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

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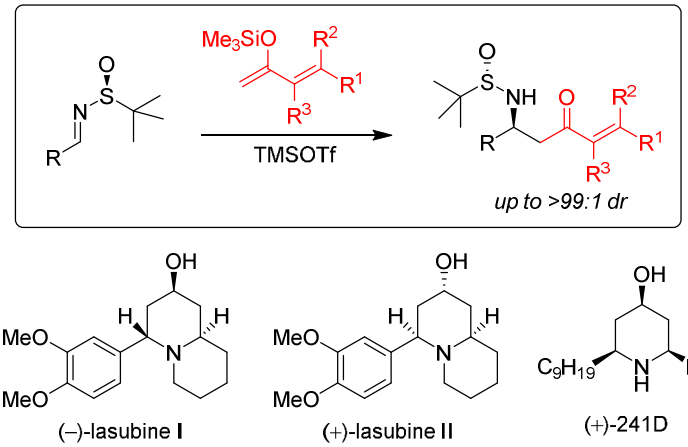


Abstract: Addition of silyl enol ethers obtained from substituted methyl enones to chiral sulfinimines afforded the β-amino substitued enones with excellent selectivity. Utility of the obtained *N*-sulfinyl β-amino ketones possessing α, β-unsaturation is exemplified in the total synthesis of the quinolizidine 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 bio-activity profiles.[1] Some of the simple quinolizidine, indolizidine and piperidine alkaloids include the lasubines **1** and **2**, indolizidines 167 B **3** and 241-D **4**, while complex alkaloids comprising these frameworks include vallesamidine **5** and aspidospermidine **6** (fig. 1).

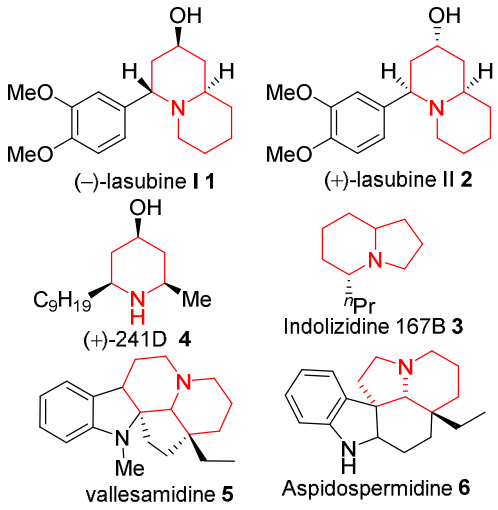
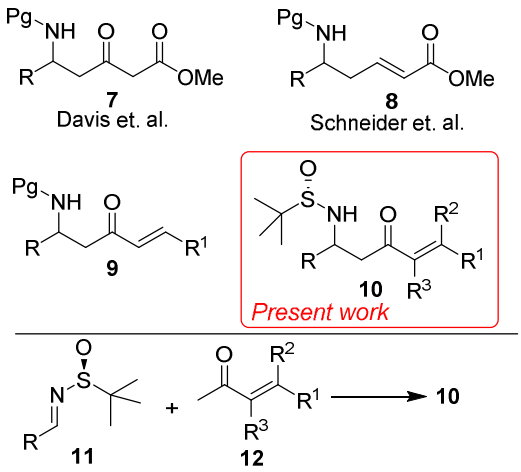


Fig. 1 Natural products possessing the quinolizidine and indolizidine framework

Over the years, impressive strategies were 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 non-racemic sulfinimines, which was also obtained by vinylogous Mukaiyama-Mannich reaction of sulfinimines with dioxinone-derived silyloxydiene.[3] Recently, the same building block was synthesized by employing chiral Bronsted acid catalyzed enantioselective addition of dioxinone-derived silyloxydiene 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 intra-molecular Michael reaction of β-amino enones **9**, generally obtained

