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Graphical Abstract

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3,3-Dimethoxypropylsulfonyl Group: A New Versatile Protecting and Activating Group for Amine Synthesis

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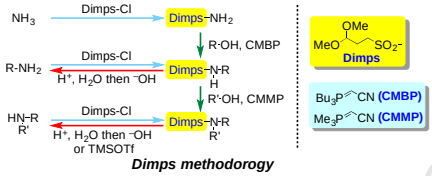
Faculty of Pharmaceutical Sciences, Tokushima Bunri University



Dimps methodorogy

Tetrahedron
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ABSTRACT

3,3-Dimethoxypropylsulfonyl (Dimps) chloride was prepared and used as a new versatile sulfonating agent for ammonia, primary and secondary amines to afford corresponding Dimps-amides in excellent yields. The resulting *N*-nonsubstituted and *N*-monosubstituted Dimps-amides, activated amines, were alkylated satisfactorily under new Mitsunobu conditions. The Dimps group was removed by treatment in aqueous solution under acidic followed by basic conditions. Furthermore, epilachnene, the defensive droplets from the Mexican bean beetle, *Epilachna varivestis*, was synthesized utilizing this Dimps methodology in short steps.

1. Introduction

In the synthesis of nitrogen-containing molecules with a wide variety of interesting biological activities, protection and/or activation of the nitrogen atom followed by deprotection procedures are common processes in the construction of nitrogen functional groups. Thus, many protecting and/or activating groups have been developed and applied to various stages of organic syntheses.[1] Among them, the Fukuyama method utilizing the *o*-nitrobenzenesulfonyl (Ns) group has been widely accepted and applied to amine synthesis because of its sufficient stability toward various reagents and mild and easy conditions to remove the group.[2] Further, the *o*-anisylsulfonyl (Ans) group was developed as an alternative activating/protecting group of the nitrogen functionality.[3]

In the course of our studies on the Mitsunobu chemistry utilizing (cyanomethylene)tributylphosphorane (CMBP) and/or (cyanomethylene)trimethylphosphorane (CMMP),[4,5] we proposed the 2-(1,3-dioxan-2-yl)ethylsulfonyl (Dios) group (**1**) (Figure 1) as a new versatile sulfonyl group for amino activation/protection and employed it for the preparation of a wide variety of primary and secondary amines.[5] To expand this chemistry, we recently designed 3,3-dimethoxypropylsulfonyl (Dimps) group (**3**), which could be removed more easily than the Dios group (**1**). Even so, the reactivity of Dimps-amides (**4**) activated amines under the Mitsunobu reaction conditions was expected to be similar to that of Dios-amides (**2**), because the pK_a values of both are estimated to be the same as that of aliphatic sulfonamides (e.g., MsNHMe: pK_a = 11.8).[6]

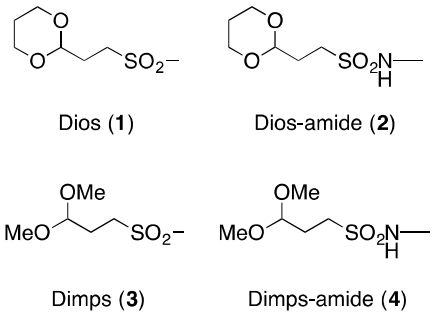

Fig. 1. Dios and Dimps Groups.

2. Results and Discussion

Dimps chloride (**7**), a sulfonyl agent, was prepared by the following reaction sequence: 1) commercially available 3,3-dimethoxypropylchloride (**5**) was converted to the corresponding sodium 3,3-dimethoxypropylsulfonate (**6**) using Na_2SO_3 (DME-H_2O, 110 °C, 72 h in an Ace pressure tube with vigorous stirring), and then 2) the sulfonate **6** was treated with 2.0 equiv of PPh_3 and 2.2 equiv of sulfuryl chloride (CH_2Cl_2, −10 °C, 2 h). The agent **7** could be purified by rapid chromatography (*n*-hex. / ether = 1 / 1) on silica gel and stored at −15 °C for at least one month (Scheme 1).

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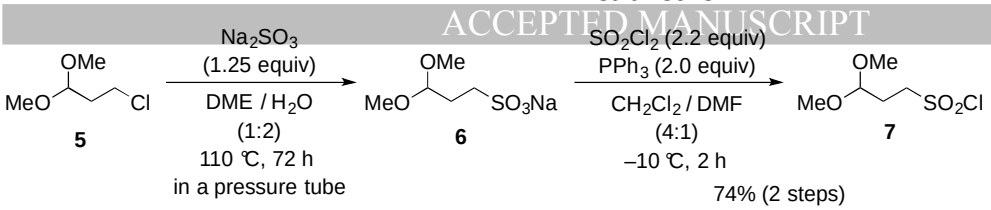
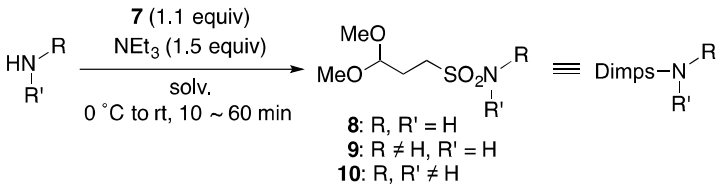
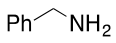
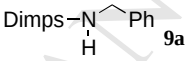
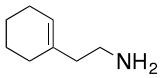
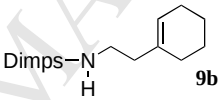
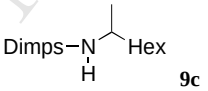
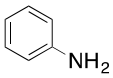
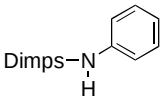
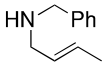
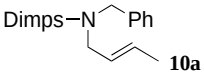


Scheme 1. Preparation of **7**.

The reaction of **7** with ammonia afforded water-soluble *N*-nonsubstituted Dimps-amide (**8**) in 95% yield (NH_3 aqueous, CH_3CN, 0 °C to room temperature, 10 min). Primary and secondary amines were also sulfonated in excellent yields (1.1 equiv of **7**, 1.5 equiv of NEt_3, CH_2Cl_2, 0 °C to room temperature, 10~30 min), as listed in Table 1.

Table 1. Reaction of Amines with **7**.

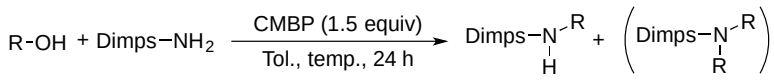


entry	amine	Solvent	Dimps-amide	Yield (%)
1	NH_3 aq.[a]	CH_3CN	Dimps−NH_2 **8**	95
2		CH_2Cl_2	 **9a**	99
3		CH_2Cl_2	 **9b**	99
4		CH_2Cl_2	 **9c**	96
5		CH_2Cl_2	 **9d**	84
6		CH_2Cl_2	 **10a**	84

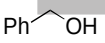
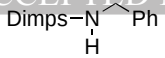
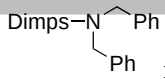
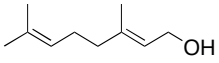
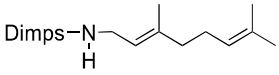
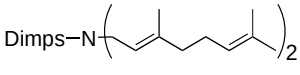
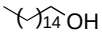
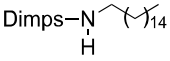
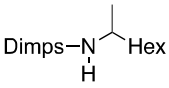
[a] Reaction was carried out without NEt_3.

The feature of the reaction of **8** in the presence of CMBP was quite similar to that of the Dios-amide reported previously.[5] Thus, the Mitsunobu alkylation of **8** proceeded in satisfactory yields to give **9** even with secondary alcohols (Table 2), even though benzylic and allylic alcohols gave overreacted product **10** (double alkylation products) to some extent because of their high reactivity.

