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Cerium ammonium nitrate (CAN) for mild and efficient reagent to remove hydroxyethyl units from 2-hydroxyethyl ethers and 2-hydroxyethyl amines

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Abstract—Cerium ammonium nitrate (CAN) removed hydroxyethyl units from 2-hydroxyethyl ethers and 2-hydroxyethyl amines to produce alcohols and amines in good yields. Especially, removal of the 2-hydroxyethyl ethers from C_2-symmetric diols, chiral 2,3-butanediol and chiral hydrobenzoin, was very useful for asymmetric syntheses using C_2-symmetric diols. The reactions using dual abilities of CAN, i.e., the ability for removal of the 2-hydroxyethyl unit and the ability for acetal hydrolysis by a single electron transfer, were also achieved successfully. The reaction conditions were very mild and efficient, and many functional groups, which can be affected under normal conditions, were unaffected during the reaction.
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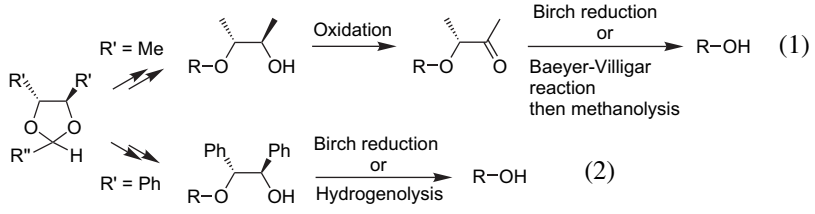
1. Introduction

Asymmetric syntheses by chemical methods are usually divided into two categories: (1) enantioselective synthesis using an asymmetric catalyst, and (2) diastereoselective synthesis using compounds having a chiral auxiliary. The diastereoselective reactions require the removal of the chiral auxiliary after the asymmetric induction. An efficient method for the removal of the chiral auxiliary is then strongly desirable for such asymmetric syntheses.

C_2-Symmetric chiral diols, such as the chiral 2,3-butanediol or chiral hydrobenzoin, are good auxiliaries and often used as C_2-symmetric chiral acetals for asymmetric syntheses. The transformation of 2-hydroxyethyl ether units to alcohols is very important especially for such an asymmetric synthesis, because such units are formed by the cleavage of the C–O bond of the dioxolane rings during the nucleophilic substitution reactions.[1] Previous methods for their removal are as follows (Scheme 1). The removal of 2-hydroxyethyl ether units from 2,3-butanediol involves a multi-step sequence, i.e., oxidation of a secondary alcohol and then Birch reduction[2] or Baeyer–Villiger reaction followed by methanolysis (Eq. 1).[3] On the other hand, for the 2-hydroxyethyl ether units derived from chiral hydrobenzoin, (1) the oxidation of the secondary alcohol followed by reductive elimination,[4] or (2) the Birch reduction or hydrogenolysis is usually used (Eq. 2).[5] However, such reactions are not applicable to the compounds having labile functions such as carbonyl, halogen, or olefin groups.

In our asymmetric synthesis using chiral hydrobenzoin as the chiral auxiliary, we produced many compounds having the 2-hydroxyethyl ether units derived from chiral



Scheme 1.

Keywords: CAN; Removal of hydroxyethyl unit; 2-Hydroxyethyl ether; 2-Hydroxyethyl amine.
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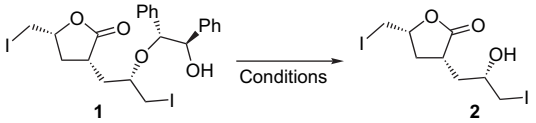
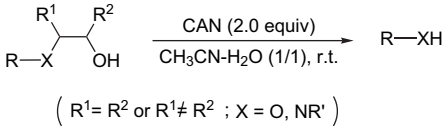
hydrobenzoin with an olefin, bromine, and iodine in the molecule. For the removal of the 2-hydroxyethyl ether units derived from the chiral hydrobenzoin, the ordinary methods affected the olefin and halogen atom. For example, the ordinary conditions were not available for the transformation of **1** to **2**, and the complex mixture was obtained (Table 1, entries 2 and 3). However, to our surprise, the use of 2.0 equiv of cerium ammonium nitrate (CAN) in CH_3CN/H_2O produced an 80% yield of the desired **2** (entry 1).[6]

Table 1. Removal of 2-hydroxy-1,2-diphenylethyl unit



Entry	Conditions	Yield
1	CAN (2.0 equiv), rt	80%
2	Birch reduction	Complex mixture
3	Hydrogenation	Complex mixture

Although CAN is recognized as a good reagent for the deprotection of 4-methoxybenzyl ether,[7] no report has described its deprotection ability of benzyl ether.[8] However, compound **1**, a kind of benzyl ether, gave the desired compound **2** in good yield. Furthermore, these conditions did not affect the ester and iodine so that the method was very mild and efficient. We then studied the reaction in detail, and reported the mild, efficient, and highly general one-pot removal method of 2-hydroxyethyl ether units to give alcohols (Scheme 2, X=O).[9] Thereafter, we also found that the conditions could transform 2-hydroxyethyl amines to amines (Scheme 2, X=NR′). We now present the full details of our study.



Scheme 2. Removal of 2-hydroxyethyl units from 2-hydroxyethyl ethers and 2-hydroxyethyl amines.

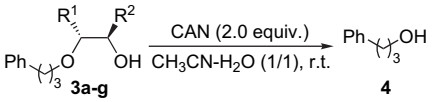
2. Results and discussion

2.1. Removal of 2-hydroxyethyl units

First of all, the effects of substituents on the 2-hydroxyethyl unit were examined (Table 2). 1,2-Diphenyl one (**3a**), 1-unsubstituted-2-phenyl one (**3b**), 1-phenyl-2-unsubstituted one (**3c**), 1,2-dimethyl one (**3d**), 1-unsubstituted-2-methyl one (**3e**), and 1-methyl-2-unsubstituted one (**3f**) afforded the desired alcohol **4** in good to moderate yields by the removal of 2-hydroxyethyl units (entries 1–6), whereas the deprotection reaction did not occur at all for the unsubstituted one (**3g**) (entry 7). These results show that the presence of at least one substituent on the 2-hydroxyethyl unit is necessary for the reaction to occur.

The scope of the substrates, which are available for this reaction, was next studied (Table 3).[10] Compounds **5a**,**b** having an ester group, affected by the Birch reduction, and compounds **5c**,**d** having an olefin, affected by the hydrogenolysis, were available for this reaction without any problems, and the desired alcohols **6a**,**b** were obtained in good yields (entries 1–4). These conditions were also applied to the compounds having a methyl ether **5e**, acetyl ester **5f**, benzyl ether **5g**, tosyl sulfonate **5h**, and iodine compound **5i**, and the respective desired alcohols **6c**–**g** were obtained in good yields (entries 5–9). These results show that the reaction is a very mild reaction available for compounds with various functional groups.

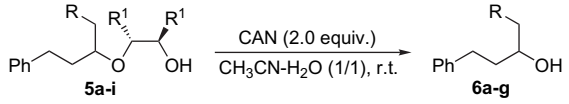
Table 2. Reaction of various 2-hydroxyethyl ethers

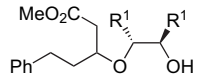
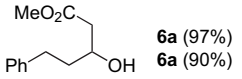
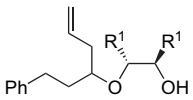
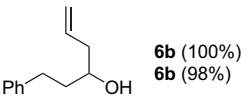
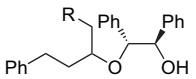
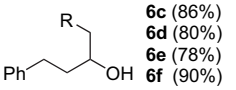


Entry	Substrate	Yield (%)
1	**3a** (R^1=R^2=Ph)	100
2	**3b** (R^1=H, R^2=Ph)	100
3	**3c** (R^1=Ph, R^2=H)	92
4	**3d** (R^1=R^2=Me)	80
5	**3e** (R^1=H, R^2=Me)	80
6	**3f** (R^1=Me, R^2=H)+**3e**[a]	66
7	**3g** (R^1=R^2=H)	No reaction

[a] Mixture of **3f** and **3e** (1:1).

Table 3. Reaction of 2-hydroxyethyl ethers with various functional groups



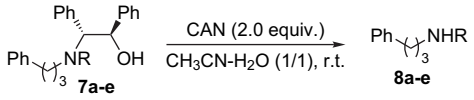
Entry	Substrate	Product (yield)
1	 **5a** (R^1 = Ph)	 **6a** (97%)
2	**5b** (R^1 = Me)	**6a** (90%)
3	 **5c** (R^1 = Ph)	 **6b** (100%)
4	**5d** (R^1 = Me)	**6b** (98%)
5	 **5e** (R = -CH_2OMe)	 **6c** (86%)
6	**5f** (R = -CH_2OAc)	**6d** (80%)
7	**5g** (R = -CH_2OBn)	**6e** (78%)
8	**5h** (R = -CH_2OTs)	**6f** (90%)
9	**5i** (R = -CH_2I)	**6g** (80%)

We next studied the need for the ether oxygen atom using 2-hydroxyethyl amines, where the ether oxygen atom is replaced by a nitrogen atom (Table 4). As a result, the 1,2-diphenyl-2-hydroxyethyl amines **7a**–**e**, having nitrogen functions such as *N*-allyl (**7a**), *N*-benzyl (**7b**), *N*-Boc (**7c**), *N*-Cbz (**7d**), and *N*-Ts (**7e**) groups, afforded the desired amines **8a**–**e** in good yields. This fact proved that the presence of the nitrogen atom in place of the oxygen atom at the 2 position of the ethyl alcohol units is important.

2.2. Study of the reaction mechanism

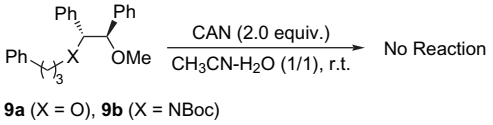
We next examined the reactions of compounds **9a**,**b**, in which the alcohol units of **3a** and **7c** are protected as

Table 4. Reaction of 1,2-diphenyl-2-hydroxyethyl amines



Entry	Substrate	Product (yield)
1	**7a** (R=allyl)	**8a** (82%)
2	**7b** (R=Bn)	**8b** (83%)
3	**7c** (R=Boc)	**8c** (80%)
4	**7d** (R=Cbz)	**8d** (68%)
5	**7e** (R=Ts)	**8e** (89%)

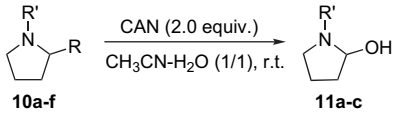
Me-ether. No reaction occurred for these compounds (Scheme 3). This shows that the first step of the reaction occurs between the alcohol unit and CAN.



Scheme 3. Reaction of Me-ethers, **9a** and **9b**.

Furthermore, cyclic 2-hydroxyethyl amines **10a**–**c** from prolinol and proline derivatives **10d**–**f** gave the *N*,*O*-acetals **11a**–**c** under the same conditions (Table 5).