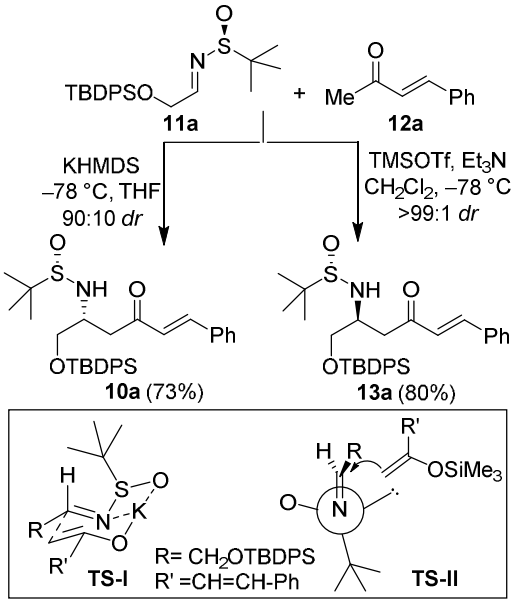
in a multi-step sequence from protected β-amino ester.[6] While the above strategies are useful, they have drawbacks in terms of generality and the multi-step sequences involved. We reasoned that the addition of silyloxy dienes or metal enolates derived from substituted methyl enones to imines[7] would 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 non-racemic sulfinimines **11**. The reliable and predictable selectivities observed in the nucleophilic addition reactions of sulfinimines[8] should yield the *N*-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.



Scheme-1 Chiral building blocks **7-9** commonly utilized in the synthesis of quinolizidine and piperidine alkaloids (Pg= protecting group).

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 >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 earlier[9] for the reaction of metal enolates with sulfinimines and Lewis acid catalyzed addition of organometallics.

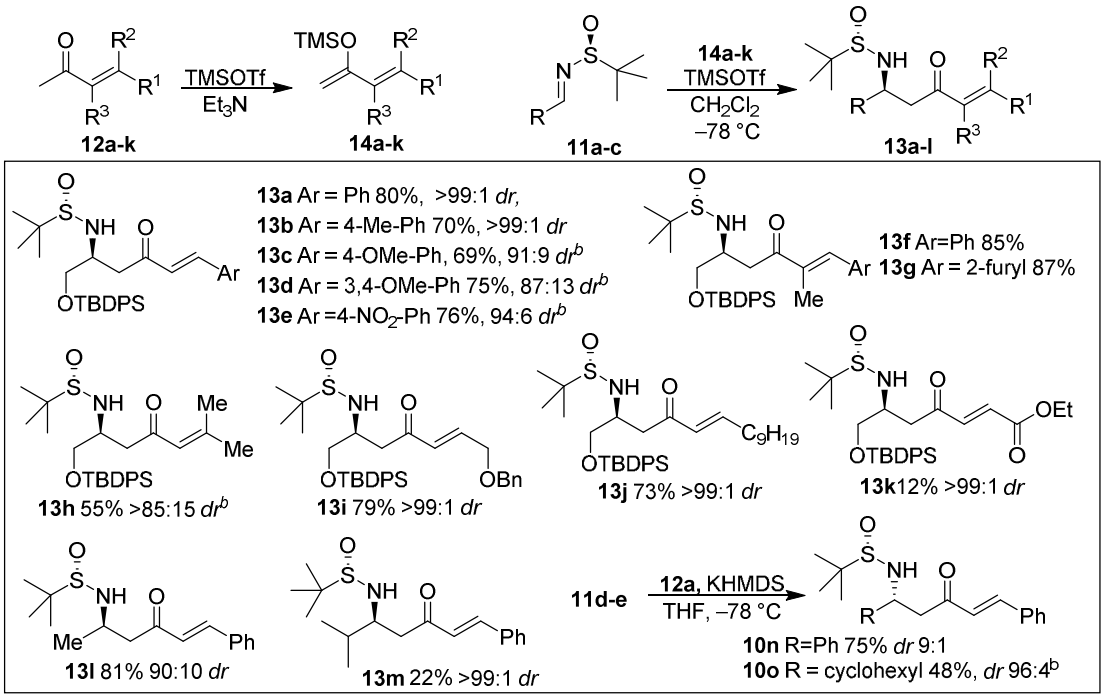


Scheme-2 Addition of metal enolate/ silylenol ether derived from α, β-unsaturated aryl methyl ketone **12a** to sulfinimine **11a**.

