Supplemental material for:

Total Synthesis of Oridamycins A and B

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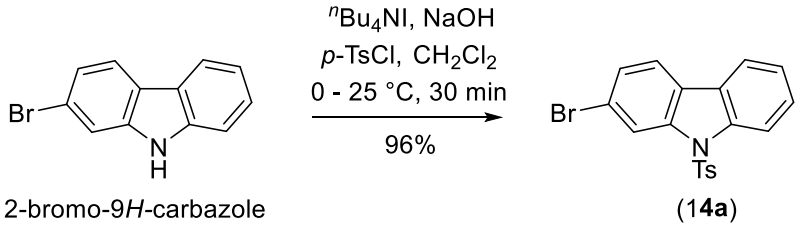
Materials and Methods

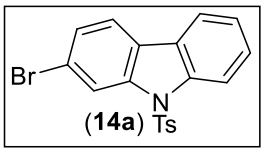
Unless otherwise stated, reactions were carried out using oven-dried glassware with Teflon-coated magnetic stirring bars used to stir the reactions. The Syringe was used to transfer solvents and liquid reagents. Tetrahydrofuran (THF) and diethyl ether (Et_2O) was distilled over sodium/benzophenone ketyl. Dichloromethane CH_2Cl_2) was distilled over calcium hydride. All other solvents like Nitromethane, MeOH, EtOAc, DMF, Dichloroethane (DCE) and reagents were used as received. Reaction temperatures above 25 °C were maintained by using an oil bath on a magnetic stirrer. Thin layer chromatography (TLC) analysis was performed by using silica gel precoated plates (0.25 mm) 60 (F-254), Visualized by UV irradiation, yellow dip stain (Cerium Ammonium Molybdate stain or CAM stain), and other stains. Silicagel of particle size 230-400 and 100-200 mesh were used to perform flash chromatography. A digital melting point apparatus is used to record the melting points.^{1}H NMR spectra were recorded by using 400 and 500 MHz spectrometers, ^{13}C NMR operating frequencies are 101, and 126 MHz respectively. Chemical shifts (δ) are reported in ppm relative to the residual solvents ($CDCl_3$) signal (δ = 7.24-7.29 for ^{1}H NMR and δ = 77.0-77.2 for ^{13}C NMR) and CD_3OD signal (δ = 3.31 for ^{1}H NMR and δ = 49.0 for ^{13}C NMR). Data for ^{1}H NMR spectra are reported as follows: chemical shift (multiplicity, coupling constants, number of hydrogen). Abbreviations are as follows: s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), and br (broad). IR spectra were recorded on an FT-IR system (Spectrum BX) and are reported in the frequency of absorption (cm^{-1}). Only selected IR absorbencies are reported. High-Resolution Mass Spectrometry (HRMS) data were recorded on MicroTOF-Q-II WATER mass spectrometer and Bruker ESI mass spectrometer using methanol as solvent. Optical rotations were measured on an automatic polarimeter.

Preparation of N-tosyl-2-bromo carbazole (14a):



2-bromo-9*H*-carbazole (**14a**)

In an oven-dried round-bottom flask 2-bromo-9*H*-carbazole (13.0 g, 73.138 mmol, 1.0 equiv.) was taken in dichloromethane (100 mL). Next, tetrabutyl ammonium iodide (1.35 g, 3.657 mmol, 0.1 equiv.) and NaOH (5.85 g, 146.277 mmol, 2.0 eq.) were added and stirred for 5 min followed by the addition of *p*-TsCl (1.84 g, 76.795 mmol, 1.05 equiv.) at 0 °C. Then the reaction mixture was allowed to warm to 25 °C for 30 min. After completion of the reaction (monitored by TLC in 20 % EtOAc and hexane) the reaction mixture was diluted with water (50 mL). The resulting biphasic mixture was transferred to a separatory funnel. The organic phase was concentrated through vacuum and the crude product was purified by column chromatography (*n*-hexane/ethyl acetate, 4:1) to afford **14a**.



***N*-Tosyl 2-bromo carbazole** (**14a**): **14a** was obtained as a white crystalline solid (MP: 144-146 °C, 73.138 mmol, 28.1 g, 96% yield); R_f = 0.4 (20% EtOAc in *n*-hexane).

