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Synthesis of β-Amino-Substituted Enones by Addition of Substituted Methyl Enones to Sulfinimines: Application to the Total Synthesis of Alkaloids (+)-Lasubine II and (+)-241D and the Formal Total Synthesis of (−)-Lasubine I

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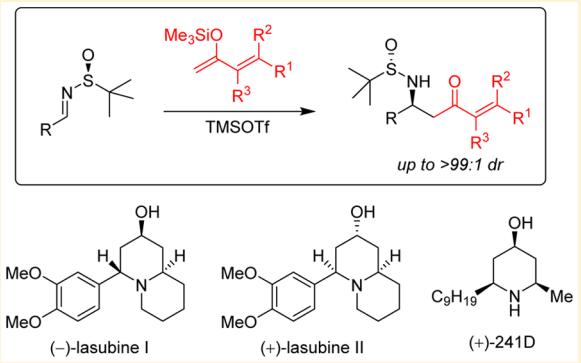
Supporting Information

ABSTRACT: Addition of silyl enol ethers obtained from substituted methyl enones to chiral sulfinimines afforded the β-amino-substituted enones with excellent selectivity. Utility of the obtained *N*-sulfinyl β-amino ketones possessing α,β-unsaturation is exemplified in the total synthesis of the quinolizidine alkaloid natural products (−)-lasubine I, (+)-lasubine II, and substituted piperidine alkaloid (+)-241-D.



Quinolizidines, indolizidines and substituted piperidines are ubiquitous structural units present in a number of diverse alkaloids possessing simple to complex structural framework exhibiting varied bioactivity profiles.[1] Some of the simple quinolizidine, indolizidine, and piperidine alkaloids include the lasubines **1** and **2** and indolizidines 167 B (**3**) and 241-D (**4**), while complex alkaloids comprising these frameworks include vallesamidine (**5**) and aspidospermidine (**6**) (Figure 1).

Over the years, impressive strategies have been developed for the synthesis of substituted piperidines, pyrrolidines which were further extended to the quinolizidine and indolidizine alkaloids. Extensively used building blocks for the synthesis of the quinolizidine alkaloids include the δ-amino-β-keto esters **7** developed by Davis' group[2] by addition of excess sodium enolate of methyl acetate to nonracemic sulfinimines, which were also obtained by vinylogous Mukaiyama−Mannich reaction of sulfinimines with dioxinone-derived silyloxy diene.[3] Recently, the same building block was synthesized by employing chiral Bronsted acid catalyzed enantioselective addition of dioxinone-derived silyloxy diene to imines.[4] Another useful building block for the synthesis of quinolizidine and indolizidine alkaloids is the γ-amino-α,β-unsaturated esters **8** derived from the vinylogous Mukaiyama−Mannich addition of vinylketene silyl acetals to imines developed by Schneider's group.[5] One of the direct syntheses of quinolizidines inter alia is the intramolecular Michael reaction of β-amino enones **9**, generally obtained in a multistep sequence from protected β-amino ester.[6] While the above strategies are useful, they have drawbacks in terms of generality and the multistep sequences involved. We reasoned that the addition of silyloxy dienes or metal enolates derived from substituted methyl enones to imines[7] would offer a straightforward single-step access to the building block **9** (Scheme 1). To accomplish this challenge, we relied on the direct addition of enolates/silyl enol ethers derived from the enones **12** to nonracemic sulfinimines **11**. The reliable and predictable selectivities observed in the nucleophilic addition reactions of sulfinimines[8] should yield the *N*-

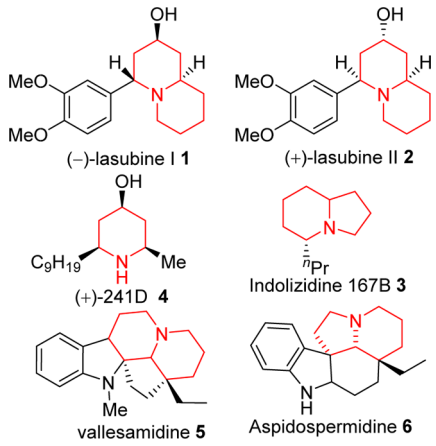


Figure 1. Natural products possessing the quinolizidine and indolizidine framework.

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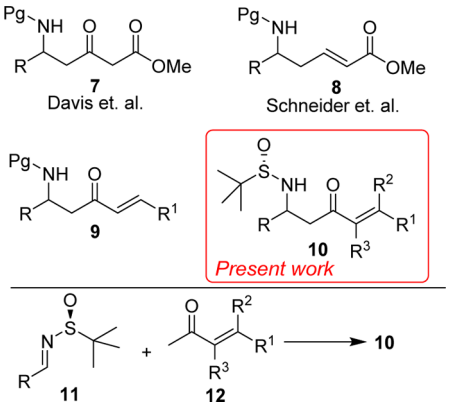
Scheme 1. Chiral Building Blocks 7−9 Commonly Utilized in the Synthesis of Quinolizidine and Piperidine Alkaloids (Pg = Protecting Group)

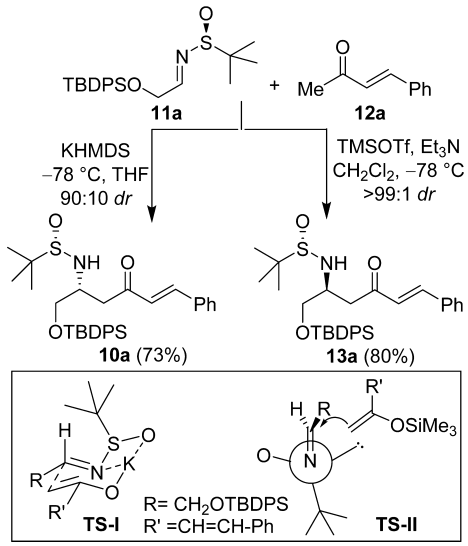


sulfinamido β-amino enones **10** structurally similar to the building block **9**. The ease in the removal of the sulfinyl auxiliary in **10** and the simultaneous intramolecular Michael addition reaction of the resultant β-amino enones should lead to functionalized piperidinone. Interestingly, in spite of a variety of nucleophilic addition reactions of sulfinimines reported, the direct addition of substituted enones to sulfinimines was never examined.

At the outset, the study commenced with the addition of α,β-unsaturated phenyl methyl ketone **12a** to sulfinimine **11a** using LHMDS as base. The reaction proceeded smoothly and afforded a 75:25 separable mixture of diastereomers **10a**/**13a** in 90% yield with the major isomer **10a** isolated in 65% yield by column chromatography. Performing the reaction with NaHMDS as base did not improve the diastereomeric ratio of the products, while the use of KHMDS as base improved the diastereomeric ratio of the products **10a**/**13a** to 90:10 (92% yield) and the major isomer **10a** was isolated in 73% yield. Interestingly, addition of the trimethylsilyl enol ether derived from **12a** furnished the products **13a**/**10a** in a >99:1 diastereomeric ratio, with **13a** as the major diastereomer isolated in 80% yield (Scheme 2). The intriguing outcome can be tentatively explained by the Davis chelation and open-chain models **TS-I** and **TS-II**, respectively, proposed previously[9] for the reaction of metal enolates with sulfinimines and Lewis acid catalyzed addition of organometallics.

The generality of the procedure was further exemplified by employing various silyl enol ethers **14a−l** derived from structurally different β-substituted enones in the reaction with sulfinimine **11a**. As evident from Chart 1, addition of silyl enol ethers obtained from β-aryl enones **12b−e** as well as β-aryl-α-methyl enones **12f−g** proceeded smoothly to afford the products **13b−g** in up to >99:1 diastereomeric ratio and in good yields. Silyl enol ether prepared from enone **12i** possessing β-benzyloxy methyl substitution afforded the product with >99:1 diastereoselectivity. Reaction of silyl enol ether **14k** having β-ester substitution furnished the product **13k** with excellent selectivity (>99:1) albeit in poor 12% yield. A quick examination of the effect of substitution on the sulfinimine in the reaction outcome was also investigated. Thus, addition of silyl enol ether **14a** to the sulfinimine **11b** derived from acetaldehyde proceeded with good dr of 90:10 (81% yield), while employing the sulfinimine **11c** obtained from isobutyraldehyde afforded the product **13m** in 22% yield

Scheme 2. Addition of Metal Enolate/Silyl Enol Ether Derived from α,β-Unsaturated Aryl Methyl Ketone 12a to Sulfinimine 11a



(dr > 99:1). It is interesting to note that the sulfinimines **11d−f** prepared from benzaldehyde, cyclohexanecarbaxaldehyde, and pivalaldehyde did not furnish the product at all. However, reaction of the potassium enolate of the enone **12a** with sulfinimines **11d** and **11e** furnished the products **10n** and **10o** in 75% and 48% yield with 90:10 and 96:4 diastereomeric ratios, respectively.

