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THE FIRST EXAMPLE OF AN AMIDE-CARBONYL STABILIZED OXIRANYL ANION: GENERATION FROM EPOXYSILANE, ITS PROPERTIES, AND TRAPPING WITH ELECTROPHILES

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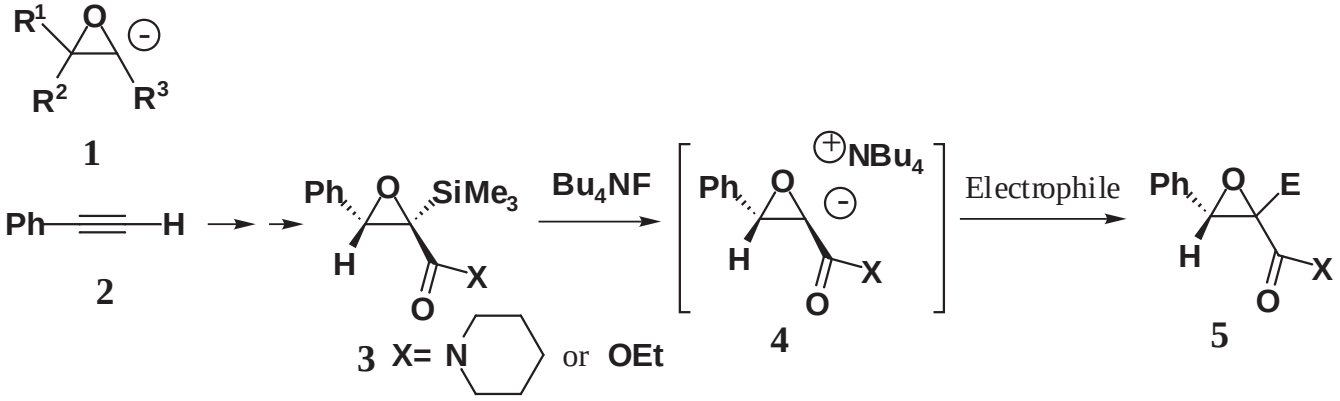
Abstract---An epoxysilane having an amide group at the α-carbon was synthesized from phenylacetylene. An amide-carbonyl stabilized oxiranyl-ammonium was generated from the epoxysilane in THF with tetrabutylammonium fluoride (TBAF). The generated oxiranyl anion was found to have enough nucleophilicity with aldehydes to give moderate to good yields of the adducts. In some reactions, the oxiranylammonium was found to be configurationally unstable to give the epimers.

Oxiranyl anions (**1**) have been recognized as very unstable compounds and as fleeting intermediates in the reaction of epoxides with strong bases.[1, 2] However, from the recent cumulative studies on the chemistry of oxiranyl anions, chemists now recognize that some oxiranyl anions can be handled as usual carbanions, though special caution must be paid in most cases.[2a] Especially, stabilized oxiranyl anions are now used as the intermediates in the total synthesis of natural products.[3]



Scheme 1. Generation of amide-carbonyl and ester-carbonyl stabilized oxiranylammoniums (**4**) and trapping with electrophiles

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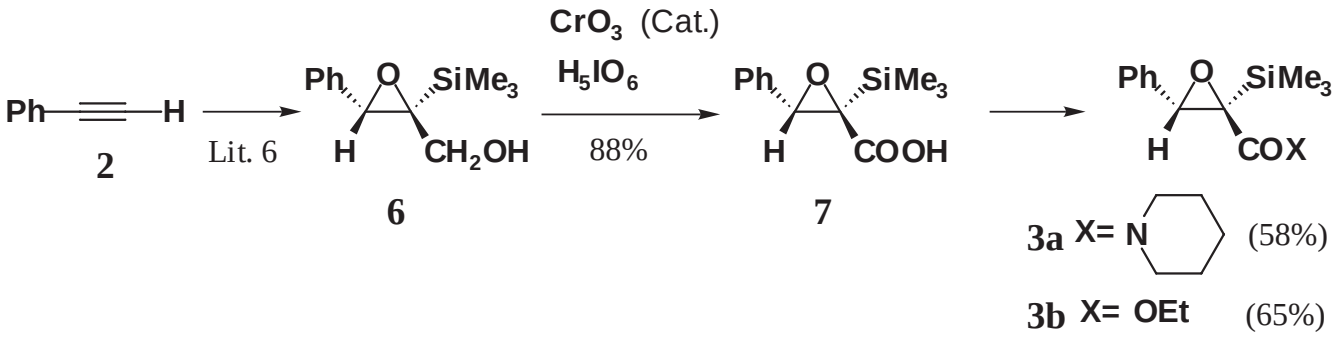
This paper is dedicated to Professor Yuichi Kanaoka on the occasion of his 75th birthday.

We recently studied the generation of some destabilized oxiranyl anions from sulfinyloxiranes with alkylmetals by sulfoxide-metal exchange and the trapping of the generated oxiranyl anions with several electrophiles.[4] In continuation of our interest in the chemistry of oxiranyl anions in synthetic organic chemistry, we were interested in amide-carbonyl stabilized oxiranyl anions because, although some ester-carbonyl stabilized oxiranyl anions were reported,[3e, 3f, 5] no report has been published on the generation of amide-carbonyl stabilized oxiranyl anions. Herein the first example of the generation and trapping of the amide-carbonyl stabilized oxiranylammonium (**4**) from epoxysilane (**3**), which were derived from phenylacetylene (**2**), are reported (Scheme 1).