Table 5. Reaction of cyclic 2-hydroxyethyl amines



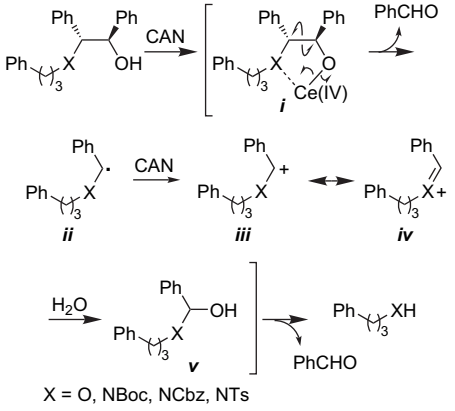
Entry	Substrate	Product (yield)
1	**10a** (R=–CH_2OH, R′=Boc)	**11a** (51%)
2	**10b** (R=–CH_2OH, R′=Cbz)	**11b** (64%)
3	**10c** (R=–CH_2OH, R′=Ts)	**11c** (48%)
4	**10d** (R=–CO_2H, R′=Boc)	**11a** (65%)
5	**10e** (R=–CO_2H, R′=Cbz)	**11b** (68%)
6	**10f** (R=–CO_2H, R′=Ts)	**11c** (63%)

2.3. Reaction mechanism

Based on the results shown in the previous sections, a plausible reaction mechanism is depicted in Scheme 4 using 1,2-diphenyl substituted compounds. First, the reaction of the alcohol unit and CAN produced the radical cleavage of the C–C bond to afford the benzyl radical species and benzaldehyde (**i**→**ii**). For this cleavage, the presence of the substituent, which stabilizes the carbon radical, is necessary. Radical species **ii** was converted to cation species **iii** and/or **iv** by a one-electron transfer oxidation of one more CAN (**ii**→**iii**→**iv**). The addition of water to the cation species forms a hemiacetal **v**, which is converted to the final compound by the removal of the benzaldehyde.[11,12]

2.4. Application (dual role of CAN)

As mentioned above, we clarified the good ability of CAN for the removal of 2-hydroxyethyl units from 2-hydroxyethyl ethers and 2-hydroxyethyl amines. CAN is already known to have the ability for acetal hydrolysis by a single



Scheme 4. Plausible reaction mechanism.

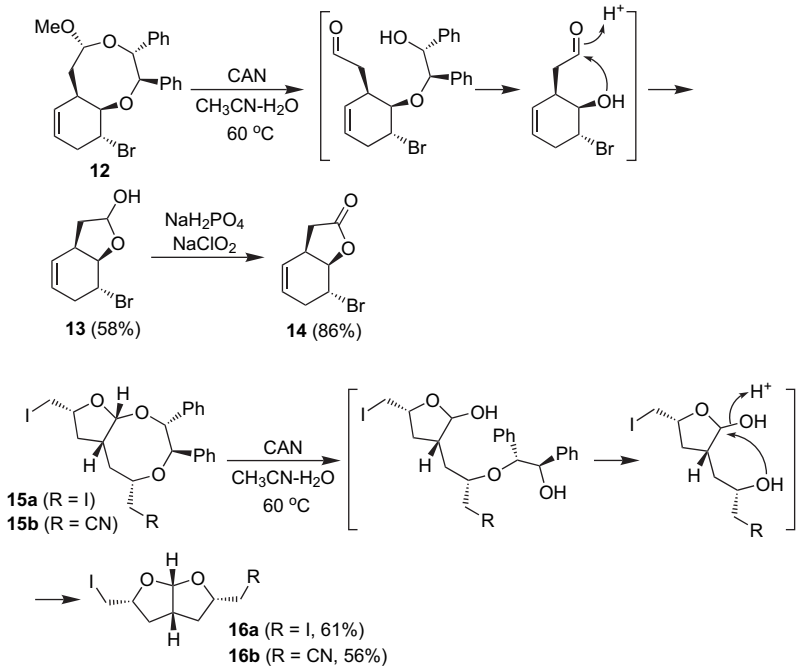
electron transfer.[13] We then tried to combine these two abilities (Scheme 5). The utility of the method was proved by the application to compounds **12**[14] and **15a**,**b**,[6] which contain functional groups such as bromine, olefin, and acetal units in **12** and iodine, acetal, and nitrile units in **15a**,**b**. Although the hydroxyethyl units in these compounds have acetal structures, a domino-type reaction, i.e., first hydrolysis of the acetals followed by the removal of hydroxyethyl units occurred in a single operation. The treatment of the mixed cyclic acetal **12** with 3.5 equiv of CAN produced the hemiacetal **13** in 58% as a 2:1 mixture. For hydrolysis of the acetal units in compounds **12** and **15a**,**b**, the reactions were carried out at 60 °C and excess amounts of CAN was used. The structure of **13** was unambiguously determined by its conversion to the lactone **14**. During the reaction from **12** to **13**, the olefin and bromine were not affected. The same tendency was observed in the reactions of the bicyclic mixed acetals **15a**,**b**, and bicyclic acetals **16a**,**b** were obtained.[15] During the reaction, the primary iodine and nitrile also survived. These facts reconfirmed the mildness of the reaction using CAN.

3. Conclusion

We proved that CAN removes hydroxyethyl units from 2-hydroxyethyl ethers and 2-hydroxyethyl amines to produce alcohols and amines in good yields. Especially, removal of the hydroxyethyl units of the 2-hydroxyethyl ethers from C_2-symmetric diols, chiral 2,3-butanediol and chiral hydrobenzoin, attained by the method described here must be very useful for asymmetric syntheses using C_2-symmetric diols as shown in the introduction of the manuscript. It is noteworthy that the reaction conditions are very mild and efficient, and many functional groups, which can be affected under the ordinary conditions, are unaffected during the reaction. This study adds a new aspect to synthetic organic chemistry.

4. Experimental

The ^{1}H NMR spectra were measured by 300 MHz or 270 MHz spectrometer with tetramethylsilane as the internal standard at 20~25 °C. IR spectra were recorded by a diffuse reflectance measurement of samples dispersed in KBr powder. E. Merck silica gel 60 for column chromatography and E. Merck pre-coated TLC plates, silica gel F_{254}, for preparative thin-layer chromatography were used.



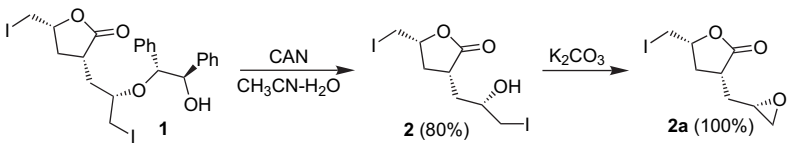
Scheme 5. Dual role of CAN.

4.1. Typical procedure for cerium ammonium nitrate (CAN) mediated C–C bond cleavage

CAN (0.2 mmol) was added to a stirred solution of the substrate (0.1 mmol) in CH_3CN (0.5 mL) and water (0.5 mL) at rt under air. The resulting mixture became immediately red-brown and the color discharged after the required time (ca. 30 min) to give a slightly yellow solution. K_2CO_3 was added to the solution and the mixture was stirred for 10 min. After filtrating K_2CO_3, the filtrate was concentrated in vacuo. The crude product was purified by SiO_2 column chromatography.

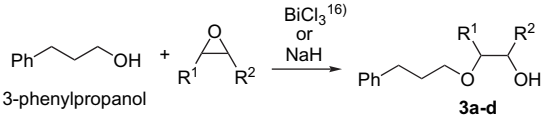
4.2. Reaction of 1 with CAN (Table 1)

Compound **1** was reacted with CAN as shown in a typical procedure. Compound **2** was rather unstable and tended to give an epoxide **2a**. Then **2** was treated with K_2CO_3 and epoxide **2a** was isolated as shown in Ref. 6.



4.3. Syntheses of the substrates in Table 2

Compounds **3a–d** were synthesized as shown below.[16] The yield of each compound was not optimized.



4.3.1. *trans*-1,2-Diphenyl-2-(3-phenylpropoxy)ethanol (3a). $BiCl_3$ (348 mg, 1.10 mmol) was added to a mixture of *cis*-stilbene oxide (866 mg, 4.41 mmol) and 3-phenylpropanol (1.2 mL, 8.81 mmol) at 0 °C under N_2. The reaction mixture was stirred at rt for 6 h. K_2CO_3 was added to the reaction mixture and stirred for 10 min. After filtrating K_2CO_3, the filtrate was concentrated in vacuo. Purification of the residue by SiO_2 column chromatography (*n*-hexane/AcOEt=5:1) gave **3a** (325 mg, 22%) as colorless crystals. Mp 74.4–74.5 °C; IR (KBr) 3549, 1092, 750 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz): δ 1.94 (2H, m), 2.64–2.9 (2H, m), 3.3–3.5 (2H, m), 3.64 (1H, br s), 4.28 (1H, d, J=8.1 Hz), 4.75 (1H, d, J=8.1 Hz), 6.9–7.4 (15H, m); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 31.4, 32.5, 68.4, 78.5, 87.5, 125.7, 127.1, 127.5, 127.5, 127.7, 127.8, 127.9, 128.2, 128.2, 137.8, 139.1, 141.6. Anal. Calcd for $C_{23}H_{24}O_2$: C, 83.10; H, 7.28. Found: C, 83.14; H, 7.31.

4.3.2. 1-Phenyl-2-(3-phenylpropoxy)ethanol (3b). 3-Phenylpropanol (1.2 mL, 8.74 mmol) was added to a solution of NaH (60% in oil, 350 mg, 8.74 mmol) in THF (40 mL) at 0 °C under N_2. The reaction mixture was stirred at rt for 1 h and styrene oxide (525 mg, 4.37 mmol) was added dropwise to the resulting mixture. The reaction mixture was stirred for 3 days at 60 °C and then poured into saturated aqueous NH_4Cl. The resulting mixture was extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. Purification of the residue by SiO_2 column chromatography

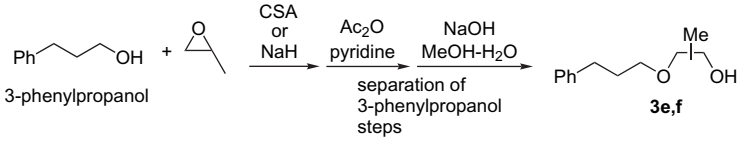
(*n*-hexane/AcOEt=5:1) gave **3b** (200 mg, 18%) as a colorless oil. IR (KBr) 3445, 1115, 750 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz): δ 1.93 (2H, m), 2.69 (2H, t, J=8.1 Hz), 2.9 (1H, br s), 3.38–3.59 (4H, m), 4.87 (1H, dd, J=10.2, 3.9 Hz), 7.15–7.36 (10H, m); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 31.1, 32.3, 70.4, 72.6, 76.3, 125.7, 125.9, 127.6, 128.2, 128.3, 140.2, 141.5; LRMS (FAB) m/z 279 (MNa^+); HRMS (FAB) calcd for $C_{17}H_{20}O_2Na$: 279.01361; found: 279.1355.