The synthetic utility of the resultant β-*N*-sulfinamido ketones was demonstrated in the total synthesis of quinolizidine alkaloids (−)-lasubine I (**1**) and (+)-lasubine II (**2**)[10] and the piperidine alkaloid (+)-241-D (**4**). Accordingly, treatment of silyl enol ether **14d** with the sulfinimine **11g** (synthesized from 5-bromopenten-1-al) afforded the product **13p** in 63% yield with 85:15 diastereomeric ratio. Removal of the sulfinyl group using HCl furnished the free amine hydrochloride salt which on treatment with DBU furnished the diastereomerically pure *cis*- and *trans*-quinolizidinones **15** and **16** in 41% and 35% yield, respectively, involving an in situ tandem Michael addition/displacement of bromine. Reduction of the ketone in **15** with LAH furnished 2-*epi*-lasubine II, which on Mitsunobu inversion provided (+)-lasubine II (**2**) in 81% yield, the spectral and physical data of which are in complete agreement with those reported in literature.[10d] Reduction of the ketone in *trans*-quinolidizinone (**16**) to (−)-lasubine I (**1**) using L-Selectride is a procedure reported in literature (Scheme 3), thus constituting the formal synthesis.[10d] Synthesis of lasubines I and II depicted in the present strategy is one of the shortest syntheses of lasubine alkaloids.

Synthesis of the alkaloid (+)-241-D (**4**) was accomplished by the following sequence. The β-sulfinamido ketone **13q** was synthesized by addition of silyl enol ether **14j** to the sulfinimine **11b** in 62% yield. Removal of the sulfinyl group in **13q** with HCl in MeOH and neutralization with Et_3N resulted in the piperidinone **17** in 84% yield. Reduction of the ketone in **17** with $NaBH_4$ as described in literature[2d,11] furnished the natural product (+)-241D (**4**) in 82% yield (Scheme 4).

In conclusion, addition of silylenol ethers obtained from substituted enones to chiral sulfinimines with very high selectivity was presented. The reaction proceeds with excellent diastereoselectivity, and products were obtained in good yields.

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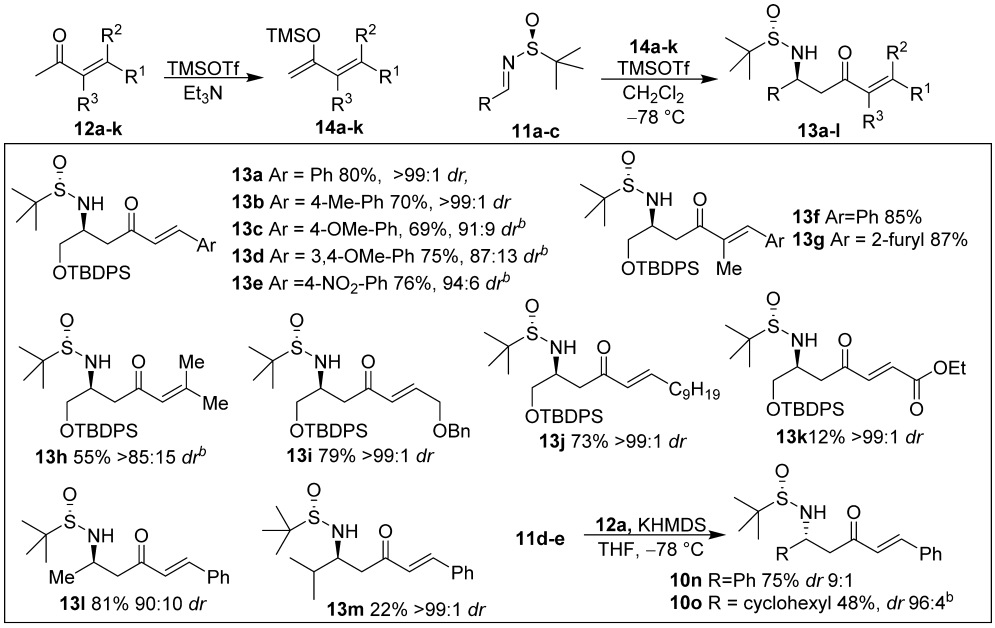
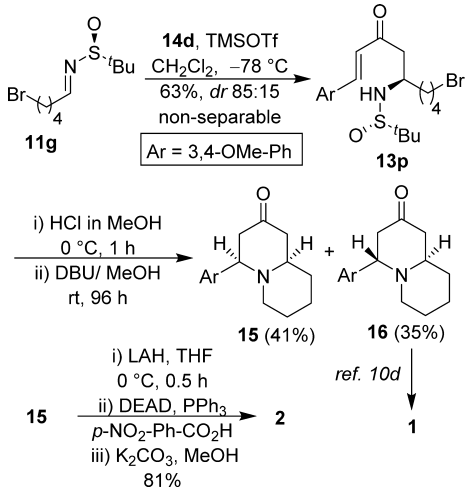
Chart 1. Addition of Silyl Enol Ethers Derived from Substituted Methyl Enones to Sulfinimines[a]



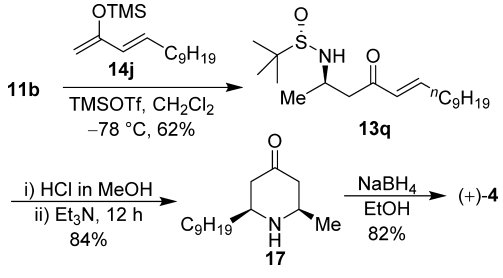
11a R = $CH_2OTBDPS$, **11b** R = Me, **11c** R = ^{i}Pr, **11d** R =Ph, **11e** R = cyclohexyl, **11f** R = ^{t}Bu
12a R^1= Ph; R^2, R^3= H, **12b** R^1= 4-MePh; R^2, R^3= H, **12c** R^1= 4-OMePh; R^2, R^3= H, **12d** R^1= 3,4-OMePh; R^2, R^3= H
12e R^1= 4-NO_2-Ph; R^2, R^3= H, **12f** R^1= Ph; R^2= H, R^3= Me, **12g** R^1= 2-furyl; R^2= H, R^3= Me, **12h** R^1= R^2= Me, R^3= H
12i R^1= CH_2OBn; R^2, R^3= H **12j** R^1= C_9H_9; R^2, R^3= H, **12k** R^1= CO_2Et; R^2, R^3= H

[a]All reactions were performed with freshly prepared silyl enol ethers **14a–k** from ketones **12a–k**. [b]Nonseparable mixture of diastereomers.

Scheme 3. Total Synthesis of (−)-Lasubine I (1) and (+)-Lasubine II (2)



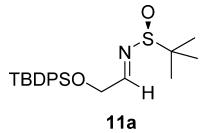
Scheme 4. Total Synthesis of (+)-241D (4)



Application of the resultant *β*-*N*-sulfinamido ketones was demonstrated in a concise enantioselective total synthesis of a collection of natural products such as quinolizidine alkaloids lasubines I and II and the piperidine alkaloid 241D.

