Dianion of *N*-Phenyl-2-[(phenylsulfonyl)methyl]propenamide as a Versatile Reagent for the Preparation of α-Methylene Carbonyl Compounds

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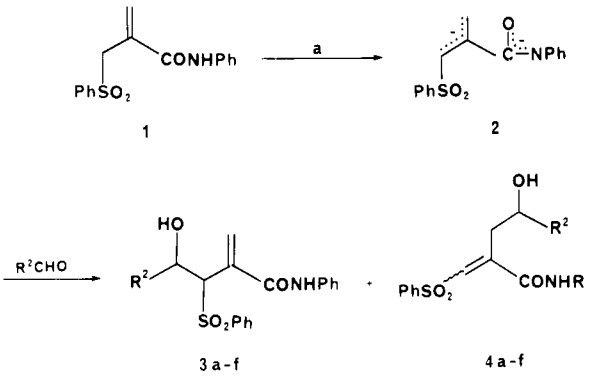
Received March 8, 1988

A general synthetic route to α-methylene β-lactams is described that involves the regioselective electrophilic substitution of the dianion **2** generated from *N*-phenyl-2-[(phenylsulfonyl)methyl]propenamide (**1**). A convergent synthesis of conocandin *N*-phenylamide was carried out. Key steps in the synthesis are the stereoselective introduction of the C-9/C-10 trisubstituted double bond of the amide using the dianion **2** and the transformation of the sulfonyl group in the intermediate amide, (*E*)-9-hydroxy-10-methyl-2-methylene-*N*-phenyl-3-(phenylsulfonyl)-9-hexadecenamide, prepared from (*E*)-7-methyl-6-tridecenal and the dianion **2**, into a hydroxy function via [2,3]-sigmatropic rearrangement of the selenoxide.

The α-methylene carbonyl unit is a common structural feature of sesquiterpenes and other naturally occurring substances possessing cytotoxic, fungitoxic, and growth-inhibitory activity.[2] As a consequence, a great deal of effort has been expended in the development of novel approaches to this class of compounds.[3] However, there had been no general method for the synthesis of α-methylene carbonyl compounds using carbanions derived from α,β-unsaturated amides owing to the tendency of these carbanions to undergo facile conjugate addition to the starting amides.[4] Beak and Kempf found that *N*-methyl-1-cyclohexenecarboxamide undergoes dilithiation on treatment with *sec*-butyllithium–*N*,*N*,*N*′,*N*′-tetramethylethylenediamine at −78 °C in THF and reacts with electrophiles to give *N*-methyl-6-substituted-1-cyclohexenecarboxamides.[5] We reported that the dianion of *N*-phenyl-2-methylpropenamide could be generated on sequential treatment with *t*-BuOK and *n*-BuLi at −78 °C in THF and serve as a reagent for the synthesis of α-methylene-γ-butyrolactones from carbonyl compounds.[6] The first asymmetric synthesis of these lactones was accomplished by the use of a variety of chiral *N*-monosubstituted 2-[(tributylstannyl)methyl]propenamides derived from L- and D-amino acids.[7] Fitt and Gschwent reported the dimetalation and electrophilic substitution of *N*-*tert*-butyl-2-methylpropenamide.[8]

Beak and Wilson reported an extensive study on the lithiation of secondary and tertiary α,β-unsaturated amides.[9] They found that the lithioamide derived from *N*,*N*-diisopropyl-2-[(phenylthio)methyl]-2-propenamide undergoes stepwise [3 + 2] cyclization with *N*-methyl-*N*-phenylacrylamide to produce cyclopentenes. They also found that *N*-methyl-2-[(phenylthio)methyl]-2-butenamide and *N*,*N*-diisopropyl-2-[(phenylthio)methyl]-2-butenamide react with azobenzene to give the dihydropyrazoles in good yields. More recently Beak and Burg discovered the facile route to cyclopentenes via [3 + 2] cyclization–elimination in the reaction of *N*,*N*-diisopropyl-2-[(phenylsulfonyl)]-methyl-2-propenamide with electron-deficient olefins.[10]

Scheme I[a]



[a] (a) *n*-BuLi/HMPA.

Table I. Reaction of Dianion 2 with Aldehydes

aldehyde	products (yield, %) 3	4
nonanal	**3a** (78)	**4a** (6)
isovaleraldehyde	**3b** (56)	**4b** (4)
cyclohexanecarbaldehyde	**3c** (77)	**4c** (6)
decanal	**3d** (65)	**4d** (4)
3,7-dimethyl-6-octenal	**3e** (65)	**4e** (3)
dodecanal	**3f** (65)	**4f** (5)

Uda and co-workers found that the dianions, prepared from (*E*)-*N*-*tert*-butyl-2-methyl-3-(phenylthio)-propenamide and *N*-*tert*-butyl-2-[(phenylthio)methyl]-propenamide, reacted with electrophiles regioselectively to give (*E*)-2-alkyl-substituted 3-(phenylthio)-propenamides.[11] We have found that the dianion **2**, generated from *N*-phenyl-2-[(phenylsulfonyl)methyl]-2-propenamide (**1**), can serve as a useful reagent for the preparation of *E*-trisubstituted olefins from alkyl halides and aldehydes, 3,4-dihydroxy-2-methylene carboxamides from aldehydes,[12a] and 5,6-dihydro-2*H*-pyrans from epoxides.[12b]

In this report we describe the stereospecific synthesis of 3-methylene β-lactams and the convergent synthesis of conocandin[13] *N*-phenylamide from common intermediates:

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(2) For a recent review, see: Hoffmann, H. M. R.; Rabe, J. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 94.
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0022-3263/89/1954-0063$01.50/0

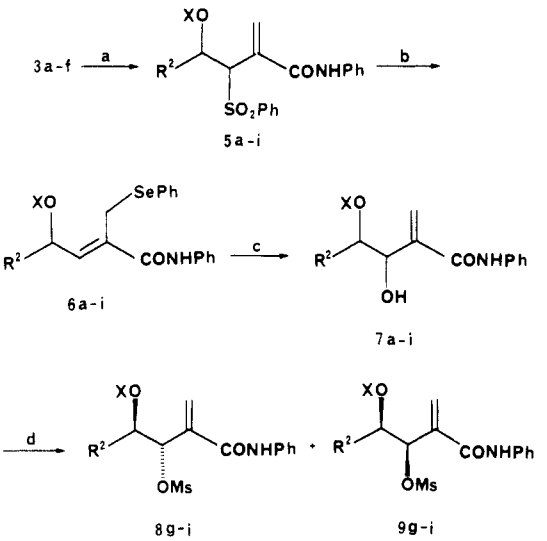
Table II. Preparation of Amides 5–7

amide	R^2	X in XCl	products (yield, %) 5	6	7
3a	n-C_8H_{17}	Me_3Si	**5a** (83)	**6a** (96)	**7a** (88)
3b	$(CH_3)_2CHCH_2$	Me_3Si	**5b** (82)	**6b** (91)	**7b** (98)
3c	$(CH_2)_5CH$	Me_3Si	**5c** (76)	**6c** (87)	**7c** (75)
3d	n-C_9H_{19}	Me_3Si	**5d** (89)	**6d** (73)	**7d** (83)
3e	$(CH_3)_2CCH(CH_2)_2CH(CH_3)CH_2$	Me_3Si	**5e** (85)	**6e** (70)	**7e** (75)
3f	n-$C_{11}H_{23}$	Me_3Si	**5f** (79)	**6f** (81)	**7f** (83)
3d	n-C_9H_{19}	t-$BuMe_2Si$	**5g** (96)	**6g** (94)	**7g** (95)
3e	$(CH_3)_2CCH(CH_2)_2CH(CH_3)CH_2$	t-$BuMe_2Si$	**5h** (95)	**6h** (91)	**7h** (84)
3f	n-$C_{11}H_{23}$	t-$BuMe_2Si$	**5i** (89)	**6i** (94)	**7i** (98)

Table III. Preparation of Methanesulfonates 8 and 9

amide	R^2	products (yield, %) 8	9
7g	n-C_9H_{19}	**8g** (48)	**9g** (40)
7h	$(CH_3)_2CCH(CH_2)_2CH(CH_3)CH_2$	**8h** (35)	**9h** (33)
7i	n-$C_{11}H_{23}$	**8i** (46)	**9i** (36)

Scheme II[a]



[a] (a) XCl; (b) PhSeNa; (c) MCPBA; (d) MsCl.

4-hydroxy-2-methylene-3-(phenylsulfonyl)alkanamides obtained by the regioselective substitution of the dianion **2** with aldehydes.

Results and Discussion

Synthesis of 3-Methylene β-Lactams. The dilithiation of *N*-phenyl-2-[(phenylsulfonyl)methyl]-propenamide (**1**) was carried out at −78 °C with butyllithium/hexamethylphosphoric triamide (*n*-BuLi/HMPA) in dry tetrahydrofuran for 30 min, followed by addition of aldehydes to give the α-adducts **3a–f** in good yields. The reactions are summarized in Scheme I and Table I. Protection of the secondary hydroxy group of the amide **3** with the silyl ether proceeded in high yield.[14] Reaction of **5** with sodium benzeneselenolate[15] afforded smoothly **6** via an addition–elimination sequence. Oxidation of **6** with MCPBA cleanly furnished 1,2-diol derivative **7** in good to high yield via [2,3]-sigmatropic rearrangement of the resulting selenoxide (Scheme II).[16] The results are shown in Table II. While the separation of the diastereomers of **7** was not possible, the mesylates **8** and **9** were readily separated by column chromatography on silica gel (Table III). The stereochemistry of **8** and **9** was determined unambiguously by convertion to epoxides **10** and **12**, respectively. Thus, desilylation of **8g**, the more mobile amide, with 2 equiv of tetrabutylammonium fluoride in THF afforded smoothly *trans*-3,4-epoxy-2-methylene-*N*-phenyltridecanamide (**10g**) in high yield (Scheme III). The less mobile isomer **9g** gave the *cis*-3,4-epoxy amide **12g** in good yield as shown in Table IV. The small vicinal coupling constant (J = 2.1 Hz) of **10g** confirmed the trans relation of C(3)-H and C(4)-H, while the larger coupling constant (J = 4.3–4.5 Hz) of **12g** was consistent with the cis stereochemistry.[17] The yields of the trans epoxides

Scheme III

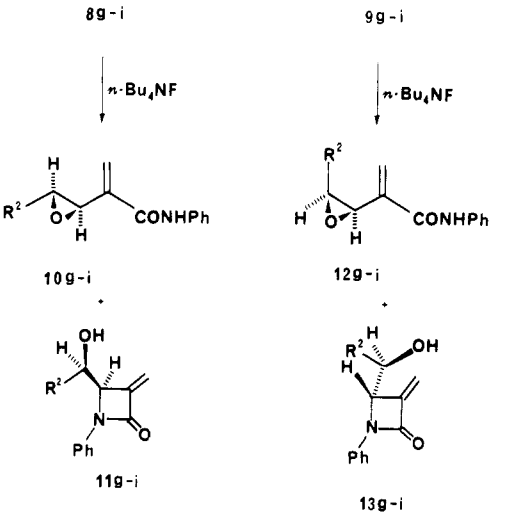


Table IV. Reaction of Methanesulfonates 8 and 9 with *n*-Bu_4NF

amide	R^2 in amide	products (yield, %) epoxide	2-azetidinone
8g	n-C_9H_{19}	**10g** (88)	**11g** (9)
9g	n-C_9H_{19}	**12g** (63)	**13g** (22)
8h	$(CH_3)_2CCH(CH_2)_2CH(CH_3)CH_2$	**10h** (89)	**11h** (10)
9h	$(CH_3)_2CCH(CH_2)_2CH(CH_3)CH_2$	**12h** (56)	**13h** (23)
8i	n-$C_{11}H_{23}$	**10i** (85)	**11i** (9)
9i	n-$C_{11}H_{23}$	**12i** (75)	**13i** (19)