4.3.3. 2-Phenyl-2-(3-phenylpropoxy)ethanol (3c). $BiCl_3$ (348 mg, 1.10 mmol) was added to a mixture of styrene oxide (525 mg, 4.37 mmol) and 3-phenylpropanol (1.2 mL, 8.81 mmol) at 0 °C under N_2. The reaction mixture was stirred at rt for 6 h. K_2CO_3 was added to the resulting mixture and stirred for 10 min. After filtrating K_2CO_3, the filtrate was concentrated in vacuo. Purification of the residue by SiO_2 column chromatography (*n*-hexane/AcOEt=5:1) gave **3c** (418 mg, 37%) as a colorless oil. IR (KBr) 3361, 1105, 750 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 1.88 (2H, m), 2.61–2.75 (3H, m), 3.31–3.50 (2H, m), 3.60–3.70 (2H, m), 4.37 (1H, dd, J=8.4, 4.3 Hz), 7.13–7.37 (10H, m); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 31.4, 32.4, 67.2, 68.3, 82.9, 125.6, 126.6, 127.8, 128.1, 128.2, 128.3, 138.7, 141.6; LRMS (FAB) m/z 257 (MH^+); HRMS (FAB) calcd for $C_{17}H_{21}O_2$: 257.1542; found: 257.1544.

4.3.4. 1,2-Dimethyl-2-(3-phenylpropoxy)ethanol (3d). $BiCl_3$ (174 mg, 0.55 mmol) was added to a mixture of 2,3-epoxybutane (cis/trans mixture, 159 mg, 2.20 mmol) and 3-phenylpropanol (0.6 mL, 4.40 mmol) at 0 °C under N_2. The reaction mixture was stirred at rt for 6 h. K_2CO_3 was added to the reaction mixture and stirred for 10 min. After filtrating K_2CO_3, the filtrate was concentrated in vacuo. Purification of the residue by SiO_2 column chromatography (*n*-hexane/AcOEt=5:1) gave diastereomeric mixture (1:1) of **3d** (229 mg, 50%) as a colorless oil. Diastereomeric mixture (1:1) of **3d** was used for the reaction.

Diastereomers could be separated by SiO_2 column chromatography (benzene/AcOEt=10:1). Less polar compound: IR (KBr) 3416, 1099, 746 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 1.07 (3H, d, J=6.5 Hz), 1.13 (3H, d, J=6.5 Hz), 1.90 (2H, m), 2.68 (2H, dd, J=8.1 Hz), 3.11 (1H, quintet, J=6.2 Hz), 3.28–3.34 (1H, m), 3.51–3.65 (2H, m), 7.16–7.26 (5H, m); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 15.4, 18.6, 31.6, 32.5, 68.6, 71.2, 80.5, 125.7, 128.2, 128.4, 141.6. Polar compound: IR (KBr) 3390, 1043, 748 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 1.09 (3H, d, J=6.5 Hz), 1.14 (3H, d, J=6.5 Hz), 1.90 (2H, m), 2.70 (3H, m), 3.27–3.50 (3H, m), 3.53–3.85 (1H, m), 7.16–7.29 (5H, m); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 13.5, 17.7, 31.4, 32.2, 67.7, 68.9, 78.6, 125.4, 127.9, 128.0, 141.5. Anal. Calcd for $C_{13}H_{20}O_2$: C, 74.96; H, 9.68. Found: C, 75.02; H, 9.69.

Compounds **3e**,**f** were synthesized as shown below. The yield of each compound was not optimized.



4.3.5. 1-(3-Phenylpropoxy)-2-propanol (3e). 3-Phenylpropanol (1.0 g, 7.34 mmol) was added to a solution of NaH (60% in oil, 294 mg, 7.34 mmol) in DMF (7.3 mL) at 0 °C under N_2. The reaction mixture was stirred at rt for 1 h and propylene oxide (5.1 mL, 73.4 mmol) was added dropwise. The reaction mixture was stirred at rt for 24 h and poured into saturated aqueous NH_4Cl. The mixture was extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. Since the resulting product **3e** and 3-phenylpropanol were not separable, we selected step-wise procedure, acetylation and separation followed by deprotection of acetate. Ac_2O (4.0 mL) was added to a solution of the crude product in pyridine (8.0 mL) at 0 °C under N_2. The reaction mixture was stirred at rt for 24 h and concentrated in vacuo. Purification of the residue by SiO_2 column chromatography (*n*-hexane/AcOEt=30:1) gave Ac-derivative of **3e** (Ac-**3e**). NaOH (118 mg, 2.95 mmol) was added to a solution of Ac-**3e** in MeOH/H_2O (2.5–0.25 mL) at 0 °C under N_2. The reaction mixture was stirred at rt for 24 h and poured into water. The mixture was extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. Purification of the residue by SiO_2 column chromatography (*n*-hexane/AcOEt=5:1) gave **3e** (453 mg, 32%) as a colorless oil. IR (KBr) 3422, 1115, 745 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz): δ 1.14 (3H, d, J=6.5 Hz), 1.86–1.97 (2H, m), 2.15 (1H, br s), 2.69 (2H, t, J=7.6 Hz), 3.21 (1H, dd, J=7.0, 8.1 Hz), 3.38–3.55 (3H, m), 3.90–3.99 (1H, m), 7.17–7.31 (5H, m); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 18.7, 31.2, 32.4, 66.4, 70.4, 76.3, 125.7, 128.2, 128.3, 141.7.

4.3.6. Mixture of 3e and 2-(3-phenylpropoxy)-1-propanol (3f). CSA (3.0 g, 12.9 mmol) was added to a mixture of propylene oxide (1 mL, 14.4 mmol) and 3-phenylpropanol (1 mL, 7.33 mmol) at 0 °C under N_2. The reaction mixture was stirred at rt for 6 h. K_2CO_3 was added to the reaction mixture and stirred for 10 min. After filtrating K_2CO_3, the filtrate was concentrated in vacuo. Since the resulting product and 3-phenylpropanol were not separable, we selected step-wise procedure, acetylation and separation followed by deprotection of acetate. Ac_2O (2.5 mL) was added to a solution of the crude product in pyridine (5.0 mL) at 0 °C under N_2. The reaction mixture was stirred at rt for 24 h and concentrated in vacuo. Purification of the residue by SiO_2 column chromatography (*n*-hexane/AcOEt=30:1) gave Ac-derivative of **3f** (Ac-**3f**). NaOH (97 mg, 2.43 mmol) was added to a solution of Ac-**3f** in MeOH/H_2O (2.0–0.2 mL) at 0 °C under N_2. The reaction mixture was stirred at rt for 24 h and poured into water. The mixture was extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. Purification of the residue by SiO_2 column

chromatography (*n*-hexane/AcOEt=5:1) gave ca. 1:1 mixture of **3f** and **3e** (367 mg, 26%) as a colorless oil. ^{1}H NMR ($CDCl_3$, 270 MHz): δ 1.86–1.14 (3H, m), 1.85–1.95 (2H, m), 2.08 (1H, br s), 2.68 (1H, t, J=7.6 Hz), 3.19 (1H, dt, J=8.4, 1.0 Hz), 3.22–3.61 (4H, m), 3.88–3.99 (1H, m), 7.17–7.31 (5H, m).

4.4. Compound 4 obtained by CAN mediated C–C bond cleavage of 3 (Table 2)

Every reaction was carried out according to the typical procedure.

Entry 1: **4** (24 mg, 100%) was obtained as a colorless oil from **3a** (60 mg, 0.18 mmol), CAN (198 mg, 0.36 mmol), and CH_3CN/water (v/v=1:1, 1.8 mL). SiO_2 column chromatography: *n*-hexane/AcOEt=3:1.

Entry 2: **4** (32 mg, 100%) was obtained as a colorless oil from **3b** (60 mg, 0.24 mmol), CAN (256 mg, 0.48 mmol), and CH_3CN/water (v/v=1:1, 2.4 mL). SiO_2 column chromatography: *n*-hexane/AcOEt=3:1.

Entry 3: **4** (26 mg, 92%) was obtained as a colorless oil from **3c** (52 mg, 0.20 mmol), CAN (220 mg, 0.40 mmol), and CH_3CN/water (v/v=1:1, 2.0 mL). SiO_2 column chromatography: *n*-hexane/AcOEt=3:1.

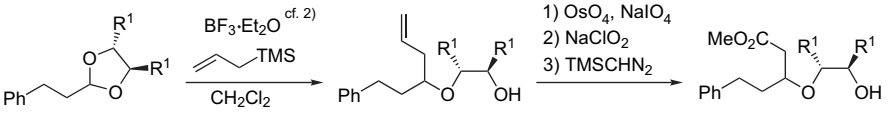
Entry 4: **4** (32 mg, 80%) was obtained as a colorless oil from **3d** (60 mg, 0.28 mmol), CAN (316 mg, 0.56 mmol), and CH_3CN/water (v/v=1:1, 2.8 mL). SiO_2 column chromatography: *n*-hexane/AcOEt=3:1.

Entry 5: **4** (28 mg, 80%) was obtained as a colorless oil from **3e** (50 mg, 0.26 mmol), CAN (564 mg, 1.03 mmol), and CH_3CN/water (v/v=1:1, 2.6 mL). SiO_2 column chromatography: *n*-hexane/AcOEt=3:1.

Entry 6: **4** (22.4 mg, 66%) was obtained as a colorless oil from **3f/3e** (1:1) (49 mg, 0.25 mmol), CAN (280 mg, 0.50 mmol), and CH_3CN/water (v/v=1:1, 2.5 mL). SiO_2 column chromatography: *n*-hexane/AcOEt=3:1.

4.5. Syntheses of substrates 5a–5d in Table 3

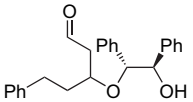
Compounds **5a**–**5d** were synthesized as shown below. The yield of each compound was not optimized. The relationship of vicinal diphenyl/dimethyl groups is trans.



17a (R^1 = Ph) **17b** (R^1 = Me) **5c** (R^1 = Ph) **5d** (R^1 = Me) **5a** (R^1 = Ph) **5b** (R^1 = Me)

4.5.1. 2-(1-Phenethyl-3-butenyloxy)-1,2-diphenylethanol (5c). Allyltrimethylsilane (7.4 mL, 46.3 mmol) and $BF_3\cdot Et_2O$ (9.9 mL, 77.2 mmol) were added to a solution of **17a** (5.1 g, 15.4 mmol) in CH_3CN (31 mL) at 0 °C under N_2. The reaction mixture was stirred at 0 °C for 2 h and poured into saturated aqueous $NaHCO_3$. The mixture was extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. Purification of the residue by SiO_2 column chromatography (*n*-hexane/AcOEt=20:1) gave **5c** (almost one isomer containing small amount of other stereo-isomer, 460 mg, 8%) as a colorless oil and the recovered **17a** (3.8 g, 75%). IR (KBr) 3560, 1454, 1063 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.86–1.94 (2H, m), 2.21–2.26 (2H, m), 2.63–2.71 (2H, m), 3.45 (1H, m), 3.53 (1H, br s), 4.32 (1H, d, J=7.8 Hz), 4.68 (1H, d, J=7.8 Hz), 4.97–5.02 (2H, m), 5.63–5.77 (1H, m), 6.92–7.30 (15H, m); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 30.8, 34.1, 38.8, 76.1, 78.4, 85.2, 116.9, 125.7, 126.9, 127.6, 127.7, 127.8, 128.1, 128.2, 128.3, 134.0, 134.3, 138.1, 139.2, 141.7. Anal. Calcd for $C_{26}H_{28}O_2$: C, 83.83; H, 7.58. Found: C, 83.55; H, 7.75.