EXPERIMENTAL SECTION

General Procedures. Column chromatography was performed on silica gel, Acme grade 100–200 mesh. TLC plates were visualized with UV, in an iodine chamber, or with phosphomolybdic acid spray, unless noted otherwise. All reagents were purchased from commercial sources and used without additional purification. THF was freshly distilled over Na–benzophenone ketyl. Melting points were uncorrected. Unless stated otherwise, ^{1}H and ^{13}C NMR spectra were recorded on a 400 MHz machine in $CDCl_3$ as solvent with TMS as reference unless otherwise indicated. High-resolution mass spectra (HRMS) were recorded on a Q-TOF micromass spectrometer using electron spray ionization mode. Sulfinimines **11a–g** were prepared according to the procedure described by Ellamn's group.[12] Aryl methyl enones **12b–d** were synthesized according to the procedure described in literature.[13] Compounds **12e–k** were synthesized according to literature procedures.[14]



11a

Preparation of (*S*$_S$,*E*)-*N*-(2-((*tert*-Butyldiphenylsilyl)oxy)-ethylidene)-2-methylpropane-1-sulfinamide (11a). To a stirred solution of ((*tert*-butyldiphenylsilyl)oxy)acetaldehyde (1.054 g, 3.55 mmol) and (*S*)-*tert*-butanesulfinamide (0.429 g, 3.5 mmol) in dry CH_2Cl_2 (11 mL) at room temperature was added oven-dried $CuSO_4$ (1.58 g, 10.5 mmol), and the reaction mixture was stirred for 12 h at the same temperature. After completion of the reaction (TLC), the reaction mixture was filtered through a short pad of Celite. Evaporation of solvent followed by silica gel column chromatography of the resulting crude residue with petroleum ether/EtOAc as eluent afforded the sulfinimine **11a** in 84% yield (1.2 g) as a colorless oil. $[\alpha]_D^{24}$ +94.6 (*c* 0.5, $CHCl_3$). IR (neat): 3359, 3070, 2857, 1630, 1427,

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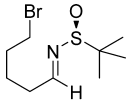
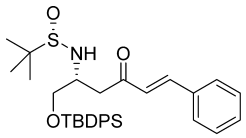
1083 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.10 (t, J = 3.2 Hz, 1H), 7.67 (d, J = 6.8 Hz, 4H), 7.50−7.32 (m, 6H), 4.56 (d, J = 2.8 Hz, 2H), 1.18 (s, 9H), 1.08 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 168.2, 135.5 (2 × C), 135.49 (2 × C), 132.8, 129.9, 127.82 (2 × C), 127.81 (2 × C), 66.1, 56.8, 26.7 (3 × C), 22.3 (3 × C), 19.2. HRMS: m/z calcd for $C_{22}H_{31}NO_2SSi$ + Na 424.1742, found 424.1743.



11g

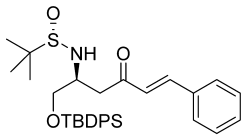
Preparation of (*S*$_S$,*E*)-*N*-(5-Bromopentylidene)-2-methylpropane-2-sulfinamide (11g). To a stirred solution of 5-bromopentanal (1.65 g, 9.8 mmol) and (*S*)-*tert*-butanesulfinamide (1.17 g, 9.7 mmol) in dry CH_2Cl_2 (30 mL) at room temperature was added oven-dried $CuSO_4$ (4.4 g, 29.4 mmol), and the mixture was stirred for 12 h. After completion of reaction (by TLC), the reaction mixture was filtered through a short pad of Celite. Evaporation of solvent followed by silica gel column chromatography of the resulting crude residue with petroleum ether/EtOAc as eluent afforded the sulfinimine **11g** in 87% yield (2.18 g) as a yellow oil. $[\alpha]_D^{24}$ +186.5 (c 0.65, $CHCl_3$). IR (neat): 1634, 1270, 1135, 1018 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.11 (t, J = 4.0 Hz, 1H), 3.5 (dt, J = 6.4, 2.8 Hz, 2H), 2.79−2.65 (m, 2H), 2.31−2.14 (m, 2H), 1.19 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.7, 56.6, 34.3, 32.5, 28.0, 22.3 (3 × C). HRMS: m/z calcd for $C_9H_{18}BrNOS$ + Na 290.0190, found 290.0193.



10a

(*Ss*)-*N*-((*R*,*E*)-1-((*tert*-Butyldiphenylsilyl)oxy)-4-oxo-6-phenylhex-5-en-2-yl)-2-methylpropane-2-sulfinamide (10a). To a precooled (−78 °C), stirred solution of benzylideneacetone **12a** (0.08 g, 0.55 mmol) in dry THF (14 mL) under argon atmosphere at −78 °C was added KHMDS (0.5 M solution in toluene 1.64 mL, 0.82 mmol). The reaction mixture was stirred for 1 h at the same temperature, and the sulfinimine **11a** (0.1 g, 0.25 mmol) dissolved in 5 mL dry THF was added at −78 °C. Then the reaction mixture was stirred at the same temperature for an additional 2 h, quenched by addition of saturated NH_4Cl solution (20 mL), and extracted with EtOAc (2 × 20 mL). The organic layer was washed with brine (20 mL) and dried over Na_2SO_4. Evaporation of solvent followed by silica gel column chromatography of the resulting crude residue with petroleum ether/EtOAc as eluent afforded the sulfinamide **10a** in 92% yield (0.125 g) as a 90:10 diastereomeric mixture). The major isomer was separated using silica gel column chromatography in 73% yield (0.102 g) as a gummy mass. $[\alpha]_D^{24}$ −25.8 (c 0.9, $CHCl_3$). IR (neat): ν_{max} 3290, 2957, 1660, 1609, 1110, 1067 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.68−7.47 (m, 7H), 7.48−7.27 (m, 9H), 6.70 (d, J = 16.4 Hz, 1H), 4.20 (d, J = 8.8 Hz, 1H), 3.94−3.69 (m, 3H), 3.25 (m, 2H), 1.19 (s, 9H), 1.06 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.8, 143.3, 135.49 (2 × C), 135.47 (2 × C), 134.3, 133.0, 132.9, 130.6, 129.8, 128.9 (2 × C), 128.4 (2 × C), 127.76 (2 × C), 127.74 (2 × C), 126.5, 65.9, 55.9, 54.8, 42.5, 26.8 (3 × C), 22.5 (3 × C), 19.3. HRMS: m/z calcd for $C_{32}H_{41}NO_3SSi$ + Na570.2474, found 570.2475.

General Procedure for the Addition of Silyl Enol Ethers 14a−l Derived from Enones 12a−l to the Sulfinimines 11a−g. The following preparation of **13a** is representative.

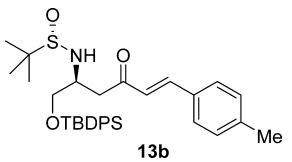


13a

Procedure A. To a precooled solution of benzylideneacetone **12a** (0.1 g, 0.68 mmol) in dry CH_2Cl_2 (5 mL) at 0 °C under argon atmosphere was added Et_3N (0.19 mL, 1.4 mmol) followed by TMSOTf (0.18 mL, 1 mmol). The reaction mixture was stirred for 1 h at the same temperature. After completion of the reaction (TLC), it was quenched by addition of saturated $NaHCO_3$ solution (20 mL). The reaction mixture was diluted with petroleum ether (30 mL) and stirred for 5 min. The organic layer was separated, washed with water (20 mL) and brine (20 mL), and dried over Na_2SO_4. Evaporation of solvent gave the silyl enol ether, which was used in the next step without further purification.

A solution of the crude silyl enol ether (obtained above) in dry CH_2Cl_2 (5 mL) under argon atmosphere was cooled to −78 °C, and sulfinimine **11a** (0.1 g, 0.25 mmol) dissolved in dry CH_2Cl_2 (5 mL) was added. TMSOTf (0.09 mL, 0.5 mmol) was introduced into the reaction mixture, and the resulting mixture was stirred for 0.5 h at −78 °C. After completion of the reaction (TLC), it was quenched by addition of saturated $NaHCO_3$ solution (20 mL) and extracted with EtOAc (2 × 20 mL). The organic layer was washed with brine and dried over Na_2SO_4. Evaporation of solvent followed by silica gel column chromatography of the resulting crude residue with petroleum ether/EtOAc as eluent afforded the product **13a** in 80% yield (0.11 g) as a colorless solid. Mp: 98−102 °C. $[\alpha]_D^{24}$ +10.6 (c 0.9, $CHCl_3$). IR (KBr): 3290, 2957, 1660, 1609, 1110, 1067 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.72−7.62 (m, 4H), 7.55−7.50 (m, 3H), 7.43−7.32 (m, 9H), 6.69 (d, J = 16.4 Hz, 1H), 4.08 (d, J = 7.2 Hz, 1H), 4.02−3.90 (m, 2H), 3.83 (dd, J = 10.0, 4.4 Hz, 1H), 3.06 (dd, J = 16.4, 6.4 Hz, 1H), 2.86 (dd, J = 16.4, 5.2 Hz 1H), 1.18 (s, 9H), 1.09 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.9, 143.1, 135.6 (2 × C), 135.5 (2 × C), 134.3, 133.1, 132.7, 130.6, 129.8, 128.9 (2 × C), 128.3 (2 × C)127.8 (5 × C), 126.2, 66.3, 55.8, 54.2, 43.3, 26.9 (3 × C), 22.5 (3 × C), 19.3. HRMS: m/z calcd for $C_{32}H_{41}NO_3SSi$ + Na 570.2474, found 570.2476.