RESULTS AND DISCUSSION

Synthesis of epoxysilanes having an amide and an ester group on the α-position

First, epoxysilanes (**3a**) and (**3b**) were synthesized starting from phenylacetylene as shown in Scheme 2. According to the procedure reported by Shipman,[6] epoxy alcohol (**6**) was synthesized from phenylacetylene (**2**) in good overall yield. The alcohol (**6**) was oxidized by a catalytic amount of CrO_3 with periodic acid (H_5IO_6) as stoichiometric oxidant[7] to give the carboxylic acid (**7**) in good yield.

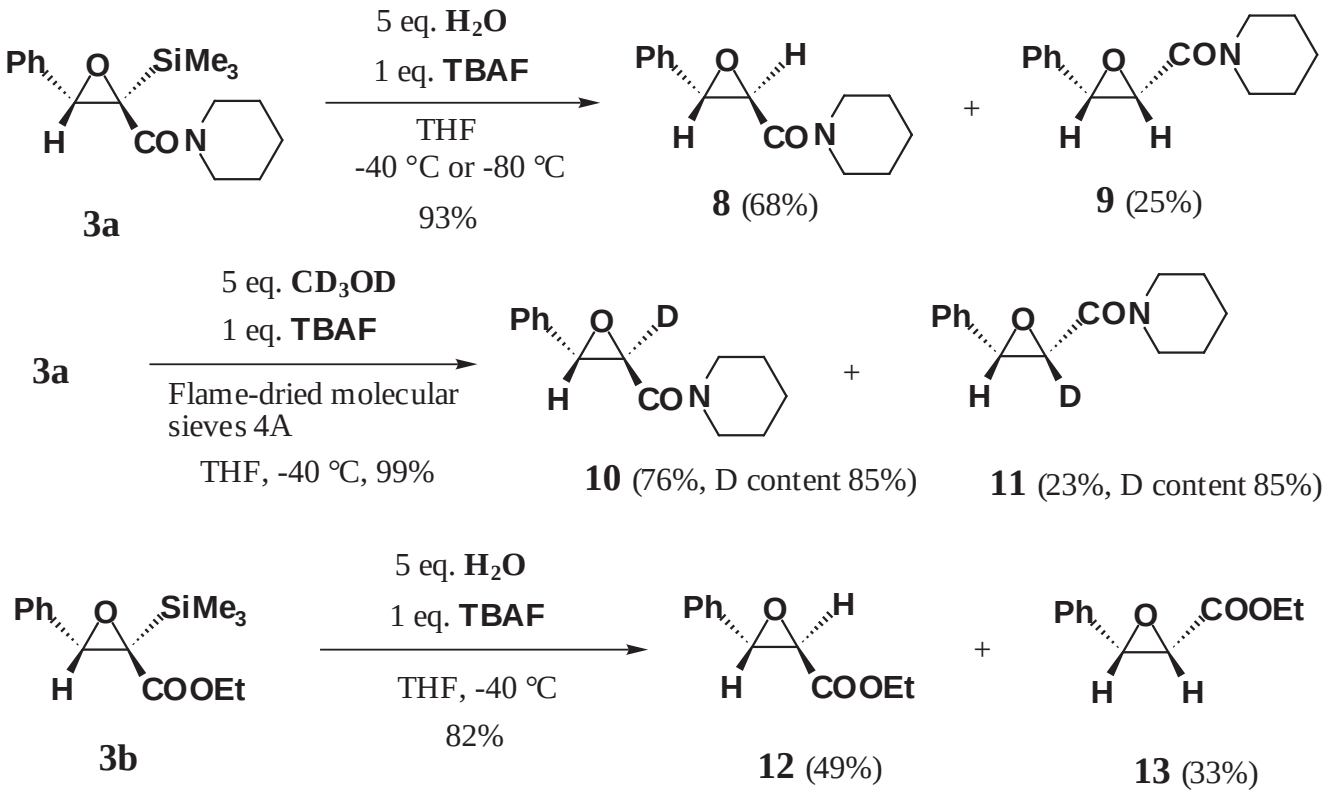


Scheme 2. Synthesis of epoxysilanes (**3a**) and (**3b**) from phenylacetylene (**2**)

The synthesis of amide (**3a**) was carried out through the pentafluorophenyl ester[8] to give the desired piperidine amide in moderate yield. We also synthesized the ethyl ester (**3b**) by esterification of (**7**) with excess iodoethane and DBU.[9] The purity of the epoxysilane (**3b**) was determined by ^{13}C NMR spectrometry.

Generation of amide-carbonyl stabilized oxiranylammoniums and trapping with some electrophiles

First of all, we investigated the feasibility for the generation of an oxiranyl anion from **3a** by reaction with a fluoride ion. Thus, the silyloxirane (**3a**) was treated with 1 equivalent of TBAF in THF containing water at -40 ℃. Instantaneous reaction took place to give the desilylated epoxides (**8**) and (**9**) (**8**:**9**=68:25) in 93% yield (Scheme 3). The structure of the products was easily determined by ^1H NMR spectrometry. Coupling constant of the hydrogens on the epoxy ring of the main product (**8**) and the minor product (**9**) were 2.0 Hz (*trans*) and 4.4 Hz (*cis*), respectively.