4.5.2. 3-(1,2-Diphenyl-2-hydroxyethoxy)-5-phenylpentanal (18a).



18a

Cat. OsO_4, $NaIO_4$ (1.9 g, 8.73 mmol), and 2,6-lutidine (0.5 mL, 4.36 mmol) were added to a solution of **5c** (813 mg, 2.18 mmol) in dioxane/water (v/v=3:1, 9 mL) at 0 °C under air. The reaction mixture was stirred at rt for 3 h. After filtration, the residue was concentrated in vacuo. Purification of the residue by SiO_2 column chromatography (*n*-hexane/AcOEt=10:1) gave **18a** (734 mg, 53%) as a colorless oil. IR (KBr) 3443, 1728, 742 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.92–2.14 (2H, m), 2.48–2.75 (4H, m), 3.63 (1H, br s), 3.92–4.00 (1H, m), 4.40 (1H, d, J=8.1 Hz), 4.76 (1H, d, J=8.1 Hz), 6.95–7.37 (15H, m), 9.53 (1H, s); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 30.7, 34.6, 48.1, 71.8, 78.0, 85.3, 125.9, 127.0, 127.5, 127.7, 127.9, 128.0, 128.1, 128.1, 128.4, 137.5, 139.0, 141.0, 201.0; LRMS (FAB) m/z 397 (MNa^+); HRMS (FAB) calcd for $C_{25}H_{26}O_3Na$: 397.1780; found: 397.1802.

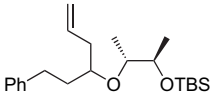
4.5.3. Methyl 3-(1,2-diphenyl-2-hydroxyethoxy)-5-phenylpentanoate (5a). NaH_2PO_4 (558 mg, 4.65 mmol), 2-methyl-2-butene (0.82 mL, 7.75 mmol), and $NaClO_2$ (263 mg, 2.33 mmol) were added to a stirred solution of **18a** (580 mg, 1.55 mmol) in *t*BuOH/water (v/v=5:1, 16 mL) at rt under air. The reaction mixture was stirred at rt for 6 h and poured into 10% aqueous HCl. The mixture was extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo to give the residue. $TMSCHN_2$ (2 M in hexane, 1 mL, 2.02 mmol) was added to a stirred solution of the residue in benzene/MeOH (v/v=4:1, 15 mL) at 0 °C. The reaction mixture was stirred at rt for 1 h and concentrated in vacuo.

Purification of the residue by SiO_2 column chromatography (*n*-hexane/AcOEt=5:1) gave **5a** (564 mg, 90% in two steps) as a colorless oil. IR (KBr) 3562, 1732, 912 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz): δ 1.80–1.91 (2H, m), 2.28–2.66 (4H, m), 3.41 (3H, s), 3.78 (1H, m), 4.26 (1H, d, J=8.7 Hz), 4.58 (1H, d, J=8.7 Hz), 6.86–7.24 (15H, m); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 30.7, 34.6, 39.8, 51.3, 73.6, 78.2, 85.1, 125.7, 126.6, 127.3, 127.5, 127.6, 127.7, 127.7, 128.0, 128.2, 137.6, 139.0, 141.2, 171.0; LRMS (FAB) *m/z* 405 (MH^+); HRMS (FAB) calcd for $C_{26}H_{29}O_4$: 405.2066; found: 405.2070.

4.5.4. 3-(1-Phenethyl-3-butenyloxy)-2-butanol (5d). Allyltrimethylsilane (2.8 mL, 17.31 mmol) and $BF_3\cdot Et_2O$ (3.7 mL, 28.85 mmol) were added to a solution of **17b** (1.19 g, 5.77 mmol) in CH_3CN (12 mL) at 0 °C under N_2. The reaction mixture was stirred at 0 °C for 3 h and poured into saturated aqueous $NaHCO_3$. The mixture was extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. Purification of the residue by SiO_2 column chromatography (*n*-hexane/AcOEt=10:1) gave **5d** (753 mg, 53%) as a colorless oil ca. 1:1 diastereomeric mixture. IR (KBr) 3450, 1454, 1063 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 1.07–1.16 (6H, m), 1.72–1.86 (2H, m), 2.29–2.34 (2H, m), 2.36~2.71 (3H, m), 3.24–3.56 (3H, m), 5.05–5.15 (2H, m), 5.75–5.90 (1H, m), 7.17–7.30 (5H, m); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 16.5, 16.6, 18.6, 18.6, 31.5, 31.8, 35.6, 36.3, 38.4, 39.2, 71.1, 71.3, 76.1, 76.5, 78.4, 78.5, 116.9, 117.8, 125.6, 125.7, 128.1, 128.2, 128.2, 128.2, 134.3, 134.7, 141.7, 142.0. Anal. Calcd for $C_{16}H_{24}O_2$: C, 77.38; H, 9.74. Found: C, 77.62; H, 9.67.

Compound **5b** was prepared from **5d** via silyl ether **19b**.

4.5.5. 3-(1-Phenethyl-3-butenyloxy)-2-*tert*-butyldimethylsilyloxybutane (19b).



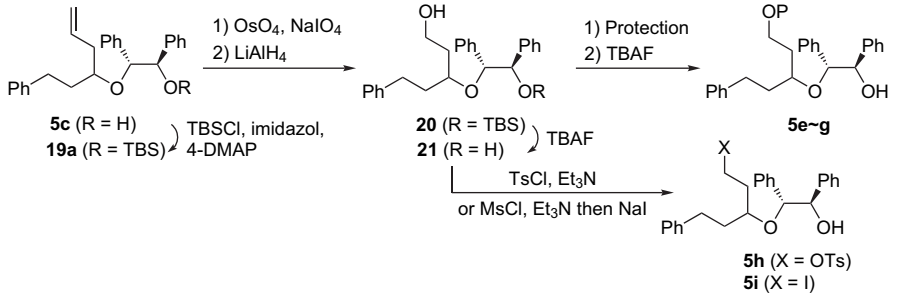
19b

tert-Butyldimethylsilyl chloride (1.19 g, 7.89 mmol) and imidazole (894 mg, 13.13 mmol) were added to a stirred solution of **5d** (652 mg, 2.63 mmol) in CH_2Cl_2 (2.6 mL) at 0 °C under N_2. The reaction mixture was stirred at rt for 24 h and poured into saturated aqueous $NaHCO_3$. The organic layer was separated and the aqueous layer was extracted with AcOEt. The combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. Purification of the residue by SiO_2 column chromatography (*n*-hexane/AcOEt=50:1) gave **19b** (902 mg, 95%) as a colorless oil. IR (KBr) 1103, 912 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ −0.01 to 0.00 (6H, m), 0.84–0.85 (9H, m), 1.02–1.06 (6H, m), 1.72–1.76 (2H, m), 2.24–2.26 (2H, m), 2.51–2.70 (2H, m), 3.36–3.38 (2H, m), 3.77–3.79 (1H, m), 5.01–5.04 (2H, m), 5.72–5.83 (1H, m), 7.13–7.26 (5H, m); ^{13}C NMR ($CDCl_3$, 270 MHz): δ −4.7, −4.6, −4.5, 13.7, 14.0, 17.1, 17.4, 25.9, 31.9, 36.0, 36.3, 39.0, 39.3, 69.1, 69.9, 76.1, 76.5, 76.8, 76.8, 116.8, 116.9, 125.6, 125.6, 128.2, 128.2, 134.8, 135.0, 142.1, 142.4; LRMS (FAB) *m/z* 363 (MH^+); HRMS (FAB) calcd for $C_{22}H_{39}O_2Si$: 363.2720; found: 363.2715.

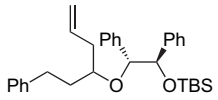
4.5.6. Methyl 3-(1,2-dimethyl-2-hydroxyethoxy)-5-phenylpentanoate (5b). OsO_4 (60 mg, 0.05 mmol), $NaIO_4$ (1.99 g, 9.29 mmol), and 2,6-lutidine (0.54 mL, 4.64 mmol) were added to a solution of **19b** (842 mg, 2.32 mmol) in dioxane/water (v/v=3:1, 6.1 mL) at 0 °C under air. The reaction mixture was stirred at rt for 3 h. After filtrating through Celite pad, the filtrate was concentrated in vacuo to give the residue. NaH_2PO_4 (843 mg, 7.03 mmol), 2-methyl-2-butene (1.2 mL, 11.71 mmol), and $NaClO_2$ (318 mg, 3.52 mmol) were added to the solution of the above residue in *t*BuOH/water (v/v=5:1, 23 mL) under air. The reaction mixture was stirred at rt for 12 h and poured into saturated 10% aqueous HCl. The mixture was extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The obtained residue was dissolved in benzene/MeOH (v/v=4:1, 14 mL). $TMSCHN_2$ (2 M in hexane, 1.52 mL, 1.52 mmol) was added to the solution at 0 °C. The reaction mixture was stirred at rt for 1 h and concentrated in vacuo. Purification of the residue by SiO_2 column chromatography (*n*-hexane/AcOEt=4:1) gave **5b** (501 mg, 77% in three steps) as a colorless oil. IR (KBr) 3459, 1730, 912 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.05–1.11 (6H, m), 1.75–1.97 (2H, m), 2.49–2.74 (4H, m), 3.24 (1H, m), 3.53 (1H, m), 3.67 (3H, s), 3.90 (1H, m), 7.17–7.27 (5H, m); ^{13}C NMR ($CDCl_3$, 270 MHz): δ 15.9, 17.39, 18.6, 31.3, 31.5, 35.8, 36.1, 38.8, 40.3, 51.6, 51.9, 70.9, 71.5, 73.3, 74.3, 78.3, 79.7, 125.8, 125.9, 128.1, 128.3, 141.2, 141.4, 171.7, 172.5. Anal. Calcd for $C_{16}H_{24}O_4$: C, 68.54; H, 8.63. Found: C, 68.47; H, 8.46.

4.6. Syntheses of substrates 5e–i in Table 3

Compounds **5e–i** were synthesized as shown below. The yield of each compound was not optimized. The compounds having alkaline labile functions, **5h** and **5i**, were synthesized via compound **21**, because TBAF treatment of the tosylate or the iodide from compound **20** gave poor results. The relationship of vicinal diphenyl groups is trans.



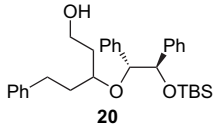
4.6.1. 1-*tert*-Butyldimethylsilyloxy-2-(1-phenethyl-3-butenyloxy)-1,2-diphenylethane (19a).