Table 2. Mitsunobu Alkylation of **8**.



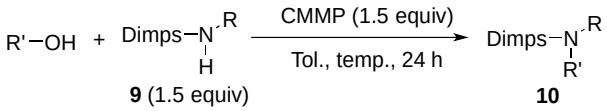
R-OH	Temp. (°C)	Yield (%)	
		9	**10**

	rt	 **9a**: 67	 **10b**: 25
	rt	 **9e**: 78	 **10c**: 12
	rt	 **9f**: 89	—[a]
	100	 **9c**: 79	—[a]

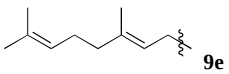
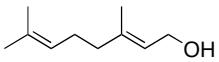
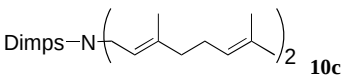
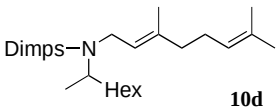
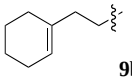
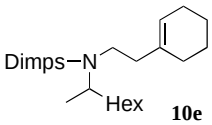
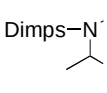
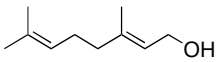
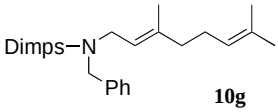
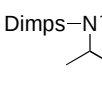
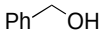
[a] Double alkylated product was not obtained.

As shown in Table 3, *N*-monosubstituted Dimps-amides (**9**) could also be subjected to the Mitsunobu alkylation utilizing CMMP[7] which possessed sufficient reactivity to afford *N*,*N*-disubstituted Dimps-amides (**10**) in excellent yields.

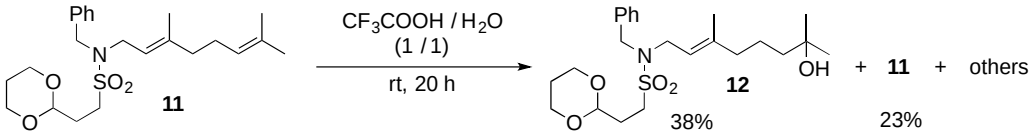
Table 3. Mitsunobu Alkylation of **9**.



9 (1.5 equiv) **10**

9: R-	R'-OH	Temp. (°C)	**10**	Yield (%)
 **9e**		rt	 **10c**	95
9e		80	 **10d**	90
 **9b**		80	 **10e**	86
 **9d**		80	 **10f**	92
 **9a**		80	 **10g**	93
9a		80	 **10h**	89
 **9c**		80	**10h**	93

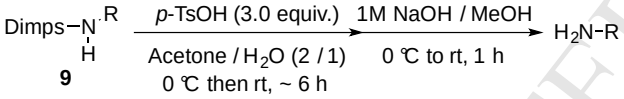
We reported previously that the Dios group (**1**) was cleaved by the treatment in hot 80% aqueous trifluoroacetic acid to afford primary and secondary amines in high yields.[5] However, the deprotection of substances with trisubstituted olefins such as the geranyl group failed to give desired amines even at room temperature and with less amounts of trifluoroacetic acid (50%) (e.g., Scheme 2).



Scheme 2. Reaction of *N*-geranyl Dios-amide (**11**) under acidic conditions.

We expected that the Dimps group (**3**) could be removed more easily than **1**. Eventually, the deprotection of **3** was accomplished with a two-step operation in one pot as follows: 1) acid-catalyzed hydrolysis of the acetal moiety to the aldehyde in an aqueous acetone or acetonitrile solution of *p*-tolenesulfonic acid (*p*-TsOH) at room temperature, and then 2) basification with the addition of 1M NaOH or solid K_2CO_3 with a small amount of water for a retro-Michael reaction,[8] giving the corresponding primary and secondary amines in high yields (Tables 4 and 5).[9] *N*-Monosubstituted Dimps-amides **9** could be cleaved more easily than *N,N*-disubstituted Dimps-amides **10**. Under these conditions, the geranyl group could survive satisfactorily. Furthermore, we confirmed that Dios-amide was sufficiently stable under these aqueous acidic conditions to recover itself (only 2% hydrolysis after 14 h). Otherwise, the Dimps group could also be cleaved by treatment with TMSOTf in good yield (Scheme 3).

Table 4. Deprotection of *N*-Monosubstituted Dimps-amide (**9**).



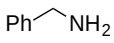
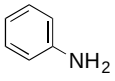
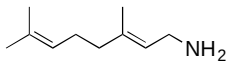
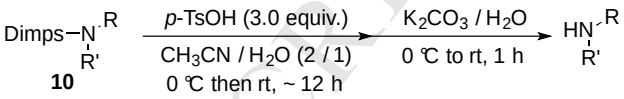
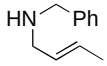
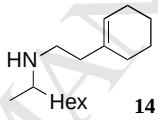
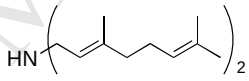
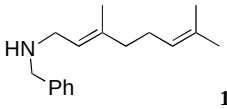
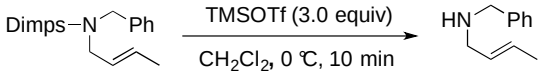
Yield of Amine (%)	
	98
	85
	88
	92

Table 5. Deprotection of *N,N*-Disubstituted Dimps-amide (**10**).

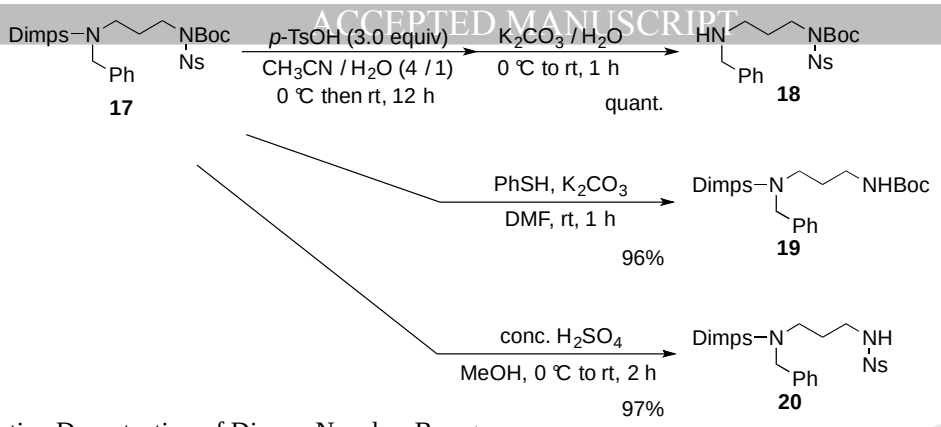


Yield of Amine (%)	
 **13**	99
 **14**	98
 **15**	95
 **16**	94



Scheme 3. Cleavage of Dimps group using TMSOTf.