Table V. Preparation of 3-Methylene-2-azetidinones 14 and 15

amide	R^2	2-azetidinone (yield, %)
8g	n-C_9H_{19}	**14g** (58)
9g	n-C_9H_{19}	**15g** (55)
8h	$(CH_3)_2CCH(CH_2)_2CH(CH_3)CH_2$	**14h** (61)
9h	$(CH_3)_2CCH(CH_2)_2CH(CH_3)CH_2$	**15h** (58)
8i	n-$C_{11}H_{23}$	**14i** (61)
9i	n-$C_{11}H_{23}$	**15i** (57)

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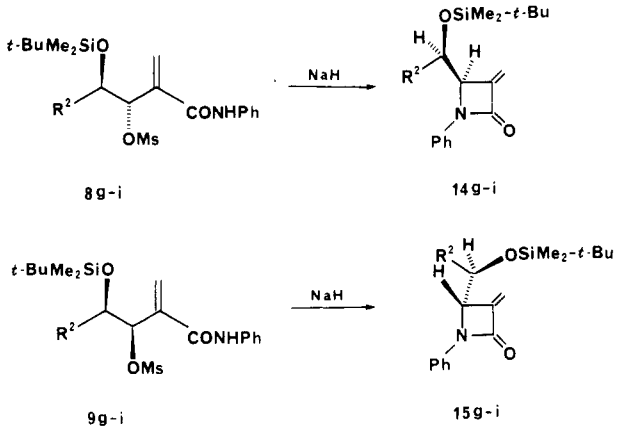
Scheme IV



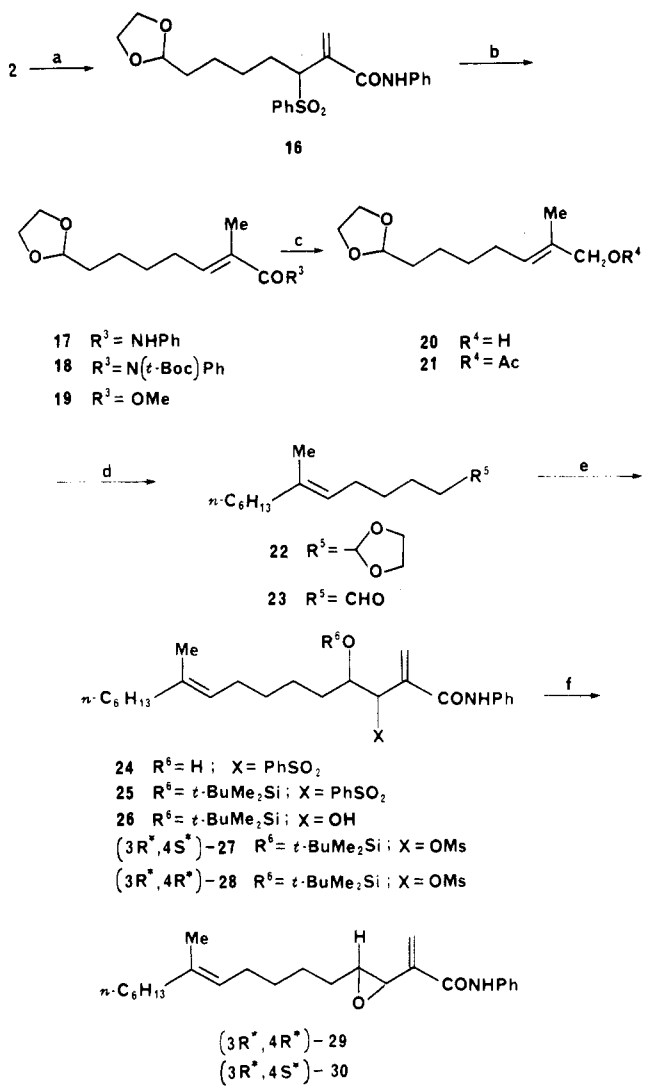
are usually high, because cis epoxidation is sterically congested compared to the trans cyclization. In each case, the 3-methylene β-lactam was isolated as the byproduct via an intramolecular displacement of the methanesulfonate by the amide nitrogen. It should be noted that the combined yields of epoxides and β-lactams are constantly high (Table IV). The use of NaH as the base in the cyclization of **8** and **9** provided improved yields of 3-methylene β-lactams **14** and **15** (Scheme IV) as shown in Table V.

Preparation of Conocandin *N*-Phenylamide. Conocandin,[13] isolated from *Hormococcus conorum*, shows high in vitro fungistatic activity. Scolastico and co-workers have recently reported the first total synthesis of its methyl ester and *tert*-butyl ester using 3-(dimethylamino)-propionate as an α-methylene carbonyl equivalent.[13f]

Our synthetic approach was based upon the utilization of the dianion **2** in the construction of both the *E* configuration of C-9/C-10 trisubstituted double bond and the 3,4-epoxy-2-methylene carbonyl unit (Scheme V). Initially we prepared (*E*)-7-methyl-6-tridecenal (**23**), the olefinic part of conocandin, by the regioselective alkylation[12] of **2** with commercially available 2-(4-chlorobutyl)-1,3-dioxolane. Thus, the reaction of the dianion **2** with the chloride produced the α-adduct **16** in 76% yield. Sodium borohydride reduction proceeded smoothly under very mild conditions (room temperature, 30 min) to furnish the *E* carboxamie **17** in 96% yield.[12] ^{1}H NMR analysis of **17** showed only one olefinic signal as a triplet at δ 6.40 ppm, consistent with the *E* geometry of the trisubstituted olefins.[18] The spectrum of a mixture of (*E*)- and (*Z*)-**17**, prepared by photochemical isomerization of **17**, showed the olefinic protons at δ 5.57 ppm (*Z* isomer) and at δ 6.40 ppm (*E* isomer). The amide **17** was converted into the methyl ester **19** (98%) via the *N*-*t*-Boc carboxamide **18** (99%).[19] Lithium aluminum hydride reduction of **19** gave the alcohol **20** (85%), which was converted into the acetate **21** (98%). Cross-coupling (90%) of **21** with pentylmagnesium bromide in the presence of Li_2CuCl_4[20] followed by acidic hydrolysis gave the desired aldehyde **23** (97%).

With the olefinic part of conocandin in hand, the construction of α-methylene-β,γ-epoxy unit was undertaken. Thus, regioselective alkylation of the dianion **2** with **23**

Scheme V[a]



[a] (a) 2-(4-chlorobutyl)-1,3-dioxolane; (b) $NaBH_4$, $(t\text{-}BuO_2C)_2O$, CH_3ONa; (c) $LiAlH_4$, CH_3COCl; (d) $C_5H_{11}MgBr$, Li_2CuCl_4, 5% HCl; (e) dianion **2**, $t\text{-}BuMe_2SiOSO_2CF_3$, MsCl; (f) $n\text{-}Bu_4NF$.

gave the hydroxyl carboxamide **24** in 50% yield. The amide **24** was converted into **20** via reaction of the silyl ether **25** (92%) with sodium benzeneselenolate in ethanol to prepare (2*Z*,9*E*)-4-[(*tert*-butyldimethylsilyl)oxy]-10-methyl-*N*-phenyl-2-[(phenylseleno)methyl]-2,9-hexadecadienamide (85%) and MCPBA oxidation (77%). Mesylation of **26** gave a separable mixture of the stereoisomers **27** (24%) and **28** (26%). Tetrabutylammonium fluoride mediated desilylation of the anti amide **27** spontaneously produced conocandin *N*-phenylamide (**29**) in 63% yield. Under identical conditions, the syn isomer **28** afforded the cis amide **30** in 36% yield.

In summary, the present work demonstrates that dianion **2** is a versatile reagent for the preparation of a wide variety of α-methylene carbonyl compounds from aldehydes. The synthetic use of the dianion is demonstrated in the stereoselective and convergent synthesis of conocandin *N*-phenylamide.

Experimental Section

General Methods. All reactions were carried out under an argon atmosphere. Tetrahydrofuran (THF) was distilled under argon from sodium benzophenone ketyl immediately before use. Dichloromethane, hexane, and HMPA were distilled from calcium hydride and stored over molecular sieves. The hexane solution

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of butyllithium was titrated by using diphenylacetic acid.[21]

Infrared spectra were recorded on a Hitachi Model 215 spectrophotometer. Nuclear magnetic resonance spectra were obtained on a JEOL Model PS-100 or a JEOL Model JMN-FX-400 spectrometer in $CDCl_3$ with tetramethylsilane as an internal standard. Mass spectra were determined on a JMS-DX-300 spectrometer.

General Procedure for the Reaction of the Dianion Derived from *N*-Phenyl-2-[(phenylsulfonyl)methyl]propenamide (1) and Aldehydes (Table I). 4-Hydroxy-2-methylene-*N*-phenyl-3-(phenylsulfonyl)dodecanamide (3a). To a solution of **1** (1.51 g, 5.0 mmol) in dry THF (40 mL) and HMPA (1.8 mL, 11 mmol) at −78 °C was added *n*-BuLi (11 mmol). After the mixture was stirred for 1 h, a solution of nonanal (0.95 mL, 5.5 mmol) in THF (3 mL) was added. The mixture was stirred for 2 h at −78 °C and quenched with saturated aqueous NH_4Cl (10 mL), and H_2O (100 mL) was added. The product was extracted with ethyl acetate (3 × 50 mL). The combined extracts were washed with brine, dried over Na_2SO_4, filtered, and evaporated. The crude product was purified by chromatography (silica gel, hexane–ethyl acetate 5:1) to give 1.72 g of **3a** (78% yield) and 0.13 g of **4a** (6% yield). **3a**: ^1H NMR δ 8.19 (m, 1 H), 7.71–7.89 (m, 2 H), 6.89–7.60 (m, 8 H), 6.13, 6.26 (s, 1 H), 6.07, 5.72 (s, 1 H), 4.20–4.72 (m, 2 H), 3.40–3.95 (br s, 1 H), 0.96–1.72 (m, 14 H), 0.60–0.96 (m, 3 H); IR (thin film) 3320, 1650, 1600, 1310, 1155, 1090 cm^{-1}. Anal. Calcd for $C_{25}H_{33}NO_4S$: C, 67.69; H, 7.50; N, 3.16. Found: C, 67.48; H, 7.27; N, 3.42.

4-Hydroxy-*N*-phenyl-2-[(phenylsulfonyl)methylene]dodecanamide (4a): ^1H NMR δ 9.85 (br s, 1 H), 6.92–8.04 (m, 11 H), 3.60–4.20 (br s, 2 H), 3.12–3.45 (m, 1 H), 2.48–2.88 (m, 1 H), 1.00–1.90 (m, 14 H), 0.68–1.00 (m, 3 H); IR (thin film) 3250, 1655, 1320, 1170, 1100 cm^{-1}. Anal. Calcd for $C_{25}H_{33}NO_4S$: C, 67.69, H, 7.50; N, 3.16. Found: C, 68.19; H, 7.72; N, 3.13.