19a

According to the same procedure for **19b**, **19a** (511 mg, 88%) was obtained as a colorless oil by purification of SiO_2 column chromatography (*n*-hexane/AcOEt=20:1) from **5c** (460 mg, 1.2 mmol) in CH_2Cl_2 (2.6 mL) and *tert*-butyldimethylsilyl chloride (559 mg, 3.7 mmol) and imidazole (421 mg, 6.2 mmol). IR (KBr) 1454, 1067 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ −0.14 (3H, s), 0.01 (3H, s), 0.86 (9H, s), 1.79–1.82 (2H, m), 2.20–2.24 (2H, m), 2.60–2.66 (2H, m), 3.30–3.40 (1H, m), 4.43 (1H, d, J=6.3 Hz), 4.75 (1H, d, J=6.3 Hz), 4.95–5.00 (2H, m), 5.60–5.91 (1H, m), 6.95–7.30 (15H, m); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ −4.8, −2.8, 18.4, 25.7 (3C), 30.6, 34.0, 39.0, 75.1, 78.8, 84.0, 116.4, 125.4, 126.8, 127.1, 127.1, 127.2, 127.3, 127.3, 128.1, 128.2, 128.2, 128.2, 135.2, 139.2, 141.4, 142.6; LRMS (FAB) *m/z* 509 (MNa^+); HRMS (FAB) calcd for $C_{32}H_{42}O_2SiNa$: 509.2852; found: 509.2860.

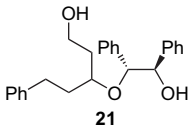
4.6.2. 1-*tert*-Butyldimethylsilyloxy-2-(1-hydroxy-5-phenyl-3-pentanoxy)-1,2-diphenylethane (20).



20

OsO_4 (95 mg, 0.37 mmol), $NaIO_4$ (3.2 g, 15.0 mmol), and 2,6-lutidine (0.87 mL, 7.4 mmol) were added to a solution of **19a** (1.8 g, 3.7 mmol) in dioxane/water (v/v=3:1, 7.5 mL) at 0 °C under air. The reaction mixture was stirred at rt for 3 h. After filtration, the filtrate was concentrated in vacuo. A solution of the obtained residue in THF (10 mL) was added to a solution of $LiAlH_4$ (147 mg, 3.90 mmol) in THF (22 mL) at 0 °C under N_2. The mixture was stirred at 0 °C for 1 h and poured into water (0.15 mL), 15% aqueous NaOH (0.15 mL), and water (0.45 mL). After filtration through Celite pad, the filtrate was concentrated in vacuo. Purification of the residue by SiO_2 column chromatography (*n*-hexane/AcOEt=4:1) gave **20** (1.30 g, 61%) as a colorless oil. IR (KBr) 3481, 1028, 742 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ −0.10 (3H, s), 0.09 (3H, s), 1.10 (9H, s), 1.89–1.98 (4H, m), 2.59 (2H, t, J=8.1 Hz), 3.79–3.82 (1H, m), 3.99–4.05 (2H, m), 4.76 (1H, d, J=4.5 Hz), 5.00 (1H, d, J=4.5 Hz), 7.26–7.52 (15H, m); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ −5.2, 5.0, 14.3, 18.2, 21.1, 25.8 (3C), 29.9, 33.4, 35.7, 60.3, 61.4, 75.4, 78.5, 83.0, 125.6, 127.0, 127.1, 127.4, 127.5, 127.6, 127.7, 127.7, 128.0, 128.1, 128.2, 138.4, 141.6, 142.0; LRMS (FAB) *m/z* 513 ($M+Na^+$); HRMS (FAB) calcd for $C_{31}H_{42}O_3Si$: 513.2801; found: 513.2804.

4.6.3. 2-(1-Hydroxy-5-phenyl-3-pentanoxy)-1,2-diphenylethanol (21).



21

tert-Butylammonium fluoride (TBAF) (1 M in toluene, 0.51 mL, 0.51 mmol) was added to a solution of **20** (167 mg, 0.34 mmol) in THF (0.34 mL) at 0 °C under N_2. The mixture was stirred at rt for 24 h and poured into saturated aqueous NH_4Cl. The mixture was extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. Purification of the residue by SiO_2 column chromatography (*n*-hexane/AcOEt=1:1) gave **21** (86 mg, 100%) as a colorless oil. IR (KBr) 3442, 1198, 773 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 1.68–1.96 (4H, m), 2.53–2.67 (2H, m), 3.02 (2H, br s), 3.48–3.51 (1H, m), 3.61 (2H, t, J=6.0 Hz), 4.33 (1H, d, J=7.8 Hz), 4.72 (1H, d, J=7.8 Hz), 6.98–7.30 (15H, m); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 30.7, 34.3, 36.4, 59.9, 74.1, 84.3, 125.7, 126.8, 127.6, 127.8, 128.0, 128.0, 128.0, 128.1, 128.2, 137.6, 139.1, 141.5. Anal. Calcd for $C_{25}H_{28}O_3$: C, 79.75; H, 7.50. Found: C, 75.92; H, 7.22; LRMS (FAB) *m/z* 377 (MH^+); HRMS (FAB) calcd for $C_{25}H_{29}O_3$: 377.2116; found: 377.2111.

4.6.4. 2-[1-(2-Methoxyethyl)-3-phenylpropoxy]-1,2-diphenylethanol (5e). Compound **20** (116 mg, 0.24 mmol) was added to a solution of NaH (60% in oil, 14 mg, 0.35 mmol) in THF (0.24 mL) at 0 °C under N_2. The mixture was stirred at 0 °C for 30 min and MeI (0.02 mL, 0.35 mmol) was added dropwise. The resulting mixture was stirred at rt for 24 h and poured into water. The mixture was extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. TBAF (1 M in toluene, 0.35 mL, 0.35 mmol) was added to the solution of the obtained residue in THF (0.24 mL) at 0 °C under N_2. The reaction mixture was stirred at rt for 24 h and poured into saturated aqueous NH_4Cl. The mixture was extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. Purification of the residue by SiO_2 column chromatography (*n*-hexane/AcOEt=4:1) gave **5e** (91 mg, 97%) as a colorless oil. IR (KBr) 3557, 912 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz): δ 1.72–1.95 (4H, m), 2.59–2.70 (2H, m), 3.16 (3H, s), 3.26–3.31 (1H, m), 3.43–3.49 (2H, m), 4.31 (1H, d, J=8.1 Hz), 4.70 (1H, d, J=8.1 Hz), 6.96–7.31 (15H, m); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 30.8, 34.4, 34.6, 58.4, 69.2, 73.4, 78.2, 84.6, 125.7, 127.0, 127.6, 127.8, 128.0, 128.2, 128.3, 137.9, 139.2, 141.8. Anal. Calcd for $C_{26}H_{30}O_3$: C, 79.97; H, 7.74. Found: C, 79.82; H, 7.80.

4.6.5. 2-[1-(2-Acetoxyethyl)-3-phenylpropoxy]-1,2-diphenylethanol (5f). Ac_2O (0.17 mL) was added to a solution of **20** (163 mg, 0.33 mmol) in pyridine (0.33 mL) at 0 °C under N_2. The mixture was stirred at rt for 24 h and concentrated in vacuo. TBAF (1 M in toluene, 0.5 mL, 0.50 mmol) was added to the solution of the obtained residue in THF (0.4 mL) at 0 °C under N_2. The reaction mixture was stirred at rt for 24 h and poured into saturated aqueous NH_4Cl. The mixture was extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. Purification of the residue by SiO_2 column chromatography (*n*-hexane/AcOEt=8:1) gave **5f** (132 mg, 96%) as a colorless oil. IR (KBr) 3560, 1730, 912 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.89 (3H, s), 1.96–2.05 (3H, m), 2.66–2.78 (2H, m), 3.49–3.56 (1H, m), 4.11–4.17 (2H, m), 4.36 (1H, d, J=8.3 Hz), 4.79 (1H, d, J=8.3 Hz), 6.95–7.38

(15H, m); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 20.7, 30.7, 32.9, 34.3, 60.9, 72.0, 77.9, 84.5, 125.8, 126.9, 127.4, 127.6, 127.8, 127.9, 128.0, 128.1, 128.2, 137.5, 139.0, 141.4, 170.6. Anal. Calcd for $C_{27}H_{30}O_4$: C, 77.48; H, 7.22. Found: C, 77.34; H, 7.21.

4.6.6. 2-[1-(2-Benzyloxyethyl)-3-phenylpropoxy]-1,2-diphenylethanol (5g). Compound **20** (182 mg, 0.37 mmol) was added to a solution of NaH (60% in oil, 22 mg, 0.56 mmol) in THF/DMF (v/v=1:1, 0.4 mL) at 0 °C under N_2. The reaction mixture was stirred at 0 °C for 30 min and BnBr (0.07 mL, 0.56 mmol) was added dropwise. The reaction mixture was stirred at rt for 3 h and poured into saturated aqueous NH_4Cl. The mixture was extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. TBAF (1 M in toluene, 0.58 mL, 0.58 mmol) was added to the solution of the obtained residue in THF (0.6 mL) at 0 °C under N_2. The reaction mixture was stirred at rt for 24 h and poured into saturated aqueous NH_4Cl. The mixture was extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. Purification of the residue by SiO_2 column chromatography (*n*-hexane/AcOEt=4:1) gave **5g** (125 mg, 72%) as a colorless oil. IR (KBr) 3560, 912 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.87–2.04 (4H, m), 2.63–2.84 (2H, m), 3.43–3.66 (3H, m), 4.37–4.38 (3H, m), 4.79 (1H, d, J=8.2 Hz), 7.03–7.44 (20H, m); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 31.2, 34.8, 35.0, 67.3, 73.1, 73.7, 78.5, 85.0, 126.1, 127.3, 127.6, 127.8, 128.0, 128.1, 128.1, 128.2, 128.3, 128.4, 128.5, 128.6, 138.3, 138.5, 140.0, 142.1. Anal. Calcd for $C_{32}H_{34}O_3$: C, 82.37; H, 7.34. Found: C, 82.15; H, 7.42.

4.6.7. 2-[1-(2-Tosyloxyethyl)-3-phenylpropoxy]-1,2-diphenylethanol (5h). Et_3N (0.12 mL, 1.22 mmol) and TsCl (117 mg, 0.91 mmol) were added to a solution of **21** (210 mg, 0.83 mmol) in CH_2Cl_2 (0.83 mL) at 0 °C under N_2. The reaction mixture was stirred at rt for 24 h and poured into water. The mixture was extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. Purification of the residue by SiO_2 column chromatography (*n*-hexane/AcOEt=4:1) gave **5h** (304 mg, 69%) as a colorless oil. IR (KBr) 3650, 1248 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz): δ 1.78–1.98 (4H, m), 2.43 (3H, s), 2.53–2.62 (2H, m), 3.21 (1H, br s), 3.40–3.44 (1H, m), 4.09–4.12 (2H, m), 4.26 (1H, d, J=8.2 Hz), 4.66 (1H, d, J=8.2 Hz), 6.87–7.33 (17H, m), 7.73 (2H, d, J=8.4 Hz); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 21.7, 30.6, 33.5, 72.3, 76.5, 78.2, 84.7, 125.9, 127.0, 127.5, 127.7, 127.9, 128.0, 128.1, 128.1, 128.1, 128.4, 129.6, 129.7, 132.9, 137.3, 138.9, 141.2, 144.6; LRMS (FAB) *m*/*z* 553 (MNa^+); HRMS (FAB) calcd for $C_{32}H_{34}O_5SNa$: 553.2025; found: 553.1990.