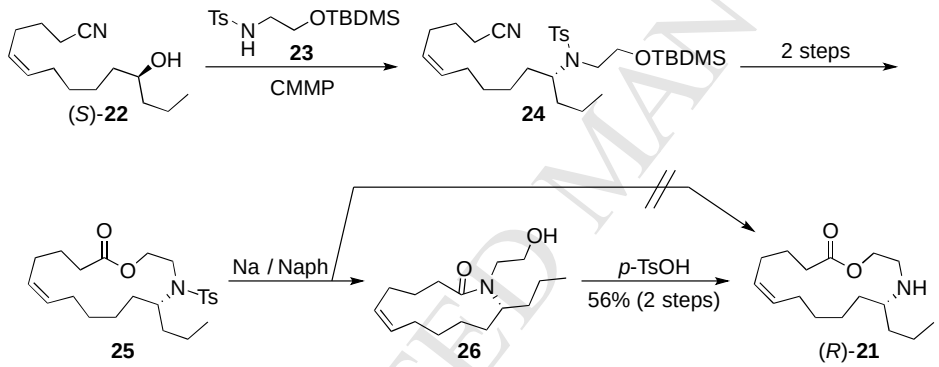
We prepared compound **17**[10] bearing the Dimps group with *tert*-butoxycarbonyl (Boc) and Ns groups on nitrogen atoms and examined the selective deprotection of each group as follows: 1) acid-catalyzed hydrolysis followed by basification cleaved the Dimps group to afford **18**, 2) treatment with thiophenol-K_2CO_3 cleaved the Ns group to give **19**, and 3) treatment with conc. H_2SO_4 in MeOH removed the Boc group quite significantly to yield **20**. Thus, the Dimps group can be utilized not only as an activating group but also as a new amine-protecting group. In conclusion, the order of the stability of Boc, Dios and Dimps group under aqueous acidic conditions[11] is Dios > Boc > Dimps.



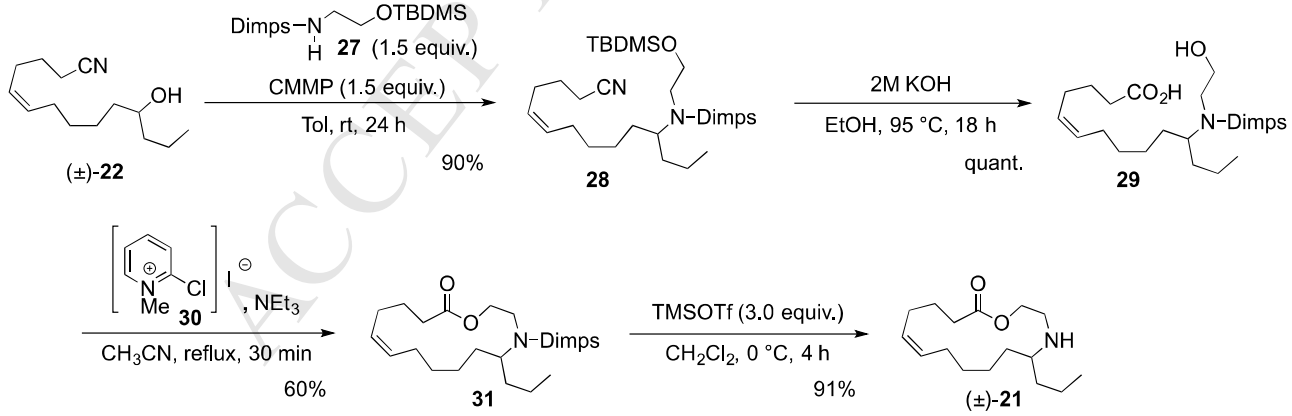
Scheme 4. Selective Deprotection of Dimps, Nosyl or Boc groups

To demonstrate the usefulness of the Dimps methodology, we synthesized epilachnene (**21**)[12] again. In the previous synthesis,[13] tosylamide **23** was employed as a nitrogen nucleophile under Mitsunobu conditions (CMMP) followed by lactonization to afford **25**, whose tosyl group was removed smoothly by reductive conditions using sodium naphthalenide at –40 °C in DME. However, the product of the reaction was undesired lactam **26** generated by intramolecular acyl migration. So, trans-lactonization of **26** was carried out by treatment with *p*-toluenesulfonic acid (Scheme 5).

This time, Dimps-amide **27**[10] was utilized to overcome this problem (Scheme 6). Alcohol **22**[14] was subjected to the Mitsunobu reaction with **27** in the presence of CMMP to yield Dimps-amide **28**, which was treated with base in hot aqueous ethanol to provide seco-acid **29**. The lactonization of **29** was successfully achieved by the reaction of 2-chloro-1-methylpyridinium iodide (**30**)[15] under highly dilute conditions to afford **31**. Finally, the Dimps group was cleaved easily by treatment with TMSOTf.



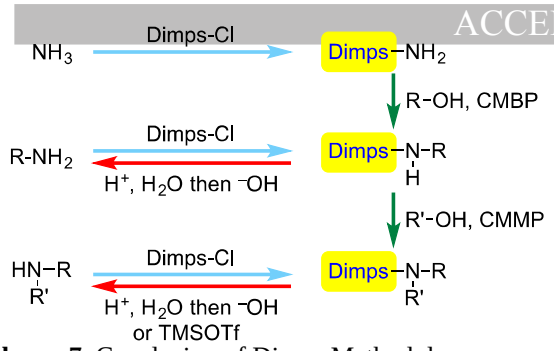
Scheme 5. Previous Synthesis of (*R*)-Epilachnene (**21**).



Scheme 6. Synthesis of (±)-**21**.

3. Conclusion

To conclude, the complete reaction sequence is illustrated in Scheme 7. The Dimps group was introduced onto an amino group, and the resulting Dimps-amide was alkylated under the new Mitsunobu conditions. Finally, the Dimps group was cleaved/deprotected under acidic followed by basic conditions. Thus, because the Dimps group can be used as a versatile activating/protecting group for amines, the reactions presented herein would be widely employed as useful methodologies in the synthesis of nitrogen-containing molecules.



Scheme 7. Conclusion of Dimps Methodology.

4. Experimental

4.1. General

Melting points (m.p.) were determined with a Yanaco MP3 apparatus. Infrared (IR) spectra were recorded using the ATR (attenuated total reflectance) technique with a JASCO Model FTIR-410 spectrophotometer. Proton nuclear magnetic resonance spectra (^{1}H NMR) were recorded with a Mercury 300 (300 MHz) spectrometers in $CDCl_3$. Chemical shifts are reported in parts per million on the δ scale relative to internal Me_4Si (δ = 0.00 ppm), and coupling constants are given in Hertz. ^{13}C NMR spectra were obtained with a Mercury 300 (75 MHz) instrument, and chemical shifts are referenced to the residual solvent signal ($CDCl_3$: δ = 77.0 ppm). Mass spectra, including high-resolution mass spectra, were recorded with a JEOL AX-500 spectrometer. Analytical thin layer chromatography (TLC) was performed on precoated silica gel 60 F-254 plates (0.2 mm layers) on glass with a fluorescent indicator, supplied by E. Merck. For column chromatography, Fuji Silysia BW-127ZH (100–270 mesh) silica was used. Reagents and solvents were commercial grades and were used without further purification unless otherwise stated. Air- and/or moisture-sensitive reactions were carried out under argon.

4.2. Dimps chloride (7)

A mixture of 3,3-dimethoxypropylchloride (**5**) (5.00 g, 36.1 mmol) and sodium sulfite (5.70 g, 45.1 mmol) in DME (15 mL) and water (30 mL) was heated at 110 °C in an Ace pressure tube with vigorous stirring for 3 days. The resulting mixture was concentrated *in vacuo*, and then the residue was dried over P_2O_5 under reduced pressure (5 mmHg) for 48 h to afford 10.4 g of crude sodium 3,3-dimethoxypropylsulfonate (**6**) containing inorganic salts. ^{1}H NMR (D_2O, acetone as an internal standard (2.22 ppm)) δ 4.65 (1H, t, J = 5.6 Hz), 3.40 (6H, s), 2.94 (2H, t-like m), 2.05 (2H, m).