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* 90:10 (81% yield), while employing the sulfinimine **11c** obtained from isobutyraldehyde afforded the product **13m** in 22% yield (*dr* >99:1). It is interesting to note that the sulfinimines **11d, 11e, 11f** 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.

Chart 1. Addition of silyl enol ethers derived from substituted methyl enones to sulfinimines.[a]

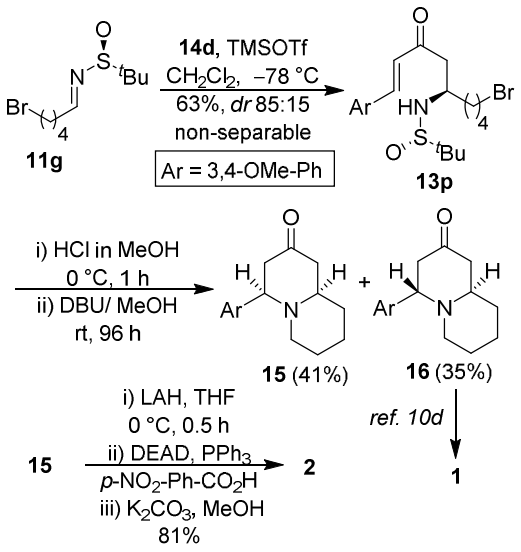


11a R = $CH_2OTBDPS$, **11b** R = Me, **11c** R = ^{i}Pr, **11d** R =Ph, **11e** R = cyclohexyl, **11f** R = ^{t}Bu
12a R^1= Ph; R^2, R^3= H, **12b** R^1= 4-MePh; R^2, R^3= H, **12c** R^1= 4-OMePh; R^2, R^3= H, **12d** R^1= 3,4-OMePh; R^2, R^3= H
12e R^1= 4-NO_2-Ph; R^2, R^3= H, **12f** R^1= Ph; R^2= 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 silylenol ethers **14a-k** from the ketones **12a-k**. [b]Non-separable mixture of diastereomers.

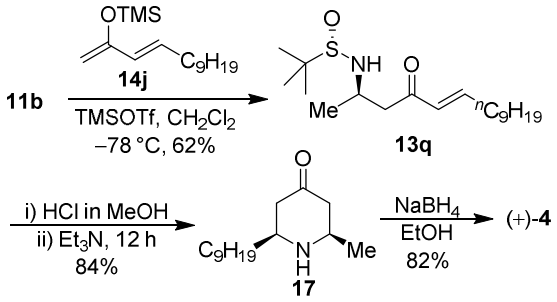
Synthetic utility of the resultant β-*N*-sulfinamido ketones was demonstrated in the total synthesis of quinolizidine alkaloids (–)-lasubine I **1** and (+)-lasubine II **2**[10] and the piperidine alkaloid (+)-241-D **4**.

Accordingly, treatment of silylenol 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 that 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.



Scheme-3 Total synthesis of (–)- lasubine I **1** (+)- lasubine II **2**

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).

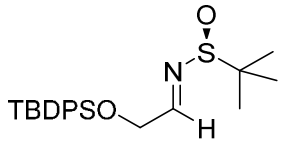


Scheme 4 Total synthesis of (+)-241D **4**

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. 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 lasubine I and lasubine II, the piperidine alkaloid 241D.