4-Hydroxy-6-methyl-2-methylene-*N*-phenyl-3-(phenylsulfonyl)heptanamide (3b): ^1H NMR δ 8.32, 8.38 (br s, 1 H), 6.93–8.00 (m, 10 H), 6.26 (d, J = 12 Hz, 1 H), 5.79, 6.15 (s, 1 H), 4.30–4.48 (m, 2 H), 3.61 (br s, 1 H), 1.04–1.96 (m, 3 H), 0.68–1.00 (m, 6 H); IR (KBr) 3320, 1660, 1600, 1315, 1160, 1090 cm^{-1}. Anal. Calcd for $C_{21}H_{25}NO_4S$: C, 65.09; H, 6.50; N, 3.62. Found: C, 64.66; H, 6.43; N, 3.53.

4-Hydroxy-6-methyl-*N*-phenyl-2-[(phenylsulfonyl)methylene]heptanamide (4b): ^1H NMR δ 9.81, (br s, 1 H), 6.87–8.10 (m, 11 H), 2.47–4.31 (m, 4 H), 0.42–2.00 (m, 9 H); IR (thin film) 3320, 1650, 1595, 1320, 1155, 1095 cm^{-1}. Anal. Calcd for $C_{21}H_{25}NO_4S$: C, 65.07; H, 6.50; N, 3.62. Found: C, 65.23; H, 6.93; N, 3.56.

4-Cyclohexyl-4-hydroxy-*N*-phenyl-3-(phenylsulfonyl)butanamide (3c): ^1H NMR δ 8.10 (br s, 1 H), 6.86–8.00 (m, 10 H), 6.40 (s, 1 H), 6.19 (s, 1 H), 4.70 (br s, 1 H), 3.90–4.34, 3.58–3.82 (m, 2 H), 0.46–2.30 (m, 11 H); IR (KBr) 3270, 1670, 1595, 1310, 1155, 1090 cm^{-1}. Anal. Calcd for $C_{23}H_{27}NO_4S$: C, 66.79; H, 6.59; N, 3.39. Found: C, 66.51; H, 6.59; N, 3.39.

4-Cyclohexyl-4-hydroxy-*N*-phenyl-2-[(phenylsulfonyl)methylene]butanamide (4c): ^1H NMR δ 9.72 (br s, 1 H), 6.93–8.05 (m, 11 H), 2.51–4.09 (m, 5 H), 0.73–2.05 (m, 11 H); IR (thin film) 3220, 1630, 1600, 1320, 1160, 1090 cm^{-1}; mass spectrum, m/e (relative intensity) 413 (M^+, 17), 395 ($M^+ - H_2O$, 37).

4-Hydroxy-2-methylene-*N*-phenyl-3-(phenylsulfonyl)tridecanamide (3d): ^1H NMR δ 7.10–8.00 (m, 11 H), 5.75, 6.10, 6.17, 6.40 (s, 2 H), 4.40–4.70 (m, 2 H), 3.35 (br s, 1 H), 0.84–1.74 (m, 19 H); IR (thin film) 3300, 1660, 1600, 770, 700 cm^{-1}. Anal. Calcd for $C_{26}H_{35}NO_4S$: C, 68.24; H, 7.71; N, 3.06. Found: C, 68.41; H, 7.93; N, 2.97.

4-Hydroxy-*N*-phenyl-3-[(phenylsulfonyl)methylene]tridecanamide (4d): mp 92 °C; ^1H NMR δ 6.96–7.84 (m, 10 H), 6.01, 6.10 (s, 1 H), 4.32–4.56 (m, 1 H), 2.24–2.54 (m, 3 H), 0.74–1.76 (m, 19 H); IR (KBr) 3280, 1660, 1605, 780, 710 cm^{-1}; exact mass calcd for $C_{26}H_{35}NO_4S$ (M^+) 457.2287, found 457.2295.

4-Hydroxy-6,10-dimethyl-2-methylene-*N*-phenyl-3-(phenylsulfonyl)-9-undecenamide (3e): ^1H NMR δ 7.09–8.00 (m, 11 H), 5.57–6.43 (m, 2 H), 4.99–5.06 (m, 1 H), 4.47–4.61 (m, 1 H), 3.33–3.57 (m, 1 H), 0.77–1.99 (m, 17 H); IR (thin film) 3300, 1650, 1595, 770, 705 cm^{-1}. Anal. Calcd for $C_{26}H_{33}NO_4S$: C, 68.54; H, 7.30; N, 3.07. Found: C, 68.24; H, 7.32; N, 2.99.

4-Hydroxy-6,10-dimethyl-2-methylene-*N*-phenyl-2-[(phenylsulfonyl)methylene]-9-undecenamide (4e): ^1H NMR δ 7.00–7.98 (m, 12 H), 4.88–5.21 (m, 1 H), 3.72–4.32 (m, 1 H), 3.16–3.46 (m, 1 H), 2.20–2.85 (m, 2 H), 0.67–1.80 (m, 16 H); IR (thin film) 3275, 1660, 1600, 770, 705 cm^{-1}; exact mass calcd for $C_{26}H_{33}NO_4S$ (M^+) 455.2131, found 455.2170.

4-Hydroxy-2-methylene-*N*-phenyl-3-(phenylsulfonyl)pentadecanamide (3f): ^1H NMR δ 7.09–8.01 (m, 11 H), 5.75, 6.10, 6.18, 6.39 (s, 2 H), 4.39–4.64 (m, 2 H), 3.46–3.59 (m, 1 H), 0.85–1.65 (m, 23 H); IR (thin film) 3300, 1660, 1600, 770, 705 cm^{-1}. Anal. Calcd for $C_{28}H_{39}NO_4S$: C, 69.24; H, 8.09; N, 2.88. Found: C, 69.16; H, 8.06; N, 2.88.

4-Hydroxy-*N*-phenyl-2-[(phenylsulfonyl)methylene]pentadecanamide (4f): mp 93.5–94 °C; ^1H NMR δ 6.96–7.93 (m, 12 H), 3.88–4.15 (m, 1 H), 3.20–3.44 (m, 1 H), 2.51–2.84 (m, 2 H), 0.72–1.72 (m, 23 H); IR (KBr) 3275, 1630, 1600, 775, 705 cm^{-1}; exact mass calcd for $C_{28}H_{39}NO_4S$ (M^+) 485.2600, found 485.2618.

2-Methylene-*N*-phenyl-3-(phenylsulfonyl)-4-[(trimethylsilyl)oxy]dodecanamide (5a) was prepared from **18a** according to the reported procedure:[14] ^1H NMR δ 8.21 (br s, 1 H), 6.82–7.90 (m, 10 H), 6.12 (d, J = 5.0 Hz, 1 H), 6.02 (d, J = 5.0 Hz, 1 H), 4.28–4.94 (m, 2 H), 0.62–1.94 (m, 17 H), 0.15 (s, 9 H); IR (thin film) 1675, 1605, 1315, 1160, 1100 cm^{-1}. Anal. Calcd for $C_{28}H_{41}NO_4S$: C, 65.20; H, 8.01; N, 2.72. Found: C, 65.15; H, 7.86; N, 2.61.

6-Methyl-2-methylene-*N*-phenyl-3-(phenylsulfonyl)-4-[(trimethylsilyl)oxy]heptanamide (5b): mp 162–165 °C; ^1H NMR δ 6.84–7.90 (m, 11 H), 6.07, (s, 1 H), 6.00 (s, 1 H), 4.76 (d, J = 5.0 Hz, 1 H), 4.30–4.60 (m, 1 H), 1.30–1.90 (m, 3 H), 0.82 (d, J = 6.0 Hz, 6 H), 0.16–0.00 (s, 9 H); IR (KBr) 1650, 1595, 1310, 1150, 1050 cm^{-1}. Anal. Calcd for $C_{24}H_{33}NO_4SSi$: C, 62.71; H, 7.24; N, 3.05. Found: C, 62.44; H, 7.09; N, 3.15.

4-Cyclohexyl-2-methylene-*N*-phenyl-2-(phenylsulfonyl)-4-[(trimethylsilyl)oxy]butanamide (5c): faster eluting diastereomer, mp 113–115 °C; ^1H NMR δ 6.60–7.66 (m, 10 H), 5.89 (s, 2 H), 4.18–4.44 (m, 2 H), 0.40–1.74 (m, 11 H), 0.00 (s, 9 H); IR (KBr) 1650, 1620, 1315, 1160, 1095 cm^{-1}; slower eluting diastereomer mp 161–162 °C; ^1H NMR δ 6.62–7.68 (m, 11 H), 5.68 (s, 1 H), 5.57 (s, 1 H), 4.64 (d, J = 9.0 Hz, 1 H), 4.16 (d, J = 9.0 Hz, 1 H), 0.52 (m, 11 H), 0.00 (s, 9 H); IR (KBr) 1670, 1600, 1310, 1160, 1095 cm^{-1}. Anal. Calcd for $C_{26}H_{35}NO_4SSi$: C, 64.29; H, 7.26; N, 2.88. Found: C, 64.51; H, 7.32; N, 2.89.

2-Methylene-*N*-phenyl-3-(phenylsulfonyl)-4-[(trimethylsilyl)oxy]tridecanamide (5d): ^1H NMR δ 6.84–7.73 (m, 11 H), 5.86–5.96 (m, 2 H), 4.17–4.62 (m, 2 H), 0.63–1.39 (m, 19 H), −0.22, −0.15 (s, 9 H); IR (thin film) 3300, 1660, 1600, 770, 700 cm^{-1}. Anal. Calcd for $C_{29}H_{43}NO_4SSi$: C, 65.74; H, 8.18; N, 2.64. Found: C, 65.59; H, 8.15; N, 2.61.

6,10-Dimethyl-2-methylene-*N*-phenyl-3-(phenylsulfonyl)-4-[(trimethylsilyl)oxy]-9-undecenamide (5e): ^1H NMR δ 7.07–7.93 (m, 11 H), 6.10–6.21 (m, 2 H), 4.37–5.14 (m, 3 H), 0.78–2.01 (m, 16 H), 0.07, 0.08, 0.23, 0.24 (s, 9 H); IR (thin film) 3325, 1660, 1600, 770, 700 cm^{-1}. Anal. Calcd for $C_{29}H_{41}NO_4SSi$: C, 65.99; H, 7.83; N, 2.65. Found: C, 65.52; H, 7.80; N, 2.60.

2-Methylene-*N*-phenyl-3-(phenylsulfonyl)-4-[(trimethylsilyl)oxy]pentadecanamide (5f): ^1H NMR δ 6.84–7.73 (m, 11 H), 5.87–5.96 (m, 2 H), 4.17–4.61 (m, 2 H), 0.63–1.39 (m, 23 H), −0.22, −0.15 (s, 9 H); IR (thin film) 3300, 1665, 1600, 770, 700 cm^{-1}. Anal. Calcd for $C_{31}H_{47}NO_4SSi$: C, 66.74; H, 8.49; N, 2.51. Found: C, 66.36; H, 8.44; N, 2.45.

