Chinese Journal of Chemistry, **2004**, *22*, 1177—1182 **Article**

Extensive Studies on the $AlEt_3$/THF-Promoted Diastereoselective Tandem Rearrangement/Reduction of α-Hydroxy (Amino) Heterocyclopropane: An Efficient Approach to 2-Quaternary 1,3-Diheteroatom Units

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A facile and highly diastereoselective method for the construction of 2-quaternary 1,3-amino alcohols and 1,3-diols has been developed on the basis of the $AlEt_3$/THF-promoted tandem rearrangement/reductive reaction of α-hydroxy (amino) aziridines (epoxides). The progressive achievement in this article included that both 2-epimers of the units could be constructed from the initially same substrate. Also a stereochemistry assignment we reported previously was corrected.

Keywords triethyl aluminium, tandem reaction, quaternary carbon, diastereoselectivity, amino alcohol

Introduction

Diastereoselective construction of 1,3-diheteroatom units, especially 1,3-amino alcohols and 1,3-diols, has always been in high demands in synthetic organic chemistry, as they are widely present in many natural products and potent drugs, such as nucleoside antibiotics and the HIV protease inhibitors.[1,2] They have also been used as chiral ligands for asymmetric catalysts and as synthetic intermediates.[3] Although several methods for the construction of 1,3-amino alcohols have been reported,[4] they are generally more complex, especially for those compounds containing the quaternary carbon center, which has long been an important class of structural units but difficult to access.[5] In our preliminary communications, we focused on a novel $AlEt_3$/THF-promoted tandem rearrangement/reduction of secondary α-hydroxy epoxides,[6] in which $AlEt_3$/THF exhibited a rare double reactivity: Lewis acidity and reduction activity. In order to extend the application of $AlEt_3$/THF and to further explore more characters of this reagent, we have made extensive investigations in terms of expanding substrates of α-hydroxy aziridines (epoxides), constructing the reversed 2-diastereoisomeric quaternary center and revising our previous reported results. Here we disclosed our detailed research, part of which was mentioned in our previous communication.[6a]

Results and discussion

In the first part, we described the construction of 2-quaternary 1,3-amino alcohols. The substrates α-hydroxy aziridines we used were prepared in racemic form from the corresponding allylic alcohols via the aziridination method developed by Sharpless.[7] Thus, as shown in Scheme 1, the substrates were subjected to treatment with an excess amount (3 equiv.) of $AlEt_3$/THF solution at a reflux temperature to afford the 2-quaternary 1,3-amino alcohols in moderate to good yields. All examples listed in Table 1 (Entries 1—9) gave only one diastereoisomer except for **7a** which generated two 1-epimers (**7b** and **7b'**), indicating the high diastereoselectivity of this sequence. The transformation involved the ring opening of aziridine with C1 to C2 carbon migration and concomitant formation of an aldehyde or ketone at the original C1 position, subsequently an immediate hydrogen-transfer from $AlEt_3$ to afford the products. The distinctive values of this sequence lie in the stereoselective derivation of two to three adjacent stereocenters with one quaternary carbon, and therefore it has been identified to be an alternative and important method for the construction of 1,3-amino alcohols. Other reductive Lewis acids, such as $Al(i\text{-}PrO)_3$ and BH_3/THF, were also tested under the same condition, but just leading to complex products (unidentified). In addition, we recently found that the

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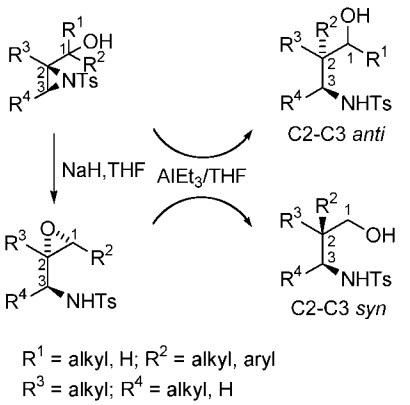
newly prepared $AlEt_3$/THF solution showed much higher reactivity than the older one.