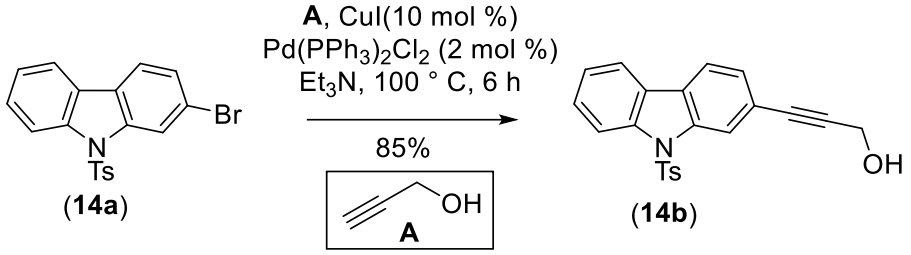
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.51 (d, *J* = 1.7 Hz, 1H), 8.28 (dd, *J* = 8.5, 0.8 Hz, 1H), 7.89 – 7.81 (m, 1H), 7.73 (d, *J* = 8.3 Hz, 1H), 7.70 (d, *J* = 8.4 Hz, 2H), 7.55 – 7.46 (m, 1H), 7.47 (dd, *J* = 8.3, 1.7 Hz, 1H), 7.35 (td, *J* = 7.5, 0.9 Hz, 1H), 7.12 (d, *J* = 8.0 Hz, 2H), 2.26 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 145.3, 139.2, 138.5, 134.8, 129.9, 129.9, 127.9, 127.3, 126.6, 126.6, 125.6, 125.4, 124.3, 121.2, 121.0, 120.1, 118.3, 115.2, 21.6.

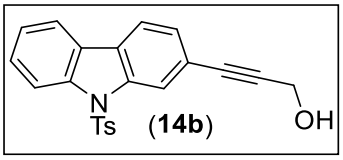
IR (neat)υ_{max} 3081,1580, 1245, 1233, 1047, 690 cm^{-1}.

HRMS (ESI) *m/z*: $[M+K]^+$ calcd. for $[C_{19}H_{14}BrO_2NS + K]^+$ 437.9560, found: 437.9570.

Synthesis of the propargyl alcohol derivative via Sonogashira coupling reaction:



In an oven dried seal tube *N*-tosyl 2-bromo carbazole **14a** (1.0 g, 2.498 mmol, 1.0 equiv.) and propargyl alcohol (216 µl, 3.747 mmol, 1.5 equiv.) was dissolved in Et_3N (10 mL), maintaining inertness with N_2 gas balloon. Then the reaction mixture was degassed by purging with Ar gas for 15 min, followed by sequential addition of CuI (47 mg, 0.249 mmol, 0.1 equiv.) and Pd $(PPh_3)_2Cl_2$ (35 mg, 0.049 mmol, 0.02 equiv.) to the reaction mixture and tube was sealed. Then the reaction mixture was allowed to heat at 100 °C on a pre-heated oil-bath for 6 h. After completion of the reaction (monitored by TLC in 20 % EtOAc and *n*-hexane) the volatiles were removed under reduced pressure. The crude product was diluted with water (15 mL) and EtOAc (15 mL). The resulting biphasic mixture was transferred to a separatory funnel. The organic phase was collected, and the aqueous phase was further extracted with EtOAc (10 mL X 2). The total organic phase was concentrated through vacuum and the crude product was purified by a solvent gradient of 20-25% EtOAc in *n*-hexane to afford the titled compound as yellow foam.



3-(9-Tosyl-9*H*-carbazol-2-yl)-prop-2-yn-1-ol (**14b**): **14b** was obtained as yellow foam (2.498 mmol, 0.796 g, 85% yield).

R_f = 0.3 (40% EtOAc in *n*-hexane).