Procedure B. To a precooled solution of benzylideneacetone **12a** (0.1 g, 0.68 mmol) in dry CH_2Cl_2 (5 mL) at 0 °C was added Et_3N (0.19 mL, 1.4 mmol) followed by TMSOTf (0.18 mL, 1 mmol) under argon atmosphere. The reaction mixture was stirred for 1 h at the same temperature and cooled to −78 °C, and sulfinimine **11a** (0.1 g, 0.25 mmol) dissolved in 5 mL of CH_2Cl_2 was added at −78 °C followed by addition of a second portion of TMSOTf (0.09 mL, 0.5 mmol). The reaction mixture was stirred for 0.5 h at −78 °C. After completion of the reaction (TLC), it was quenched by addition of saturated $NaHCO_3$ solution (20 mL) and extracted with EtOAc (2 × 20 mL). The organic layer was washed with water and brine (20 mL) and dried over Na_2SO_4. Evaporation of solvent followed by silica gel column chromatography of the resulting crude residue with petroleum ether/EtOAc as eluent afforded the product **13a** in 78% yield (0.11 g) as a colorless solid. The spectral data are same as described above.



13b

Compound **13b** was prepared from 4-methylbenzylideneacetone (**12b**) (0.1 g, 0.62 mmol) and sulfinimine **11a** (0.1 g, 0.25 mmol) using procedure A described above in 70% yield (0.097 g) as a gummy mass. $[\alpha]_D^{24}$ +7.7 (c 0.66, $CHCl_3$). IR (neat): 3709, 2958, 2855, 1659, 1425, 1111 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.71−7.58 (m, 4H), 7.49 (d, J = 16.4 Hz, 1H), 7.48−7.29 (m, 8H), 7.21 (d, J = 8.0 Hz, 2H), 6.67 (d, J = 16.0 Hz, 1H), 4.09 (d, J = 7.2 Hz, 1H), 4.05−3.86 (m, 2H), 3.83 (dd, J = 10.0, 4.4 Hz, 1H), 3.05 (dd, J = 16.4, 6.8 Hz, 1H), 2.85 (dd, J = 16.4, 5.6 Hz, 1H), 2.39 (s, 3H), 1.18 (s, 9H), 1.09 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.0, 143.2, 141.2, 135.6 (2 × C), 135.5 (2 × C), 133.1, 132.8, 131.5, 129.8, 129.7 (2 × C), 128.4 (2 × C), 127.8 (5 × C), 125.3, 66.4, 55.8, 54.3, 43.2, 26.9 (3 × C), 22.5 (3 × C), 21.5, 19.3. HRMS: m/z calcd for $C_{33}H_{43}NO_3SSi$ + Na 584.2631, found 584.2631.

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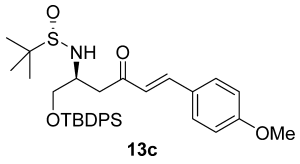
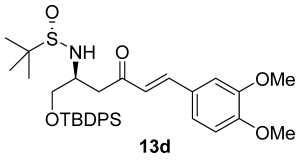


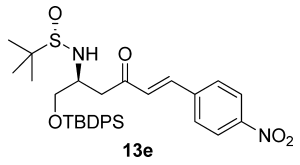
13c

Compound **13c** was prepared from 4-methoxybenzylideneacetone (**12c**) (0.1 g, 0.57 mmol) and sulfinimine **11a** (0.1 g, 0.25 mmol) using procedure A described above in 69% yield (0.09 g) as an inseparable mixture (91:9) of diastereomers as a gummy mass. $[\alpha]_D^{24}$ +6.4 (*c* 1.09, $CHCl_3$). IR (neat): 3069, 2839, 1683, 1600, 1250, 1111, 1027 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.72−7.58 (m, 4.5H), 7.54−7.45 (m, 3.4H), 7.44−7.29 (m, 6.5H), 6.92 (d, *J* = 8.8 Hz, 2H), 6.57 (d, *J* = 16.4 Hz, 1H, major), 6.05 (d, *J* = 12.8 Hz, 0.1H, minor), 4.09 (d, *J* = 7.2 Hz, 1H), 4.03−3.85 (m, 2H), 3.85 (s, 3H), 3.84−3.81 (m, 1H), 3.80−3.69 (m, 1H), 3.03 (dd, *J* = 16.4, 6.8 Hz, 1H), 2.83 (dd, *J* = 16.0, 5.2 Hz, 1H), 1.2 (s, 9H, major), 1.16 (s 1H, minor), 1.08 (s, 9H, major), 1.04 (s, 1H, minor). ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.9, 161.7, 142.9, 135.6 (2 × C), 135.5 (2 × C), 133.1, 132.8, 130.1(2 × C), 129.8, 127.8 (5 × C), 126.96, 124.0, 114.4 (2 × C), 66.4, 55.8, 55.4, 43.2, 26.9 (3 × C), 22.5 (3 × C), 19.3. HRMS: *m*/*z* calcd for $C_{33}H_{43}NO_4$ SSi + Na 600.2580, found 600.2580.



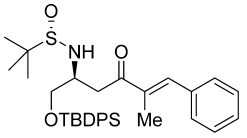
13d

Compound **13d** was prepared from 3,4-dimethoxybenzylideneacetone (**12d**) (0.1 g, 0.48 mmol) and sulfinimine **11a** (0.1 g, 0.25 mmol) using procedure A described above in 75% yield (0.12 g) as an inseparable mixture (87:13) of diastereomers as a gummy mass. $[\alpha]_D^{24}$ +4.7 (*c* 4.9, $CHCl_3$). IR (neat): 3198, 2929, 2819, 1678, 1456, 1085 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.77−7.55 (m, 4.5H), 7.46 (d, *J* = 16 Hz, 1H), 7.48−7.29 (m, 6.7H), 7.16 (dd, *J* = 8.4, 2.0 Hz, 0.13H, minor), 7.11 (dd, *J* = 8.0, 1.6 Hz, 1H, major), 7.05 (d, *J* = 2 Hz, 1H), 6.88 (d, *J* = 8.0 Hz, major), 6.81 (d, *J* = 8.4 Hz, minor) (1 H), 6.58 (d, *J* = 16.4 Hz, major), 6.08 (d, *J* = 12.8 Hz, minor) (1 H), 4.10 (d, *J* = 7.2 Hz, 1H), 4.07−3.93 (m, 9H), 3.83 (dd, *J* = 9.6, 4.4 Hz, 1H), 3.06 (dd, *J* = 16.4, 6.8 Hz, 1H), 2.86 (dd, *J* = 16.0, 5.2 Hz, major), 2.71 (dd, *J* = 16.8, 5.6 Hz, minor) (1 H), 1.18 (s, major), 1.16 (s, minor) (9 H), 1.09 (s, major), 1.05 (s, minor) (9 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.8, 151.4, 149.2, 143.2, 135.6 (2 × C), 133.1, 132.8, 129.8, 129.7, 127.7 (3 × C), 127.2, 124.2, 123.2, 111.0, 109.7, 66.3, 56.0, 55.9, 55.8, 54.3, 43.1, 26.9 (3 × C), 22.5 (3 × C), 16.3. HRMS: *m*/*z* calcd for $C_{34}H_{45}NO_5SSi$ + Na 630.2685, found 630.2687.