Scheme 1

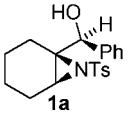
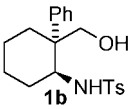
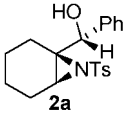
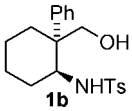
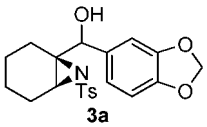
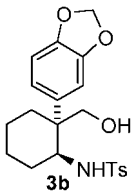
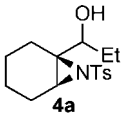
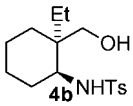
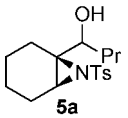
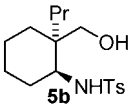
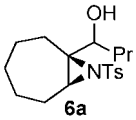
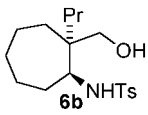
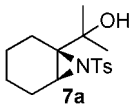
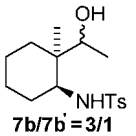
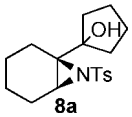
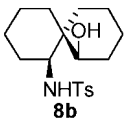
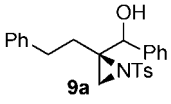
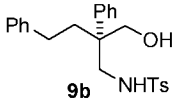
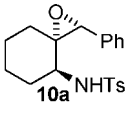
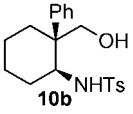


As shown in Table 1, various substrates were effective for this procedure, but normally the alkyl and aryl group were good migrating group while the hydrogen was not. From Entries 1 and 2, we can see that the two 2-epimers **1a** and **2a** could generate the same diastereoisomer product **1b**, indicating that the migration from C1 to C2 depended highly upon its migrating ability of R^2. Results showed that the aromatic group with an electron-donating group also had a good result for this reaction (Entry 3). By comparing the reaction yields of Entries 1—5, we could see that the aromatic group was more favorable than the aliphatic group (Entries 4 and 5). This could be due to that aryl group has a better transferring ability than alkyl group. The substrate with a bigger cycle of cycloheptane moiety also proceeded smoothly under the general reaction condition (Entry 6). In Entry 7, the tertiary substrate **7a** afforded the secondary 1,3-amino alcohol **7b** and its C1 epimer **7b'**. For the cyclic tertiary substrate **8a,** we successfully got a single diastereoisomeric 1,3-amino alcohol **8b**. Furthermore, we examined the acyclic substrate (Entry 9), which was prepared via a Shapiro reaction by benzaldehyde and the hydrazone of benzylacetone followed by azirination of the allylic alcohol.[8] The tandem reaction of this acyclic α-hydroxy aziridine **9a** proceeded smoothly to afford the corresponding 1,3-amino alcohol **9b**, indicating that this method was applicable to broad scope of the substrates.

To determine the relative stereochemistry of the products of the α-hydroxy aziridines, we prepared the benzylidene acetal of the amino alcohol. The 1D NOE spectrum (Figure 1) revealed an obvious spatial

Figure 1 The determination of C2 and C3 relative stereo-chemistry of the products of the α-hydroxy aziridines.

Table 1 Experimental results of the reaction of 2-hydroxy (amino) aziridines (epoxide) with $AlEt_3$/THF

Entry	Substrate[a]	Product	Yield[b]/%	*t*/h
1	 **1a**	 **1b**	92	1.5
2	 **2a**	 **1b**	91	1.5
3	 **3a**	 **3b**	85	2
4	 **4a**	 **4b**	68	10
5	 **5a**	 **5b**	75	9
6	 **6a**	 **6b**	69	8
7	 **7a**	 **7b/7b' = 3/1**	82	16
8	 **8a**	 **8b**	85	4
9	 **9a**	 **9b**	89	2
10	 **10a**	 **10b**	80	5

[a] The substrates are diastereomerically pure. [b] Isolated yields.

correlation between the migrating group R^2 and H, as shown in *cis*-**A** in Figure 1. If the group R^2 was *trans* to H, no correlation would occur in the benzylidene acetal of *trans*-**B**, therefore, the amine group was *trans* to the migrating group, which was just the same as the communication reported before.[6a,7b] To assign the configuration of the newly generated C1-OH in Entries 7 and 8, we prepared the benzylidene acetal of **8b**. Its molecular model examination suggested that the relative configuration would be C1-C2 *syn*. Again a further investiga-

tion to it with the 1D NOE technique also showed the presence of C1-C2 *syn* configuration. On the basis of the above results, we presumed that the C2 methyl was *syn* to C1-OH in the major product **7b**, which was further confirmed by the 1D NOE spectrum of the benzylidene acetal of **7b**.