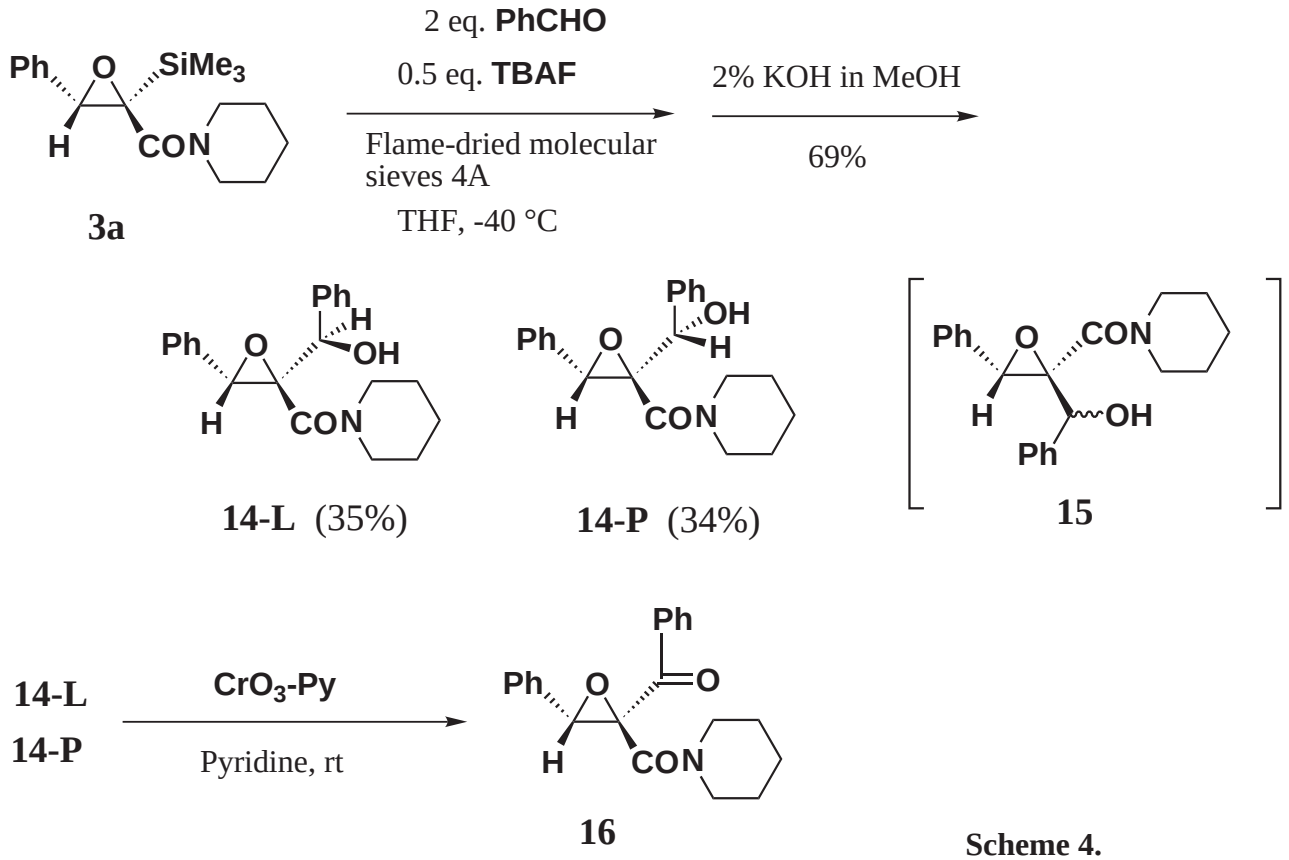
Scheme 3.

We were somewhat surprised by the observation of a considerable amount of inverted product (**9**), because the configurational stability of the oxiranyl anions was recognized to be very high.[2] We also investigated this reaction at much lower temperature (-80 ℃); however, the ratio of the isomers did not change at all.

Inversion of the configuration of the oxiranylammonium was also observed in the reaction with the ester (**3b**). In this case the ratio of the retained product (**12**) and the inverted product (**13**) was 49:33. This result shows that the configuration of the oxiranylammonium derived from ester (**3b**) is less stable than that from amide (**3a**).