4.6.8. 2-[1-(2-Iodoethyl)-3-phenylpropoxy]-1,2-diphenylethanol (5i). Et_3N (0.09 mL, 0.62 mmol) and MsCl (0.04 mL, 0.62 mmol) were added to a solution of **21** (128 mg, 0.51 mmol) in CH_2Cl_2 (0.5 mL) at 0 °C under N_2. The reaction mixture was stirred at 0 °C for 3 h and poured into water. The mixture was extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. NaI (227 mg, 1.53 mmol) was added to the solution of the obtained residue in acetone (0.5 mL) under N_2. The reaction mixture was refluxed for 3 h. After filtration by Celite pad, the filtrate was concentrated in vacuo. Purification of the residue by SiO_2 column chromatography (*n*-hexane/AcOEt=8:1) gave **5i** (44 mg, 18%) as a colorless oil. IR (KBr) 3560, 912, 743 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz) δ 1.95–2.10 (4H, m), 2.59–2.67 (2H, m), 2.97–3.03 (1H, m), 3.19–3.28 (1H, m), 3.38–3.42 (1H, m), 4.28 (1H, d, J=8.2 Hz), 4.73 (1H, d, J=8.2 Hz), 6.94–7.37 (15H, m); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 2.1, 30.7, 34.0, 38.8, 75.8, 78.0, 84.6, 125.8, 126.8, 126.9, 127.4, 127.6, 127.9, 128.0, 128.1, 128.3, 137.4, 138.9, 141.2; LRMS (FAB) *m*/*z* 487 (MH^+); HRMS (FAB) calcd for $C_{25}H_{28}O_2I$: 487.1145; found: 487.1124.

4.7. Compounds 6 obtained by CAN mediated C–C bond cleavage of 5 (Table 3)

Every reaction was carried out according to the typical procedure.

4.7.1. Methyl 3-hydroxy-5-phenylpentanoate (6a). Entry 1: **6a** (30 mg, 97%) was obtained as a colorless oil from **5a** (60 mg, 0.14 mmol), CAN (162 mg, 0.30 mmol), and CH_3CN/water (v/v=1:1, 1.4 mL). SiO_2 column chromatography: *n*-hexane/AcOEt=4:1.

Entry 2: **6a** (43 mg, 90%) was obtained as a colorless oil from **5b** (64 mg, 0.23 mmol), CAN (251 mg, 0.46 mmol), and CH_3CN/water (v/v=1:1, 2.2 mL). SiO_2 column chromatography: *n*-hexane/AcOEt=4:1.

Compound **6a**: IR (KBr) 3526, 1728, 912 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz): δ 1.65–1.80 (2H, m), 2.33–2.48 (2H, m), 2.57–2.76 (2H, m), 2.94 (1H, br s), 3.63 (3H, s), 3.95 (1H, m), 7.11–7.24 (5H, m); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 31.8, 38.1, 41.1, 51.8, 67.2, 125.8, 128.3, 128.3, 141.5, 173.2. Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74. Found: C, 69.01; H, 7.73.

4.7.2. 1-Phenyl-5-hexen-3-ol (6b). Entry 3: **6b** (28 mg, 100%) was obtained as a colorless oil from **5c** (60 mg, 0.16 mmol), CAN (176 mg, 0.32 mmol), and CH_3CN/water (v/v=1:1, 1.6 mL). SiO_2 column chromatography: *n*-hexane/AcOEt=10:1.

Entry 4: **6b** (35 mg, 98%) was obtained as a colorless oil from **5d** (50 mg, 0.20 mmol), CAN (220 mg, 0.40 mmol), and CH_3CN/water (v/v=1:1, 2.0 mL). SiO_2 column chromatography: *n*-hexane/AcOEt=4:1.

Compound **6b**: IR (KBr) 3361, 912, 743 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz): δ 1.67 (1H, br s), 1.67–1.76 (2H, m), 2.10–2.23 (2H, m), 2.56–2.73 (2H, m), 3.60 (1H, m), 5.04–5.10 (2H, m), 5.67–5.79 (1H, m), 7.11–7.24 (5H, m); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 32.1, 38.5, 42.1, 69.9, 118.3, 125.7, 128.3, 128.3, 134.5, 141.9. Anal. Calcd for $C_{12}H_{16}O$: C, 81.77; H, 9.15. Found: C, 81.81; H, 9.19.

4.7.3. 1-Methoxy-5-phenyl-3-pentanol (6c). Compound **6c** (32 mg, 86%) was obtained as a colorless oil from **5e** (75 mg, 0.19 mmol), CAN (209 mg, 0.38 mmol), and

CH_3CN/water (v/v=1:1, 2 mL). SiO_2 column chromatography: *n*-hexane/AcOEt=2:1. Compound **6c**: IR (KBr) 3472, 1454, 1113 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz): δ 1.71–1.86 (4H, m), 2.66–2.85 (2H, m), 3.10 (1H, br s), 3.37 (3H, s), 3.52–3.69 (2H, m), 3.81–3.86 (1H, m), 7.17–7.33 (5H, m); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 32.0, 36.3, 39.2, 58.9, 70.9, 71.8, 125.6, 128.2, 128.3, 142.1. Anal. Calcd for $C_{12}H_{18}O$: C, 74.19; H, 9.34. Found: C, 73.90; H, 9.22.

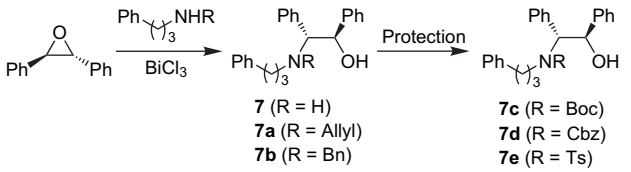
4.7.4. 1-Acetoxy-5-phenyl-3-pentanol (6d). Compound **6d** (26 mg, 80%) was obtained as a colorless oil from **5f** (62 mg, 0.15 mmol), CAN (162 mg, 0.3 mmol), and CH_3CN/water (v/v=1:1, 1.4 mL). SiO_2 column chromatography: *n*-hexane/AcOEt=3:1. Compound **6d**: IR (KBr) 3420, 1732, 912 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz): δ 1.67–1.83 (4H, m), 1.98 (3H s), 2.55–2.79 (2H, m), 3.57–3.66 (1H, m), 4.02–4.10 (1H, m), 4.25–4.34 (1H, m), 7.11–7.24 (5H, m); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 21.1, 32.1, 36.5, 39.1, 61.7, 68.0, 125.8, 128.3, 128.3, 141.7, 171.3. Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.24; H, 8.16. Found: C, 70.29; H, 8.20.

4.7.5. 1-Benzyloxy-5-phenyl-3-pentanol (6e). Compound **6e** (26 mg, 78%) was obtained as a colorless oil from **5g** (60 mg, 0.12 mmol), CAN (140 mg, 0.26 mmol), and CH_3CN/water (v/v=1:1, 1.2 mL). SiO_2 column chromatography: *n*-hexane/AcOEt=5:1. Compound **6e**: IR (KBr) 3420, 1192, 912 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz): δ 1.75–1.79 (4H, m), 2.61–2.85 (2H, m), 3.01 (1H, br s), 3.61–3.75 (2H, m), 3.77–3.89 (1H, m), 4.52 (2H, s), 7.18–7.32 (10H, m); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 32.0, 36.5, 39.2, 69.3, 70.9, 73.3, 125.6, 127.6, 127.7, 128.2, 128.3, 128.4, 142.1. Anal. Calcd for $C_{18}H_{22}O_2$: C, 79.96; H, 8.20. Found: C, 79.90; H, 8.32.

4.7.6. 1-Tosyloxy-5-phenyl-3-pentanol (6f). Compound **6f** (42 mg, 90%) was obtained as a colorless oil from **5h** (76 mg, 0.14 mmol), CAN (156 mg, 0.28 mmol), and CH_3CN/water (v/v=1:1, 1.4 mL). SiO_2 column chromatography: *n*-hexane/AcOEt=3:1. Compound **6f**: IR (KBr) 3539, 1356, 1175 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz): δ 1.68–1.93 (5H, m), 2.45 (3H, s), 2.61–2.79 (2H, m), 3.73–3.79 (1H, m), 4.08–4.16 (1H, m), 4.22–4.31 (1H, m), 7.15–7.32 (7H, m), 7.77 (2H, d, J=8.4 Hz); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 21.7, 32.0, 36.4, 39.1, 67.3, 67.7, 125.8, 127.8, 128.2, 128.4, 129.8, 132.7, 141.5, 144.7. Anal. Calcd for $C_{18}H_{22}O_4S$: C, 64.64; H, 6.63; S, 9.59. Found: C, 64.44; H, 6.74; S, 9.10; LRMS (FAB) *m/z* 335 (MH^+); HRMS (FAB) calcd for $C_{18}H_{23}O_4S$: 335.1317; found: 335.1332.

4.7.7. 1-Iodo-5-phenyl-3-pentanol (6g). Compound **6g** (46 mg, 80%) was obtained as a colorless oil from **5i** (96 mg, 0.2 mmol), CAN (216 mg, 0.40 mmol), and CH_3CN/water (v/v=1:1, 2.0 mL). SiO_2 column chromatography: *n*-hexane/AcOEt=5:1. Compound **6g**: IR (KBr) 3366, 1495, 912 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz): δ 1.69–1.99 (5H, m), 2.55–2.78 (2H, m), 3.19–3.25 (2H, m), 3.66–3.73 (1H, m), 7.11–7.25 (5H, m); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 3.0, 32.0, 38.9, 40.7, 71.3, 125.9, 128.2, 128.4, 141.4. Anal. Calcd for $C_{11}H_{15}IO$: C, 45.54; H, 5.21; I, 43.74. Found: C, 45.83; H, 5.16; I, 43.00; LRMS (FAB) *m/z* 291 (MH^+); HRMS (FAB) calcd for $C_{11}H_{16}OI$: 291.0246; found: 291.0251.

4.8. Synthesis of substrates 7a–e in Table 4



4.8.1. 1,2-Diphenyl-2-(3-phenylpropylamino)ethanol (7). $BiCl_3$ (200 mg, 0.64 mmol) was added to a mixture of *trans*-stilbene oxide (500 mg, 2.54 mmol) and 3-phenylpropylamine (689 mg, 5.09 mmol) at 0 °C under N_2. The reaction mixture was stirred at 40 °C for 12 h. K_2CO_3 was added to the reaction mixture at 0 °C and stirred for 10 min. After filtrating K_2CO_3, the filtrate was concentrated in vacuo. Purification of the residue by SiO_2 column chromatography (*n*-hexane/AcOEt=1:1) gave **7** (400 mg, 47%) as white crystals. Mp 135.5–135.6 °C; IR (KBr) 3307, 1602 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz): δ 1.73 (2H, quintet, J=7.2 Hz), 2.41–2.57 (4H, m), 3.86 (1H, d, J=5.7 Hz), 4.78 (1H, d, J=5.7 Hz), 7.06–7.34 (15H, m); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 31.6, 33.4, 46.6, 68.7, 76.4, 125.7, 126.7, 127.4, 127.5, 127.9, 128.0, 128.0, 128.2, 139.2, 140.4, 141.8. Anal. Calcd for $C_{23}H_{25}NO$: C, 83.34; H, 7.60; N, 4.23. Found: C, 83.22; H, 7.60; N, 4.26.