4-[(*tert*-Butyldimethylsilyl)oxy]-2-methylene-*N*-phenyl-3-(phenylsulfonyl)tridecanamide (5g): ^1H NMR δ 7.06–7.93 (m, 11 H), 6.06–6.47 (m, 2 H), 4.76–4.86 (m, 1 H), 4.53–4.61 (m, 1 H), 0.84–1.58 (m, 19 H), 0.77, 0.91, 0.93 (s, 9 H), 0.01–0.27 (m, 6 H); IR (thin film) 3300, 1660, 1600, 770, 700 cm^{-1}. Anal. Calcd for $C_{32}H_{49}NO_4SSi$: C, 67.21; H, 8.64; N, 2.45. Found: C, 67.22; H, 8.67; N, 2.39.

4-[(*tert*-Butyldimethylsilyl)oxy]-6,10-dimethyl-2-methylene-*N*-phenyl-3-(phenylsulfonyl)-9-undecenamide (5h): ^1H NMR δ 7.06–7.93 (m, 11 H), 6.10–6.53 (m, 2 H), 4.84–5.14 (m, 2 H), 4.51–4.60 (m, 1 H), 0.91, 0.93, 0.94 (s, 9 H), 0.71–2.04 (m, 16 H), 0.00–0.31 (m, 6 H); IR (thin film) 3300, 1660, 1600, 770, 700 cm^{-1}. Anal. Calcd for $C_{32}H_{47}NO_4SSi$: C, 67.44; H, 8.31; N, 2.46. Found: C, 67.47; N, 8.27; N, 2.41.

(21) Koflon, W. G.; Baclawski, L. M. *J. Org. Chem.* **1976**, *41*, 1879.

4-[(*tert*-Butyldimethylsilyl)oxy]-2-methylene-*N*-phenyl-3-(phenylsulfonyl)pentadecanamide (5i): ^{1}H NMR δ 7.06–7.93 (m, 11 H), 6.06–6.47 (m, 2 H), 4.74–4.86 (m, 1 H), 4.53–4.61 (m, 1 H), 0.80–1.55 (m, 23 H), 0.77, 0.91, 0.93 (s, 9 H), 0.00–0.27 (m, 6 H); IR (thin film) 3300, 1660, 1600, 770, 700 cm^{-1}. Anal. Calcd for $C_{34}H_{53}NO_4SSi$: C, 68.07; H, 8.90; N, 2.33. Found: C, 67.97, H, 9.24; N, 2.29.

General Procedure for the Preparation of *N*-Phenyl-2-[(phenylseleno)methyl] Carboxamides (Table II). To a stirred solution of diphenyl diselenide (1.41 g, 4.38 mmol) in absolute EtOH (50 mL) was added $NaBH_4$ (0.35 g, 9.2 mmol).[15] A solution of the amide **5a** (2.76 g, 4.38 mmol) in dry THF (10 mL) was added at room temperature, and the reaction mixture was stirred for 2 h. The solvent was evaporated and the residue was partioned between ether and water. The product was extracted with ether, dried over Na_2SO_4, filtered, and evaporated, and the crude product was purified by chromatography (silica gel, hexane–ethyl acetate 10:1), to give 2.24 g of ***N*-phenyl-2-[(phenylseleno)methyl]-4-[(trimethylsilyl)oxy]-2-dodecenamide (6a)** (96%) yield: mp 67–68 °C; ^{1}H NMR δ 7.72 (br s, 1 H), 6.81–7.57 (m, 10 H), 6.14 (d, J = 8.0 Hz, 1 H), 4.25 (br s, 1 H), 3.61–3.92 (m, 2 H), 0.61–1.57 (m, 17 H), 0.00 (s, 9 H); IR (KBr) 1655, 1605, 1105 cm^{-1}. Anal. Calcd for $C_{28}H_{41}NO_2SiSe$: C, 63.37; H, 7.79; N, 2.64. Found: C, 63.40; H, 7.64; N, 2.71.

6-Methyl-*N*-phenyl-2-[(phenylseleno)methyl]-4-[(trimethylsilyl)oxy]-2-heptenamide (6b): mp 91–93 °C; ^{1}H NMR δ 7.66 (br s, 1 H), 6.86–7.58 (m, 10 H), 6.18 (d, J = 8.0 Hz, 1 H), 4.20–4.58 (m, 1 H), 3.64–3.98 (m, 2 H), 0.54–1.80 (m, 9 H), 0.00 (s, 9 H); IR (KBr) 1630, 1600, 1085 cm^{-1}. Anal. Calcd for $C_{24}H_{33}NO_2SiSe$: C, 60.74; H, 7.01; N, 2.95. Found: C, 60.96; H, 7.28; N, 2.93.

4-Cyclohexyl-*N*-phenyl-2-[(phenylseleno)methyl]-4-[(trimethylsilyl)oxy]-2-butenamide (6c): mp 96–97 °C; ^{1}H NMR δ 7.68 (br s, 1 H), 6.83–7.59 (m, 10 H), 6.17 (d, J = 8.0 Hz, 1 H), 3.67–4.20 (m, 3 H), 0.55–1.87 (m, 11 H), 0.00 (s, 9 H); IR (KBr) 1650, 1595, 1060 cm^{-1}. Anal. Calcd for $C_{26}H_{35}NO_2SiSe$: C, 62.38; H, 7.05; N, 2.80. Found: C, 62.09; H, 7.05; N, 3.07.

***N*-Phenyl-2-[(phenylseleno)methyl]-4-[(trimethylsilyl)oxy]-2-tridecenamide (6d)**: ^{1}H NMR δ 6.97–7.63 (m, 11 H), 6.16 (d, J = 8.2 Hz, 1 H), 4.22–4.27 (m, 1 H), 3.83 (d, J = 22 Hz, 1 H), 3.80 (d, J = 22 Hz, 1 H), 0.75–1.23 (m, 19 H), –0.12 (s, 9 H); IR (thin film) 3275, 1660, 1600, 760, 700 cm^{-1}. Anal. Calcd for $C_{29}H_{43}NO_2SiSe$: C, 63.45; H, 7.96; N, 2.57. Found: C, 63.42; H, 7.83; N, 2.50.

6,10-Dimethyl-*N*-phenyl-2-[(phenylseleno)methyl]-4-[(trimethylsilyl)oxy]-2,9-undecadienamide (6e): ^{1}H NMR δ 7.01–7.96 (m, 11 H), 6.32 (d, J = 8.2 Hz, 1 H), 5.04–5.24 (m, 1 H), 4.42–4.73 (m, 1 H), 3.80–4.07 (m, 2 H), 0.75–2.20 (m, 16 H), –0.12 (s, 9 H); IR (thin film) 3250, 1660, 1600, 765, 700 cm^{-1}. Anal. Calcd for $C_{29}H_{41}NO_2SiSe$: C, 64.18; H, 7.62; N, 2.58. Found: C, 64.20; H, 7.50; N, 2.58.

***N*-Phenyl-2-[(phenylseleno)methyl]-4-[(trimethylsilyl)oxy]-2-pentadecenamide (6f)**: ^{1}H NMR δ 6.98–7.62 (m, 11 H), 6.16 (d, J = 8.2 Hz, 1 H), 4.22–4.27 (m, 1 H), 3.83 (d, J = 22 Hz, 1 H), 3.80 (d, J = 22 Hz, 1 H), 0.74–1.46 (m, 23 H), –0.12 (s, 9 H); IR (thin film) 3275, 1660, 1600, 760, 700 cm^{-1}. Anal. Calcd for $C_{31}N_{47}NO_2SiSe$: C, 65.01; H, 8.27, N, 2.45. Found: C, 64.82; H, 8.12; N, 2.39.

4-[(*tert*-Butyldimethylsilyl)oxy]-*N*-phenyl-2-[(phenylseleno)methyl]-2-tridecenamide (6g): ^{1}H NMR δ 7.09–7.75 (m, 11 H), 6.29 (d, J = 8.2 Hz, 1 H), 4.36–4.41 (m, 1 H), 3.92 (s, 2 H), 0.88 (s, 9 H), 0.84–1.57 (m, 19 H), –0.02 (m, 6 H); IR (thin film) 3275, 1660, 1600, 790, 700 cm^{-1}. Anal. Calcd for $C_{32}H_{49}NO_2SiSe$: C, 65.50; H, 8.42; N, 2.39. Found: C, 65.15; H, 8.22; N, 2.40.

4-[(*tert*-Butyldimethylsilyl)oxy]-6,10-dimethyl-*N*-phenyl-2-[(phenylseleno)methyl]-2,9-undecadienamide (6h): ^{1}H NMR δ 7.10–7.74 (m, 11 H), 6.29–6.32 (m, 1 H), 5.09–5.13 (m, 1 H), 4.52–4.58 (m, 1 H), 3.89–3.95 (m, 2 H), 0.88, 0.89 (s, 9 H), 0.87–2.16 (m, 16 H), –0.01 to 0.15 (m, 6 H); IR (thin film) 3250, 1650, 1600, 750, 700 cm^{-1}. Anal. Calcd for $C_{32}H_{47}NO_2SiSe$: C, 65.72; H, 8.10; N, 2.40. Found: C, 65.73; H, 8.03; N, 2.42.

4-[(*tert*-Butyldimethylsilyl)oxy]-*N*-phenyl-2-[(phenylseleno)methyl]-2-pentadecenamide (6i): ^{1}H NMR δ 7.09–7.91 (m, 11 H), 6.29 (d, J = 8.2 Hz, 1 H), 4.36–4.41 (m, 1 H), 3.92 (s, 2 H), 0.88 (s, 9 H), 0.84–1.59 (m, 23 H), –0.02 (m, 6 H); IR (thin film) 3275, 1650, 1600, 750, 700 cm^{-1}. Anal. Calcd for $C_{34}H_{53}NO_2SiSe$: C, 66.42; H, 8.69; N, 2.28. Found: C, 66.55; H, 8.57; N, 2.31.

General Procedure for the Preparation of 3-Hydroxy-2-methylene-*N*-phenyl Carboxamides (Table II). 3-Hydroxy-2-methylene-*N*-phenyl-4-[(trimethylsilyl)oxy]dodecanamide (7a). To a solution of **6a** (0.86 g, 1.60 mmol) in dry CH_2Cl_2 (10 mL) at –78 °C was added dropwise a solution of MCPBA (0.35 g, 1.60 mmol) in dry CH_2Cl_2 (5 mL). After 1 h, aqueous $NaHCO_3$ (2 mL) was added. The organic layer was washed with brine, dried over Na_2SO_4, and evaporated, and the crude product was purified by chromatography (silica gel, hexane–ethyl acetate 4:1) to give 0.56 g of the desired amide **7a** (88% yield): ^{1}H NMR δ 8.81, 8.59 (br s, 1 H), 6.92–7.60 (m, 5 H), 5.99 (d, J = 7.0 Hz, 1 H), 5.54 (s, 1 H), 4.36 (br s, 1 H), 3.26–3.96 (m, 2 H), 0.64–1.64 (m, 17 H), 0.00, 0.04 (s, 9 H); IR (thin film) 3280, 1660, 1600, 1085 cm^{-1}. Anal. Calcd for $C_{22}H_{37}NO_3Si$: C, 67.47; H, 9.52; N, 3.58. Found: C, 67.17; H, 9.41; N, 3.56.