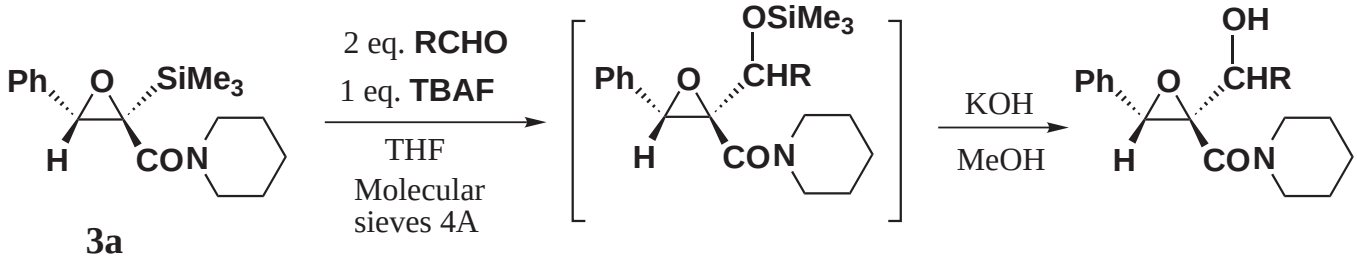
In order to generate the oxiranylammonium and trap it with some electrophiles other than water, we set up the reaction conditions as follows. First, molecular sieve 4A was flame-dried under argon atmosphere in a round-bottom flask. After cooling to room temperature, to the flask were added dry THF, the epoxysilane (**3a**), and 5 equivalents of D_2O. The reaction mixture was cooled to -40 ℃, then TBAF was added. The desilylated epoxides (**10** and **11**) containing over 85% of deuterium were obtained in quantitative yield. This result indicated that the reaction undoubtedly gave the desired amide-carbonyl stabilized oxiranyl anion.

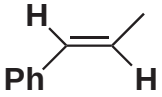
Next, we investigated trapping of the generated oxiranylammonium (**4**) with carbonyl compounds (Scheme 4 and Table 1). Under the conditions described for the synthesis of deuterated epoxides (**10**) and (**11**), the epoxide (**3a**) was treated with TBAF in the presence of 2 equivalents of benzaldehyde at -40 ℃. After 30 min the reaction mixture was treated with a base to afford the desired adducts and some amounts of the desilylated products (**8**) and (**9**). As the products, four isomers (**14** and **15**) were expected; however,



Scheme 4.

Table 1. Generation of oxiranylammonium and trapping with aldehydes



Entry	R	Temp. / °C	Time / min	Product	Yield / %	(diastereomeric ratio)
1	**Ph**	-40	30	**14**	69	(50:50)
2	**$PhCH_2CH_2$**	-80	30	**17**	51	(55:45)
3		-40	30	**18**	36	(60:40)

only two adducts, a less polar adduct (expressed as L) and a more polar adduct (expressed as P), were obtained in this experiment and the ratio of the two products was almost 1:1.
First of all, these two products (**14-L** and **14-P**) were separated and both were oxidized to give ketones. The produced ketones were found to be the same **16**. From this fact, the two products were established to be the diastereomers concerning the carbon bearing a hydroxyl group. In order to know whether the adducts were the retained products (**14**) or the inverted products (**15**), we examined in detail the spectral data; however, we could not determine the structure of the adducts. The structure of the adduct (**14-L**) was finally determined to be the retained product as shown in Scheme 4 by X-Ray crystallographic analysis. Stereoview of the adduct (**14-L**) is shown in Figure 1. At present we are not sure of the exact reason why the inverted adducts (**15**) were not produced in this reaction.

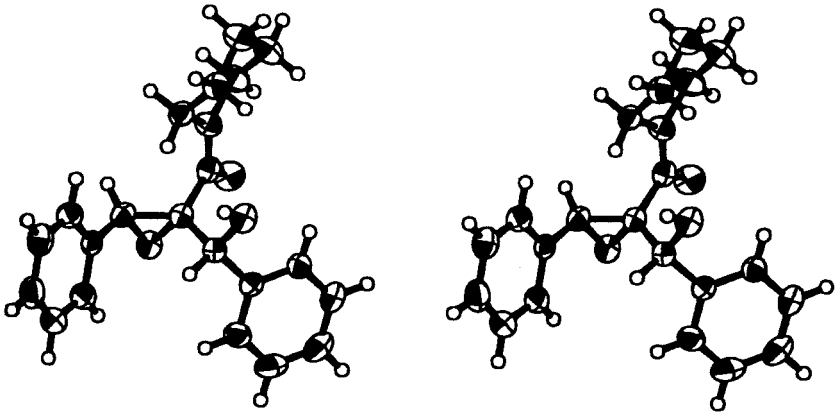


Figure 1. Stereoview of the adduct (**14-L**)

We investigated this reaction with 3-phenylpropanal and cinnamaldehyde, and the results are summarized in Table 1. The yields of the adducts (**17**) and (**18**) were somewhat lower than that of **14**. Again, only two products were obtained. We investigated the reaction of this oxiranylammonium with acetone, benzoyl chloride and ethyl chloroformate; however, no reaction product was obtained.

In conclusion, we were able to generate the oxiranylammonium stabilized by an amide-carbonyl group. The reactivity of the oxiranyl anion was found to be low, and only aldehydes gave the adducts; however, from the adduct, highly oxidized epoxides like **16** could be synthesized by this method.

EXPERIMENTAL

Melting points were measured with a Yanagimoto micro melting point apparatus and are uncorrected. ^{1}H NMR spectra were measured in a $CDCl_3$ solution with JEOL JNM-LA 400 and 500 spectrometer. Electron-impact MS spectra were obtained at 70 eV by direct insertion. Silica gel 60 (MERCK) containing

0.5% fluorescence reagent 254 and a quartz column were used for column chromatography and the products having UV absorption were detected by UV irradiation. In experiments requiring a dry solvent, THF was distilled from benzophenone ketyl; HMPA and diisopropylamine were distilled from CaH_2. The molecular sieves 4A used in this study were flame-dried under Ar atmosphere before use.