To a solution of triphenylphosphine (26.4 g, 101 mmol) in CH_2Cl_2 (100 mL) under an argon atmosphere was added slowly sulfuryl chloride (9.0 mL, 111 mmol) at 0 °C. After stirring for 10 min, DMF (25 mL) was added and the resulting mixture was cooled to −10 °C. To this mixture was added the crude product **6** (above) rapidly. After vigorous stirring for 2 h, the reaction mixture was carefully poured into a mixture of water (100 mL) and *n*-hexane (100 mL). The organic layer was separated and the aqueous layer was extracted with *n*-hexane (2 x 100 mL). The combined organic layers were washed with water (5 x 100 mL), dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The residue was dissolved in *n*-hexane (100 mL), and then insoluble material ($O=PPh_3$) was filtered off. The filtrate was concentrated *in vacuo*, and the crude product was subjected to quick purification through a short silica gel column chromatography (eluent: ether/*n*-hexane, 1/1, v/v) to yield Dimps chloride (**7**) as a colorless oil (5.44 g, 74% in 2 steps). **7** was stored at −15 °C for a month without decomposition. ^{1}H NMR ($CDCl_3$) δ 4.53 (1H, t, J = 4.9 Hz), 3.80-3.75 (2H, m), 3.38 (6H, s), 2.35-2.28 (2H, m); ^{13}C NMR ($CDCl_3$) δ 101.8, 60.7, 54.2, 27.9; IR (ATR) 2938, 2837, 1366, 1167, 1119, 1070 cm^{-1}; MS (FAB) *m/z* 201 ([M-H]$^+$); HRMS *m/z* 201.0008 (200.9988 calcd for $C_5H_{10}ClO_4S$).

4.3. Dimps-amide (8)

To a cooled solution of **7** (1.01 g, 4.96 mmol) in acetonitrile (5 mL) was added dropwise aqueous ammonia (15 mL) over a period of 3 min at 0 °C. The resulting mixture was stirred for 10 min at room temperature, and concentrated *in vacuo*. The crude product was purified by silica gel column chromatography (eluent: *n*-hexane/AcOEt, 1/1, v/v) to yield **8** as a colorless solid (861 mg, 95%). m.p. 49.9-51.0 °C (colorless needles, *n*-hexane-AcOEt); ^{1}H NMR ($CDCl_3$) δ 4.89 (2H, br.s), 4.50 (1H, t, J = 5.1 Hz), 3.37 (6H, s), 3.19-3.26 (2H, m), 2.12-2.21 (2H, m); ^{13}C NMR ($CDCl_3$) δ 102.8, 53.9, 50.6, 27.6; IR (KBr) 3343, 3266, 1376, 1365, 1170 cm^{-1}; MS (CI) *m/z* 184 ([M+H]$^+$), 152, 123, 71 (100); HRMS *m/z* 184.0619 (184.0644 calcd for $C_5H_{14}NO_4S$).

4.4. General procedure for sulfonylation of amines

*4.4.1. N-Benzyl-3,3-dimethoxypropylsulfonamide (**9a**): (Reaction of **7** with benzylamine)*

To a cooled solution (0 °C) of benzylamine (220 µL, 2.0 mmol) and Et_3N (420 µL, 3.0 mmol) in CH_2Cl_2 (10 mL) was added **7** (446 mg, 2.2 mmol) slowly with stirring. The mixture was stirred at room temperature for 1 h and then quenched with a sat. NH_4Cl aq. sol. (15 mL). The reaction mixture was extracted with CH_2Cl_2 (3 x 25 mL), and the combined organic extracts were dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The residue was subjected to purification by column chromatography on silica gel (eluent: *n*-hexane/AcOEt, 3/1 - 1/1, v/v) to give 542 mg (99%) of **9a** as colorless solid. m.p. 56.4-57.2 °C (colorless needles, *n*-hexane-AcOEt); ^{1}H NMR ($CDCl_3$) δ 7.27-7.41 (5H, m), 4.81 (1H, br.t, J = 6.0 Hz), 4.40 (1H, t, J = 5.2 Hz), 4.29 (2H, d, J = 6.3 Hz), 3.31 (6H, s), 3.00-3.08 (2H, m), 2.01-2.11 (2H, m); ^{13}C NMR ($CDCl_3$) δ 136.8, 128.9, 128.1, 127.9, 102.7, 53.7, 48.2, 47.3, 27.2; IR (KBr) 3261, 2960, 2940, 1359, 1193 cm^{-1}; MS (CI) *m/z* 272 ([M-H]$^+$), 242, 210, 146, 106, 91, 75 (100); HRMS *m/z* 272.0948 (272.0956 calcd for $C_{12}H_{18}NO_4S$).

4.5. General procedure for Mitsunobu alkylation

*4.5.1. N-(Oct-2-yl)-3,3-dimethoxypropylsulfonamide (**9c**): (Reaction of **8** with octan-2-ol)*

An Ace pressure tube was used as a reaction vessel. To a solution of **8** (279 mg, 1.5 mmol) and octan-2-ol (160 µL, 1.0 mmol) in dry toluene (5 mL) was added CMBP (380 µL, 1.5 mmol) at room temperature under an argon atmosphere. The resulting mixture was sealed and stirred for 24 h at 100 °C. After concentrating *in vacuo*, the residue was purified by silica gel column chromatography (eluent: *n*-hexane/AcOEt, 2/1 - 1/1 - 1/2 - 1/5, v/v) to yield **9c** as a colorless oil (235 mg, 79%). ^{1}H NMR ($CDCl_3$) δ 4.48 (1H, t, J = 5.2 Hz), 4.07 (1H, br.d, J = 8.5 Hz), 3.40-3.51 (1H, m), 3.36 (6H, s), 3.05-3.12 (2H, m), 2.05-2.14 (2H, m), 1.25-1.52 (10H, m), 1.23 (3H, d, J = 6.6 Hz), 0.88 (3H, t, J = 6.9 Hz); ^{13}C NMR ($CDCl_3$) δ 102.8, 53.7, 50.4, 49.2, 38.0, 31.7, 29.0, 27.4, 25.7, 22.6, 22.4, 14.0; IR (neat) 3280, 2931, 1124 cm^{-1}; MS (CI) *m/z* 296 ([M+H]$^+$), 264 (100), 232; HRMS *m/z* 296.1888 (296.18954 calcd for $C_{13}H_{30}NO_4S$).

*4.5.2. N-(Geranyl)-N-(oct-2-yl)-3,3-dimethoxypropylsulfonamide (**10d**): (Reaction of **9e** with octan-2-ol)*

An Ace pressure tube was used as a reaction vessel. To a solution of **9e** (320 mg, 1.5 mmol) and octan-2-ol (160 µL, 1.0 mmol) in dry toluene (5 mL) was added CMMP (170 mg, 1.5 mmol) at room temperature under an argon atmosphere. The resulting mixture was sealed and stirred for 24 h at 80 °C. After concentrating *in vacuo*, the residue was purified by silica gel column chromatography (eluent: *n*-hexane/AcOEt, 5/1 - 1/1, v/v) to yield **10d** as a colorless oil (392 mg, 90%). ^{1}H NMR ($CDCl_3$) δ 5.21 (1H, br.t, J = 6.8 Hz), 5.07 (1H, br.t, J = 6.6 Hz), 4.46 (1H, t, J = 5.4 Hz), 3.74-3.90 (3H, m), 3.34 (6H, s), 2.93-3.01 (2H, m), 1.96-2.14 (6H, m), 1.68 (6H, s), 1.60 (3H, br.s), 1.24-1.33 (10H, m), 1.20 (3H, d, J = 6.9 Hz), 0.8 (3H, br.t, J = 6.3Hz); ^{13}C NMR ($CDCl_3$) δ 138.1, 131.7, 123.9, 122.1, 103.0, 54.0, 53.6, 49.0, 40.7, 39.6, 35.7, 31.7, 29.1, 27.2, 26.8, 26.3, 25.6, 22.6, 20.1, 17.6, 16.1, 14.0; IR (neat) 2930, 1334, 1194 cm^{-1}; MS (CI) *m/z* 431 (M^+), 400, 367, 264, 232, 137 (100); HRMS *m/z* 431.3072 (M^+) (431.30691 calcd for $C_{23}H_{45}NO_4S$).