3-Hydroxy-6-methyl-2-methylene-*N*-phenyl-4-[(trimethylsilyl)oxy]heptanamide (7b): ^{1}H NMR δ 9.00, 8.83 (br s, 1 H), 6.87–7.54 (m, 5 H), 5.78–6.02 (m, 1 H), 5.32–5.50 (m, 1 H), 3.52–4.42 (m, 3 H), 1.00–1.82 (m, 3 H), 0.52–0.92 (m, 6 H), 0.00 (s, 9 H); IR (thin film) 3280, 1650, 1595, 1070 cm^{-1}; exact mass calcd for $C_{18}H_{29}NO_3Si$ (M^+) 335.1891, found 335.1893.

4-Cyclohexyl-3-hydroxy-2-methylene-*N*-phenyl-4-[(trimethylsilyl)oxy]butanamide (7c): ^{1}H NMR δ 8.64 (br s, 1 H), 6.90–7.70 (m, 5 H), 6.00 (s, 1 H), 5.53 (d, J = 3.0 Hz, 1 H), 4.27–4.57 (m, 1 H), 3.53–3.93, 3.09–3.30 (m, 2 H), 0.75–1.99 (m, 11 H), 0.06, 0.00 (s, 9 H); IR (thin film) 3230, 1655, 1595, 1060 cm^{-1}. Anal. Calcd for $C_{20}H_{31}NO_3Si$: C; 66.45; H, 8.64; N; 3.87. Found: C, 66.32; H, 8.55; N, 3.85.

3-Hydroxy-2-methylene-*N*-phenyl-4-[(trimethylsilyl)oxy]tridecanamide (7d): ^{1}H NMR δ 7.07–7.60 (m, 6 H), 5.92–6.31 (m, 1 H), 5.49–5.62 (m, 1 H), 4.23–4.44 (m, 1 H), 3.97–3.89 (m, 2 H), 0.85–1.63 (m, 19 H), 0.04–0.22 (m, 9 H); IR (thin film) 3250, 1660, 1600, 765, 700 cm^{-1}. Anal. Calcd for $C_{23}H_{39}NO_3Si$: C, 68.10; H, 9.69; N, 3.45. Found: C, 68.45; H, 9.51; N, 3.38.

3-Hydroxy-6,10-dimethyl-2-methylene-*N*-phenyl-4-[(trimethylsilyl)oxy]-9-undecenamide (7e: ^{1}H NMR δ 8.74–9.31 (m, 1 H), 6.88–7.98 (m, 5 H), 5.96–6.20 (m, 1 H), 5.10–5.57 (m, 2 H), 4.18–4.47 (m, 1 H), 3.40–4.10 (m, 2 H), 0.64–2.10 (m, 16 H), 0.00–0.22 (m, 9 H); IR (thin film) 3275, 1660, 1600, 760, 700 cm^{-1}; exact mass calcd for $C_{23}H_{37}NO_3Si$ (M^+) 403.2539, found 403.2539.

3-Hydroxy-2-methylene-4-[(trimethylsilyl)oxy]-*N*-phenylpentadecanamide (7f): ^{1}H NMR δ 8.54–9.36 (m, 1 H), 7.07–7.56 (m, 5 H), 5.92–6.31 (m, 1 H), 5.51–5.62 (m, 1 H), 4.23–4.44 (m, 1 H), 3.67–3.89 (m, 2 H), 0.86–1.63 (m, 23 H), 0.04–0.21 (m, 9 H); IR (thin film) 3250, 1660, 1600, 765, 700 cm^{-1}. Anal. Calcd for $C_{25}H_{43}NO_3Si$: C, 69.23; H, 9.93; N, 3.23. Found: C, 69.05; H, 10.08; N, 3.16.

4-[(*tert*-Butyldimethylsilyl)oxy]-3-hydroxy-2-methylene-*N*-phenyltridecanamide (7g): ^{1}H NMR δ 8.54, 8.87 (s, 1 H), 7.09–7.57 (m, 5 H), 5.64–6.15 (m, 2 H), 4.39–4.53 (m, 1 H), 3.88–3.94 (m, 1 H), 3.29–3.46 (m, 1 H), 0.89, 0.92 (s, 9 H), 0.08, 0.09, 0.10 (s, 6 H); IR (thin film) 3250, 1660, 1600, 790, 770 cm^{-1}. Anal. Calcd for $C_{26}H_{45}NO_3Si$: C, 69.75; H, 10.13; N, 3.13. Found: C, 69.25; H, 9.93; N, 3.09.

4-[(*tert*-Butyldimethylsilyl)oxy]-3-hydroxy-6,10-dimethyl-2-methylene-*N*-phenyl-9-undecenamide (7h): ^{1}H NMR δ 8.43–8.74 (m, 1 H), 7.09–7.56 (m, 5 H), 6.02–6.11 (m, 1 H), 5.62–5.67 (m, 1 H), 5.02–5.07 (m, 11 H), 4.32–4.60 (m, 1 H), 3.96–4.12 (m, 1 H), 3.20–3.50 (m, 1 H), 0.87, 0.89, 0.90, 0.91 (s, 9 H), 0.80–1.98 (m, 16 H), 0.01–0.26 (m, 6 H); IR (thin film) 3250, 1660, 1600, 790, 770 cm^{-1}; exact mass calcd for $C_{26}H_{43}NO_3S$ (M^+) 445.3011, found 445.2994.

4-[(*tert*-Butyldimethylsilyl)oxy]-3-hydroxy-2-methylene-*N*-phenylpentadecanamide (7i): ^{1}H NMR δ 8.86, 8.52 (s, 1 H), 7.09–7.57 (m, 5 H), 6.06–6.15 (m, 1 H), 5.64–5.66 (m, 1 H), 4.39–4.53 (m, 1 H), 3.88–3.94 (m, 1 H), 3.29–3.44 (m, 1 H), 0.88, 0.89, 0.92 (s, 9 H), 0.85–1.60 (m, 23 H), 0.08, 0.09, 0.10 (s, 6 H); IR (thin film) 3250, 1660, 1600, 770 cm^{-1}. Anal. Calcd for $C_{28}H_{49}NO_3Si$: C, 70.68; H, 10.38; N, 2.94. Found: C, 70.63; H, 10.15; N, 2.85.

General Procedure for the Preparation of the Mesylates (Table III). To a solution of **7g** (1.00 g, 2.24 mmol) in dry CH_2Cl_2 (20 mL) were added dry Et_3N (0.47 mL, 3.37 mmol) and methanesulfonyl chloride (0.18 mL, 2.33 mmol). After the mixture was

stirred for 0.5 h, the reaction was quenched by addition of H_2O (10 mL) and the mixture was extracted with CH_2Cl_2 (2 × 20 mL). The organic extracts were washed with 5% HCl and saturated aqueous $NaHCO_3$, dried over Na_2SO_4, filtered, and evaporated, and the crude product was purified by chromatography (silica gel, hexane–ethyl acetate 8:1) to give 0.56 g of (3*R**,4*S**)-4-[(*tert*-butyldimethylsilyl)oxy]-2-methylene-3-(mesyloxy)-*N*-phenyltridecanamide (**8g**) (48% yield) and 0.47 g of (3*R**,4*R**)-4-[(*tert*-butyldimethylsilyl)oxy]-2-methylene-3-(mesyloxy)-*N*-phenyltridecanamide (**9g**).

8g: ^{1}H NMR δ 7.86 (s, 1 H), 7.12–7.54 (m, 5 H), 6.08 (s, 1 H), 5.94 (s, 1 H), 5.48 (d, *J* = 3.4 Hz, 1 H), 4.13–4.17 (m, 1 H), 3.07 (s, 3 H), 0.90 (s, 9 H), 0.83–1.51 (m, 19 H), 0.12, 0.16 (s, 6 H); IR (thin film) 3300, 1660, 1600, 790, 700 cm^{-1}. Anal. Calcd for $C_{27}H_{47}NO_5SSi$: C, 61.67; H, 9.01; N, 2.66. Found: C, 61.66; H, 8.79; N, 2.59.

9g: ^{1}H NMR δ 7.91 (s, 1 H), 7.11–7.58 (m, 5 H), 6.03 (s, 1 H), 5.71 (s, 1 H), 5.33 (d, *J* = 6.1 Hz, 1 H), 4.07–4.11 (m, 1 H), 3.02 (s, 3 H), 0.86 (s, 9 H), 0.82–1.71 (m, 19 H), 0.08 (s, 6 H); IR (thin film) 3300, 1660, 1600, 770 cm^{-1}; exact mass calcd for $C_{27}H_{47}NO_5SSi$ (M^+) 525.2944, found 525.2956.

(3*R,4*S**)-4-[(*tert*-Butyldimethylsilyl)oxy]-6,10-dimethyl-2-methylene-3-(mesyloxy)-*N*-phenyl-9-undecenamide (8h)**: ^{1}H NMR δ 8.09 (s, 1 H), 7.00–7.60 (m, 5 H), 6.03 (d, *J* = 3.0 Hz, 1 H), 5.90 (s, 1 H), 5.50–5.57 (m, 1 H), 4.89–5.17 (m, 1 H), 4.15–4.35 (m, 1 H), 3.04 (s, 1 H), 0.89 (s, 9 H), 0.74–2.01 (m, 16 H), 0.20, 0.13 (s, 6 H); IR (thin film) 3300, 1660, 1600, 790, 770 cm^{-1}. Anal. Calcd for $C_{27}H_{45}NO_5SSi$: C, 61.61; H, 8.66; N, 2.67. Found: C, 61.44; H, 8.45; N, 2.48.

(3*R,4*R**)-4-[(*tert*-Butyldimethylsilyl)oxy]-6,10-dimethyl-2-methylene-3-(mesyloxy)-*N*-phenyl-9-undecenamide (9h)**: ^{1}H NMR δ 7.58–8.03 (m, 1 H), 6.99–7.65 (m, 5 H), 5.98–6.07 (m, 1 H), 5.73–5.84 (m, 1 H), 5.13–5.48 (m, 1 H), 4.94–5.09 (m, 1 H), 4.08–4.29 (m, 1 H), 2.98 (s, 3 H), 1.60 (d, *J* = 8.5 Hz, 6 H), 0.81 (s, 9 H), 0.75–2.25 (m, 10 H), 0.07, 0.06 (s, 6 H); IR (thin film) 3325, 1660, 1600, 790, 770 cm^{-1}; exact mass calcd for $C_{27}H_{45}NO_5SSi$ (M^+) 523.2788, found 523.2792.

(3*R,4*S**)-4-[(*tert*-Butyldimethylsilyl)oxy]-2-methylene-3-(mesyloxy)-*N*-phenylpentadecanamide (8i)**: ^{1}H NMR δ 7.87 (s, 1 H), 7.13–7.54 (m, 5 H), 6.08 (s, 1 H), 5.94 (s, 1 H), 5.47 (d, *J* = 2.8 Hz, 1 H), 4.13–4.17 (m, 1 H), 3.07 (s, 3 H), 0.90 (s, 9 H), 0.84–1.51 (m, 23 H), 0.12, 0.16 (s, 6 H); IR (thin film) 3300, 1660, 1600, 790, 770 cm^{-1}; exact mass calcd for $C_{29}H_{51}NO_5SSi$ (M^+) 553.3257, found 553.3261.