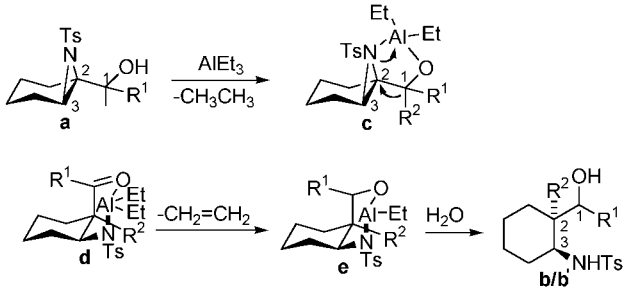
In order to construct the opposite configurational 2-quaternary center of the 1,3-amino alcohols, we examined the other kind of substrates of epoxy amines **10a (**Table 1, Entry 10), which was prepared through an aza-payne rearrangement of **1a** to form the corresponding α-hydroxy aziridine by reported method.[9] The epoxy amine also exhibited a good reactivity and high diastereoselectivity in the $AlEt_3$/THF system to generate the reversed configurational 2-quaternary center of the 1,3-amino alcohol in comparison with Entries 1—9. This tandem reaction involved another semipinacol-type rearrangement with C1 to C2 carbon rearrangement and a subsequent reduction. Therefore the relative stereochemistry of the amine group and the migrating group in the products of epoxy amines was assigned to be C2-C3 *syn*. This experimental result demonstrated a new and efficient approach to construct the reversed configuration of the quaternary carbon, which was not readily accessible by the previous procedure.[7b,10]

On the basis of the tandem reaction of α-hydroxy aziridines mentioned above and the relative configuration of the products, a possible reaction mechanism of this rearrangement/reduction was proposed in Scheme 2, in which $AlEt_3$ firstly coordinated to the aziridine nitrogen and the hydroxyl oxygen in **a** to afford the complex **c,** subsequently cleavage of the activated C—N bond of the aziridine then occurred concomitantly with 1, 2-migration of the migrating group in a transition state geometry resembling that of ordinary nucleophilic substitution proceeding with inversion of configuration. Thus the C1-carbocation intermediate **d** was formed, then a hydride shift from the ethyl carbon of the aluminium complex to the C1-carbocation center in **d** followed by elimination of volatile ethylene, finally, the hydrolysis released product **b**. Actually, the intermediate aldehyde or ketone was unobserved (except for Entry 7 in Table 1) during this tandem reaction, which means that the hydride shift progress was much faster than the former rearrangement progress.

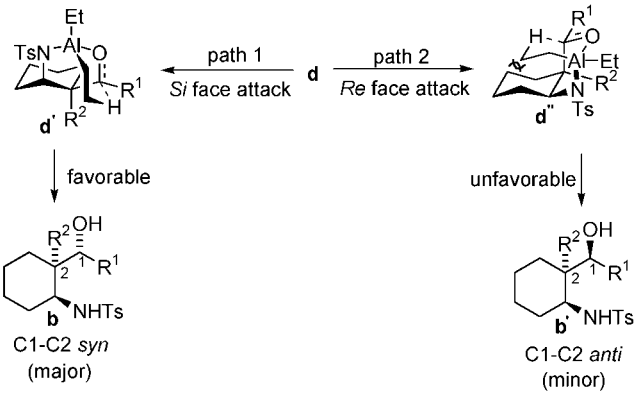
As for Entries 7 and 8 in Table 1, two possible pathways exist for the hydride shift, which brings about two corresponding 1,3-amino alcohols, the C1-C2 *syn* **b** and the C1-C2 *anti* **b'** respectively. As shown in Scheme 3, because of an obvious steric effect in path 2, the formation of **d"** was unfavorable. Thus the C1-C2 *syn* product **b** was more abundant than the C1-C2 *anti* product **b'**. In fact, Entry 8 gave the exclusive C1-C2 *syn* product **8b**.