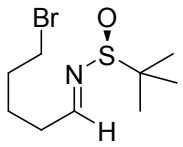
Experimental:

General Procedures: Column chromatography was performed on silica gel, Acme grade 100-200 mesh. TLC plates were visualized either 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 NMR 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 micro-mass 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

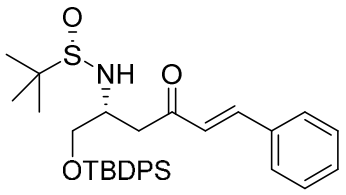
Preparation of (S_S,*E*)-*N*-(2-((*tert*-butyldiphenylsilyl)oxy)ethylidene)-2-methylpropane-1-sulfinamide (11a): To a stirred solution of ((*tert*-butyldiphenylsilyl)oxy)acetaldehyde (1.054 g, 3.55 mmol) and (*S*)-*t*-butanesulfinamide (0.429 g, 3.5 mmol) in dry CH_2Cl_2 (11 mL) at room temperature was added oven dried $CuSO_4$ (1.58 g, 10.5 mmol) and the reaction mixture was stirred for 12 hours at the same temperature. After completion of 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, 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*)-*t*-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 was stirred for 12 hours. 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)

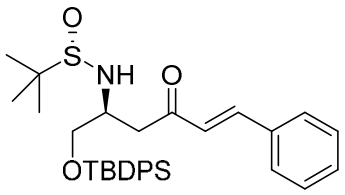
as yellow oil. $[\alpha]_D^{24}$ +186.5 (*c* 0.65, $CHCl_3$). IR (neat) 1634, 1270, 1135, 1018 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 8.11 (t, *J* = 4.0 Hz, 1H), 3.5 (dt, *J* = 6.4, 2.8 Hz, 2H), 2.79-2.65 (m, 2H), 2.31-2.14 (m, 2H), 1.19 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.7, 56.6, 34.3, 32.5, 28.0, 22.3 (3 × C)**.** HRMS: *m/z* calcd for $C_9H_{18}BrNOS$+Na 290.0190; found: 290.0193.



10a

(*S*s)-*N*-((*R*,*E*)-1-((*tert*-butyldiphenylsilyl)oxy)-4-oxo-6-phenylhex-5-en-2-yl)-2-methylpropane-2-sulfinamide (**10a)**: To a pre-cooled (−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 additional 2 hours which was quenched by addition of saturated NH_4Cl solution (20 mL) and was 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). 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:



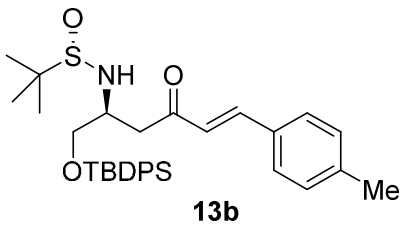
13a

Procedure A: To a pre-cooled 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 was stirred for 5 minutes. The organic layer was separated and was washed with water (20 mL), brine (20 mL) and was dried over Na_2SO_4. Evaporation of solvent gave the silylenolether which was used in the next step without further purification.

A solution of the crude silylenolether (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 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 was 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,

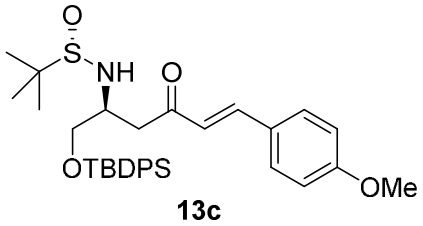
129.8, 128.9 (2 × C), 128.3 (2 × C)127.8 (5 × C), 126.2, 66.3, 55.8, 54.2, 43.3, 26.9 (3 × C), 22.5 (3 × C), 19.3. HRMS: *m/z* calcd for $C_{32}H_{41}NO_3SSi$+Na 570.2474; found: 570.2476.

Procedure B: To a pre-cooled 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, cooled to −78 °C and sulfinimine **11a** (0.1 g, 0.25 mmol) dissolved in 5 mL CH_2Cl_2 was added at −78 °C, followed by addition of 2nd 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, 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 is same as described above.



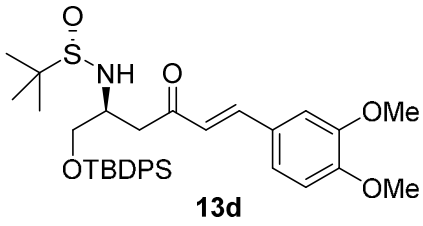
13b

Compound **13b** was prepared from 4-methyl benzylideneacetone **12b** (0.1 g, 0.62 mmol) and sulfinimine **11a** (0.1 g, 0.25 mmol) using the 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, $CDCl_3$): δ198.0, 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.