*4.5.3. N-2-(Cyclohex-1-enyl)ethyl-3,3-dimethoxypropylsulfonamide (**9b**)*

The title compound was isolated as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 5.52 (1H, br.s), 4.48 (1H, t, J = 5.2 Hz), 4.22 (1H, br.t, J = 5.5 Hz), 3.36 (6H, s), 3.18 (2H, dd, J = 12.3, 6.6 Hz), 3.05-3.13 (2H, m), 2.19 (2H, br.t, J = 6.6 Hz), 2.05-2.13 (2H, m), 1.97-2.04 (2H, m), 1.87-1.94 (2H. m), 1.57-1.68 (4H, m); ^{13}C NMR ($CDCl_3$) δ 133.6, 124.8, 102.8, 53.8, 47.7, 40.8, 38.3, 27.8, 27.3, 25.2, 22.7, 22.2; IR (neat) 3287, 2930, 2834 cm^{-1}; MS (FAB) *m/z* 314 ([M+Na]$^+$), 289, 260, 228 (100); HRMS *m/z* 314.1420 (314.14019 calcd for $C_{13}H_{25}NO_4SNa$).

*4.5.4. N-Phenyl-3,3-dimethoxypropylsulfonamide (**9d**)*

The title compound was isolated as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 7.15-7.39 (5H, m), 6.61 (1H, br.s), 4.47 (1H, t, J = 5.2 Hz), 3.31 (6H, s), 3.16-3.22 (2H, m), 2.08-2.16 (2H, m); ^{13}C NMR ($CDCl_3$) δ 136.7, 129.6, 125.3, 120.8, 102.6, 53.7, 47.0, 27.0 IR (neat) 3260, 2939, 1344 cm^{-1}; MS (CI) *m/z* 260 ([M+H]$^+$), 228 (100), 132, 196; HRMS *m/z* 259.0866 (259.08782 calcd for $C_{11}H_{17}NO_4S$).

*4.5.5. N-Geranyl-3,3-dimethoxypropylsulfonamide (**9e**)*

The title compound was isolated as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 5.22(1H, br.t, J = 7.1 Hz), 5.06 (1H, br.t, J = 6.6 Hz), 4.47 (1H, t, J = 5.1 Hz), 4.14 (1H, br.s), 3.72 (2H, t, J = 6.6 Hz), 3.36 (6H, s), 3.06-3.13 (2H, m), 1.98-2.15 (6H, m), 1.68 (6H, br. s), 1.60 (3H, br.s); ^{13}C NMR ($CDCl_3$) δ 141.1, 131.9, 123.6, 119.3, 102.8, 53.7, 48.1, 41.0, 39.4, 27.3, 26.3, 25.6, 17.7, 16.3; IR (neat) 3286, 2930, 1381, 1193 cm^{-1}; MS (CI) *m/z* 320 (M^+), 288, 256, 137 (100); HRMS *m/z* 319.1824 (319.18172 calcd for $C_{15}H_{29}NO_4S$).

*4.5.6. N-Hexadecanyl-3,3-dimethoxypropylsulfonamide (**9f**)*

m.p. 67-69 °C (colorless needles, *n*-hexane-AcOEt); ^{1}H NMR ($CDCl_3$) δ 4.48 (1H, t, J = 5.1 Hz), 4.21(1H, br.t, J = 6.0 Hz), 3.36 (6H, s), 3.05-3.15 (4H, m), 2.06-2.14 (2H, m), 1.48-1.60 (4H, m), 1.18-1.40 (14H, br.s), 0.88 (3H, t, J = 6.6 Hz); ^{13}C NMR ($CDCl_3$) δ 102.8, 53.8, 47.7, 43.4, 32.9, 30.3, 29.7, 29.7, 29.7, 29.6, 29.6, 29.6, 29.5, 29.5, 29.3, 29.1, 27.3, 26.6, 22.7, 14.1; IR (KBr) 3273, 2917, 2849, 1310, 1131 cm^{-1}; MS (CI) *m/z* 408 ([M+H]$^+$), 376 (100), 348, 280, 278, 252, 164, 110; HRMS *m/z* 408.3137 (408.31473 calcd for $C_{21}H_{46}NO_4S$).

*4.5.7. N-(Benzyl)-N-crotyl-3,3-dimethoxypropylsulfonamide (**10a**)*

m.p. 51.0-52.0 °C (colorless needles, *n*-hexane-AcOEt). ^{1}H NMR ($CDCl_3$) δ 7.26-7.39 (5H, m), 5.54-5.67 (1H, m), 5.37-5.50 (1H, m), 4.58 (1H, t, J = 5.2 Hz), 4.38 (2H, s), 3.70 (2H, d, J = 6.9 Hz), 3.35 (6H, s), 2.99-3.07 (2H, m), 2.05-2.15 (2H, m), 1.71 (3H, dd, J = 6.5, 1.2 Hz); ^{13}C NMR ($CDCl_3$) δ 136.3, 131.4, 128.6, 128.4, 127.8, 125.1, 102.9, 53.7, 49.8, 48.5, 48.4, 27.0, 17.6; IR (neat) 2938, 1332, 1193, 1123 cm^{-1}; MS (CI) *m/z* 328 (([M+H]$^+$), 296, 242, 210 (100), 159, 91; HRMS *m/z* 328.1600 (328.15824 calcd for $C_{16}H_{26}NO_4S$).

*4.5.8. N,N-Dibenzyl-3,3-dimethoxypropylsulfonamide (**10b**)*

The title compound was isolated as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 7.27-7.39 (10H, m), 4.41 (1H, s), 4.35 (4H, s), 3.32 (6H, s), 2.94-3.02 (2H, m), 2.04-2.12 (2H, m); ^{13}C NMR ($CDCl_3$) δ 135.6, 128.7, 128.7, 128.0, 102.6, 53.6, 50.0, 48.8, 26.8; IR (neat) 2937, 2832, 1332, 1124 cm^{-1}; MS (CI) *m/z* 362 ([M-H]$^+$), 332, 300, 268, 244, 210 (100), 195, 181, 131, 120, 91, 71, 44; HRMS *m/z* 362.1433 (362.14259 calcd for $C_{19}H_{24}NO_4S$).

*4.5.9. N,N-Digeranyl-3,3-dimethoxypropylsulfonamide (**10c**)*

The title compound was isolated as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 5.19 (2H, br.t, J = 6.6 Hz), 5.04-5.11 (2H, m), 4.47 (1H, t, J = 5.5 Hz), 3.83 (4H, d, J = 6.9 Hz), 3.35 (6H, s), 2.95-3.03 (2H, m), 1.99-2.15 (10H, m), 1.68 (6H, br.s), 1.64 (6H, br.s), 1.61 (6H, br.s); ^{13}C NMR ($CDCl_3$) δ 140.4, 131.8, 123.8, 119.4, 103.0, 53.7, 48.2, 44.0, 39.7, 27.0, 26.4, 25.6, 17.7, 16.1; IR (neat) 2925, 1376, 1337, 144, 1124 cm^{-1}; MS (CI) *m/z* 455 (M^+), 424, 392, 360, 256, 137 (100); HRMS *m/z* 455.3070 (455.30691 calcd for $C_{25}H_{45}NO_4S$).