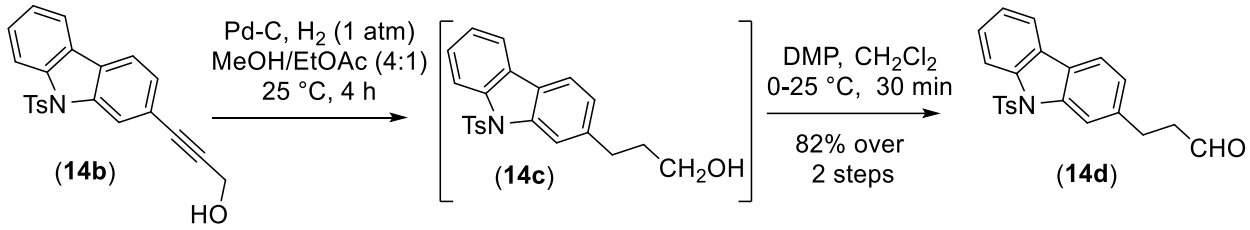
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.42 (dd, *J* = 1.4, 0.7 Hz, 1H), 8.28 (dt, *J* = 8.4, 0.8 Hz, 1H), 7.79 (ddd, *J* = 7.7, 1.3, 0.7 Hz, 1H), 7.73 (dd, *J* = 8.0, 0.7 Hz, 1H), 7.67 (d, *J* = 8.4 Hz, 2H), 7.46 (ddd, *J* = 8.5, 7.3, 1.3 Hz, 1H), 7.38 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.36 – 7.26 (m, 1H), 7.03 (d, *J* = 7.9 Hz, 2H), 4.58 (s, 2H), 2.17 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 145.2, 138.9, 138.1, 134.8, 129.8, 129.8, 128.0, 127.6, 126.6, 126.6, 126.5, 125.9, 124.2, 121.5, 120.3, 120.0, 118.4, 115.2, 88.0, 86.2, 51.8, 21.5.

IR (neat) υ_{max} 3584, 2981, 2895, 2240, 1698, 1387, 1280, 1152, 836 cm^{-1}.

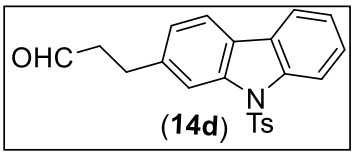
HRMS (ESI) *m/z*: $[M+Na]^+$ calcd. for $[C_{22}H_{17}O_3NS + Na]^+$ 398.0821, found: 398.0808; $[M+K]^+$ calcd. for $[C_{22}H_{17}O_3NS + K]^+$ 414.0561, found: 414.0547.

Synthesis aldehyde 14d:



The propargyl alcohol derivative **14b (**1.4 g, 3.728 mmol, 1.0 equiv.) was dissolved in 4:1 mixture of MeOH/EtOAc (15 mL) in an oven dried round bottom flask. The reaction mixture was degassed with Ar gas for 10 min. Then Pd/C (5 % w/w) was added followed by continuous purging with hydrogen gas (1 atm) for 4 h. After complete consumption of starting material (monitored by TLC), the solvent was evaporated and filtered with celite funnel. The crude product obtained was then charged for the next step without purification.

In an oven dried round bottom flask, the crude primary alcohol (3.728 mmol, 1.0 equiv.) was dissolved in DCM (15 mL) followed by addition of Dess-Martin Periodinane (1.74 g, 4.101 mmol, 1.1 equiv.) at 0 ºC over a period of 10 min with continuous stirring over an ice bath. After the complete addition of DMP, the ice bath was removed, and the reaction mixture was allowed to stir for an additional 30 min until the full consumption of the starting material (monitored by TLC analysis). After completion of the reaction, was quenched with saturated $NaHCO_3$ (8 mL) at 0 ºC. The biphasic mixture was then transferred to a separatory funnel and the organic part was collected. The aqueous part was further extracted with CH_2Cl_2 (8 mL X 2). The combined organic layers were washed with brine, dried over Na_2SO_4 and concentrated in vacuo under reduced pressure. Finally, the crude product was purified through flash column chromatography using 10% EtOAc in *n*-hexane. Pure aldehyde **14d** was obtained after column chromatography as yellowish foam.



(**14d**)

3-(9-Tosyl-9*H*-carbazol-2-yl) propanal (**14d**): **14d** was obtained as yellowish foam (3.728 mmol, 1.15 g, 82% over 2 steps); R_f = 0.5 (30% EtOAc in *n*-hexane).