Our secondary investigation was toward the construction of 2-quaternary 1,3-diols through the $AlEt_3$/THF promoted tandem reaction of secondary α-hydoxy epoxides. The general method was indicated in Scheme 4, and the selected examples were listed in Table 2. Particular notice was that if the un-protected substrates **11a** and **13a** were used, the C1-C3 *syn* diols products **11b** and **13b** could be obtained (Entries 1 and 3 in Table 2). This reaction process could be explained by means of the mechanism reported in previous communication.[6a] However if the secondary hydroxy of **11a** and **13a** was protected with benzyl, the reaction products **12b** and **14b** possessed the reversed configuration of 2-quaternary carbon in comparison with **11b** and **13b,** respectively (Entries 2 and 4 in Table 2). The configuration was confirmed by means of the 1D NOE spectrum of the acetonide of the de-protected products **12c** and **14c** (Figure 2). In fact, compound **11b** and **12c** were identical with the known products,[11] which was a further confirmation for the stereochemistry assignment. This

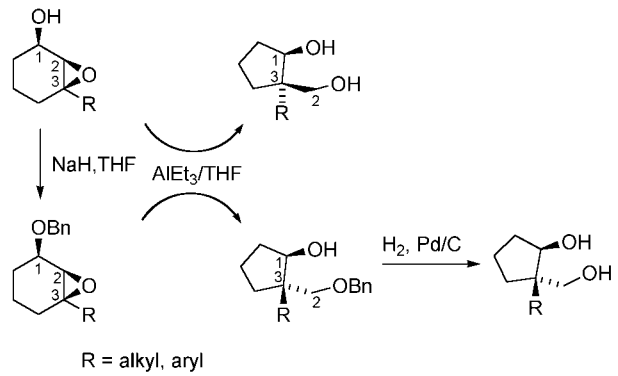
Scheme 2



Scheme 3

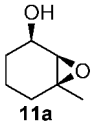
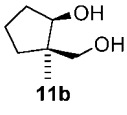
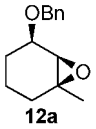
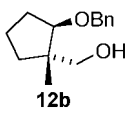
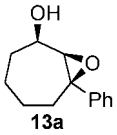
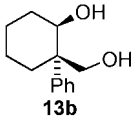
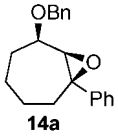
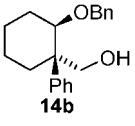


Scheme 4

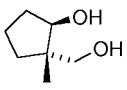


results revised the stereochemistry assignment which we have ever reported in the previous communication,[6b] and we are apologized for our misassignment before. The mechanism of this reaction was unclear now, which was still on going in our group. Thus, by means of $AlEt_3$/THF, we successfully constructed the 2-quaternary 1,3-diol units with high diastereoselectivity from the initially same secondary α-hydroxy epoxide substrates. The noteworthy feature of this method was that the configuration of the quaternary carbon center can be controlled optionally.

Table 2 Experimental results of the reaction of secondary α-hydroxy (benzyloxy) epoxides with $AlEt_3$/THF

Entry	Substrate[a]	Product	Yield[b]/%	*t*/h
1	 **11a**	 **11b**	58	14
2	 **12a**	 **12b**	92	11
3	 **13a**	 **13b**	84	7
4	 **14a**	 **14b**	80	6

[b] Isolated yields.


12c

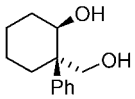

14c

Figure 2 The de-protected products **12c** and **14c**.

In conclusion, we have developed a facile and highly diastereoselective method for the construction of the 2-quaternary 1,3-diheteroatom units. Various types of substrates were examined to demonstrate the generality of this tandem reaction, and the way to construct the quaternary carbon with different configuration would be of great use for the synthesis of natural products.[5,12]

Experimental

Melting points were determined with a Kofler hot-stage microscope and were uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded on an Avance DRX-200 MHz and a Varian Mercury-plus 300BB or a Bruker AM 400 MHz instrument with TMS as internal standard. IR spectra were recorded on a Nicolet NEXUS 670 FT-IR instrument. MS data were measured with EI (70 eV). FABMS spectra were recorded by using xenon ionization techniques with an m-nitrobenzyl alcohol (MNBA) matrix on a ZAB-HS instrument and HRMS data were measured with ESI techniques (Bruker ApexII). The compounds were purified by column chromatography on silica gel H, from the Qingdao Marine Chemical Factory, eluting with the solvent mixture of petroleum (b.p. 60—90 ℃) and ethyl acetate.