*4.5.10. N-2-(Cyclohex-1-enyl)ethyl-N-(oct-2-yl)-3,3-dimethoxypropylsulfonamide (**10e**)*

The title compound was isolated as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 5.45 (1H, br.s), 4.47 (1H, t, J = 5.2 Hz), 3.75 (1H, sextet, J = 6.9 Hz), 3.36 (6H, s), 3.15 (2H, dd, J = 7.8, 10.0 Hz), 1.42-1.66 (6H, m), 1.24-1.40 (8H, m), 1.21 (3H, d, J = 6.9 Hz), 0.88 (3H, t, J = 6.6 Hz); ^{13}C NMR ($CDCl_3$) δ 134.9, 123.0, 102.9, 54.1, 53.7, 48.2, 42.3, 40.1, 35.9, 31.7, 29.1, 28.4, 27.1, 26.8, 25.2, 22.8, 22.6, 22.3, 19.8, 14.1; IR (neat) 2929, 1379, 1334 cm^{-1}; MS (CI) *m/z* 403 (M^+), 372, 308, 212, 142, 71 (100); HRMS *m/z* 402.2674 (402.26779 calcd for $C_{21}H_{40}NO_4S$).

*4.5.11. N-(Oct-2-yl)-N-phenyl-3,3-dimethoxypropylsulfonamide (**10f**)*

The title compound was isolated as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 7.36-7.45 (3H, m), 7.25-7.31 (2H, m), 4.45 (1H, t, J = 5.1Hz), 4.27 (1H, sextet, J = 6.9 Hz), 3.34 (2H, m), 2.05-2.17 (2H, m), 1.20-1.55 (10H, m), 1.17 (3H, d, J = 6.9 Hz), 0.88 (3H, br.t, J = 6.3 Hz); ^{13}C NMR ($CDCl_3$) δ 135.3, 132.3, 129.0, 128.6, 102.9, 55.6, 53.7, 48.0, 35.9, 31.7, 29.0, 27.2, 26.7, 22.5, 20.7, 14.0; IR (neat) 2931, 1338, 1153 cm^{-1}; MS (CI) *m/z* 371 (M^+), 340 (100), 286, 252; HRMS *m/z* 371.2120 (371.21301 calcd for $C_{19}H_{33}NO_4S$).

*4.5.12. N-Benzyl-N-geranyl-3,3-dimethoxypropylsulfonamide (**10g**)*

The title compound was isolated as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 7.28-7.40 (5H, m), 5.19 (1H, br.t J = 7.6 Hz), 5.03-5.11 (1H, m), 4.47 (1H, t, J = 5.4 Hz), 4.38 (2H, s), 3.78 (2H, t, J = 7.1 Hz), 3.35 (6H, s), 2.29-3.08 (2H, m), 1.98-2.17 (6H, m), 1.69 (3H, br.d, J = 1.2 Hz), 1.61 (3H, br.s), 1.49 (3H, br.d, J = 1.5 Hz); ^{13}C NMR ($CDCl_3$) δ 141.2, 136.3, 131.9, 128.6, 128.3, 127.7, 123.8, 118.3, 102.8, 53.7, 49.9, 48.3, 43.9, 39.6, 26.9, 26.2, 25.7, 17.7, 16.1; IR (neat) 2929, 1143 cm^{-1}; MS (CI) *m/z* 409 (M^+), 378, 345, 242, 210, 137 (100); HRMS *m/z* 409.2286 (409.22866 calcd for $C_{22}H_{35}NO_4S$).

*4.5.13. N-Benzyl-N-(oct-2-yl)-3,3-dimethoxypropylsulfonamide (**10h**)*

The title compound was isolated as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 7.22-7.46 (5H, m), 4.40 (1H, t, J = 5.1 Hz), 4.38 (1H, d, J = 15.6 Hz), 4.29 (1H, d, J = 15.6 Hz), 3.86 (1H, sextet, J = 6.9 Hz), 3.32 (6H, s), 2.76-2.96 (2H, m), 1.98-2.11 (2H, m), 1.10-1.52 (13H, m), 0.86 (3H, t, J = 6.6 Hz); ^{13}C NMR ($CDCl_3$) δ 138.1, 128.4, 128.3,127.5, 102.7, 54.6, 53.6, 48.5, 46.9, 35.7, 31.6, 28.9, 26.9, 26.7, 22.5, 19.8, 14.0; IR (neat) 2931, 2857, 1334, 1139, 1124 cm^{-1}; MS (CI) *m/z* 384 ([M-H]$^+$), 354 (100), 290, 266, 232, 210, 204, 174, 134, 71; HRMS *m/z* 384.2210 (384.22084 calcd for $C_{20}H_{34}NO_4S$).

4.6. General procedure for Desulfurization

*4.6.1. Desulfurization of N-geranyl-3,3-dimethoxypropylsulfonamide (**9e**)*

To a solution of **9e** (639 mg, 2.00 mmol) in acetone (4 mL) and water (2 mL) was added slowly *p*-toluenesufonic acid monohydrate (1.14 g, 6.00 mmol) at 0 °C. After 5 min, the reaction mixture was allowed to warm to room temperature and stirred for 6 h. After completion of the reaction was checked by TLC, the mixture was cooled again at 0 °C, and then MeOH (10 mL) and a 1M aqueous solution of NaOH (3 mL) were added to the mixture. After stirring for 5 min at 0 °C and 1 h at room temperature, water (15 mL) was added and the mixture was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was subjected to purification by column chromatography (treated by NH_3) on silica gel (eluent: *n*-hexane, AcOEt/Et_3N = 99/1, then MeOH/Et_3N = 99/1, v/v) to afford 282 mg (92 %) of geranylamine as a pale yellow oil, whose spectra data were identified with an authentic sample.

*4.6.2. Desulfurization of N-benzyl-N-geranyl-3,3-dimethoxypropylsulfonamide (**10g**)*

To a solution of **10g** (306 mg, 0.748 mmol) in acetonitrile (5 mL) and water (2.5 mL) was added slowly *p*-toluenesufonic acid monohydrate (450 mg, 2.37 mmol) at 0 °C. After 5 min, the reaction mixture was allowed to warm to room temperature and stirred for 10 h. After completion of the reaction was checked by TLC, the mixture was cooled again at 0 °C, and then water (2 mL) and K_2CO_3 (550 mg, 3.98 mmol) were added slowly to the mixture. After stirring for 10 min at 0 °C and 1 h at room temperature, water (20 mL) was added and the mixture was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic extracts were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The residue was subjected to purification by column chromatography on silica gel (eluent: *n*-hexane/AcOEt, 10/1 - 4/1 - 1/1, v/v then AcOEt only) to afford 172 mg (94 %) of **16** as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 7.4-7.2 (5H, m), 5.26 (1H, br.t, J = 6.7 Hz), 5.10 (1H, br.t, J = 6.6 Hz), 3.78 (2H, s), 3.25 (2H, d, J = 6.6 Hz), 2.15-1.95 (4H, m), 1.68 (3H, s), 1.61 (6H, s); ^{13}C NMR ($CDCl_3$) δ 140.5, 137.8, 131.4, 128.3, 128.1, 126.8, 124.1, 122.8, 53.4, 46.6, 39.6, 26.5, 25.6, 17.6, 16.2; IR (ATR) 3275, 3061, 2967 cm^{-1}; MS (EI) *m/z* 243 (M$^+$) 174, 91 (100); HRMS *m/z* 243.1992 (243.1987 calcd for $C_{17}H_{25}N$).