13c

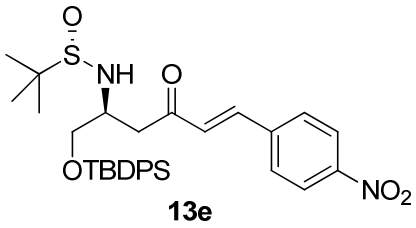
Compound **13c** was prepared from 4-methoxy benzylideneacetone **12c** (0.1 g, 0.57 mmol) and sulfinimine **11a** (0.1 g, 0.25 mmol) using the procedure **A** described above in 69% yield (0.09 g) as an inseparable mixture (91:9) of diastereomers as a gummy mass. $[\alpha]_D^{24}$ +6.4 (*c* 1.09, $CHCl_3$). 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 $C_{33}H_{43}NO_4SSi$+Na 600.2580; found: 600.2580.



13d

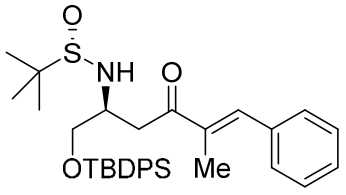
Compound **13d** was prepared from 3,4-dimethoxy benzylideneacetone **12d** (0.1 g, 0.48 mmol) and sulfinimine **11a** (0.1 g, 0.25 mmol) using the procedure **A** described above in 75% yield (0.12 g) as an inseparable mixture (87:13) of diastereomers as a gummy mass. $[\alpha]_D^{24}$ +4.7 (*c* 4.9, $CHCl_3$). 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.



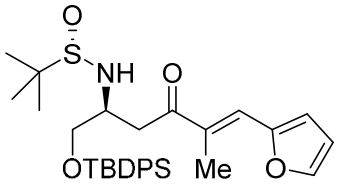
13e

Compound **13e** was prepared from 4-Nitro benzylideneacetone **12e** (0.1 g, 0.5 mmol) and sulfinimine **11a** (0.1 g, 0.25 mmol) using the 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}. ^{1}H 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

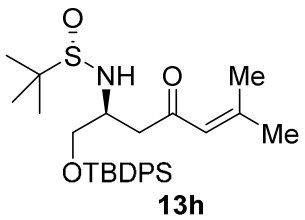
Compound **13f** was prepared from (*E*)-3-methyl-4-phenylbut-3-en-2 one **12f** (0.15 g, 0.94 mmol) and sulfinimine **11a** (0.1 g, 0.25 mmol) using the procedure **A** described above in 85% yield (0.12 g) as a gummy mass. $[\alpha]_D^{24}$ +14.9 (*c* 0.7, $CHCl_3$). IR (neat) 3062, 2956, 2858, 1663, 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

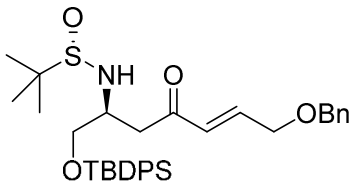
Compound **13g** was prepared from (*E*)-4-(furan-2-yl)-3-metylbut-3-en-2 one **12g** (0.1 g, 0.625 mmol) and sulfinimine **11a** (0.1 g, 0.25 mmol) using the procedure **A** described above in 87% yield (0.119 g) as a yellow gummy mass. $[\alpha]_D^{24}$ +8.1 (*c* 2.25, $CHCl_3$). IR (neat) 3068, 2932, 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

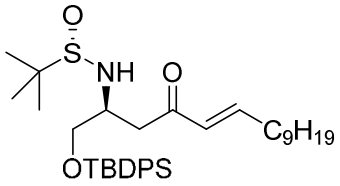
Compound **13h** was prepared from mesityl oxide **12h** (0.15 g, 1.53 mmol) and sulfinimine **11a** (0.1 g, 0.25 mmol) using the procedure **A** described above in 55% yield (0.068 g as an inseparable 85:15 mixture of diastereomers) as a pale yellow liquid. $[\alpha]_D^{24}$ +18.4 (*c* 0.83, $CHCl_3$). 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.