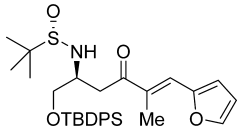
13e

Compound **13e** was prepared from 4-nitrobenzylideneacetone (**12e**) (0.1 g, 0.5 mmol) and sulfinimine **11a** (0.1 g, 0.25 mmol) using procedure A described above in 76% yield (0.112 g) as an inseperable mixture (94:6) of diastereomeric ratio as a gummy mass. $[\alpha]_D^{24}$ +12.6 (*c* 1.63, $CHCl_3$). IR (neat): 3419, 2929, 2856, 1656, 1600, 1344, 1112 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.25 (d, *J* = 8.4 Hz, 1.84H, major), 8.15 (d, *J* = 8.4 Hz, 0.12H, minor), 7.70−7.60 (m, 6H), 7.52 (d, *J* = 16.4 Hz, 1H), 7.47−7.31 (m, 6H), 6.78 (d, *J* = 16.0 Hz, 1H, major), 6.34 (d, *J* = 12.8 Hz 0.06H, minor), 4.12 (d, *J* = 6.8 Hz, 1H), 4.07−3.86 (m, 2H), 3.84 (dd, *J* = 9.6, 4.4 Hz, 1H), 3.11 (dd, *J* = 16.8, 6.8 Hz, 1H), 2.90 (dd, *J* = 16.8, 5.2 Hz, 1H), 1.18 (s, 9H, major), 1.16 (s, 0.7H, minor), 1.08 (s, 9H, major), 1.05 (s, 0.6H, minor). ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.3, 148.6, 140.5, 139.8, 135.6 (2 × C), 135.5 (2 × C), 133.0, 132.7, 129.9, 129.4, 128.8 (2 × C), 127.8 (5 × C), 124.1, 66.2, 55.9, 53.9, 43.9, 26.8 (3 × C), 22.5 (3 × C), 19.3. HRMS: *m*/*z* calcd for $C_{32}H_{40}N_2O_5SSi$ + Na 615.2325, found 615.2318.



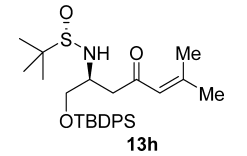
13f

Compound **13f** was prepared from (*E*)-3-methyl-4-phenylbut-3-en-2 one (**12f**) (0.15 g, 0.94 mmol) and sulfinimine **11a** (0.1 g, 0.25 mmol) using procedure A described above in 85% yield (0.12 g) as a gummy mass. $[\alpha]_D^{24}$ +14.9 (*c* 0.7, $CHCl_3$). IR (neat): 3062, 2956, 2858, 1663, 1111, 1067 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.71−7.58 (m, 4H), 7.51−7.31 (m, 12H), 4.09 (d, *J* = 7.6 Hz, 1H), 4.04−3.87 (m, 2H), 3.84 (d, *J* = 6.4 Hz, 1H), 3.19 (dd, *J* = 16.8, 6.8 Hz, 1H), 2.98 (dd, *J* = 16.8, 5.2 Hz, 1H), 2.01 (s, 3H), 1.18 (s, 9H), 1.09 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 200.1, 139.2, 137.5, 135.7, 135.6 (2 × C), 135.5 (2 × C), 133.2, 132.8, 129.8, 129.7 (2 × C), 128.6, 128.5 (2 × C), 127.8 (5 × C), 66.4, 55.8, 54.8, 40.2, 26.9 (3 × C), 22.5 (3 × C), 19.3, 13.0. HRMS: *m*/*z* calcd for $C_{33}H_{43}NO_3SSi$ + Na 584.2631, found 584.2631.



13g

Compound **13g** was prepared from (*E*)-4-(furan-2-yl)-3-metylbut-3-en-2 one (**12g**) (0.1 g, 0.625 mmol) and sulfinimine **11a** (0.1 g, 0.25 mmol) using procedure A described above in 87% yield (0.119 g) as a yellow gummy mass. $[\alpha]_D^{24}$ +8.1 (*c* 2.25, $CHCl_3$). IR (neat): 3068, 2932, 2860, 1659, 147, 1111, 1068 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.70−7.60 (m, 4H), 7.59 (s, 1H), 7.48−7.29 (m, 6H), 7.22 (s, 1H), 6.67 (d, *J* = 3.6 Hz, 1H), 6.54 (dd, *J* = 3.2, 2.0 Hz, 1H), 4.06 (d, *J* = 7.2 Hz, 1H), 4.01−3.85 (m, 2H), 3.82 (dd, *J* = 9.6, 4.0 Hz, 1H), 3.12 (dd, *J* = 16.4, 6.8 Hz, 1H), 2.91 (dd, *J* = 16.8, 5.6 Hz, 1H), 2.09 (s, 3H), 1.17 (s, 9H), 1.08 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.0, 151.6, 144.5, 135.5 (2 × C), 135.4 (2 × C), 133.6, 133.1, 132.8, 129.8, 127.7 (5 × C), 126.1, 115.5, 112.3, 66.3, 55.7, 54.7, 39.8, 26.8 (3 × C), 22.4 (3 × C), 19.2, 12.8. HRMS: *m*/*z* calcd for $C_{31}H_{41}NO_4SSi$ + Na 574.2423, found 574.2421.



13h

Compound **13h** was prepared from mesityl oxide (**12h**) (0.15 g, 1.53 mmol) and sulfinimine **11a** (0.1 g, 0.25 mmol) using procedure A described above in 55% yield (0.068 g as an inseparable 85:15 mixture of diastereomers) as a pale yellow liquid. $[\alpha]_D^{24}$ +18.4 (*c* 0.83, $CHCl_3$). IR (neat): 3437, 2931, 1685, 1621, 1427, 1110, 1068 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.71−7.57 (m, 4H), 7.49−7.30 (m, 6H), 6.15 (s, minor), 6.03 (s, major) (1 H), 4.26 (d, *J* = 8.4 Hz, minor), 4.03 (d, *J* = 7.2 Hz, major) (1H), 3.95−3.84 (m, 2H), 3.83−3.69 (m, 1H), 2.78 (dd, *J* = 16.4, 6.8 Hz, 1H), 2.62 (dd, *J* = 16.4, 5.2 Hz, 1H, major), 2.54 (dd, *J* = 12.8, 4.8 Hz, 0.15H, minor), 2.13 (s, 0.42H), 2.10 (s, 3H), 1.88 (s, 3H, major), 1.85 (s, 0.47H), 1.17 (s, major), 1.14 (s, minor) (9H), 1.08 (s, minor), 1.07 (s, major) (9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.3, 156.0, 135.6 (2 × C), 135.5 (2 × C), 133.2, 132.8, 129.77, 129.76, 127.74 (2 × C), 127.73 (2 × C), 123.8, 66.4, 55.7, 54.2, 46.7, 27.7, 26.8 (3 × C), 22.5 (3 × C), 20.8, 19.3. HRMS: *m*/*z* calcd for $C_{28}H_{41}NO_3SSi$ + Na 522.2474, found 522.2474.

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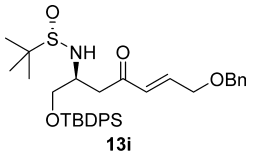
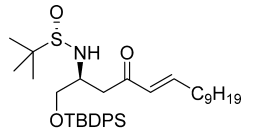


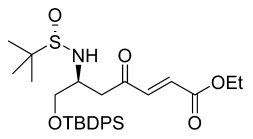
13i

Compound **13i** was prepared from (*E*)-5-(benzyloxy)pent-3-en-2-one (**12i**) (0.1 g, 0.5 mmol) and sulfinimine **11a** (0.1 g, 0.25 mmol) using procedure A described above in 79% yield (0.12 g) as a gummy mass. $[\alpha]_D^{24}$ +23.5 (*c* 1.0, $CHCl_3$). IR (neat): 3359, 3060, 2954, 1669, 1684, 1256, 1070 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.70−7.57 (m, 3H), 7.48−7.25 (m, 11H), 6.79 (dt, *J* = 16.0, 4.0 Hz, 1H), 6.36 (d, *J* = 16.0 Hz, 1H), 4.56 (s, 2H), 4.18 (dd, *J* = 4.0, 1.6 Hz, 2H), 4.01 (d, *J* = 6.8 Hz, 1H), 3.99−3.38 (m, 2H), 3.82−3.71 (m, 1H), 2.95 (dd, *J* = 16.8, 6.4 Hz, 1H), 2.75 (dd, *J* = 16.8, 5.2 Hz, 1H), 1.17 (s, 9H), 1.07 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.7, 142.7, 137.5, 135.6 (2 × C), 135.5 (2 × C), 133.1, 132.8, 129.8, 129.3, 128.5 (2 × C), 127.9, 127.8 (5 × C), 127.6 (2 × C), 72.9, 68.7, 66.3, 55.8, 53.9, 43.1, 26.9 (3 × C), 22.5 (3 × C), 19.2. HRMS: *m*/*z* calcd for $C_{34}H_{45}NO_4SSi$ + Na 0.614.2736, found 614.2735.