*4.6.3. N-(Oct-2-yl)-2-(cyclohex-1-enyl)ethylamine (**14**)*

The title compound was isolated as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 5.47(1H, br s), 2.71(1H, dt, J = 11.1, 6.9 Hz), 2.60 (2H, dt, J = 11.4, 6.9 Hz), 2.13 (2H, t, J = 6.9 Hz), 1.95-2.04 (2H, m), 1.87-1.95 (2H, m), 1.50-1.67 (4H, m), 1.24-1.34 (10H, m), 1.03 (3H, d, J = 6.3 Hz), 0.88 (3H, t, J = 6.6 Hz); ^{13}C NMR ($CDCl_3$) δ 135.4, 122.8, 53.2, 44.8, 38.4, 37.1, 31.9, 29.5, 28.0, 26.1, 25.2, 22.9, 22.6, 22.5, 20.4, 14.1; IR (neat) 3310, 2956, 2925, 2856 cm^{-1}; MS (CI) *m/z* 238 ([M+H]$^+$, 100), 236, 193, 156, 142, 89; HRMS *m/z* 238.2534 (238.25346 calcd for $C_{16}H_{32}N$).

*4.6.4. Desulfurization of **10a** using TMSOTf*

To a solution of **10a** (327 mg, 1.0 mmol) in dry CH_2Cl_2 (5 mL) was added TMSOTf (550 µL, 3.0 mmol) at 0 °C under an argon atmosphere. After stirring for 10 min, a saturated $NaHCO_3$ aqueous solution (10 mL) was added and extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were dried over K_2CO_3, filtrated and evaporated. The residue was purified by silica gel column chromatography (eluent: *n*-hexane/AcOEt, 1/1, 1/3, v/v) to yield **13** as a pale yellow oil (140 mg, 87%), whose spectra data were identified with an authentic sample.

4.7. Selective Cleavage of Protective Group

*4.7.1. N-Benzyl-N'-Boc-N'-Ns-propane-1,3-diamine (**18**): (Selective cleavage of Dimps group)*

The title compound was isolated as a colorless oil. ^{1}H NMR ($CDCl_3$) δ 8.31-8.27 (1H, m), 7.76-7.70 (3H, m), 7.34-7.21 (5H, m), 3.87 (2H, t, J = 7.0 Hz), 3.81 (2H, s), 2.75 (2H, t, J = 7.0 Hz), 2.29 (1H, br.s), 1.97 (2H, quintet, J = 7.0 Hz), 1.34 (9H, s); ^{13}C NMR ($CDCl_3$) δ 150.4, 147.5, 140.1, 134.1, 133.5, 133.2, 131.7, 128.4, 128.2, 126.9, 124.3, 85.0, 53.8, 46.2, 46.1, 30.3, 27.8; IR (ATR) 3335, 2979, 2934, 2360, 2341, 1729, 1541, 1454, 1361, 1282, 1256, 1149, 1120 cm^{-1}; MS (FAB) *m/z* 450 ([M+H]$^+$); HRMS *m/z* 450.1707 (450.16987 calcd for $C_{21}H_{28}N_3O_6S$).

*4.7.2. N-Benzyl-N-Dimps-N'-Boc-propane-1,3-diamine (**19**): (Selective cleavage of Nosyl group)*

To a mixture of **17** (123 mg, 0.20 mmol) and K_2CO_3 (55 mg, 0.40 mmol) in DMF (2 mL) was added PhSH (26.5 µL, 0.26 mmol) at rt. After stirring for 1 h, a saturated $NaHCO_3$ aqueous solution (10 mL) was added and extracted with ether (3 x 10 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtrated and evaporated. The residue was purified by silica gel column chromatography (eluent: *n*-hexane/AcOEt, 2/1, v/v) to yield **19** as a colorless solid (85.2 mg, 96%). m.p. 58.0-59.0 °C (colorless needles, *n*-hexane-EtOAc); ^{1}H NMR (300MHz, $CDCl_3$) δ 7.37-7.31 (5H, m), 4.80 (1H, s), 4.45 (1H, t, J = 5.3 Hz), 4.38 (2H, s), 3.35 (6H, s), 3.24 (2H, t, J = 6.9 Hz), 3.05 (2H, m), 3.03-2.98 (2H, m), 2.13-2.06 (2H, m) 1.57 (2H, m), 1.42 (9H, s); ^{13}C NMR ($CDCl_3$) δ 156.0, 136.2, 128.8, 128.5, 128.1, 102.7, 79.1, 53.8, 51.7, 47.2, 45.1, 36.9, 28.4, 26.8; IR (ATR) 3427, 2940, 2359, 1712, 1508, 1313, 1239, 1160, 1120, 1068, 1022 cm^{-1}; MS (FAB) *m/z* 453 ([M+Na]$^+$); HRMS *m/z* 453.2062 (453.20351 calcd for $C_{20}H_{34}N_2O_6SNa$).

*4.7.3. N-Benzyl-N-Dimps-N'-Ns-propane-1,3-diamine (**20**): (Selective cleavage of Boc group)*

To a solution of **17** (123 mg, 0.20 mmol) in MeOH (1 mL) was added conc. H_2SO_4 (32 µL, 0.60 mmol) at 0 °C. After stirring for 2 h at room temperature, a saturated $NaHCO_3$ aqueous solution (10 mL) was added and extracted with ether (3 x 10 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtrated and evaporated. The residue was purified by silica gel column chromatography (eluent: *n*-hexane/AcOEt, 2/1, v/v) to yield **20** as a colorless oil (100 mg, 97%). ^{1}H NMR ($CDCl_3$) δ 8.08-8.03 (1H, m), 7.86-7.81 (1H, m), 7.74-7.69 (2H, m), 7.38-7.30 (5H, m), 5.74 (1H, t, J = 6.5 Hz), 4.45 (1H, t, J = 5.1 Hz), 4.35 (2H, s), 3.36 (6H, s), 3.31 (2H, t, J = 6.5 Hz), 3.08-2.99 (4H, m), 2.12-2.05 (2H, m), 1.53 (2H, quintet, J = 6.5 Hz); ^{13}C NMR ($CDCl_3$) δ 148.0, 136.1, 133.9, 133.4, 132.7, 130.7, 128.8, 128.5, 128.3, 125.3, 102.7, 53.9, 52.4, 46.7, 45.2, 40.0, 28.9, 26.8; IR (ATR) 3336, 2939, 1732, 1540, 1442, 1415, 1335, 1239, 1214, 1165, 1142, 1120, 1072 cm^{-1}; MS (FAB) *m/z* 538 ([M+Na]$^+$); HRMS *m/z* 538.1317 (538.12936 calcd for $C_{21}H_{29}N_3O_8S_2Na$).

4.8. Application of Dimps-amide: the Synthesis of (±)-Epilachnene

*4.8.1. Dimps-amide **28***

To a solution of **27** (496 mg, 1.5 mmol) and **22** (222 mg, 1.0 mmol) in dry toluene (6 mL) was added CMMP (182 mg, 1.6 mmol) at room temperature under an argon atmosphere. The resulting mixture was stirred for 24 h at room temperature. After concentrating *in vacuo*, the residue was purified by silica gel column chromatography (eluent: *n*-hexane/AcOEt, 5/1 - 4/1, v/v) to yield **28** as a colorless oil (490 mg, 90%). ^{1}H NMR ($CDCl_3$) δ 5.47(1H, dtt, J = 10.8, 7.2, 1.5 Hz), 5.29(1H, dtt, J = 10.8, 7.2, 1.5 Hz), 4.49 (1H, t, J = 5.4 Hz), 3.66-3.80 (2H, m), 3.54-3.65 (1H, m), 3.35 (6H, s), 3.14-3.22 (2H, m), 2.97-3.05 (2H, m), 2.34 (2H, t, J = 7.2 Hz), 2.20 (2H, qd, J = 7.4, 1.2 Hz), 2.05-2.17 (4H, m), 1.72 (2H, quintet, J = 7.2 Hz), 1.28-1.55 (13H, m), 0.90(9H, m), 0.07(6H, s); ^{13}C NMR ($CDCl_3$) δ 132.0, 127.1, 119.8, 102.8, 62.6, 58.5, 53.6, 48.3, 45.2, 36.2, 33.9, 29.4, 27.1, 27.0, 26.4, 25.9, 25.9, 25.3, 20.1, 18.1, 16.4, 14.0, -5.4; IR (neat) 2954, 2933, 2857, 2245, 1335, 1145, 1123 cm^{-1}; MS (CI) *m/z* 564, 545 ([M-H]$^+$), 532, 489, 451 (100), 419, 381, 352, 326, 278, 235, 206, 156, 106, 71; HRMS *m/z* 545.3434 (545.34442 calcd for $C_{27}H_{53}N_2O_5SSi$).