4.8.2. 1,2-Diphenyl-2-(*N*-allyl-3-phenylpropylamino)-ethanol (7a). $BiCl_3$ (286 mg, 0.44 mmol) was added to a mixture of *trans*-stilbene oxide (342 mg, 1.74 mmol) and *N*-allyl-3-phenylpropylamine (611 mg, 3.49 mmol) at 0 °C under N_2. The reaction mixture was stirred at 50 °C for 12 h. K_2CO_3 was added to the reaction mixture at 0 °C and stirred for 10 min. After filtrating K_2CO_3, the filtrate was concentrated in vacuo. Purification of the residue by SiO_2 column chromatography (*n*-hexane/AcOEt=10:1) gave **7a** (549 mg, 85%) as a colorless oil. IR (KBr) 3573, 1602 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 1.70 (2H, m), 2.3–2.5 (2H, m), 2.6 (1H, m), 2.9 (1H, m), 3.34 (1H, m), 3.82 (1H, m), 5.0–5.25 (4H, m), 5.68 (1H, m), 7.09–7.27 (15H, m); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 28.3, 33.4, 49.5, 53.2, 71.1, 72.7, 117.1, 125.5, 126.4, 127.0, 127.2, 127.5, 127.6, 128.1, 128.2, 129.4, 135.6, 136.0, 141.7, 142.1; LRMS (FAB) *m/z* 372 (MH^+); HRMS (FAB) calcd for $C_{26}H_{30}ON$: 372.2328; found: 372.2325.

4.8.3. 1,2-Diphenyl-2-(*N*-benzyl-3-phenylpropylamino)-ethanol (7b). $BiCl_3$ (152 mg, 0.23 mmol) was added to a mixture of *trans*-stilbene oxide (181 mg, 0.92 mmol) and *N*-benzyl-3-phenylpropylamine (416 mg, 1.85 mmol) at 0 °C under N_2. The reaction mixture was stirred at 50 °C for 12 h. K_2CO_3 was added to the reaction mixture at 0 °C and stirred for 10 min. After filtrating K_2CO_3, the filtrate was concentrated in vacuo. Purification of the residue by SiO_2 column chromatography (*n*-hexane/AcOEt=10:1) gave **7b** (114 mg, 29%) as a colorless oil. IR (KBr) 3566, 3440, 1600 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz): δ 1.64–1.72 (2H,

m), 2.16–2.42 (3H, m), 2.57–2.68 (1H, m), 3.21 (1H, d, J=14 Hz), 3.82 (1H, d, J=14 Hz), 3.90 (1H, d, J=8.1 Hz), 5.21 (1H, d, J=8.1 Hz), 6.99–7.35 (20H, m); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 28.5, 33.5, 49.4, 54.8, 70.4, 73.5, 125.6, 126.6, 127.0, 127.4, 127.5, 127.8, 127.9, 128.0, 128.1, 128.2, 128.5, 129.5, 135.7, 139.4, 141.9, 142.2: LRMS (FAB) m/z 422 (MH^+); HRMS (FAB) calcd for $C_{30}H_{32}ON$: 422.2484; found: 422.2485.

4.8.4. 1,2-Diphenyl-2-(*N*-*tert*-butoxycarbonyloxy-3-phenylpropylamino)ethanol (7c). Boc_2O (0.21 mL, 0.91 mmol) was added to a solution of **7** (200 mg, 0.60 mmol) in CH_2Cl_2 (1.2 mL) at 0 °C under N_2. The reaction mixture was stirred at rt for 3 h and poured into saturated aqueous $NaHCO_3$. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2. The combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. Purification of the residue by SiO_2 column chromatography (*n*-hexane/AcOEt=4:1) gave **7c** (267 mg, 100%) as a colorless oil. IR (KBr) 3593, 3421, 1681, 912 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz): δ 1.29 (9H, s), 1.52–1.62 (2H, m), 2.31 (2H, t, J=7.8 Hz), 2.85–2.95 (1H, m), 3.11–3.20 (1H, m), 5.34 (1H, br s), 6.95 (2H, d, J=6.4 Hz), 7.12–7.41 (15H, m); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 28.2, 33.2, 51.1, 61.3, 64.8, 79.7, 80.6, 125.8, 125.9, 127.1, 127.8, 128.0, 128.1, 128.3, 128.4, 128.5, 128.6, 129.1, 141.7; LRMS (FAB) m/z 432 (MH^+); HRMS (FAB) calcd for $C_{28}H_{34}O_3N$: 432.2538; found: 432.2520.

4.8.5. 1,2-Diphenyl-2-(*N*-benzyloxycarbonyloxy-3-phenylpropylamino)ethanol (7d). CbzCl (0.29 mL, 0.67 mmol) was added to a solution of **7** (201 mg, 0.61 mmol) in EtOH/H_2O (v/v=1:1, 1.2 mL) at 0 °C under N_2. The reaction mixture was stirred at rt for 3 h and poured into saturated aqueous $NaHCO_3$. The mixture was extracted with CH_2Cl_2. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. Purification of the residue by SiO_2 column chromatography (*n*-hexane/AcOEt=4:1) gave **7d** (244 mg, 86%) as a colorless oil. IR (KBr) 3427, 1681, 912, 742 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz): δ 1.55 (2H, br s), 2.30 (2H, t, J=7.5 Hz), 2.94–3.02 (1H, m), 3.15–3.24 (1H, m), 5.16 (2H, br s), 6.92 (2H, d, J=6.7 Hz), 7.14–7.41 (20H, m); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 29.7, 32.9, 47.1, 66.9, 73.5, 125.6, 126.6, 127.7, 127.7, 128.0, 128.2, 128.3, 128.9, 136.3, 137.3, 141.0; LRMS (FAB) m/z 466 (MH^+); HRMS (FAB) calcd for $C_{31}H_{32}O_3N$: 466.2383; found: 466.2381.

4.8.6. 1,2-Diphenyl-2-(*N*-*p*-toluenesulfonyl-3-phenylpropylamino)ethanol (7e). Et_3N (0.11 mL, 0.80 mmol) and TsCl (129 mg, 0.68 mmol) were added to a solution of **7** (201 mg, 0.61 mmol) in CH_2Cl_2 (1.2 mL) at 0 °C under N_2. The reaction mixture was stirred at rt for 12 h and poured into water. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2. The combined organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. Purification of the residue by SiO_2 column chromatography (*n*-hexane/AcOEt=6:1) gave **7e** (121 mg, 41%) as a colorless oil. IR (KBr) 3506, 912, 742 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.4 (1H, m), 1.7 (1H, m), 2.29–2.32 (2H, m), 2.33 (3H, s), 2.93–3.04 (1H, m), 3.09–3.19 (1H, m), 5.03 (1H, d, J=7.2 Hz), 5.47 (1H, d, J=7.2 Hz), 6.97–7.42 (19H, m); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 21.5, 30.6, 33.1, 46.6, 66.9, 74.9, 125.7, 127.1, 127.2, 127.8, 128.0, 128.1, 128.2, 128.3, 129.0, 129.7, 135.6, 137.3, 140.8, 141.0, 142.5; LRMS (FAB) m/z 508 (MNa^+); HRMS (FAB) calcd for $C_{30}H_{31}O_3NSNa$: 508.1922; found: 508.1940.

4.9. Compounds 8 obtained by CAN mediated C–C bond cleavage of 7 (Table 4)

The spectral data of **8a–e** were identical with those reported in the literatures.[17]

Entry 1: *N*-allyl-3-phenylpropylamine **8a** (19 mg, 82%) was obtained as a colorless oil from **7a** (50 mg, 0.13 mmol), CAN (147 mg, 0.26 mmol), and CH_3CN/water (v/v=1:1, 1.3 mL). SiO_2 column chromatography: AcOEt only.

Entry 2: *N*-benzyl-3-phenylpropylamine **8b** (25 mg, 83%) was obtained as a colorless oil from **7b** (56 mg, 0.13 mmol), CAN (147 mg, 0.26 mmol), and CH_3CN/water (v/v=1:1, 1.3 mL). SiO_2 column chromatography: AcOEt only.

Entry 3: *N*-*tert*-butoxycarbonyl-3-phenylpropylamine **8c** (22 mg, 80%) was obtained as a colorless oil from **7c** (50 mg, 0.12 mmol), CAN (127 mg, 0.24 mmol), and CH_3CN/water (v/v=1:1, 1.2 mL). SiO_2 column chromatography: *n*-hexane/AcOEt=20:1.

Entry 4: *N*-benzyloxycarbonyl-3-phenylpropylamine **8d** (22 mg, 68%) was obtained as a colorless oil from **7d** (57 mg, 0.12 mmol), CAN (134 mg, 0.24 mmol), and CH_3CN/water (v/v=1:1, 1.2 mL). SiO_2 column chromatography: *n*-hexane/AcOEt=10:1.

Entry 5: *N*-*p*-toluenesulfonyl-3-phenylpropylamine **8e** (31 mg, 89%) was obtained as a colorless oil from **7d** (58 mg, 0.12 mmol), CAN (131 mg, 0.24 mmol), and CH_3CN/water (v/v=1:1, 1.2 mL). SiO_2 column chromatography: *n*-hexane/AcOEt=5:1.

4.10. Synthesis of substrates 9a and 9b in Scheme 3

4.10.1. *trans*-1,2-Diphenyl-1-methoxy-2-(3-phenylpropoxy)ethane (9a). Compound **3a** (50 mg, 0.15 mmol) was added to a solution of NaH (60% in oil, 7 mg, 0.18 mmol) in THF (1.5 mL) at 0 °C under N_2. The reaction mixture was stirred at rt for 1 h, and MeI (43 mg, 0.30 mmol) was added dropwise. The reaction mixture was stirred at rt for 3 h and poured into saturated aqueous NH_4Cl. The mixture was extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. Purification of the residue by SiO_2 column chromatography (*n*-hexane/AcOEt=5:1) gave **9a** (52 mg, 100%) as a colorless oil. IR (KBr) 1111, 748 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.79 (2H, m), 2.50–2.60 (2H, m), 3.20–3.40 (2H, m), 3.21 (3H, s), 4.25 (1H, d, J=6.3 Hz), 4.32 (1H, d, J=6.3 Hz), 6.99–7.17 (15H, m); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 31.4, 32.2, 57.5, 68.6, 85.9, 87.5, 125.6, 127.4, 127.5, 127.7, 127.7, 127.8, 128.2, 128.4, 138.6, 139.1, 142.1; LRMS (FAB) m/z 369 (MNa^+); HRMS (FAB) calcd for $C_{24}H_{26}O_2Na$: 369.1830; found: 369.1841.