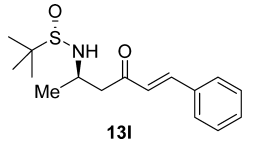
13j

Compound **13j** was prepared from (*E*)-tridec-3-en-2-one (**12j**) (0.098 g, 0.5 mmol) and sulfinimine **11a** (0.1 g, 0.25 mmol) using procedure A described above in 73% yield (0.107 g) as a gummy mass. $[\alpha]_D^{24}$ +18.2 (*c* 1.0, $CHCl_3$). IR (neat): 3406, 2989, 1647, 1015 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.70−7.57 (m, 4H), 7.49−7.31 (m, 6H), 6.79 (dt, *J* = 16.0, 6.8 Hz, 1H), 6.05 (d, *J* = 16.0 Hz, 1H), 4.02 (d, *J* = 6.8 Hz, 1H), 3.98−3.82 (m, 2H), 3.81−3.71 (m, 1H), 2.93 (dd, *J* = 16.4, 5.2 Hz, 1H), 2.72 (dd, *J* = 16.8, 5.2 Hz, 1H), 2.19 (q, *J* = 7.2 Hz, 2H), 1.51−1.38 (m, 2H), 1.27 (m, 12H), 1.17 (s, 9H), 1.07 (s, 9H), 0.88 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.2, 148.3, 135.6 (2 × C), 135.5 (2 × C), 133.2, 132.8, 130.4, 129.8, 127.8 (5 × C), 66.4, 55.8, 54.2, 42.5, 32.5, 31.8, 29.5, 29.4, 29.3, 29.2, 28.0, 26.9 (3 × C), 22.6, 22.5 (2 × C), 19.3, 14.1. HRMS: *m*/*z* calcd for $C_{35}H_{55}NO_3SSi$ + Na 620.3570, found 620.3571.



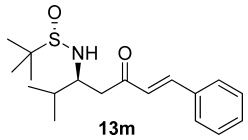
13k

Compound **13k** was prepared from (*E*)-ethyl 4-oxopent-2-enoate (**12k**) (0.08 g, 0.56 mmol) and sulfinimine **11a** (0.09 g, 0.22 mmol) using procedure A described above in 12% yield (0.015 g) as a gummy mass. $[\alpha]_D^{24}$ +8.7 (*c* 0.765, $CHCl_3$). IR (neat): 3726, 2928, 2861, 2313, 1727, 1644, 1018 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.70−7.56 (m, 3H), 7.50−7.31 (m, 6H), 6.99 (d, *J* = 16.0 Hz, 1H), 6.58 (d, *J* = 16.0 Hz, 1H), 4.27 (q, *J* = 7.2 Hz, 2H), 3.98 (d, *J* = 7.2 Hz, 1H), 3.95−3.83 (m, 2H), 3.82−3.71 (m, 1H), 2.99 (dd, *J* = 17.2, 6.8 Hz, 1H), 2.80 (dd, *J* = 17.2, 4.8 Hz, 1H), 1.33 (t, *J* = 7.2 Hz, 3H), 1.17 (s, 9H), 1.07 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 197.5, 165.3, 139.1, 135.9 (2 × C), 135.5 (2 × C), 132.9, 132.6, 131.2, 129.9 (2 × C), 127.8 (4 × C), 66.2, 61.5, 55.9, 53.7, 44.1, 26.9 (3 × C), 19.2, 14.1. HRMS: *m*/*z* calcd for $C_{29}H_{41}NO_5SSi$ + Na 566.2372, found 566.2372.



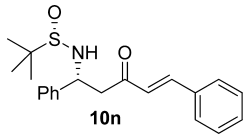
13l

Compound **13l** was prepared from benzylideneacetone **12l** (0.146 g, 1 mmol) and (S_S,*E*)-*N*-ethylidene-2-methylpropane-2-sulfinamide (**11b**) (0.07 g, 0.5 mmol) using procedure A described above in 81% yield (0.12 g) as a 90:10 separable mixture of diastereomers. Major diastereomer was isolated using silicagel column chromatography in 63% yield (0.087 g) as a gummy mass. $[\alpha]_D^{24}$ +22.4 (*c* 1.0, $CHCl_3$).IR (neat): 3386, 2957, 2924, 2854, 1714, 1243, 1017 cm-1.^1H NMR (400 MHz, $CDCl_3$) δ 7.59−7.49 (m, 3H), 7.43−7.34 (m, 3H), 6.71 (d, *J* = 16.2 Hz, 1H), 4.0−3.84 (m, 1H), 3.71 (d, *J* = 6.2 Hz, 1H), 3.06 (dd, *J* = 16.6, 7.6 Hz, 1H), 2.78 (dd, *J* = 16.6, 5.2 Hz, 1H), 1.94 (s, 1H), 1.39 (d, *J* = 6.7 Hz, 3H), 1.21 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.4, 143.2, 134.2, 130.6, 128.9, 128.3, 126.2, 55.6, 49.1, 48.5, 22.5, 22.0. HRMS: *m*/*z* for $C_{16}H_{23}NO_2S$ + Na calcd 316.1347, found 316.1351.



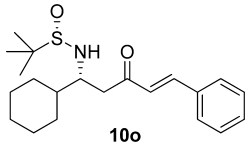
13m

Compound **13m** was prepared from benzylideneacetone **12a** (0.15 g, 1.0 mmol) and sulfinimine **11d** (0.09 g, 0.5 mmol) using procedure A described above in 22% yield (0.036 g) as a colorless liquid. $[\alpha]_D^{24}$ +22.4 (*c* 0.25, $CHCl_3$). IR (neat): 3410, 1651, 1602, 1458, 1130, 1018 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.62−7.45 (m, 3H), 7.44−7.34 (m, 3H), 6.76 (d, *J* = 16.0 Hz, 1H), 3.72−3.60 (m, 2H), 3.07−2.91 (m, 1H), 2.80 (dd, *J* = 16.0, 3.2 Hz, 1H), 2.22−1.99 (m, 1H), 1.17 (s, 9H), 1.02 (t, *J* = 6.0 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.7, 143.0, 134.3, 130.6, 128.9, 128.4, 126.2, 58.9, 56.1, 43.8, 32.1, 22.6, 16.3, 18.5. HRMS: *m*/*z* calcd for $C_{18}H_{27}NO_2S$ + Na 344.1660, found 344.1657.



10n

Compound **10n** was synthesized using procedure B as follows: To a precooled stirred solution (−78 °C) of benzylideneacetone **12a** (0.14 g, 0.96 mmol) in dry THF (14 mL) under argon atmosphere at −78 °C was added KHMDS (2.88 mL of 0.5 M solution in toluene, 1.44 mmol). The reaction mixture was stirred for 1 h at the same temperature. A solution of (*E*)-N-benzylidene-2-methylpropane-2-sulfinamide (**11c**) (0.1 g, 0.25 mmol) dissolved in 5 mL of dry THF was introduced at −78 °C, and the reaction mixture was stirred for 2 h at the same temperature. After completion of the reaction (TLC), it was quenched by addition of saturated NH_4Cl (20 mL) and extracted with EtOAc (2 × 20 mL). The organic layer was separated, washed with brine (20 mL), and dried over Na_2SO_4. Evaporation of solvent followed by silica gel column chromatography of the resulting crude residue with petroleum ether/EtOAc as eluent afforded the product **10n** in 96% yield (0.163 g in 90:10 diastereomeric ratio). Major isomer was separated using silica gel column chromatography in 75% yield (0.127 g) as a gummy mass. $[\alpha]_D^{24}$ +89.8 (c 0.215, $CHCl_3$). IR (neat): 3446, 3270, 2868, 1680, 1048 cm^{-1}. ^1H NMR (400 MHz, CDCl3): δ 7.59−7.44 (m, 3H), 7.45−7.28 (m, 8H), 6.68 (d, *J* = 16.4 Hz, 1H), 4.96−4.85 (pen, *J* = 3.6 Hz, 1H), 4.83 (d, *J* = 4.0 Hz, 1H), 3.28 (dd, *J* = 16.8, 4.4 Hz, 1H), 3.19 (dd, *J* = 16.8, 7.6 Hz, 1H), 1.23 (s, 9H). 13C NMR (100 MHz, $CDCl_3$): δ 198.5, 143.9, 140.95, 134.1, 130.8, 128.96 (2 × C), 128.6 (2 × C) 128.4, (2 × C), 127.9, 127.5 (2 × C), 125.96, 55.6, 55.3, 47.3, 22.6 (3 × C). HRMS: *m*/*z* calcd for $C_{21}H_{25}NO_2S$ + Na 378.1504, found 378.1504.



