 (t, *J* 6.9, 1H); δ_C **9b**: 19.1, 21.2, 33.7, 34.3, 35.6, 38.8, 58.7, 80.3, 224.8; **9c**: 19.5, 20.7, 30.2, 33.6, 34.4, 38.3, 60.2, 76.6, 223.6; *m*/*z* (GC-MS) **9b**: 154 (M^+, 12%), 136 (29), 97 (100), 94 (29), 67 (54), 55 (38), 41 (32); **9c**: 154 (M^+, 4%), 136 (4), 110 (26), 97 (100), 79 (29), 55 (51), 41 (57); HRMS (EI): found 154.0982; calc. for $C_9H_{14}O_2$: 154.0993.

1-Hydroxyspiro[4.5]decan-6-one 10b/c. Following the typical procedure above (rt, 7 h), the epoxide **10a** (200 mg, 1.19 mmol) was treated with $ZnBr_2$ (18.8 mg, 0.083 mmol) to afford the

product **10b/c** (120 mg, 64 : 36) in 60% total yield. δ_H 1.44–2.41 (m, 28H), 3.77 (dd, *J* 2.9, 6.3, 1H), 4.44 (t, *J* 6.5, 1H); δ_C 19.6, 20.5, 21.9, 25.8, 27.4, 29.6, 29.9, 30.6, 31.3, 31.6, 32.3, 33.8, 37.8, 40.0, 59.6, 62.7, 74.5, 77.3, 213.3, 215.0; *m*/*z* (GC-MS) **10b**: 168 (M^+, 8%), 150 (11), 124 (39), 111 (100), 98 (36), 67 (50), 55 (54); **10c**: 168 (M^+, 2%), 150 (29), 124 (23), 111 (100), 83 (21), 67 (29), 55 (48); HRMS (EI): found 168.1139; calc. for $C_{10}H_{16}O_2$: 168.1150.

1-Hydroxyspiro[4.6]undecan-6-one 11b/c. Following the typical procedure above (rt, 240 h), the epoxide **11a** (200 mg, 1.10 mmol) was treated with $ZnBr_2$ (19.8 mg, 0.088 mmol) to afford the product **11b/c** (110 mg, 84 : 16) in 55% total yield. δ_H 1.18–2.52 (m, 32H), 3.80 (d, *J* 6.0, 1H), 3.94 (br s, 1H); δ_C 20.7, 21.4, 22.0, 22.4, 25.2, 25.9, 26.0, 27.6, 28.6, 30.2, 32.4, 33.5, 34.0, 36.0, 37.7, 42.7, 54.6, 62.3, 77.5, 81.7, 215.2, 218.8; *m*/*z* (GC-MS) **11b**: 182 (M^+, 33%), 164 (15), 138 (18), 111 (63), 83 (53), 67 (100), 55 (72); **11c**: 182 (M^+, 11%), 164 (6), 138 (25), 125 (100), 97 (44), 67 (45), 55 (57); HRMS (EI): found 182.1345; calc. for $C_{11}H_{18}O_2$: 182.1307.

1-Hydroxyspiro[4.7]dodecan-6-one 12b/c. Following the typical procedure above (rt, 3 h), the epoxide **12a** (200 mg, 1.02 mmol) was treated with $ZnBr_2$ (13.8 mg, 0.061 mmol) to afford the product **12b/c** (136 mg, 72 : 28) in 68% total yield. δ_H 1.26–2.48 (m, 36H), 3.29 (br, OH), 3.77 (dd, *J* 2.2, 5.9, 1H), 4.02 (t, *J* 5, 1H); δ_C 20.6, 20.7, 22.9, 23.6, 24.6, 24.7, 25.7, 28.2, 29.4, 29.8, 30.2, 30.4, 31.1, 33.1, 34.1, 34.2, 37.4, 39.1, 57.3, 61.0, 77.0, 80.2, 214.7, 221.2; *m*/*z* (GC-MS) **12b**: 196 (M^+, 6%), 168 (3), 139 (46), 125 (9), 98 (28), 97 (67), 67 (100), 55 (81); **12c**: 196 (M^+, 10%), 168 (2), 139 (11), 126 (30), 97 (45), 81 (83), 67 (60), 55 (100); HRMS (EI): found 196.1490; calc. for $C_{12}H_{20}O_2$: 196.1463.

1,7-Dihydroxyspiro[5.5]undecane 1d. To a stirred solution of **1b** (200 mg, 0.7 mmol) in dry CH_2Cl_2 (10 ml) was added DIBAL-H (2.2 ml, 1 M in toluene) under argon at −78 °C. The mixture was stirred until the temperature went up to room temperature. Then the reaction mixture was added to saturated NH_4Cl (10 ml) solution, extracted with CH_2Cl_2 (3 × 10 ml), the organic extract dried over $MgSO_4$ and purified by column chromatography to give **1d** (166 mg) in 83% yield. The ^1H and ^{13}C NMR and MS data are consistent with the reported date.[8]

1,6-Dihydroxyspiro[4.4]nonane 9d/e. To a stirred solution of **9b** (200 mg, 1.30 mmol) in MeOH (10 ml) was added $NaBH_4$ (197 mg, 5.20 mmol) at 0 °C. The mixture was stirred for 5 minutes. Then the solvent was removed under reduced pressure. To the residue was added dilute 2 M HCl (10 ml) solution and the mixture was extracted with ether (3 × 10 ml). The combined extracts were dried over $MgSO_4$ and purified by column chromatography to give **9d/e** (184 mg, 56 : 44) in 92% total yield. The ^1H, ^{13}C NMR and MS data are identical to those previously reported.[12]

1,6-Dihydroxyspiro[4.4]nonane 9d/f. Following the procedure as for **1d**, the products **9d** (91 mg) and **9f** (71 mg) were obtained from **9c** (200 mg, 1.30 mmol) in 81% total yield. The ^1H and ^{13}C NMR and MS data were in accordance with those reported.[12]

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