*4.8.2. Seco-acid **29***

An Ace pressure tube was used as a reaction vessel. A mixture of **28** (896 mg, 1.6 mmol) in 2M KOH solution (15 mL) and EtOH (15 mL) was sealed and stirred for 18 h at 95 °C. After cooling, the resulting mixture was poured into hexane (50 mL) and extracted with 1M NaOH solution (3 x 30 mL). The combined basic aqueous layers were acidified with 2M HCl solution (pH 1) and extracted with CH_2Cl_2 (4 x 30 mL), dried over $MgSO_4$, filtrated and evaporated. The residue was purified by silica gel column chromatography (eluent: *n*-hexane/AcOEt, 2/1 - 1/1, v/v, then AcOEt with 1% AcOH) to yield **29** as a colorless oil (724 mg, 100%). ^{1}H NMR ($CDCl_3$) δ 5.27-5.48 (2H, m), 4.51(1H, t, J = 5.4 Hz), 3.74 (2H, t, J = 5.7 Hz), 3.62 (1H, quintet, J = 6.3 Hz), 3.37 (6H, s), 3.30 (2H, dd, J = 12.5, 5.7 Hz), 3.01-3.10 (2H, m), 2.35 (2H, t, J = 6.9 Hz), 1.96-2.18 (6H, m), 1.62-1.75 (2H, m), 1.25-1.58 (11H, m), 0.93 (3H, t, J = 6.9 Hz); ^{13}C NMR ($CDCl_3$) δ 178.1, 130.7, 128.6, 102.7, 62.2, 58.9, 53.7, 47.7, 45.1, 36.0, 33.8, 33.0, 29.4, 26.9, 26.9, 26.5, 26.2, 24.4, 20.0, 13.9; IR (neat) 3460, 2936, 2871, 1709, 1320, 1123 cm^{-1}; MS (CI) *m/z* 469, 450 ([M-H]$^+$), 437, 420, 388, 356 (100), 324, 282, 254, 242, 181, 164, 137, 116, 71; HRMS *m/z* 450.2542 (450.25253 calcd for $C_{21}H_{40}NO_7S$).

*4.8.3. N-Dimps-epilachnene **31***

The reaction was carried out under a dry argon atmosphere in a 500-mL three-necked round-bottomed flask equipped with a reflux condenser, a septum for adding the reagents and sampling the reaction mixture, and an inlet for purging the flask with dried argon. A mixture of **29** (215 mg, 0.48 mmol) and dry Et_3N (840 µL, 6.0 mmol) in dry CH_3CN (8 mL) was added dropwise using a syringe over 60 min to a refluxing solution of **30** (767 mg, 3.0 mmol) in dry CH_3CN (170 mL), and the resulting mixture was refluxing for 3 h. After cooling to 0 °C, water (100 mL) and ether (200 mL) were added. The resulting mixture was separated, and the ethereal solution was washed with water (3 x 100 mL) and brine (100 mL), dried over $MgSO_4$, filtrated and evaporated. The residue was purified by silica gel column chromatography (eluent: *n*-hexane/AcOEt, 4/1 - 3/1 - 2/1, v/v, and then AcOEt) to yield **31** as a colorless solid (125 mg, 60%). m.p. 71.0-72.0 °C (colorless needles, *n*-hexane-ether); ^{1}H NMR ($CDCl_3$) δ 5.31-5.43 (1H, m), 5.20-5.31 (1H, m), 4.49 (1H, t, J = 5.1 Hz), 4.24-4.36 (1H, m), 4.06 (1H, ddd, J = 12.5, 4.2, 2.7 Hz), 3.25-3.60 (2H, m), 3.36 (6H, s), 2.96-3.17 (2H, m), 2.33-2.44 (2H, m), 1.98-2.30 (2H, m), 1.80-1.96 (1H, m), 1.10-1.78 (12H, m), 0.93 (3H, t, J = 7.2 Hz); ^{13}C NMR ($CDCl_3$) δ 173.3, 131.3, 129.4, 102.8, 63.5, 61.2, 53.6, 49.4, 44.9, 36.4, 33.5, 31.6, 28.8, 26.8, 26.4, 25.6, 25.3, 23.3, 20.3, 14.0; IR (KBr) 2954, 2935, 2870, 1736, 1330, 1146, 1123 cm^{-1}; MS (CI) *m/z* 474, 433 (M$^+$), 432, 402, 390, 338 (100), 306, 266, 224, 71; HRMS *m/z* 433.2513 (433.24979 calcd for $C_{21}H_{39}NO_6S$).

*4.8.4. (±)-Epilachnene (**21**)*

To a solution of **31** (217 mg, 0.50 mmol) in dry CH_2Cl_2 (10 mL) was added TMSOTf (270 µL, 1.5 mmol) at 0 °C under an argon atmosphere. After stirring for 4 h, a saturated $NaHCO_3$ aqueous solution (10 mL) was added and extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were dried over K_2CO_3, filtrated and evaporated. The residue was purified by silica gel column chromatography (eluent: *n*-hexane/AcOEt, 2/1, v/v and then AcOEt) to yield (±)-**21** as a colorless oil (121 mg, 91%). ^{1}H NMR (C_6D_6) δ 5.38 (1H, dtt, J = 18.5, 8.1, 1.8 Hz), 5.14-5.26 (1H, m), 4.18 (1H, ddd, J = 11.3, 7.5, 2.1 Hz), 3.85 (1H, ddd, J = 11.3, 6.5, 2.1 Hz), 2.68 (1H, ddd, J = 14.0, 7.5, 2.1 Hz), 2.48 (1H, ddd, J = 14.0, 6.5, 2.1 Hz), 2.31 (1H, m), 2.06-2.24 (4H, m), 1.92-2.04 (2H, m), 1.46-1.60 (1H, m), 1.60-1.76 (1H, m), 1.02-1.42 (10H, m), 0.88-0.94 (3H, t-like m); ^{13}C NMR (C_6D_6) δ 172.9, 131.6, 129.8, 63.8, 56.5, 45.9, 38.7, 34.8, 32.0, 29.3, 27.9, 26.0, 25.8, 24.3, 19.3, 14.8; IR (KBr) 2928, 2855, 2360, 1736, 1459, 1159 cm^{-1}; MS (EI) *m/z* 267 (M$^+$), 252, 224, 170, 157, 116, 97; HRMS *m/z* 267.2203 (267.21981 calcd for $C_{16}H_{29}NO_2$).

Acknowledgments

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10. See Supplementary Material for spectra data.
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Supplementary Material

^{1}H NMR spectra of **6**-**8**, **9a**-**f**, **10a**-**h**, **14**, **16**-**20**, **27**-**29**, **31** and (±)-epilachnene (**21**); Spectra data of **17** and **27**.