10o

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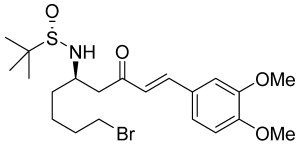
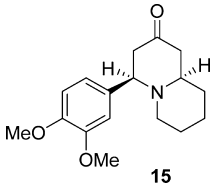
To a precooled stirred solution (−78 °C) of benzylideneacetone **12a** (0.12 g, 0.8 mmol) in dry THF (14 mL) under argon atmosphere at −78 °C was added KHMDS (2.5 mL of 0.5 M solution in toluene, 1.2 mmol). The reaction mixture was stirred for 1 h at the same temperature. A solution of sulfinimine **11e** (0.1 g, 0.47 mmol) dissolved in 5 mL of dry THF was introduced at −78 °C, and the reaction mixture was stirred for 2 h at the same temperature. After completion of the reaction (TLC), it was quenched by addition of saturated NH_4Cl (20 mL) and extracted with EtOAc (2 × 20 mL). The organic layer was separated, washed with brine (20 mL), and dried over Na_2SO_4. Evaporation of solvent followed by silica gel column chromatography of the resulting crude residue with petroleum ether/EtOAc as eluent afforded the product **10o** in 48% yield (0.08 g in 96:4 inseperable diastreomeric ratio). $[\alpha]_D^{24}$ +36.7 (c 1.4, $CHCl_3$). IR (neat): 3406, 2926, 2856, 1735, 1643, 1132, 1018 cm^{-1}. ^1H NMR (400 MHz, CDCl3): δ 7.64−7.49 (m 3H), 7.45−7.35 (m, 3H), 6.72 (d, J = 16.4 Hz, 1H), 4.19 (d, J = 8.8 Hz, 1H), 3.51−3.34 (m, 1H), 3.12 (d, J = 4.8 Hz, 2H), 1.93 (d, J = 12.4 Hz, 1H), 1.82−1.57 (m, 5H), 1.32−1.05 (m, 14H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 199.5, 143.2, 134.2, 130.6, 128.9, 128.4, 126.4, 59.0, 56.0, 43.2, 41.4, 29.9, 29.4, 26.3, 26.1, 26.0, 22.7. HRMS: m/z calcd for $C_{21}H_{31}NO_2S$ + Na 384.1973, found 384.1973.



13p

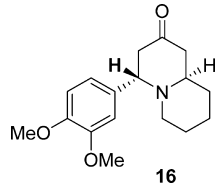
Compound **13p** was prepared from 3,4 dimethoxybenzylideneacetone (**12d**) (0.17 g, 0.8 mmol) and sulfinimine **11g** (0.1 g, 0.37 mmol) using procedure A described above in 63% yield (0.12 g as an inseparable mixture of diastereomers) as a green yellow oil. $[\alpha]_D^{24}$ +46.7 (c 2.4, $CHCl_3$). IR (neat): 3442, 2931, 2856, 1650, 1513, 1023 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.51 (d, J = 16.0 Hz, 1H), 7.20 (dd, J = 8.4, 1.6 Hz, 0.15H, minor), 7.13 (dd, J = 8.4, 1.6 Hz, 1H, major), 7.07 (d, J = 2.0 Hz, 1H), 6.87 (d, J = 8.4 Hz, 1H), 6.61 (d, J = 16.0 Hz, major), 6.11 (d, J = 12.8 Hz, minor) (1H), 3.98−3.82 (m, 8.8H), 3.43 (t, J = 6.8, 2H), 3.14 (dd, J = 16.8, 8 Hz, 1H), 2.82 (dd, J = 16.8, 4.4 Hz, 1H), 1.99−1.78 (m, 3H), 1.74−1.59 (m 3H), 1.19 (s, major), 1.16 (s, minor) (9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 198.4, 151.4, 149.2, 143.3, 127.2, 124.3, 123.2, 111.0, 109.7, 55.9, 55.8, 55.7, 53.0, 46.6, 34.0, 33.5, 32.2, 24.6, 22.5 (3 × C). HRMS: m/z calcd for $C_{21}H_{32}BrNO_4S$ + Na 496.1133, found 496.1131.

Preparation of Compounds 15 and 16. To a precooled, stirred solution of **13p** (0.1 g, 0.21 mmol) in MeOH (5 mL) at 0 °C was added a saturated solution of HCl in MeOH (0.5 mL). The reaction mixture was stirred for 1 h at the same temperature. After completion of the reaction (TLC), the solvent was evaporated off, and the resultant solid was dissolved in MeOH (12 mL), DBU (0.125 mL, 0.84 mmol) was added. The reaction mixture was stirred for 4 days at rt. The solvent was evaporated off, and the residue was diluted with water (20 mL) and extracted with EtOAc (2 × 20 mL). The organic layer was washed with brine and dried over Na_2SO_4. Evaporation of solvent followed by silica gel column chromatography of the resulting crude residue with petroleum ether/EtOAc as eluent afforded the products **15** in 41% yield (0.025 g) as a greenish yellow oil and **16** in 35% yield (0.021 g) as a greenish yellow oil.



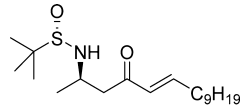
15

$[\alpha]_D^{24}$ +70.0 (c 2.5, $CHCl_3$) [lit.[15] $[\alpha]_D^{24}$ +71 (c 0.25, $CHCl_3$)]. IR (neat): 2930, 2855, 1721, 1513, 1261, 1138, 1027 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 6.92 (s, 1H), 6.90−6.75 (m, 2H), 3.90 (s, 3H), 3.87 (s, 3H), 3.20 (dd, J = 12.0, 2.8 Hz, 1H), 2.79 (m, 1H), 2.68 (t, J = 13.2 Hz, 1H), 2.58−2.19 (m, 4H), 1.80−1.19 (m, 7H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.7, 149.3, 148.3, 135.1, 119.5, 111.0, 109.8, 69.9, 62.4, 55.9, 55.8, 52.7, 50.8, 48.7, 34.3, 25.8, 24.1. HRMS: m/z calcd for $C_{17}H_{23}NO_3$ + H 290.1756, found 290.1756.



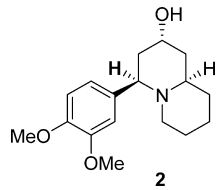
16

$[\alpha]_D^{24}$ +11.3 (c 1.0, $CHCl_3$) [lit.[16] $[\alpha]_D^{24}$ +10.8 (c 1.31, $CHCl_3$); IR (neat): 2930, 2855, 1721, 1513, 1261, 1138, 1027 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 6.81 (d, J = 8.8 Hz, 1 H), 6.74−6.62 (m, 2 H), 4.24 (dd, J = 6.4, 4.4 Hz, 1 H), 3.87 (s, 3H), 3.86 (s, 3H), 2.98−2.81 (m, 3H), 2.60 (m, 2H), 2.38 (dd, J = 14.8, 8.4 Hz 1H), 2.20 (dt, J = 11.6, 2.8 Hz, 1H), 1.75−1.12 (m, 6H). ^{13}C NMR: δ 209.5, 148.7, 148.4, 131.4, 120.9, 111.8, 110.6, 63.8, 55.9, 55.8, 54.3, 51.3, 47.5, 46.7, 31.8, 23.9, 23.3. HRMS: m/z calcd for $C_{17}H_{23}NO_3$ + H 290.1756, found 290.1760.