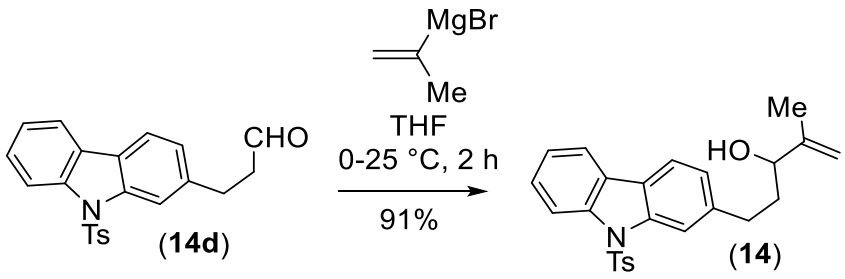
^{1}H NMR (400 MHz, $CDCl_3$): δ 9.85 (t, *J* = 1.4 Hz, 1H), 8.30 (dt, *J* = 8.4, 0.9 Hz, 1H), 8.17 (dd, *J* = 1.5, 0.7 Hz, 1H), 7.83 (ddd, *J* = 7.8, 1.3, 0.7 Hz, 1H), 7.77 (d, *J* = 7.9 Hz, 1H), 7.67 (d, *J* = 8.4 Hz, 2H), 7.45 (ddd, *J* = 8.5, 7.3, 1.3 Hz, 1H), 7.35 – 7.29 (m, 1H), 7.18 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.08 (d, *J* = 8.0 Hz, 2H), 3.15 (t, *J* = 7.5 Hz, 2H), 2.87 (td, *J* = 7.5, 1.4 Hz, 2H), 2.23 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 201.4, 145.0, 140.2, 138.9, 138.6, 135.0, 129.8, 129.8, 127.2, 126.6, 126.6, 126.3, 124.9, 124.5, 124.0, 120.2, 119.9, 115.2, 114.9, 45.7, 28.9, 21.6.

IR (neat) υ_{max} 2981, 2895, 1740, 1698, 1280, 1152, 836 cm^{-1}.

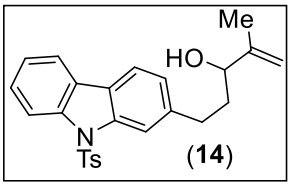
HRMS (ESI) *m/z*: $[M+Na]^+$calcd. for $[C_{22}H_{19}O_3NS + Na]^+$ 400.0978, found: 400.0974.

Synthesis of allyl alcohol derivative 14:



An oven-dried round-bottom flask was charged with the aldehyde **14d** (4.8 g, 12.716 mmol, 1.0 equiv.) in anhydrous THF (60 mL), maintaining inertness with N_2 gas balloon and was cooled to 0 °C, over an ice bath followed by addition of isopropenyl magnesium bromide (0.5 M in THF, 28 mL, 13.988 mmol, 1.1 equiv.) over 30 min with continuous stirring at the same temperature. After the complete addition of the Grignard reagent, the ice bath was removed and stirred at 25 °C for an additional 2 h until the full consumption of the starting material. After completion of the reaction (as judged by running TLC) was quenched with saturated NH_4Cl solution (20 mL). The organic layer from the biphasic solution was separated by a

separatory funnel and the aqueous phase was further extracted with EtOAc (20 mL X 2). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo under reduced pressure. Finally, the crude product was purified through column chromatography using EtOAc in *n*-hexane (10% EtOAc in *n*-hexane) to afford the allyl alcohol **14** as a pale-yellow oil.



2-Methyl-5-(9-tosyl-9*H*-carbazol-2-yl)-pent-1-en-3-ol 14: **14** was obtained as a pale-yellow oil (12.716 mmol, 4.85 g of product, 91% yield); R_f = 0.3 (10% EtOAc in *n*-hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.29 (d, *J* = 8.4 Hz, 1H), 8.17 (d, *J* = 1.4 Hz, 1H), 7.84 (dt, *J* = 7.8, 0.8 Hz, 1H), 7.78 (d, *J* = 7.9 Hz, 1H), 7.67 (d, *J* = 8.4 Hz, 2H), 7.47 – 7.40 (m, 1H), 7.36 – 7.30 (m, 1H), 7.20 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.07 (d, *J* = 8.2 Hz, 2H), 4.99 (dd, *J* = 1.9, 1.0 Hz, 1H), 4.90 (t, *J* = 1.6 Hz, 1H), 4.11 (t, *J* = 6.4 Hz, 1H), 2.96 – 2.78 (m, 2H), 2.24 (s, 3H), 1.95 (td, *J* = 8.0, 6.4 Hz, 2H), 1.77 (t, *J* = 1.1 Hz, 3H).