(3*R,4*R**)-4-[(*tert*-Butyldimethylsilyl)oxy]-2-methylene-3-(mesyloxy)-*N*-phenylpentadecanamide (9i)**: ^{1}H NMR δ 7.87 (s, 1 H), 7.11–7.54 (m, 5 H), 6.03 (s, 1 H), 5.80 (s, 1 H), 5.33 (d, *J* = 5.8 Hz, 1 H), 4.07–4.11 (m, 1 H), 3.03 (s, 3 H), 0.86 (s, 9 H), 0.82–1.69 (m, 23 H), 0.08 (s, 6 H); IR (thin film) 3325, 1660, 1600, 790, 770 cm^{-1}; exact mass calcd for $C_{29}H_{51}NO_5SSi$ (M^+) 553.3257, found 553.3265.

General Method for the Preparation of 3,4-Epoxy-2-methylene Carboxamides and 3-Methylene-2-azetidinones. To a solution of **8g** (1.84 g, 3.50 mmol) in dry THF (20 mL) at 0 °C was added *n*-Bu_4NF (8.8 mmol). After 4 h, ethyl acetate (50 mL) was added, and the product was extracted with ethyl acetate. The organic layer was washed with saturated aqueous $NaHCO_3$ and brine, dried over Na_2SO_4, filtered, and evaporated, and the crude product was purified by chromatography (silica gel, hexane–ethyl acetate 5:1) to give 0.97 g of (3*R**,4*R**)-3,4-epoxy-2-methylene-*N*-phenyltridecanamide (**10g**) (88% yield) and 0.10 g of (4*R**)-4-[(1*R**)-1-hydroxydecyl]-3-methylene-*N*-phenyl-2-azetidinone (**11g**) (9% yield).

10g: mp 51–52 °C; ^{1}H NMR δ 8.78 (s, 1 H), 7.08–7.57 (m, 5 H), 6.21 (s, 1 H), 5.73 (s, 1 H), 3.54 (d, *J* = 2.1 Hz, 1 H), 3.04–3.08 (m, 1 H), 0.84–1.68 (m, 19 H); IR (thin film) 3275, 1660, 1600, 760, 700 cm^{-1}. Anal. Calcd for $C_{20}H_{29}NO_2$: C, 76.15; H, 9.27; N, 4.44. Found: C, 76.15; H, 9.07; N, 4.38.

11g: ^{1}H NMR δ 7.06–7.57 (m, 5 H), 5.85 (s, 1 H), 5.38 (s, 1 H), 4.62–4.65 (m, 1 H), 4.04–4.15 (m, 1 H), 2.76–3.25 (m, 1 H), 0.85–1.59 (m, 19 H); IR (thin film) 3375, 1730, 770, 700 cm^{-1}; exact mass calcd for $C_{20}H_{29}NO_2$ (M^+) 315.2197, found 315.2185.

(3*R,4*S**)-3,4-Epoxy-2-methylene-*N*-phenyltridecanamide (12g)**: ^{1}H NMR δ 8.40 (s, 1 H), 7.11–7.59 (m, 5 H), 6.30 (s, 1 H), 5.68 (s, 1 H), 3.89 (d, *J* = 4.3 Hz 1 H), 3.25–3.26 (m, 1 H), 0.81–1.62 (m, 19 H); IR (thin film) 3250, 1660, 1600, 770, 710, cm^{-1}; exact mass calcd for $C_{20}H_{29}NO_2$ (M^+) 315.2199, found 315.2214.

(4*R)-4-[(*S**)-1-Hydroxydecyl]-3-methylene-*N*-phenyl-2-azetidinone (13g)**: ^{1}H NMR δ 7.05–7.52 (m, 5 H), 5.85 (s, 1 H), 5.30 (s, 1 H), 4.59 (d, *J* = 1.2 Hz, 1 H), 4.12–4.15 (s, 1 H), 2.59–2.63 (m, 1 H), 0.86–1.59 (m, 19 H); IR (thin film) 3350, 1720, 770, 700 cm^{-1}; exact mass calcd for $C_{20}H_{29}NO_2$ (M^+) 315.2198, found 315.2183.

(3*R,4*R**)-3,4-Epoxy-6,10-dimethyl-2-methylene-*N*-phenyl-9-undecenamide (10h)**: ^{1}H NMR δ 8.77 (s, 1 H), 7.09–7.62 (m, 5 H), 6.27 (s, 1 H), 5.76 (s, 1 H), 5.06–5.10 (m, 1 H), 3.52–3.55 (m, 1 H), 3.10–3.14 (m, 1 H), 0.96–2.17 (m, 16 H); IR (thin film) 3250, 1660, 1600, 770, 700 cm^{-1}. Anal. Calcd for $C_{20}H_{27}NO_2$: C, 76.64; H, 8.68; N, 4.47. Found: C, 76.41; H, 8.71; N, 4.46.

(4*R)-4-[(*R**)-1-Hydroxy-3,7-dimethyl-6-octenyl]-2-methylene-*N*-phenyl-2-azetidinone (11h)**: ^{1}H NMR δ 7.07–7.54 (m, 5 H), 5.86 (s, 1 H), 5.38 (s, 1 H), 4.99–5.07 (m, 1 H), 4.63–4.64 (m, 1 H), 4.15–4.28 (m, 1 H), 2.32–2.42 (br s, 1 H), 0.82, 0.92 (d, *J* = 6.4 Hz, 3 H), 0.81–2.04 (m, 13 H); IR (thin film) 3400, 1720, 770, 705 cm^{-1}; exact mass calcd for $C_{20}H_{27}NO_2$ (M^+) 313.2041, found 313.2027.

(3*R,4*S**)-3,4-Epoxy-6,10-dimethyl-2-methylene-*N*-phenyl-9-undecenamide (12h)**: ^{1}H NMR δ 8.43 (s, 1 H), 7.11–7.63 (m, 5 H), 6.30 (s, 1 H), 5.67 (s, 1 H), 5.03–5.07 (s, 1 H), 3.90 (dd, *J* = 12.5, 4.3 Hz, 1 H), 3.28–3.34 (m, 1 H), 0.88–2.04 (m, 16 H); IR (thin film) 3300, 1660, 1600, 770, 700 cm^{-1}; exact mass calcd for $C_{20}H_{27}NO_2$ (M^+) 313.2042, found 313.2052.

(4*R)-4-[(*S**)-1-Hydroxy-3,7-dimethyl-6-octenyl]-2-methylene-*N*-phenyl-2-azetidinone (13h)**: ^{1}H NMR δ 7.07–7.65 (m, 5 H), 5.86 (s, 1 H), 5.31 (s, 1 H), 5.06–5.11 (m, 1 H), 4.58–4.59 (m, 1 H), 4.25–4.30 (m, 1 H), 2.30–2.38 (br s, 21 H), 0.92, 0.98 (d, *J* = 6.7 Hz, 3 H), 0.80–2.13 (m, 13 H); IR (thin film) 3350, 1720, 770, 705 cm^{-1}; exact mass calcd for $C_{20}H_{27}NO_2$ (M^+) 313.2042, found 313.2045.

(3*R,4*R**)-3,4-Epoxy-2-methylene-*N*-phenylpentadecanamide (10i)**: mp 62 °C; ^{1}H NMR δ 8.73 (s, 1 H), 7.09–7.62 (m, 5 H), 6.25 (s, 1 H), 5.75 (s, 1 H), 3.55 (d, *J* = 2.1 Hz, 1 H), 3.08–3.11 (m, 1 H), 0.82–1.71 (m, 23 H); IR (thin film) 3275, 1650, 1600, 760, 700 cm^{-1}. Anal. Calcd for $C_{22}H_{33}NO_2$: C, 76.92; H, 9.68; N, 4.08. Found: C, 76.89; H, 9.68; N, 4.02.

(4*R)-4-[(*R**)-1-Hydroxydodecenyl]-2-methylene-*N*-phenyl-2-azetidinone (11i)**: ^{1}H NMR δ 7.07–7.54 (m, 5 H), 5.86 (s, 1 H), 5.38 (s, 1 H), 4.65 (d, *J* = 6.1 Hz, 1 H), 4.05–4.09 (m, 1 H), 2.62 (s, 1 H), 0.86–1.59 (m, 23 H); IR (thin film) 3400, 1730, 770, 705 cm^{-1}; exact mass calcd for $C_{22}H_{33}NO_2$ (M^+) 343.2512, found 343.2538.

(3*R,4*S**)-3,4-Epoxy-2-methylene-*N*-phenylpentadecanamide (12i)**: ^{1}H NMR δ 8.41 (s, 1 H), 7.11–7.59 (m, 5 H), 6.30 (s, 1 H), 5.68 (s, 1 H), 3.89 (d, *J* = 4.6 Hz, 1 H), 3.24–3.27 (m, 1 H), 0.84–1.53 (m, 23 H); IR (thin film) 3250, 1660, 1600, 770, 705 cm^{-1}; exact mass calcd for $C_{21}H_{33}NO_2$ (M^+) 343.2511, found 343.2525.

(4*R)-4-[(*S**)-1-Hydroxydodecyl]-2-methylene-*N*-phenyl-2-azetidinone (13i)**: ^{1}H NMR δ 7.05–7.49 (m, 5 H), 5.85 (s, 1 H), 5.30 (s, 1 H), 4.59 (s, 1 H), 4.13–4.15 (m, 1 H), 2.45 (s, 1 H), 0.86–1.58 (m, 23 H); IR (thin film) 3350, 1720, 770, 705 cm^{-1}; exact mass calcd for $C_{22}H_{33}NO_2$ (M^+) 343.2511, found 343.2511.

General Procedure for the Preparation of 3-Methylene-2-azetidinones. (4*R)-4-[(*R**)-1-[(*tert*-Butyldimethylsilyl)oxy]decyl]-3-methylene-*N*-phenyl-2-azetidinone (14g) (Table V).** To a suspension of NaH (0.16 g, 4.0 mmol) in dry THF (25 mL) at −78 °C was added a solution of **8g** (1.05 g, 2.0 mmol) in dry THF (10 mL). The mixture was stirred at −78 °C for 30 min and allowed to warm to 0 °C over 4 h. Saturated aqueous NH_4Cl (5 mL) was added, and the product was extracted with ethyl acetate (3 × 25 mL), dried over Na_2SO_4, filtered, and evaporated. The crude product was purified by chromatography (silica gel, hexane–ethyl acetate 3:1) to give **14g** (58% yield): ^{1}H NMR δ 7.06–7.41 (m, 5 H), 5.84 (s, 1 H), 5.40 (s, 1 H), 4.60 (d, *J* = 4.6 Hz, 1 H), 4.20–4.24 (m, 1 H), 0.93 (s, 9 H), 0.85–1.45 (m, 19 H), 0.09, 0.12 (s, 6 H); IR (thin film) 1755, 1600, 790, 770 cm^{-1}; exact mass calcd for $C_{26}H_{43}NO_2Si$ (M^+) 429.3063, found 429.3083.

(4*R)-4-[(*S**)-1-[(*tert*-Butyldimethylsilyl)oxy]decyl]-3-methylene-*N*-phenyl-2-azetidinone (15g)**: ^{1}H NMR δ 7.06–7.58 (m, 5 H) 5.82 (s, 1 H), 5.25 (s, 1 H), 4.57 (s, 1 H), 4.14 (t, *J* = 6.0 Hz, 1 H), 0.88 (s, 9 H), 0.86–1.57 (m, 19 H), −0.12 (s, 6 H); IR (thin

film) 1750, 1600, 795, 770 cm^{-1}; exact mass calcd for $C_{26}H_{43}NO_2Si$ (M^+) 429.3062, found 429.3051.