13i

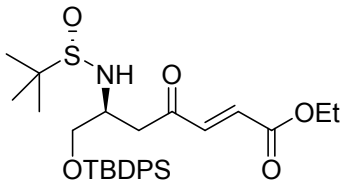
Compound **13i** was prepared from (*E*)-5-(benzyloxy)pent-3-en-2-one **12i** (0.1 g, 0.5 mmol) and sulfinimine **11a** (0.1 g, 0.25 mmol) using the procedure **A** described above in 79% yield (0.12 g) as a gummy mass. $[\alpha]_D^{24}$ + 23.5 (*c* 1.0, $CHCl_3$). IR (neat) 3359, 3060, 2954, 1669, 1684, 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 .614.2736.; found 614.2735.



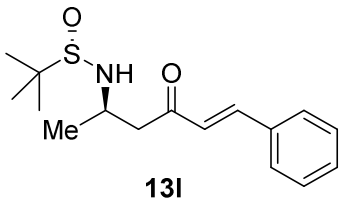
13j

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 the 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}. ^{1}H 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.



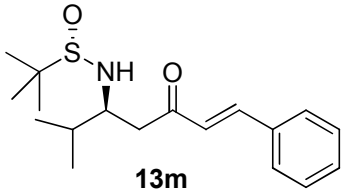
13k

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 the 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.



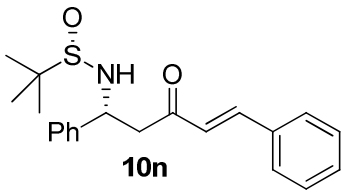
13l

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 the procedure **A** described above in 81% yield (0.12 g) as a 90:10 seperable 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

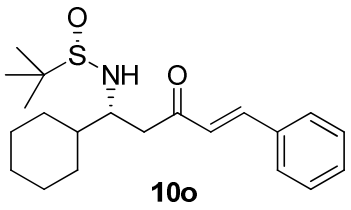
Compound **13m** was prepared from benzylideneacetone **12a** (0.15 g, 1.0 mmol) and sulfinimine **11d** (0.09 g, 0.5 mmol) using the procedure **A** described above in 22% yield (0.036 g) as a colorless liquid. $[\alpha]_D^{24}$ +22.4 (*c* 0.25, $CHCl_3$). IR (neat) 3410, 1651, 1602, 1458, 1130, 1018 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

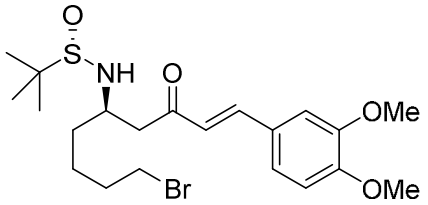
Compound **10n** was synthesized using procedure **B** as follows: To a pre-cooled stirred solution (−78 °C) of benzylideneacetone **12a** (0.14 g, 0.96 mmol) in dry THF (14 mL) under argon atmosphere at −78 °C was added KHMDS (2.88 mL of 0.5M solution in toluene, 1.44 mmol). The reaction mixture was 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 dry THF was introduced at −78 °C and the reaction mixture was stirred 2 h at the same temperature. After completion of the reaction (TLC), it was quenched by addition of saturated NH_4Cl (20 mL) and was extracted with EtOAc (2 × 20 mL). The organic layer was separated and 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 diastreomeric 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

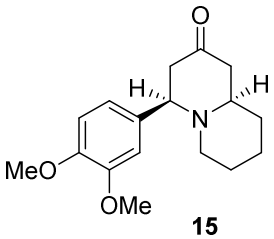
To a pre-cooled stirred solution (−78 °C) of benzylideneacetone **12a** (0.12 g, 0.8 mmol) in dry THF (14 mL) under argon atmosphere at −78 °C was added KHMDS (2.5 mL of 0.5M solution in toluene, 1.2 mmol). The reaction mixture was stirred for 1 h at the same temperature. A solution of sulfinimine **11e** (0.1 g, 0.47 mmol) dissolved in 5 mL dry THF was introduced at −78 °C and the reaction mixture was stirred 2 h at the same temperature. After completion of the reaction (TLC), it was quenched by addition of saturated NH_4Cl (20 mL) and was extracted with EtOAc (2 × 20 mL). The organic layer was separated and 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