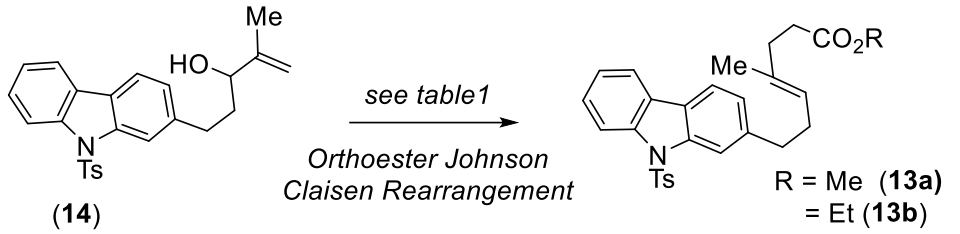
^{13}C NMR (101 MHz, $CDCl_3$): δ 147.5, 144.9, 142.1, 138.9, 138.6, 135.1, 129.7, 129.7, 127.0, 126.6, 126.6, 126.5, 124.7, 124.5, 124.0, 119.9, 119.8, 115.3, 115.0, 111.4, 75.2, 37.1, 32.7, 21.6, 17.8.

IR (neat) υ_{max} 2981, 2895, 1698, 1680, 1280, 1152, 836 cm^{-1}.

HRMS (ESI**)** *m/z*: $[M+Na]^+$ calcd. for $[C_{25}H_{25}O_3NS + Na]^+$ 442.1447, found: 442.1442.

Attempt towards the Synthesis of *E*-selective γ,δ-unsaturated ester via Johnson-Claisen rearrangement:

Table 1: Optimization forJohnson - Claisen Orthoester Rearrangement.

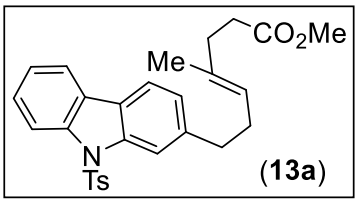


Entry	Solvent	Reagent (10 equiv.)	H^+ source (10 mol%)	Temp.(°C)	Time	Yield (%)[a,b]
1	neat	$MeC(OMe)_3$	$C_2H_5CO_2H$	140	28 h	43
2	neat	$MeC(OEt)_3$	*p*-NO_2-C_6H_4OH	160	28 h	47
3	*o*-xylene	$MeC(OMe)_3$	$C_2H_5CO_2H$	180	36 h	56
4	*o*-xylene	$MeC(OEt)_3$	$C_2H_5CO_2H$	180	36 h	61
5	*o*-xylene	$MeC(OEt)_3$	*p*-NO_2-C_6H_4OH	180	30 h	64
6	*p*-xylene	$MeC(OEt)_3$	*p*-NO_2-C_6H_4OH	180	30 h	68
7	*p*-xylene	$MeC(OEt)_3$	*p*-NO_2-C_6H_4OH	microwave (180)	30 min	61
8	*p*-xylene	$MeC(OMe)_3$	*p*-NO_2-C_6H_4OH	microwave (210)	15 min	71
9	*p*-xylene	$MeC(OEt)_3$	*p*-NO_2-C_6H_4OH	microwave (210)	15 min	76
10	*o*-xylene	$MeC(OEt)_3$	$C_2H_5CO_2H$	microwave (210)	15 min	68

[a]Optimization reactions were carried out on 0.40 mmol of substrate. [b]Yields are isolated after column chromatography.

Allyl alcohol **14** (900 mg, 2.145 mmol, 1.0 equiv.) was dissolved in minimum volume of *p*-xylene (6 mL) with triethylorthoacetate (3.9 mL, 21.452 mmol, 10.0 equiv.) in a microwave vial and *p*-nitrophenol (30 mg, 1.0 mmol, 0.1 equiv.) was added to it. The resulting solution was charged under microwave irradiation maintaining the temperature at 210 °C for 15 min. After 15 min, the reaction mixture was cooled down to 25 °C and was diluted with EtOAc (10 mL) and water (10 mL). The resulting biphasic mixture was transferred to a separatory funnel

and the layers that formed were separated. The aqueous phase was further extracted with EtOAc (15 mL X 2). The combined organic layers were washed with 2N HCl solution (20 mL), brine and dried over Na_2SO_4, and concentrated under reduced pressure. Then the crude product was purified by flash chromatography by eluting with a gradient of 5% EtOAc/*n*-hexane to afford the γ, δ-unsaturated ester compound **13a/13b**