(2*S,3*S**)-2,3-Epoxy-3-phenyl-2-trimethylsilylpropanoic acid (7).** A stock solution of H_5IO_6 / CrO_3 was prepared by dissolving H_5IO_6 (11.4 g, 50.0 mmol) and CrO_3 (69 mg 3.6 mol %) in wet MeCN (0.75 v / water) to a volume of 114 mL (complete dissolution typically required 1-2 h). To a solution of the epoxy alcohol (**7**) (2.0 g; 8.5 mmol) in MeCN (85 mL) was added the stock solution (46.5 mL) at 0 ℃ and the reaction mixture was stirred at 0 ℃ for 1 h. The reaction was quenched by adding an aqueous solution of Na_2HPO_4 (0.6 g in 10 mL of H_2O). The carboxylic acid was extracted with ether and the organic layer was separated. The ether layer was washed with water and then 2 % aqueous sodium hydroxide solution was added and the water layer was separated. The water layer was acidified carefully with 4 % hydrochloric acid in an ice bath. Ether was added to the solution and the carboxylic acid was extracted with ether. The organic layer was separated, washed with brine, then dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure to give the carboxylic acid (**7**) (1.86 g, 88 %) as yellow viscus oil. IR (neat) 3062, 2957, 1722, 1402, 1251, 847 cm^{-1}; ^1H NMR δ -0.09 (9H, s), 4.30 (1H, s), 7.33-7.67 (5H, m). MS *m/z* (%) 236 (M^+, 20), 221 (13), 179 (9), 147 (21), 118 (100), 105 (21), 90 (30),73 (58)). Calcd for $C_{12}H_{16}O_3Si$: M, 236.0867. Found: *m/z* 236.0883.

***N*-[(2*S**,3*S**)-2,3-Epoxy-3-phenyl-2-trimethylsilylpropanoyl]piperidine (3a).** To a solution of **7** (236 mg, 1 mmol) in ethyl acetate (2 mL) was added pentafluorophenol (239 mg, 1.3 mmol) followed by dicyclohexylcarbodiimide (268 mg; 1.3 mmol) at 0 ℃ with stirring. The reaction mixture was cooled and stirred for 2 h. The precipitated *N*,*N*'-dicyclohexylurea was filtered off and piperidine (255 mg, 3 mmol) was added to the filtrate at 0 ˚C, then the reaction mixture was stirred and allowed to warm to rt for 1 h. The reaction mixture was diluted with ethyl acetate and the solution was washed successively with 2 % aqueous sodium hydroxide and sat. aq. NH_4Cl, then dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by column chromatography (50 % ethyl acetate in hexane) to give **3a** (177 mg, 58 %) as a light yellow low melting solid. IR (neat) 2945, 1648, 1436, 1256, 848 cm^{-1}; ^1H NMR δ -0.12 (9H, s), 1.49-1.75 (6H, m), 3.35-3.85 (4H, m), 4.24 (1H, s), 7.29-7.39 (5H, m). MS *m/z* (%) 303 (M^+, 44), 288 (100), 184 (6), 174 (15), 112 (12), 73 (61). Calcd for $C_{17}H_{25}NO_2Si$: M, 303.1653. Found: *m/z* 303.1670.

Ethyl (2*S,3*S**)-2,3-epoxy-3-phenyl-2-trimethylsilylpropanoate (3b).** A solution of the carboxylic acid (**7**) (1.0 g, 4.2 mmol) and DBU (3.15 mL, 21.0 mmol) in benzene (30 mL) was stirred at rt and iodoethane (1.68 mL, 21.0 mmol) was added. The reaction mixture was stirred for 2 h and poured into water and the layers were separated. The aqueous layer was extracted with ether. The combined organic extracts were washed with sat. aq. NH_4Cl, then dried over anhydrous $MgSO_4$. The solvent was

removed under reduced pressure and the residue was purified by column chromatography (5 % ethyl acetate in hexane) to give ester (**3b**) (732 mg, 65 %) as a colorless oil. IR (neat) 2979, 1744, 1714, 1250, 1224, 846 cm^{-1}; ^1H NMR δ -0.10 (9H, s), 1.34 (3H, t, *J*=7.2 Hz), 4.21 (1H, s), 4.27 (2H, m), 7.27-7.38 (5H, m); ^{13}C NMR δ –2.0, 14.2, 57.4, 61.2, 61.9, 126.7, 128.0, 128.1, 135.2, 172.4. MS *m/z* (%) 264 (M^+, 4), 221 (6), 179 (62), 135 (37), 103 (30), 73 (100). Calcd for $C_{14}H_{20}O_3Si$: M, 264.1182. Found: *m/z* 264.1201.