13q

Compound **13q** was prepared from (*E*)-tridec-3-en-2-one **12j** (0.190 g, 1.0 mmol) and sulfinimine **11b** (0.074 g, 0.5 mmol) using procedure A described above in 62% yield (0.106 g) as a colorless oil. $[\alpha]_D^{24}$ +59.4 (c 0.75, $CHCl_3$). IR (neat): 3403, 3269, 2926, 2855, 1736, 1666, 1629, 1462, 1369, 1243, 1050 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 6.83 (dt, J = 16.0, 6.9 Hz, 1H), 6.07 (d, J = 16.0 Hz, 1H), 3.9−3.78 (m, 1H), 3.66 (d, J = 6.2 Hz, 1H), 2.92 (dd, J = 16.7, 7.6 Hz, 1H), 2.66 (dd, J = 16.7, 5.2 Hz, 1H), 2.19 (dt, J = 8.0, 4.0 Hz, 2H), 1.72 (s, 1H), 1.51−1.39 (m, 2H), 1.35 (d, J = 6.8 Hz, 3H), 1.25 (s, 12H), 1.16 (s, 9H), 0.87 (t, J = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ. 198.7, 148.5, 130.4, 55.6, 49.1, 47.7, 32.4, 31.8, 29.4, 29.3, 29.2, 29.2, 28.0, 22.6, 22.5, 22.0, 14.1. HRMS: m/z for $C_{19}H_{37}NO_2S$ + Na calcd 366.2447, found 366.2443.



2

Preparation of (2*R*,4*R*,9a*R*)-4-(3,4-Dimethoxyphenyl)-octahydro-1*H*-quinolizin-2-ol (2). To a precooled stirred solution of **15** (0.045 g, 0.16 mmol) in dry THF (2 mL) under argon atmosphere at 0 °C was added $LiAlH_4$ (8.8 mg, 0.23 mmol). The reaction mixture was stirred for 0.5 h. After completion of the reaction (by TLC), it was quenched with MeOH (0.5 mL) and stirred for 2 h. The resultant reaction mixture was filtered through a Celite pad. Evaporation of solvent gave the crude alcohol which was taken to further reaction without purification.

To a precooled (0 °C) solution of crude alcohol in dry toluene (5.2 mL) were added triphenylphosphine (0.086 g, 0.31 mmol) and *p*-nitrobenzoic acid (0.052 g, 0.31 mmol) under argon atmosphere and the mixture allowed to stir for 10 min. DEAD (0.026 mL, 0.16 mmol) was introduced into the reaction mixture over a period of 10 min at the same temperature. The reaction mixture was warmed to room temperature and stirred for 1 h. After the reaction was complete (TLC), the volatiles were removed under reduced pressure, and the crude residue thus obtained was subjected to next reaction without further purification. To a solution of the *p*-nitrobenzoate (obtained

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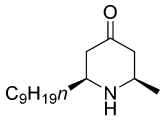
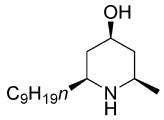
above) in MeOH (3 mL) was added K_2CO_3 (0.038 g, 0.28 mmol) at room temperature and the mixture stirred for 1.5 h. After completion of the reaction, saturated $NaHCO_3$ solution (5 mL) was added and then the mixture extracted with EtOAc (15 mL) and washed with brine (5 mL). Evaporation of solvent followed by neutral alumina column chromatography of the resulting crude residue with petroleum ether/EtOAc as eluent afforded the alcohol **2** (0.035 g, 81% for two steps) as a yellow oil. $[\alpha]_D^{24}$ +47.9 (*c* 1.1, $CHCl_3$) [lit.[17a] + 43.4 (*c* 1.0, $CHCl_3$). IR (neat): 2928, 1594, 1513, 1460, 1261, 1139, 1062 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 6.97−6.73 (m, 3H), 4.20−4.08 (m, 1H), 3.88 (s, 3H), 3.86 (s, 3H), 3.32 (dd, *J* = 11.6, 3.2 Hz, 1H), 2.75−2.62 (m, 1H), 2.48−2.30 (m, 1H), 1.96−1.21 (m, 12H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.9, 147.8, 137.2, 119.6, 110.9, 110.4, 64.9, 63.4, 56.4, 55.9, 55.8, 53.2, 42.8, 40.3, 33.6, 26.1, 24.8. HRMS: *m*/*z* calcd for $C_{17}H_{25}NO_3H$ 292.1913, found 292.1918.



17

Preparation of (2*S*,6*R*)-2-Methyl-6-nonylpiperidin-4-one (17). To a precooled, stirred solution of **13q** (0.068 g, 0.2 mmol) in MeOH (5 mL) at 0 °C was added saturated HCl in MeOH (0.5 mL). The reaction mixture was stirred for 1 h at the same temperature. After completion of reaction (TLC), solvent was evaporated, the resultant residue was dissolved in MeOH (6 mL), Et_3N (0.04 mL, 0.27 mmol) was added, and the resulting solution was stirred for 12 h at rt. Most of the solvent was evaporated, and the solution was diluted with water (10 mL) and extracted with EtOAc (2 × 20 mL). Solvent was evaporated, and product was purified using silica gel column chromatography to yield **17** as a colorless oil in 84% (0.039 g) yield. $[\alpha]_D^{24}$ −1.4 (*c* 0.5, $CHCl_3$) [lit.[11a] $[\alpha]_D^{24}$ −1.1 (*c* 1.56, $CHCl_3$)]. IR (neat): 3386, 2957, 2924, 2854, 1714, 1243, 1017 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 3.43 (dd, *J* = 12.0, 6.7 Hz, 1H), 3.28 (dt, *J* = 12.2, 6.2 Hz, 1H), 2.54−2.42 (m, 2H), 2.14 (td, *J* = 12.7, 6.7 Hz, 2H), 1.61 (s, 2H), 1.25 (s, 15H), 1.16 (d, *J* = 6.5 Hz, 3H), 0.87 (t, *J* = 6.7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 209.9, 52.6, 49.6, 47.8, 47.7, 34.7, 31.8, 29.6, 29.5, 29.2, 26.1, 22.6, 21.6, 14.1. HRMS: *m*/*z* for $C_{15}H_{29}NO$ + H calcd 240.2327, found 240.2326.



4

Preparation of (2*S*,4*R*,6*R*)-2-Methyl-6-nonylpiperidin-4-ol (4). To a stirred solution of **17** (0.023 g 0.1 mmol) in ethanol (2 mL) at 0 °C was added $NaBH_4$ (0.01 g, 0.25 mmol), and stirring was continued for 1 h at 0 °C. After completion of the reaction (TLC), the solvent was removed under reduced pressure and the crude residue was taken up with a 15% ammonia solution (1 mL) and extracted with diethyl ether (2 × 3 mL). The combined organic layers were dried over $NaSO_4$. Evaporation of solvent followed by silica gel column chromatography of the resulting crude residue with EtOAc/MeOH as eluent afforded the product **4** in 82% yield (0.019 g). $[\alpha]_D^{24}$ +5.4 (*c* 0.5, MeOH) [lit.[18] $[\alpha]_D^{24}$ +5.66 (*c* 0.60, MeOH)]. IR (neat): 3359, 2924, 2853, 1655, 1461, 1026 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 3.66 (td, *J* = 11.1, 5.5 Hz, 1H), 2.7−2.65 (m, 1H), 2.54 (dd, *J* = 9.1, 6.1 Hz, 1H), 2.00−1.92 (m, 2H), 1.40 (d, *J* = 8.0 Hz, 2H), 1.26 (s, 15H), 1.12 (d, *J* = 6.4 Hz, 3H), 1.00 (dd, *J* = 19.1, 11.5 Hz, 2H), 0.88 (t, *J* = 6.7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 69.5, 54.8, 50.2, 43.9, 41.7, 36.8, 31.9, 29.7, 29.6, 29.5, 29.3, 26.0, 22.7, 22.4, 14.1. HRMS: *m*/*z* for $C_{15}H_{31}NO$ + H calcd 242.2484, found 242.2495.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01541.

^1H and ^{13}C NMR spectra of the new compounds (PDF)

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Notes

The authors declare no competing financial interest.

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