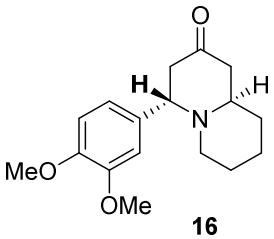
Compound **13p** was prepared from 3,4 dimethoxy benzylideneacetone **12d** (0.17 g, 0.8 mmol) and sulfinimine **11g** (0.1 g, 0.37 mmol) using the procedure **A** described above in 63% yield (0.12 g as an inseparable mixture of diastereomers) as a green yellow oil. $[\alpha]_D^{24}$ +46.7 (*c* 2.4, $CHCl_3$). 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 pre-cooled 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 was 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.



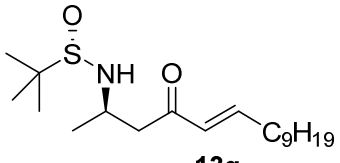
15

$[\alpha]_D^{24}$ +70.0 (*c* 2.5, $CHCl_3$) [lit.[15] +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.



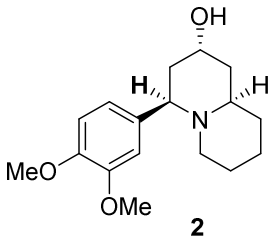
16

$[\alpha]_D^{24}$ +11.3 (*c* 1.0, $CHCl_3$) [lit[16] +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 the 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.

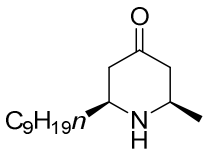


2

Preparation of (2*R*,4*R*,9a*R*)-4-(3,4-dimethoxyphenyl)octahydro-1H-quinolizin-2-ol (2): To a pre-cooled 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 reaction (by TLC) it was quenched with MeOH (0.5 mL) and it was 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 pre−cooled (0 °C) solution of crude alcohol in dry toluene (5.2 mL) was added triphenyl phosphine (0.086 g, 0.31 mmol) and *p*-nitrobenzoic acid (0.052 g, 0.31 mmol) under argon atmosphere and allowed to stirred for 10 min. DEAD (0.026 mL, 0.16 mmol) was introduced into the reaction mixture over period of 10 min at the same temperature. The reaction mixture was warmed up to room temperature and was 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

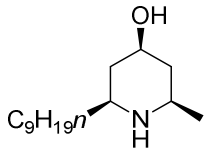
further purification. To a solution of the *p*-nitrobenzoate (obtained above) in MeOH (3 mL) was added K_2CO_3 (0.038 g, 0.28 mmol) at room temperature and stirred for 1.5 h. After completion of the reaction to it was added saturated $NaHCO_3$ solution (5 mL) and extracted with EtOAc (15 mL) and washed 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 2 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, 1062cm^{-1}. ^{1}H 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 pre–cooled 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 and the resultant residue was dissolved in MeOH (6 mL), Et_3N (0.04 mL, 0.27 mmol) was added and was stirred for 12 h at rt. Most of the solvent was evaporated off and 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] –1.1 (*c* 1.56, $CHCl_3$) IR (neat) 3386, 2957, 2924, 2854, 1714, 1243, 1017 cm^{-1}. ^{1}H 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 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] +5.66 (*c* 0.60, MeOH)]. IR (neat) 3359, 2924, 2853, 1655, 1461, 1026 cm^{-1}. ^{1}H 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.

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Supporting information: Supporting information containing ^{1}H and ^{13}C NMR spectra of all the new compounds is provided. “This material is available free of charge via the Internet at http://pubs.acs.org.”

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