4.10.2. *trans*-1,2-Diphenyl-1-methoxy-2-(*N*-*tert*-butoxycarbonyl-3-phenylpropylamino)ethane (9b). Compound **7c** (50 mg, 0.15 mmol) was added to a solution of NaH (60% in oil, 7 mg, 0.18 mmol) in THF (1.5 mL) at 0 °C under N_2. The reaction mixture was stirred at rt for 1 h and MeI (43 mg, 0.30 mmol) was added dropwise. The reaction mixture was stirred at rt for 3 h and poured into saturated aqueous NH_4Cl. The mixture was extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. Purification of the residue by SiO_2 column chromatography (*n*-hexane/AcOEt=5:1) gave **9b** (52 mg, 78%) as a colorless oil. IR (KBr) 1681, 912 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz): δ 1.18 (9H, s), 1.22–1.53 (2H, m), 2.07–2.30 (2H, m), 2.62–2.81 (1H, m), 2.82–3.06 (1H, m), 3.07 (3H, s), 4.70 (1H, d, *J*=7.3 Hz), 5.03 (1H, *J*=7.3 Hz), 7.02–7.36 (15H, m); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 28.2, 33.2, 46.2, 53.4, 56.7, 79.0, 82.0, 82.6, 125.4, 127.2, 127.4, 127.6, 127.7, 128.0, 128.1, 128.4, 128.6, 138.7, 129.1, 141.7; LRMS (FAB) *m*/*z* 446 (MH^+); HRMS (FAB) calcd for $C_{29}H_{36}O_3N$: 446.2696; found: 446.2706.

4.11. Oxidative fragmentation of proline derivatives in Table 5

The spectral data of **11a–c** were identical with those reported in the literatures.[18]

4.11.1. *N*-*tert*-Butoxycarbonyl-2-hydroxypyrrolidine (11a). Entry 1: **11a** (26 mg, 51%) was obtained as a colorless oil from **10a** (56 mg, 0.28 mmol), CAN (302 mg, 0.55 mmol), and CH_3CN/water (v/v=1:1, 2.6 mL). SiO_2 column chromatography: *n*-hexane/AcOEt=4:1.

Entry 4: **11a** (33 mg, 65%) was obtained as a colorless oil from **10d** (59 mg, 0.27 mmol), CAN (300 mg, 0.55 mmol), and CH_3CN/water (v/v=1:1, 2.7 mL). SiO_2 column chromatography: *n*-hexane/AcOEt=4:1.

4.11.2. *N*-Benzyloxycarbonyl-2-hydroxypyrrolidine (11b). Entry 2: **11b** (37 mg, 64%) was obtained as a colorless oil from **10b** (61 mg, 0.26 mmol), CAN (284 mg, 0.52 mmol), and CH_3CN/water (v/v=1:1, 2.6 mL). SiO_2 column chromatography: *n*-hexane/AcOEt=2:1.

Entry 5: **11b** (31 mg, 68%) was obtained as a colorless oil from **10e** (52 mg, 0.21 mmol), CAN (229 mg, 0.42 mmol), and CH_3CN/water (v/v=1:1, 2.0 mL). SiO_2 column chromatography: *n*-hexane/AcOEt=2:1.

4.11.3. *N*-*p*-Toluenesulfonyl-2-hydroxypyrrolidine (10c). Entry 3: **11c** (22 mg, 48%) was obtained as a colorless oil from **10c** (49 mg, 0.19 mmol), CAN (211 mg, 0.38 mmol), and CH_3CN/water (v/v=1:1, 1.9 mL). SiO_2 column chromatography: *n*-hexane/AcOEt=2:1.

Entry 6: **11c** (28 mg, 63%) was obtained as a colorless oil from **10f** (49 mg, 0.18 mmol), CAN (199 mg, 0.36 mmol), and CH_3CN/water (v/v=1:1, 1.8 mL). SiO_2 column chromatography: *n*-hexane/AcOEt=2:1.

4.12. Reactions in Scheme 5

4.12.1. (3a*R*,7a*R*,7*R*)-7-Bromo-2,3,3a,6,7,7a-hexahydrobenzofuran-2-ol (13). CAN (462 mg, 0.84 mmol) was added to a stirred solution of **12** (104 mg, 0.24 mmol) in acetonitrile (0.6 mL) and water (0.6 mL) at rt under air. The reaction mixture was stirred at 60 °C for 30 min. K_2CO_3 was added to the resulting solution. After filtrating K_2CO_3, the filtrate was concentrated in vacuo. Purification of the residue by SiO_2 column chromatography (*n*-hexane/AcOEt=5:1) gave **12** (30 mg, 58%) as a colorless oil (2:1 mixture of anomeric carbon by ^1H NMR). IR (KBr) 3379, 1649 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz): δ 1.7–1.9 (1H, m), 2.13–2.41 (1H, m), 2.45–2.6 (1H, m), 2.6–2.9 (1H, m), 2.91–3.11 (1H, m), 4.04–4.07 (2/3H, dt, *J*=5, 8 Hz), 4.33 (1/3H, t, *J*=5.7 Hz), 4.44–4.53 (1H, m), 5.58–5.73 (3H, m); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 30.1, 32.5, 36.4, 37.6, 39.5, 39.5, 47.6, 49.8, 80.6, 81.0, 98.1, 100.0, 124.1, 124.1, 127.8, 128.9; LRMS (FAB) *m*/*z* 241 (MNa^+); HRMS (FAB) calcd for $C_8H_{11}O_2{}^{79}BrNa$: 240.9840; found: 240.9865, calcd for $C_8H_{11}O_2{}^{81}BrNa$: 242.9819; found: 242.9857.

4.12.2. (3a*R*,7a*R*,7*R*)-7-Bromo-3a,6,7,7a-tetrahydro-3*H*-benzofuran-2-one (14). NaH_2PO_4 (35 mg, 0.29 mmol), 2-methyl-2-butene (0.05 mL, 0.48 mmol), and $NaClO_2$ (13 mg, 014 mmol) were added to a stirred solution of **13** (21 mg, 0.10 mmol) in *t*BuOH/water (v/v=5:1, 1.0 mL) at rt under air. The reaction mixture was stirred at rt for 6 h and poured into saturated 10% aqueous HCl. The mixture was extracted with AcOEt. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. Purification of the residue by SiO_2 column chromatography (*n*-hexane/AcOEt=4:1) gave **14** (18 mg, 86%) as a colorless oil. IR (KBr) 1788, 1217 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz): δ 2.40–2.51 (2H, m), 2.77–2.89 (2H, m), 3.28 (1H, br s), 4.44–4.46 (1H, m), 4.78–4.80 (1H, m), 5.56–5.60 (1H, m), 5.72–5.76 (1H, m); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 28.8, 33.3, 35.1, 43.3, 79.2, 124.2, 125.2, 175.3; LRMS (FAB) *m*/*z* 217 (MH^+); HRMS (FAB) calcd for $C_8H_{10}O_2{}^{79}Br$: 216.9865; found: 216.9870, calcd for $C_8H_{10}O_2{}^{81}Br$: 218.9844; found: 218.9870.

4.12.3. (2*S*,3a*RS*,5*R*,6a*SR*)-2,5-Bisiodomethylhexahydrofuro[2,3-*b*]furan (16a). CAN (428 mg, 0.78 mmol) was added to a stirred solution of **15a** (116 mg, 0.20 mmol) in acetonitrile (1.0 mL) and water (1.0 mL) at rt under air. The reaction mixture was stirred at 60 °C for 30 min. K_2CO_3 was added to the reaction mixture. After filtrating K_2CO_3, the filtrate was concentrated in vacuo. Purification of the residue by SiO_2 column chromatography (*n*-hexane/AcOEt=4:1) gave **16a** (46 mg, 61%) as a colorless oil. IR (KBr) 1018, 742 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz): δ 1.68–1.77 (2H, m), 2.36–2.41 (2H, m), 2.88–3.07 (1H, m), 3.37–3.43 (4H, m), 4.18–4.22 (2H, m), 5.75 (1H, d, *J*=5.4 Hz); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 9.9, 37.9, 43.6, 80.2, 110.6; LRMS (FAB) *m*/*z* 395 (MH^+); HRMS (FAB) calcd for $C_8H_{13}O_2I_2$: 394.9005; found: 394.8982.

4.12.4. (1*S*,3*R*,4*R*,6*S*,8*R*,10*R*)-6-Cyanomethyl-3,4-diphenyl-10-iodomethyl-2,5,11-trioxabicyclo[6.3.0]undecane (15b). NaCN (106 mg, 2.16 mmol) was added to a stirred solution of **15a** (850 mg, 1.44 mmol) in DMSO (2.9 mL) at rt under air. The reaction mixture was stirred at 70 °C for 2 h and poured into water. The mixture was extracted with AcOEt. The organic layer was washed with

brine, dried over Na_2SO_4, and concentrated in vacuo. Purification of the residue by SiO_2 column chromatography (*n*-hexane/AcOEt=4:1) gave **15b** (284 mg, 40%) as a colorless oil. IR (KBr) 1452, 742 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz): δ 1.52–1.61 (1H, m), 2.31–2.45 (6H, m), 3.11 (1H, t, J=9.2 Hz), 3.35 (1H, q, J=4.8 Hz), 4.19–4.65 (4H, m), 5.92 (1H, d, J=3.8 Hz), 6.86–6.88 (4H, m), 7.10–7.13 (6H, m); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 11.0, 22.6, 32.4, 37.1, 44.5, 73.5, 78.8, 80.7, 86.6, 107.2, 127.0, 127.2, 127.3, 127.5, 127.6, 127.7, 127.9, 137.9, 138.1; LRMS (FAB) *m/z* 490 (MH^+); HRMS (FAB) calcd for $C_{23}H_{25}O_3NI$: 490.0879; found: 490.0861.

4.12.5. (2*R*,3a*R*,5*S*,6a*S*)-5-Cyanomethyl-2-iodomethylhexahydrofuro[2,3-*b*]furan (16b). CAN (420 mg, 0.78 mmol) was added to a stirred solution of **15b** (108 mg, 0.22 mmol) in acetonitrile (1.1 mL) and water (1.1 mL) at rt under air. The reaction mixture was stirred at 60 °C for 30 min. K_2CO_3 was added to the reaction mixture. After filtrating K_2CO_3, the filtrate was concentrated in vacuo. Purification of the residue by SiO_2 column chromatography (*n*-hexane/AcOEt=2:1) gave **16b** (36 mg, 56%) as a colorless oil. IR (KBr) 1456, 912 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz): δ 1.60–1.82 (2H, m), 2.35–2.5 (2H, m), 2.80–3.0 (3H, m), 3.35–3.45 (2H, m), 4.15–4.40 (2H, m), 5.68 (1H, d, J=5.4 Hz); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 9.7, 24.8, 37.0, 37.8, 43.5, 75.4, 80.4, 110.3, 117.0; LRMS (FAB) *m/z* 294 (MH^+); HRMS (FAB) calcd for $C_9H_{13}O_2NI$: 293.9991; found: 293.9993.

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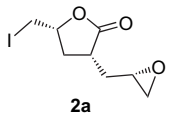

2a

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