(4*R)-4-[(*R**)-1-[(*tert*-Butyldimethylsilyl)oxy]-3,7-dimethyl-6-octenyl]-2-methylene-*N*-phenyl-2-azetidinone (14h)**: ^1H NMR δ 7.07–7.40 (m, 5 H), 5.85 (s, 1 H), 5.42 (s, 1 H), 4.96, 5.02, J = 7.0 Hz, 1 H), 4.60 (d, J = 4.3 Hz, 1 H), 4.35–4.41 (m, 1 H), 0.94 (s, 9 H), 0.85–1.96 (m, 13 H), 0.68, 0.83 (d, J = 6.7 Hz, 3 H), 0.00, 0.14, 0.16 (s, 6 H); IR (thin film) 1755, 1600, 795, 770 cm^{-1}; exact mass calcd for $C_{26}H_{41}NO_2Si$ (M^+) 427.2906, found 427.2884.

(4*R)-4-[(*S**)-1-[(*tert*-Butyldimethylsilyl)oxy]-3,7-dimethyl-6-octenyl]-2-methylene-*N*-phenyl-2-azetidinone (15h)**: ^1H NMR δ 7.07–7.61 (m, 5 H), 5.82 (s, 1 H), 5.24 (s, 1 H), 5.04–5.12 (m, 1 H), 4.57 (d, J = 8.5 Hz, 1 H), 4.21–4.28 (m, 1 H), 0.87–2.17 (m, 16 H), 0.86, 0.89 (s, 9 H), –0.14, –0.08, –0.01 (s, 6 H); IR (thin film) 1755, 1600, 795, 770 cm^{-1}; exact mass calcd for $C_{26}H_{41}NO_2Si$ (M^+) 427.2906, found 427.2881.

(4*R)-4-[(*R**)-1-[(*tert*-Butyldimethylsilyl)oxy]dodecenyl]-2-methylene-*N*-phenyl-2-azetidinone (14i)**: ^1H NMR δ 7.07–7.41 (m, 5 H), 5.84 (s, 1 H), 5.39 (s, 1 H), 4.59 (d, J = 4.9 Hz, 1 H), 4.20–4.24 (m, 1 H), 0.93 (s, 9 H), 0.85–1.50 (m, 23 H), 0.09, 0.12 (s, 6 H); IR (thin film) 1755, 1600, 765, 770 cm^{-1}; exact mass calcd for $C_{28}H_{47}NO_2Si$ (M^+) 547.3375, found 457.3353.

(4*R)-4-[(*S**)-1-[(*tert*-Butyldimethylsilyl)oxy]dodecenyl]-2-methylene-*N*-phenyl-2-azetidinone (15i)**: ^1H NMR δ 7.06–7.58 (m, 5 H), 5.82 (s, 1 H), 5.25 (s, 1 H), 4.57 (s, 1 H), 4.14 (t, J = 6.0 Hz, 1 H), 0.88 (s, 9 H), 0.86–1.57 (m, 23 H), –0.12 (s, 6 H); IR (thin film) 1750, 1600, 795, 770 cm^{-1}; exact mass calcd for $C_{28}H_{47}NO_2Si$ (M^+) 457.3375, found 457.3354.

2-Methylene-7-(1,3-dioxacyclopent-2-yl)-*N*-phenyl-3-(phenylsulfonyl)heptanamide (16). To a solution of **1** (2.11 g, 7.00 mmol) in dry THF–TMEDA–HMPA (1:1:1, 15 mL) at –78 °C was added *n*-BuLi (15.4 mmol). After being stirred for 30 min at –78 °C, 2-(4-chlorobutyl)-1,3-dioxolane (1.15 mL, 7.70 mmol) was added. The reaction mixture was warmed to room temperature over 5 h and aqueous saturated NH_4Cl (10 mL) was added. The product was extracted with ethyl acetate, dried over Na_2SO_4, filtered, and evaporated, and the crude product was purified by chromatography (silica gel, hexane–ethyl acetate 3:1) to give 2.29 g of **16** (76% yield): ^1H NMR δ 8.42 (s, 1 H), 7.02–8.03 (m, 10 H), 6.24 (s, 1 H), 5.75 (s, 1 H), 4.80 (t, J = 4.0 Hz, 1 H), 4.46–4.66 (m, 1 H), 3.70–4.41 (m, 4 H), 1.24–2.31 (m, 8 H); IR (thin film) 3320, 1660, 1600, 775, 740, 705 cm^{-1}; exact mass calcd for $C_{23}H_{27}NO_5S$ (M^+) 429.1610, found 429.1636.

(*E*)-2-Methyl-7-(1,3-dioxacyclopent-2-yl)-*N*-phenyl-2-heptenamide (17). To a solution of **16** (5.56 g, 12.9 mmol) in absolute EtOH (60 mL) was added $NaBH_4$ (1.13 g, 30.0 mmol). After the mixture was stirred for 0.5 h, the solution was poured into brine (200 mL). The product was extracted with ethyl acetate (3 × 60 mL), dried over Na_2SO_4, filtered, and evaporated, and the crude product was purified by chromatography (silica gel, hexane–ethyl acetate 4:1) to give 3.50 g of **17** (96%) as a white solid: mp 68 °C; ^1H NMR δ 7.61 (s, 1 H), 7.06–7.56 (m, 5 H), 6.40 (t, J = 7.3 Hz, 1 H), 4.83 (t, J = 4.6 Hz, 1 H), 3.82–3.95 (m, 4 H), 2.16–2.20 (m, 2 H), 1.92 (s, 3 H), 1.65–1.70 (m, 2 H), 1.45–1.49 (m, 4 H); IR (KBr) 3275, 1660, 1600, 770, 710 cm^{-1}; exact mass calcd for $C_{17}H_{23}NO_3$ (M^+) 289.1678, found 289.1695.

(*E*)-*N*-(*tert*-Butoxycarbonyl)-7-(1,3-dioxacyclopent-2-yl)-2-methyl-*N*-phenyl-2-heptenamide (18) was prepared from **17** (3.23 g, 11.2 mmol) by the reported procedure:[19] ^1H NMR δ 6.92–7.47 (m, 5 H), 6.09–6.31 (m, 1 H), 4.82 (t, J = 9.0 Hz, 1 H), 3.68–4.12 (m, 4 H), 2.00–2.31 (m, 2 H), 1.09 (s, 3 H), 1.42 (s, 9 H), 1.24–1.71 (m, 6 H); IR (thin film) 1730, 1680, 715 cm^{-1}; exact mass calcd for $C_{22}H_{31}NO_5$ (M^+) 389.2202, found 389.2202.

Methyl (*E*)-2-methyl-7-(1,3-dioxacyclopent-2-yl)-2-heptenoate (19) was prepared from **18** by the reported procedure:[19] ^1H NMR δ 6.80 (t, J = 7.0 Hz, 1 H), 4.87 (t, J = 4.0 Hz, 1 H), 3.82–4.04 (m, 4 H), 3.76 (s, 3 H), 1.98–2.34 (m, 2 H), 1.83 (s, 3 H), 1.12–1.73 (m, 6 H); IR (thin film) 1715, 765 cm^{-1}; exact mass calcd for $C_{12}H_{20}O_4$ (M^+) 228.1361, found 228.1370.

(*E*)-2-Methyl-7-(1,3-dioxacyclopent-2-yl)-2-hepten-1-ol (20). To a suspension of $LiAlH_4$ (0.72 g, 19.0 mmol) in dry ether (50 mL) at 0 °C was added a solution of the methyl ester **19** (3.72 g, 17.0 mmol) in dry ether (10 mL). After being stirred for 3 h at room temperature, the reaction mixture was quenched with saturated aqueous NH_4Cl (10 mL). The mixture was filtered through Hyflo Super-Cel and the salts were washed several times with fresh portions of ether. The product was extracted with ethyl acetate (4 × 50 mL). The combined organic extracts were washed with brine, dried over Na_2SO_4, filtered, and evaporated, and the crude product was purified by chromatography (silica gel, hexane–ethyl acetate 2:1) to give 2.88 g of **20** (85% yield): ^1H NMR δ 5.44 (t, J = 7.0 Hz, 1 H), 4.88 (t, J = 4.0 Hz, 1 H), 3.78–4.09 (m, 6 H), 2.80 (br s, 1 H), 1.90–2.16 (m, 2 H), 1.64 (s, 3 H), 1.23–1.83 (m, 6 H); IR (thin film) 3400, 880 cm^{-1}; exact mass calcd for $C_{11}H_{20}O_3$ (M^+) 200.1412, found 200.1410.

(*E*)-2-Methyl-7-(1,3-dioxacyclopent-2-yl)-2-heptenyl Acetate (21). To a solution of **20** (1.39 g, 6.94 mmol) and dry pyridine (1.12 mL, 13.9 mmol) in dry CH_2Cl_2 (30 mL) at room temperature was added acetyl chloride (0.74 g, 10.4 mmol). After the mixture was stirred for 2 min, 2% NaOH (30 mL) was added. The product was extracted with CH_2Cl_2 (3 × 30 mL), dried over Na_2SO_4, filtered, and evaporated, and the crude product was purified by chromatography (silica gel, hexane–ethyl acetate 5:1) to give 1.64 g of **21** (98% yield): ^1H NMR δ 5.52 (t, J = 7.0 Hz, 1 H), 4.89 (t, J = 4.0 Hz, 1 H), 4.50 (s, 2 H), 3.80–4.08 (m, 4 H), 2.06 (s, 3 H), 1.91–2.24 (m, 2 H), 1.65 (s, 3 H), 1.22–1.79 (m, 6 H); IR (thin film) 1730, 880, 750 cm^{-1}; exact mass calcd for $C_{13}H_{22}O_4$ (M^+) 242.1519, found; 242.1540.

(*E*)-1-(1,3-Dioxacyclopent-2-yl)-6-methyl-5-dodecene (22). To a solution of **21** (2.74 g, 11.3 mmol) in dry THF (20 mL) at –78 °C was added a solution of $C_5H_{11}MgBr$ (33.0 mmol) in dry ether (16 mL), and then a solution of Li_2CuCl_4[20] (0.1 M, 2 mL) in dry THF was added. The mixture was gently warmed to room temperature over 6 h and quenched with saturated aqueous NH_4Cl (30 mL), and the resulting solid was filtered. The product was extracted with ethyl acetate (3 × 30 mL), dried over Na_2SO_4, filtered, and evaporated, and the crude product was purified by chromatography (silica gel, hexane–ethyl acetate 10:1) to give 2.58 g of **22** (90% yield) as a colorless oil: ^1H NMR δ 5.14 (t, J = 7.0 Hz, 1 H), 4.88 (t, J = 4.0 Hz, 1 H), 3.84–4.06 (m, 4 H), 1.84–2.07 (m, 4 H) 1.56 (s, 3 H), 0.72–1.48 (m, 17 H); IR (thin film) 1150, 740 cm^{-1}; exact mass calcd for $C_{16}H_{30}O_2$ (M^+) 254.2246, found 254.2256.