***N*-[(2*R**,3*S**)-2,3-Epoxy-3-phenylpropanoyl]piperidine (8) and *N*-[(2*S**,3*S**)-2,3-Epoxy-3-phenylpropanoyl]piperidine (9).** To a solution of amide (**3a**) (100 mg, 0.32 mmol) in THF (1.0 mL) and water (0.029 mL, 1.60 mmol) at -40 ℃ was added a solution of TBAF (1.0M solution in THF; 0.32 mL, 0.32 mmol). The reaction mixture was stirred at the temperature for 10 min. The reaction mixture was poured into water and the whole was extracted with ethyl acetate. The organic layer was washed with aq. NH_4Cl and dride over $MgSO_4$. The products were separated by silica gel column chromatography (50 % ethyl acetate in hexane) to give **8** (51.7 mg, 68 %) as colorless crystals and the isomer (**9**) (18.8 mg, 25 %) as colorless crystals. **8:** mp 77-77.5 ˚C (AcOEt-hexane); IR (KBr) 2947, 1651, 1444, 1256, 911, 758 cm^{-1}; ^1H NMR δ 1.58-1.76 (6H, m), 3.46-3.69 (4H, m), 3.64 (1H, d, *J*=2.0 Hz), 4.07 (1H, d, *J*=2.0 Hz), 7.31-7.41 (5H, m). MS *m/z* (%) 231 (M^+, 40), 214 (21), 174 (10), 125 (23), 112 (42), 96 (100), 84 (39), 69 (53). Calcd for $C_{14}H_{17}NO_2$: M, 231.1259. Found: *m/z* 231.1263. Anal. Calcd for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41; N, 6.06. Found: C, 72.48; H, 7.29; N, 5.85. Isomer (**9**)**:** mp 85-86 ˚C (AcOEt-hexane); IR (KBr) 2933, 1635, 1448, 1228, 914, 699 cm^{-1}; ^1H NMR δ 0.73-0.87 (1H, m), 1.08-1.17 (1H, m), 1.39-1.50 (4H, m), 3.08-3.16 (1H, m), 3.31-3.34 (2H, m), 3.58-3.66 (1H, m), 3.88 (1H, d, *J*=4.4 Hz), 4.25 (1H, d, *J*=4.4 Hz), 7.30-7.37 (5H, m). MS *m/z* (%) 231 (M^+, 53), 174 (6), 125 (24), 112 (26), 96 (100), 69 (33). Calcd for $C_{14}H_{17}NO_2$: M, 231.1258. Found: *m/z* 231.1258. Anal. Calcd for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41; N, 6.06. Found: C, 72.57; H, 7.35; N, 5.86.

(2*R,3*S**)-Ethyl 2,3-epoxy-3-phenylpropanoate (12) and (2*S**,3*S**)-Ethyl 2,3-epoxy-3-phenylpropanoate (13).** The ester (**3a**) (100 mg, 0.38 mmol) was treated with TBAF (0.38 mL, 0.38 mmol) in THF (1 mL) containing water (0.034 mL, 1.90 mmol) at -40 ˚C. The mixture was stirred for 10 min and poured into water and the whole was extracted with ether. The combined organic extracts were washed with saturated aqueous NH_4Cl, then dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by column chromatography (10 % ethyl acetate in hexane) to give a mixture of **12** and the isomer (**13**) (59.4 mg, 82 %) (**12**= 49 %, **13**= 33 %; calculated from ^1H NMR) as a colorless oil. IR (neat) 2983, 1750, 1203, 1026, 697 cm^{-1}; ^1H NMR δ 1.01 (1.2H, t, *J*=7.2 Hz), 1.33 (1.8H, t, *J*=7.2 Hz), 3.50 (0.6H, d, *J*=1.9 Hz), 3.82 (0.4H, d, *J*=4.6 Hz), 4.00 (0.8H, m), 4.09 (0.6H, d, *J*=1.9 Hz), 4.25 (0.4H, d, *J*=4.3 Hz), 4.28 (1.2H, m), 7.28-7.42 (5H, m). MS *m/z* (%) 192 (M^+, 5), 135 (100), 118 (23), 107 (65), 91 (67), 79 (62). Calcd for $C_{11}H_{12}O_3$: M, 192.0785. Found: *m/z* 192.0789.

***N*-[(2*R**,3*S**)-2-Deuterio-2,3-epoxy-3-phenylpropanoyl]piperidine (10) and *N*-[(2*S**,3*S**)-2-Deuterio-2,3-epoxy-3-phenylpropanoyl]piperidine (11).** Molecular sieve 4A (150 mg / 1 mL of THF) was flame-dried under argon atmosphere in a round-bottom flask. After cooling to rt, to the flask were added dry THF (1 mL), the amide (**3a**) (100 mg; 0.32 mmol) and CD_3OD (0.034 mL; 1.6 mmol). The mixture was cooled to -40 ˚C, then TBAF (0.32 mL, 0.32 mmol) was added. The mixture was stirred for 10 min. The reaction was quenched by adding sat. aq. NH_4Cl and the whole was extracted with ethyl acetate. The combined organic extracts were washed with sat. aq. NH_4Cl, then dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by column chromatography (50 % ethyl acetate / hexane) to give **10** (58.2 mg, 76 %) as a colorless, low-melting solid and isomer (**11**) (17.5 mg, 23 %) as a colorless low-melting solid. **10:** IR (KBr) 2942, 1648, 1441, 1252, 740, 692 cm^{-1}; ^1H NMR δ 1.57-1.73 (6H, m), 3.45-3.67 (4H, m), 4.07 (1H, s), 7.31-7.40 (5H, m); D-content = 85 %. MS *m/z* (%) 232 (M^+, 31), 215 (15), 174 (8), 127 (8), 126 (20), 112 (34), 96 (100), 84 (33), 69 (49). Calcd for $C_{14}H_{16}DNO_2$. M, 232.1321. Found: *m/z* 232.1314. **11:** IR (KBr) 2933, 1634, 1448, 1227, 699 cm^{-1}; ^1H NMR δ 0.79-0.85 (1H, m), 1.10-1.16 (1H, m), 1.38-1.48 (4H, m), 3.09-3.16 (1H, m), 3.29-3.34 (2H, m), 3.58-3.64 (1H, m), 4.24 (1H, s), 7.29-7.37 (5H, m), D-content = 85 %. MS *m/z* (%) 232 (M^+, 42), 174 (9), 126 (20), 112 (23), 96 (100), 69 (32). Calcd for $C_{14}H_{16}DNO_2$: M, 232.1321. Found: *m/z* 232.1329.