General experimental procedure for the $AlEt_3$/THF promoted tandem reaction

Under Ar atmosphere, a solution (0.5 mL, 1.5 mmol, 3 mol•L^{-1}) of $AlEt_3$ in THF was added dropwise to a stirred solution of **3a** (200 mg, 0.5 mmol) in 10 mL of dry THF. The reaction mixture was refluxed under Ar atmosphere. After TLC analysis showed that the reaction was complete, the reaction mixture was poured into aqueous HCl (2 N) at 0 ℃ and extracted three times with ethyl acetate. The combined extracts were dried over Na_2SO_4, concentrated *in vacuo* and purified on silica gel eluting with a mixture solvent of petroleum and ethyl acetate to give **3b** (172 mg, 85%).

***Trans*-[2-(4-methylphenylsulfonylamino)-1-phenyl-cyclohexyl]-methanol (1b):** White solid, m.p. 98 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.80 (d, J=8.0 Hz, 2H), 7.33—7.19 (m, 7H), 5.75 (d, J=8.8 Hz, 1H), 4.10 (dd, J=11.2, 3.6 Hz, 1H), 4.05 (dd, J=11.2, 2.8 Hz, 1H), 3.42 (dd, J=10.4, 8.0 Hz, 1H), 2.87 (brs, 1H), 2.45 (s, 3H), 1.92—1.89 (m, 1H), 1.49—1.13 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 143.4, 141.8, 137.5, 129.8, 128.5, 127.0, 126.9, 126.3, 68.8, 53.7, 46.8, 29.0, 27.2, 21.5, 21.2, 20.4; IR (KBr) ν: 3463, 3295, 2933, 1304, 1150, 1093, 1007, 815, 670 cm^{-1}; EI-MS *m/z* (%): 341 (M^+−18, 2), 328 (<1), 210 (4), 186 (76), 158 (53), 91 (100); ESI-HRMS calcd for $C_{20}H_{26}NO_3S$ $[M+H]^+$ 360.1628, found 360.1630.

***Trans*-[2-(4-methylphenylsulfonylamino)-1-(3,4-methylenedioxy-phenyl)-cyclohexyl]-methanol (3b):** White solid, m.p. 109 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.77 (d, J=8.0 Hz, 2H), 7.33 (d, J=8.0 Hz, 2H), 6.82 (d, J=1.6 Hz, 1H), 6.79—6.73 (m, 2H), 5.96 (s, 2H), 5.41 (d, J=8.4 Hz, 1H), 4.05—3.94 (m, 2H), 3.38 (dd, J=10.8, 8.0 Hz, 1H), 2.70 (brs, 1H), 2.45 (s, 3H), 1.83—1.81 (m, 1H), 1.62—1.39 (m, 6H), 1.13—1.10 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 147.9, 145.8, 143.4, 137.4, 135.7, 129.7, 126.9, 120.1, 108.1, 107.6, 100.9, 68.7, 54.1, 46.6, 29.6, 27.3, 21.5, 21.3, 20.4; IR (KBr) ν: 3461, 3196, 2926, 1489, 1240, 1157, 1095, 815, 666 cm^{-1}; EI-MS *m/z* (%): 403 (M^+, 1), 385 (9), 230 (100), 202 (38), 155 (30), 91 (98); ESI-HRMS calcd for $C_{21}H_{26}NO_5S$ $[M+H]^+$ 404.1526, found 404.1525.

***Trans*-[2-(4-methylphenylsulfonylamino)-1-ethyl-cyclohexyl]-methanol (4b):** White solid, m.p. 100 ℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.76 (d, J=8.4 Hz, 2H),

7.28 (d, J=8.4 Hz, 2H), 5.81 (d, J=8.1 Hz, 1H), 3.92 (dd, J=4.8, 11.7 Hz, 1H), 3.33(dd, J=6.6, 11.7 Hz, 1H), 3.17—3.10 (m, 1H), 2.42 (s, 3H), 1.67—1.49 (m, 2H), 1.41—1.16 (m, 8H), 0.77 (t, J=6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 143.4, 138.4, 129.9, 127.2, 64.8, 56.9, 40.7, 28.8, 28.2, 25.2, 22.9, 21.7, 20.4, 7.3; IR (KBr) ν: 3544, 3278, 2940, 2921, 1325, 1151, 1028, 816, 669 cm^{-1}; EI-MS *m/z* (%): 311 (M^+, 2), 293 (M^+−18, 14), 210 (22), 155 (68), 91 (100); ESI-HRMS calcd for $C_{16}H_{29}N_2O_3S$ [$M+NH_4$]$^+$ 329.1893, found 329.1896.