(*E*)-7-Methyl-6-tridecenal (23). To a solution of **22** (2.15 g, 8.45 mmol) in THF (60 mL) and H_2O (60 mL) was added *p*-toluenesulfonic acid monohydrate (2.00 g, 10.5 mmol), and the mixture was stirred for 9 h at room temperature. The product was extracted with ethyl acetate (3 × 50 mL), dried over $MgSO_4$, filtered, and evaporated, and the crude product was purified by chromatography (silica gel, hexane–ethyl acetate 7:1) to give 1.72 g (8.17 mmol) of **23** (97% yield): ^1H NMR δ 9.76 (t, J = 1.8 Hz, 1 H), 5.09 (td, J = 7.0, 1.2 Hz, 1 H), 2.42 (td, J = 7.3, 1.8 Hz, 2 H), 1.94–2.04 (m, 4 H), 1.58 (s, 3 H), 0.86–1.68 (m, 15 H); IR (thin film) 1730, 740 cm^{-1}; exact mass calcd for $C_{14}H_{26}O$ (M^+) 210.1983, found 210.1964.

(*E*)-9-Hydroxy-10-methyl-2-methylene-*N*-phenyl-3-(phenylsulfonyl)-9-hexadecenamide (24) was prepared in 50% yield from **23** (0.70 g, 3.3 mmol) by the procedure described for the preparation of the hydroxy amide **3a**: ^1H NMR δ 8.12 (s, 1 H), 7.00–8.01 (m, 10 H), 5.80, 6.14, 6.20, 6.39 (s, 2 H), 5.08 (t, J = 6.5 Hz, 1 H), 4.33–4.76 (m, 2 H), 3.49–3.81 (m, 1 H), 0.80–2.24 (m, 24 H); IR (thin film) 3320, 1660, 1600, 1440, 1310, 1160, 770, 705 cm^{-1}; exact mass for $C_{30}H_{42}NO_4S$ (M^+) 512.283, found 512.283.

(*E*)-4-[(*tert*-Butyldimethylsilyl)oxy]-10-methyl-2-methylene-*N*-phenyl-3-(phenylsulfonyl)-9-hexadecenamide (25) was prepared in 92% yield from **24** (0.29 g, 0.57 mmol) by the reported procedure:[14] ^1H NMR δ 7.04–7.92 (m, 11 H), 6.06, 6.17, 6.47 (s, 2 H), 5.06 (t, J = 6.5 Hz, 1 H), 4.31–4.90 (m, 2 H), 0.76–2.10 (m, 33 H), 0.00–0.24 (m, 6 H); IR (thin film) 3330, 1670, 1600, 1440, 1310, 1160, 850 cm^{-1}.

(2*Z*,9*E*)-4-[(*tert*-Butyldimethylsilyl)oxy]-10-methyl-*N*-phenyl-2-[(phenylseleno)methyl]-2,9-hexadecadienamide was prepared in 85% yield from **25** (1.77 g, 2.83 mmol) by the procedure described for the preparation of the amide **6a**: ^1H NMR δ 7.77 (s, 1 H), 7.00–7.64 (m, 10 H), 6.28 (d, J = 8.0 Hz, 1 H), 5.12 (t, J = 6.5 Hz, 1 H), 4.28–4.52 (m, 1 H), 3.93 (s, 2 H), 1.79–2.12 (m, 4 H), 1.12–1.76 (m, 17 H), 0.72–1.00 (m, 12 H), 0.04, 0.06 (s, 6 H); IR (thin film) 3250, 1640, 1580, 1430, 830 cm^{-1}.

(*E*)-4-[(*tert*-Butyldimethylsilyl)oxy]-3-hydroxy-10-methyl-2-methylene-*N*-phenyl-9-hexadecenamide (26) was prepared in 77% yield from (2*Z*,9*E*)-4-[(*tert*-butyldimethyl-

silyl)oxy]-10-methyl-*N*-phenyl-2-[(phenylseleno)methyl]-2,9-hexadecadienamide (0.60 g, 0.936 mmol) by the procedure described for the preparation of the amide **7a**: ^{1}H NMR δ 8.72, 8.95 (s, 1 H), 7.00–7.68 (m, 5 H), 6.08, 6.10 (s, 1 H), 5.65 (s, 1 H), 5.11 (t, J = 6.5 Hz, 1 H), 4.35–4.76 (m, 1 H), 3.95 (br s, 1 H), 3.58–3.73 (m, 1 H), 1.79–2.11 (m, 9 H), 1.05–1.61 (m, 17 H), 0.63–1.03 (m, 12 H), 0.08 (s, 6 H); IR (thin film) 3300, 1670, 1600, 1450, 850 cm^{-1}; exact mass calcd for $C_{30}H_{51}NO_3Si$ (M^+) 501.3637, found 501.3617.

(3*R,4*S**)-(*E*)-4-[(*tert*-Butyldimethylsilyl)oxy]-3-(mesyloxy)-10-methyl-2-methylene-*N*-phenyl-9-hexadecenamide (27)**: ^{1}H NMR δ 7.85 (s, 1 H), 7.13–7.54 (m, 5 H), 6.08 (s, 1 H), 5.94 (s, 1 H), 5.48 (d, J = 3.7 Hz, 1 H), 5.09 (t, J = 7.1 Hz, 1 H), 4.11–4.15 (m, 1 H), 3.07 (s, 3 H), 1.91–1.97 (m, 4 H), 1.19–1.55 (m, 17 H), 0.86–0.95 (m, 12 H), 0.12–0.16 (s, 6 H); IR (thin film) 3330, 1670, 1600, 1440, 1360, 1180, 850 cm^{-1}; exact mass calcd for $C_{23}H_{35}NO_5SSi$ ($M^+ - C_4H_9$) 522.2710, found 522.2735.

(3*R,4*R**)-(*E*)-[(*tert*-Butyldimethylsilyl)oxy]-3-(mesyloxy)-10-methyl-2-methylene-*N*-phenyl-9-hexadecenamide (28)**: ^{1}H NMR δ 7.85 (s, 1 H), 7.14–7.54 (m, 5 H), 6.02 (s, 1 H), 5.79 (s, 1 H), 5.33 (d, J = 5.8 Hz, 1 H), 5.08 (t, J = 7.2 Hz, 1 H), 4.09–4.13 (m, 1 H), 3.03 (s, 3 H), 1.92–1.98 (m, 4 H), 1.19–1.59 (m, 17 H), 0.85–0.90 (m, 12 H), 0.74 (s, 6 H); IR (thin film) 3320, 1660, 1590, 1440, 1360, 1180, 850 cm^{-1}; exact mass calcd for $C_{31}H_{53}NO_5SSi$ (M^+) 579.3412, found 579.3387.

(3*R,4*R**)-(*E*)-3,4-Epoxy-10-methyl-2-methylene-*N*-phenyl-9-hexadecenamide (29) (Conocandin *N*-phenylamide)**. From **27** (0.20 g, 0.345 mmol), **29** was obtained in 63% yield (0.08 g, 0.216 mmol): ^{1}H NMR δ 8.73 (s, 1 H), 7.10–7.58 (m, 5 H), 6.27 (s, 1 H), 5.77 (s, 1 H), 5.10 (t, J = 7.0 Hz, 1 H), 3.56 (d, J = 2.4 Hz, 1 H), 3.09–3.13 (m, 1 H), 1.94–2.04 (m, 4 h), 1.21–1.70 (m, 17 H), 0.86–0.92 (m, 3 H); IR (thin film) 3270, 1660, 1660, 1440 cm^{-1}; exact mass calcd for $C_{24}H_{35}NO_2$ (M^+) 369.2668, found 369.2653.

(3*R,4*S**)-(*E*)-3,4-Epoxy-10-methyl-2-methylene-*N*-phenyl-9-hexadecenamide (30)**. From **28** (0.24 g, 0.414 mmol), the amide **30** was obtained in 36% yield (0.06 g, 0.102 mmol): mp 37–40 °C; ^{1}H NMR δ 8.38 (s, 1 H), 7.11–7.59 (m, 5 H), 6.31 (s, 1 H), 5.68 (s, 1 H), 5.06 (t, J = 7.0 Hz, 1 H), 3.90 (d, J = 4.3 Hz, 1 H), 3.25–3.26 (m, 1 H), 1.91–2.04 (m, 4 H), 1.21–1.59 (m, 17 H), 0.88–0.92 (m, 3 H); exact mass calcd for $C_{24}H_{35}NO_2$ (M^+) 369.2668, found 369.2686.

Acknowledgment. This work was supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Science and Culture, Japan. K.T. thanks the Kurata Foundation for financial support.

Reversible and in Situ Formation of Organic Arsenates and Vanadates as Organic Phosphate Mimics in Enzymatic Reactions: Mechanistic Investigation of Aldol Reactions and Synthetic Applications

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Received June 15, 1988

A synthetic strategy is developed that uses organic phosphate utilizing enzymes as catalysts and a mixture of an organic alcohol and inorganic arsenate or vanadate to replace the organic phosphate substrate. In this process, inorganic arsenate or vanadate reacts with the alcohol reversibly in situ to form a mixture of esters, one of which is accepted by the enzyme as a substrate. Examples of the utility of this approach are demonstrated in enzymatic aldol condensations catalyzed by fructose-1,6-diphosphate aldolase, fuculose-1-phosphate aldolase, and rhamnulose-1-phosphate aldolase with a mixture of dihydroxyacetone and inorganic arsenate as substrate. Several uncommon sugars and deoxy sugars are prepared on 5–17-mmol scales. Mechanistic studies on an aldol reaction indicate that the redox reaction between dihydroxyacetone and inorganic vanadate prohibits the use of such a mixture to replace dihydroxyacetone phosphate in enzymatic aldol condensations.

Introduction

Organic phosphate utilizing enzymes hold potential for the preparation of many multifunctional or complex organic compound, especially sugars.[1] Enzymatic synthesis of organic phosphates that require ATP and ATP regeneration has been successfully developed.[2] When an analogue of the naturally occurring organic phosphate is desired, the enzymatic preparation, however, is limited by the substrate specificity of the enzyme used. In some instances, phosphorylated substrates or products are unstable and difficult to manipulate in solution, and the phosphate moiety of the product may have to be removed. This overall reaction sequence is shown in eq 1.

$$\mathrm{ROH} \xrightarrow[\text{kinase}]{\text{ATP}} \mathrm{ROPO_3^{2-}} \xrightarrow{\text{enzyme}} \mathrm{R'OPO_3^{2-}} \xrightarrow[\text{H}^+ \text{ or phosphatase}]{\mathrm{H_2O}} \mathrm{R'OH} \quad (1)$$

Several organic phosphate utilizing enzymes are known to catalyze transformations of their nonphosphorylated substrates in the presence of inorganic arsenate; the reactions are detected spectroscopically under assay conditions.[3] These enzymes include glucose-6-phosphate dehydrogenase, glucose phosphate isomerase, α-glycerophosphate dehydrogenase, phosphofructokinase, and 6-phosphogluconate dehydrogenase. More recently it has been shown that vanadate also stimulates the oxidation of glucose by glucose-6-phosphate dehydrogenase.[4] These reactions may involve the reversible, nonenzymatic formation of organic arsenate or vanadate esters, which are analogous to organic phosphates and accepted by the en-

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0022-3263/89/1954-0070$01.50/0