***N*-[(2*R**,3*S**)-2,3-Epoxy-2-((*R**)-hydroxybenzyl)-3-phenylpropanoyl]piperidine (14-L) and *N*-[(2*R**,3*S**)-2,3-Epoxy-2-((*S**)-hydroxybenzyl)-3-phenylpropanoyl]piperidine (14-P).** Molecular sieve 4A (150 mg) was flame-dried under argon atmosphere in a round-bottom flask. After cooling to rt, to the flask were added dry THF (1 mL), the amide (**3a**) (200 mg, 0.64 mmol) and benzaldehyde (0.13 mL, 1.28 mmol). The mixture was cooled to -40 ˚C, then TBAF (0.64 mL, 0.64 mmol) was added. The reaction mixture was stirred for 30 min and a solution of 2% KOH in MeOH was added and the mixture was stirred for 10 min. The reaction was quenched by adding sat. aq. NH_4Cl and the whole was extracted with ethyl acetate. The combined organic extracts were washed with sat. aq. NH_4Cl, then dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by column chromatography (50 % ethyl acetate in hexane) to give **14-L** (76.9 mg, 35 %) as colorless crystals and **14-P** (75.1 mg, 34 %) as colorless crystals. **14-L:** mp 137-138 ˚C (AcOEt-hexane); IR (KBr) 3262 (OH), 2934, 1615, 1441, 1270, 704 cm^{-1}; ^1H NMR δ 0.53 (1H, m), 1.18 (1H, m), 1.36-1.45 (4H, m), 3.04-3.27 (3H, m), 3.54-3.57 (1H, m), 4.27 (1H, d, *J*=7.3 Hz), 4.28 (1H, s), 4.95 (1H, s, OH), 7.27-7.54 (10H, m). MS *m/z* (%) 337 (M^+, 17), 319 (44), 231 (29), 214 (33), 174 (32), 118 (57), 112 (100), 84 (99). Calcd for $C_{21}H_{23}NO_3$: M, 337.1677. Found: *m/z* 337.1679. Anal. Calcd for $C_{21}H_{23}NO_3$: C, 74.75; H, 6.87; N, 4.15. Found: C, 74.45; H, 6.56; N, 4.06. **14-P:** mp 158-159 ˚C (AcOEt-hexane); IR (KBr) 3361 (OH), 2936, 1614, 1451, 1256, 758, 699 cm^{-1}; ^1H NMR δ 0.88-0.90 (1H, m), 1.24-1.54 (5H, m), 2.70 (1H, m), 3.22-3.34 (2H, m), 3.54-3.60 (1H, m), 3.87 (1H, s, OH), 4.40 (1H s), 4.62 (1H, d *J*=5.6 Hz), 6.81-6.83 (2H, m), 7.16-7.23 (3H, m), 7.41-7.50 (5H, m). MS *m/z* (%) 337 (M^+, 20), 319 (7), 304 (8) 231 (40), 214 (13), 174 (12), 118 (30), 112 (100),91 (38), 77 (49), 69

(53). Calcd for $C_{21}H_{23}NO_3$: M, 337.1676. Found: *m/z* 337.1662. Anal. Calcd for $C_{21}H_{23}NO_3$: C, 74.75; H, 6.87; N 4.15. Found: C, 74.59; H, 6.65; N 4.09.

***N*-[(2*R**, 3*S**)-2,3-Epoxy-2-(1-hydroxy-3-phenylpropyl)-3-phenylpropanoyl]piperidine (17-L and 17-P).** In a similar procedure as described above, the reaction of **3a** with 3-phenylpropanal gave a mixture of the adduct (**17-L**) and (**17-P**) (61.3 mg; 51%) as colorless crystals. Only **17-L** could be separated in pure form. **17-L:** mp 162-164 ˚C (AcOEt-hexane); IR (KBr) 3386 (OH), 2937, 1624, 1449, 1254, 700 cm^{-1}; ^1H NMR δ 1.59-1.93 (8H, m), 2.37-2.52 (2H, m), 3.27-3.31 (1H, m), 3.54-3.77 (4H, m), 4.23 (1H, s), 6.79-6.81 (2H, m), 7.06-7.12 (3H, m), 7.28-7.32 (5H, m). MS *m/z* (%) 365 (M^+, 52), 348 (5), 261 (11), 260 (40), 232 (27), 203 (22), 187 (47), 174 (38), 112 (82), 91 (100), 84 (47), 69 (38). Calcd for $C_{23}H_{27}NO_3$: M, 365.1990. Found: *m/z* 365.1998. Anal. Calcd for $C_{23}H_{27}NO_3$: C, 75.59; H, 7.45; N, 3.83. Found: C, 75.44; H, 7.26; N, 3.79.