***Trans*-[2-(4-methylphenylsulfonylamino)-1-propyl-cyclohexyl]-methanol (5b):** White solid, m.p. 103 ℃; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.78 (d, J= 8.0 Hz, 2H), 7.32 (d, J=8.0 Hz, 2H), 5.75 (d, J=8.4 Hz, 1H), 3.97 (dd, J=11.4, 4.8 Hz, 1H), 3.35 (dd, J=11.4, 6.0 Hz, 1H), 3.17 (t, J=8.0 Hz, 1H), 1.67—1.04 (m, 12H), 0.82 (t, J=6.8 Hz, 3H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 143.1, 138.1, 129.6, 126.9, 65.0, 57.1, 40.4, 35.4, 29.5, 28.2, 22.8, 21.4, 20.3, 15.7, 14.7; IR (KBr) ν: 3432, 3266, 2956, 2930, 1322, 1152, 1087, 817, 665 cm^{-1}; EI-MS *m/z* (%): 325 (M^+, <1), 307 (6), 210 (17), 155 (51), 91 (100); ESI-HRMS calcd for $C_{17}H_{28}NO_3S$ $[M+H]^+$ 326.1784, found 326.1785.

***Trans*-[2-(4-methylphenylsulfonylamino)-1-propyl-cycloheptyl]-methanol (6b):** White solid, m.p. 79 ℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.77 (d, J= 8.1 Hz, 2H), 7.31 (d, J=8.1 Hz, 2H), 5.71 (d, J=9.0 Hz, 1H), 3.68 (d, J=11.4 Hz, 1H), 3.31 (d, J=11.4 Hz, 1H), 3.22 (t, J=7.8 Hz, 1H), 2.42 (s, 3H), 1.67—1.12 (m, 12H), 1.09—0.85 (m, 2H), 0.79 (t, J=6.9 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 143.4, 138.3, 129.9, 127.3, 66.8, 60.4, 43.6, 36.2, 31.3, 30.9, 29.3, 25.5, 22.0, 21.7, 16.9, 15.0; IR (KBr) ν: 3471, 3215, 2956, 2923, 1460, 1153, 811, 666 cm^{-1}; EI-MS *m/z* (%): 321 (M^+−18, 6), 210 (7), 184 (11), 155 (38), 91 (100); ESI-HRMS calcd for $C_{18}H_{30}NO_3S$ $[M+H]^+$ 340.1941, found 340.1939.

***Trans*-[2-(4-methylphenylsulfonylamino)-1-methyl-cyclohexyl]-ethanol (7b):** White solid, m.p. 94 ℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.83 (d, J=8.1 Hz, 2H), 7.30 (d, J=8.1 Hz, 2H), 5.63 (d, J=6.6 Hz, 1H), 3.59—3.56 (m, 1H), 3.13 (dd, J=3.9, 3.0 Hz, 1H), 2.42 (s, 3H), 1.19—1.58 (m, 8H), 1.10 (d, J=3.6 Hz, 3H), 0.74 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 143.7, 138.7, 130.2, 127.6, 74.2, 58.4, 40.6, 28.3, 28.0, 22.1, 21.2, 21.0, 20.3, 18.7; IR (KBr) ν: 3533, 3288, 2938, 1420, 1157, 812, 669 cm^{-1}; EI-MS *m/z* (%): 293 (M^+−18, 1), 278 (<1), 172 (35), 155 (49), 91 (81), 43 (100); ESI-HRMS cacld for $C_{16}H_{26}NO_3S$ $[M+H]^+$ 312.1628, found 312.1643.

***Trans*-[2-(4-methylphenylsulfonylamino)-1-methyl-cyclohexyl]-ethanol (7b'):** White solid, m.p. 117 ℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.76 (d, J=8.4 Hz, 2H), 7.29 (d, J=8.4 Hz, 2H), 6.14 (d, J=7.8 Hz, 1H), 4.19 (t, J=6.0 Hz, 1H), 3.17 (t, J=7.5 Hz, 1H), 2.40 (s, 3H), 1.63—1.56 (m, 1H), 1.42—1.21 (m, 6H), 1.09—1.07 (m, 1H), 1.06 (d, J=6.3 Hz, 3H), 0.74 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 143.3, 138.4, 129.8, 127.2, 69.6, 58.5, 40.5, 33.4, 28.0, 22.6, 21.7, 20.6, 17.4, 17.4; IR (KBr) ν: 3528, 3288, 2930, 1420, 1151, 815, 675 cm^{-1}; EI-MS *m/z* (%): 311 (M^+, <1), 298 (M^+−18, 2), 210 (12), 155 (58), 122 (81), 91 (100).

(*Trans*, *cis*)-7-(4-methylphenylsulfonylamino)-spiro[5.5]undecan-1-ol (8b): White solid, m.p. 117 ℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.81 (d, J=8.4 Hz, 2H), 7.31 (d, J=8.4 Hz, 2H), 7.08 (s, 1H), 3.20 (d, J=10.0 Hz, 1H), 2.91 (brs, 1H), 2.43 (s, 3H), 1.97 (m, 1H), 1.82—1.11 (m, 14H), 0.72 (m, 1H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 143.0, 137.2, 129.4, 127.3, 76.5, 60.7, 40.0, 31.5, 30.9, 26.4, 24.3, 21.5, 20.8, 20.1, 19.9, 19.8; IR (KBr) ν: 3363, 3294, 2928, 1429, 1329, 1156, 816, 676 cm^{-1}; EI-MS *m/z* (%): 337 (M^+, <1), 319 (<1), 210 (7), 155 (28), 148 (100), 91 (78); ESI-HRMS calcd for $C_{18}H_{28}NO_3S$ $[M+H]^+$ 338.1784, found 338.1785.

2-(4-Methylphenylsulfonylaminomethyl)-2,4-diphenylbutan-1-ol (9b): White solid, m.p. 58 ℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ: 7.71 (d, J=7.5 Hz, 2H), 7.03—7.39 (m, 12H), 4.81 (t, J=6.6 Hz, 1H), 4.16 (d, J=11.1 Hz, 1H), 3.94 (d, J=11.1 Hz, 1H), 3.37 (dd, J=8.7, 12.0 Hz, 1H), 3.23 (dd, J=5.4, 12.0 Hz, 1H), 2.42 (s, 3H), 2.40—2.18 (m, 2H), 2.09—1.99 (m, 1H), 1.88—1.80 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 143.8, 142.4, 141.2, 137.0, 130.0, 129.2, 128.6, 128.4, 127.2, 127.2, 126.7, 126.0, 64.8, 48.6, 46.8, 37.0, 30.0, 21.8; IR (KBr) ν: 3472, 3253, 2922, 1453, 1152, 751, 699 cm^{-1}; FABMS (MNBA): *m/z* 410 (M+1); ESI-HRMS calcd for $C_{24}H_{31}N_2O_3S$ $[M+NH_4]^+$ 427.2050, found 427.2041.

***Cis*-[2-(4-methylphenylsulfonylamino)-1-phenyl-cyclohexyl]-methanol (10b):** White solid, m.p. 93 ℃; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 7.84 (d, J=9.2 Hz, 2H), 7.33—7.19 (m, 7H), 5.56 (d, J=8.6 Hz, 1H), 4.07 (dd, J=11.4, 5.2 Hz, 2H), 3.45 (dd, J=11.4, 7.8 Hz, 1H), 2.44 (s, 3H), 2.10—1.11 (m, 8H); ^{13}C NMR (50 MHz, $CDCl_3$) δ: 143.4, 141.8, 137.6, 129.8, 128.5, 127.0, 126.9, 126.2, 68.8, 53.7, 46.8, 29.1, 27.2, 21.5, 21.2, 20.4; IR (KBr) ν: 3464, 3295, 2932, 1304, 1151, 1094, 1007, 815, 670 cm^{-1}; EI-MS *m/z* (%): 341 (M^+−18, 2), 260 (19), 186 (63), 158 (46), 91 (100); ESI-HRMS calcd for $C_{20}H_{29}N_2O_3S$ $[M+NH_4]^+$ 377.1893, found 377.1892.