***N*-[(2*R**,3*S**)-2,3-Epoxy-2-(1-hydroxy-3-phenyl-2-propenyl)-3-phenylpropanoyl]-piperidine (18-L and 18-P).** In a similar procedure as described above, the reaction of **3a** with cinnamaldehyde gave a mixture of the adduct **18-L** and **18-P** (45.6 mg; 39%) as colorless crystals. Only **18-L** could be separated in pure form. **18-L:** mp 133.5-135.0 ˚C (AcOEt-hexane); IR (KBr) 3306 (OH), 2941, 1613, 1447, 1248, 952, 700 cm^{-1}; ^1H NMR δ 1.58-1.70 (6H, m), 2.33 (1H, m), 3.49-3.54 (1H, m), 3.64-3.73 (3H, m), 4.01-4.04 (1H, m), 4.29 (1H, s), 5.75 (1H, d, *J*=15.8 Hz), 6.16 (1H, dd, *J*=7.6 Hz, 15.8 Hz), 7.17-7.39 (10H, m). MS *m/z* (%) 363 (M^+, 16), 345 (4), 272 (6), 256 (6), 231 (14), 180 (16), 131 (25), 112 (79), 84 (100), 69 (34). Calcd for $C_{23}H_{25}NO_3$: M, 363.1834. Found: *m/z* 363.1831. Anal. Calcd for $C_{23}H_{25}NO_3$: C, 76.01; H, 6.93; N, 3.85. Found: C, 75.66; H, 6.76; N 3.76.

***N*-[(2*S**,3*S**)-2-Benzoyl-2,3-Epoxy-3-phenylpropanoyl]piperidine (16).** A solution of CrO_3 in pyridine was prepared by dissolving CrO_3 (45.0 mg, 0.45 mmol) in pyridine (0.45 mL). To the CrO_3-pyridine solution was added a solution of **14-L** (50.0 mg, 0.15 mmol) in pyridine (1 mL). The reaction mixture was stirred for 2 h at rt. To the reaction was added water and the whole was extracted with ethyl acetate and the organic layer was washed with water, then dried over anhydrous $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by column chromatography (33 % ethyl acetate in hexane) to give the ketone (**16**) (40 mg, 80%) as colorless crystals. mp 123-125 ℃ (AcOEt-hexane); IR (KBr) 2941, 1675, 1653, 1442, 1256, 1243, 946, 738, 697 cm^{-1}; ^1H NMR δ 1.43-1.69 (6H, m), 3.41-3.47 (1H, m), 3.53-3.65 (2H, m), 3.76-3.81 (1H, m), 4.73 (1H, s), 7.16-7.51 (8H, m), 8.05-8.08 (2H, m). MS *m/z* (%) 335 (M^+, 34), 230 (30), 174 (8), 105 (100), 77 (44). Calcd for $C_{21}H_{21}NO_3$: M, 335.1521. Found: *m/z* 335.1517. Anal. Calcd for $C_{21}H_{21}NO_3$: C, 75.20; H, 6.31; N, 4.18. Found: C, 74.85; H, 6.42; N, 3.90.

X-Ray Crystallography. A quality single crystal of **14-L** was mounted on a glass fiber. Diffraction data were collected on a Bruker Smart APEX CCD X-ray diffractometer with graphite-monochromated Mo

Kα radiation (λ= 0.71073 ① ⑭ Crystallographic data are summarized below. The data were corrected for Lorentz and polarization effects, and for absorption using the SADABS program.[10] The structure was solved by the direct method.[11] All non-hydrogen atoms were refined anisotropically on F^2 by full-matrix least-squares using the SHELXL-97 program.[12] The KenX program[13] was used to visualize the molecules and to locate new atoms during the refinement procedures. Hydrogen atoms were refined isotropically. The teXsan program[14] was also used to generate ORTEP diagrams. **Crystallographic date for 14-L**: $C_{21}H_{23}NO_3$, *M*=337.40, *monoclinic*, space group $P2_1/c$ (#14), a=21.7616(10), b=11.8178(5), c=13.8845(6) A, b=93.826(1)°, *V*=3562.8(3) A^3, Z=8, F(000)=1440, D_{calc}=1.258 gcm^{-3}, μ(Mo Kα)=0.084 mm^{-1}, T=293(2) K, *R*1=0.0304 for $I>2.0\sigma(I)$, W*R*2=0.0920 for all data (5132), GOF=1.004 (635 Parameters), crystal dimensions 0.37x0.21x0.20 mm^3. Data deposited at the Cambridge Crystallographic Data Centre; deposition number CCDC 182943.

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