***Cis*-2-(hydroxymethyl)-2-methylcyclopentanol (11b):** ^{1}H NMR (400 MHz, $CDCl_3$) δ: 3.94 (dd, J=5.7, 4.2 Hz, 1 H), 3.71 (d, J=11.1 Hz, 1H), 3.56 (d, J=11.1 Hz, 1H), 2.05—1.25 (m, 6H), 0.97 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 82.0, 68.5, 46.2, 34.5, 33.4, 23.1, 21.1; EI-MS *m/z* (%): 94 (M^+−36, 55), 84 (100), 68 (97), 56 (73); ESI-HRMS calcd for $C_7H_{14}O_2Na$ $[M+Na]^+$ 153.0886, found 153.0886.

***Trans*-(2-benzyloxy-1-methylcyclopentyl)-methanol (12b):** ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.34—7.27 (m, 5H), 7.61 (d, J=11.8 Hz, 1H), 4.45 (d, J= 11.8 Hz, 1H), 3.69 (d, J=7.4 Hz, 1H), 3.45 (s, 2H), 2.04—1.98 (m, 2H), 1.77—1.39 (m, 4H), 1.05 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 138.9, 128.2, 127.4, 127.3, 84.3, 71.5, 70.9, 46.1, 33.3, 29.1, 19.3, 17.1; EI-MS *m/z* (%): 220 (M^+, <1), 169 (<1), 159 (<1), 91 (100), 65 (47), 55 (64), 43 (69), 39 (62); HRMS

calcd for $C_{14}H_{20}O_2Na$ $[M+Na]^+$ 243.1356, found 243.1353.

De-protected product of 12b: To a solution of **12b (**110 mg, 0.5 mmol) in THF (5 mL), Pd (10%) on activated charcoal (10 mg) was added. The reaction funnel was connected with a plastic balloon containing H_2 at the pressure of 100000 Pa. After TLC analysis showed that the reaction was complete, the Pd was filtered off and the THF was concentrated in vacuum and purified on silica gel eluting with a mixture solvent of petroleum and ethyl acetate to give an oil (62 mg, 95%). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 3.99 (m, 1H), 3.56 (d, J=10.2 Hz, 1H), 3.48 (d, J=10.2 Hz, 1H), 2.00 (m, 1H), 1.95 (brs , 1H, OH), 1.78—1.55 (m, 5H), 1.40—1.37 (m, 1H), 1.01 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 79.1, 72.1, 45.6, 33.4, 32.2, 19.2, 16.4.

***Cis*-2-(hydroxymethyl)-2-phenylcyclohexanol (13b):** ^{1}H NMR (400 MHz, CDCl3) δ: 7.24—7.52 (m, 5H), 4.51 (t, J=3.2 Hz, 1H), 4.10 (d, J=12 Hz, 1H), 3.86 (d, J=12 Hz, 1H), 1.95—1.21 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 143.4, 128.7, 127.0, 126.5, 73.7, 68.7, 47.1, 30.8, 30.2, 22.2, 21.4; EI-MS *m/z* (%): 188 (M^+—18, 23), 169 (96), 91 (100), 77 (46), 43 (38); ESI-HRMS calcd for $C_{13}H_{18}O_2Na$ $[M+Na]^+$ 229.1199, found 229.1195.

***Trans*-[2-(benzyloxy)-1-phenylcyclohexyl]-methanol (14b):** ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.67 (s, 1H), 7.65 (s, 1H), 7.38—7.23 (m, 8H), 4.74 (d, J=11.6 Hz, 1H), 4.41 (d, J=11.6 Hz, 1H), 3.80 (dd, J=9.4, 3.2 Hz, 1H), 3.78 (d, J=11.1 Hz, 1H), 3.71 (d, J=11.0 Hz, 1H), 2.24—2.19 (m, 1H), 1.93—1.37 (m, 7H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 142.1, 138.4, 128.6, 128.3, 128.1, 127.5, 127.5, 126.0, 83.3, 70.9 (2C), 49.0, 30.8, 25.7, 23.6, 21.2; EI-MS *m/z* (%): 296 (M^+, <1), 278 (<1), 265 (<1), 223 (<1), 169 (9), 105 (11), 91 (100), 65 (10); HRMS calcd for $C_{20}H_{24}O_2Na$ $[M+Na]^+$ 319.1669, found 319.1663.

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