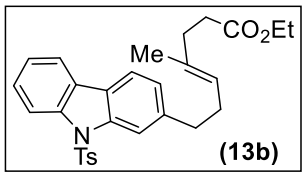
Methyl (*E*)-**4-methyl-7-(9-tosyl-9*H*-carbazol-2-yl) hept-4-enoate 13a**: **13a** was obtained as pale-yellow oil; R_f = 0.6 (10% EtOAc in *n*-hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.29 (dt, *J* = 8.4, 0.9 Hz, 1H), 8.15 (dd, *J* = 1.4, 0.7 Hz, 1H), 7.84 – 7.82 (m, 1H), 7.76 (dd, *J* = 7.9, 0.6 Hz, 1H), 7.67 (d, *J* = 8.4 Hz, 2H), 7.43 (ddd, *J* = 8.5, 7.3, 1.3 Hz, 1H), 7.34 – 7.30 (m, 1H), 7.17 – 7.14 (m, 1H), 7.09 – 7.06 (m, 2H), 5.24 (ddd, *J* = 5.8, 4.3, 3.0 Hz, 1H), 3.65 (s, 3H), 2.82 (t, *J* = 7.7 Hz, 2H), 2.43 – 2.38 (m, 4H), 2.31 (ddd, *J* = 6.2, 5.0, 2.6 Hz, 2H), 2.24 (s, 3H), 1.56 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 174.0, 144.9, 142.2, 138.9, 138.5, 135.2, 134.5, 129.7, 129.7, 127.0, 126.6, 126.6, 126.5, 124.8, 124.5, 124.3, 123.9, 119.8, 119.7, 115.3, 115.0, 51.6, 36.7, 34.7, 33.1, 30.4, 21.6, 16.1.

IR (neat) υ_{max} 2981, 2895, 1735, 1668, 1450, 1233, 956, 835 cm^{-1}.

HRMS (ESI) *m/z*: $[M+Na]^+$calcd. for $[C_{28}H_{29}O_4NS + Na]^+$ 498.1710, found: 498.1698.



Ethyl (*E*)-**4-methyl-7-(9-tosyl-9*H*-carbazol-2-yl) hept-4-enoate (13b)**: **(13b)**: was obtained as a pale-yellow oil (2.145 mmol, 798 mg, 76% yield); R_f = 0.55 (10% EtOAc in *n*-hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.33 (d, *J* = 8.4 Hz, 1H), 8.19 (s, 1H), 7.87 (d, *J* = 7.7 Hz, 1H), 7.80 (d, *J* = 7.9 Hz, 1H), 7.72 – 7.68 (m, 2H), 7.47 (t, *J* = 8.0 Hz, 1H), 7.35 (t, *J* = 7.5 Hz, 1H), 7.20 (d, *J* = 8.0 Hz, 1H), 7.11 (d, *J* = 8.0 Hz, 2H), 5.29 (t, *J* = 7.2 Hz, 1H), 4.15 (q, *J* = 7.1 Hz,

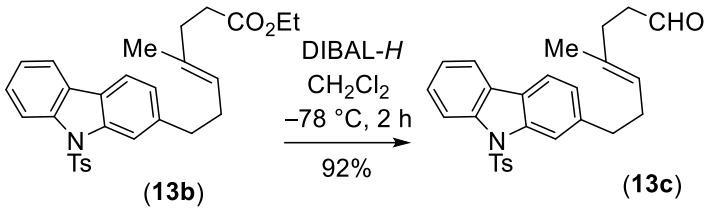
2H), 2.86 (t, *J* = 7.7 Hz, 2H), 2.43 (dd, *J* = 8.5, 6.1 Hz, 4H), 2.34 (t, *J* = 7.8 Hz, 2H), 2.27 (s, 3H), 1.60 (s, 3H), 1.27 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 173.6, 144.9, 142.3, 138.9, 138.6, 135.2, 134.6, 129.8, 129.8, 127.0, 126.7, 126.6, 126.6, 124.9, 124.5, 124.3, 124.0, 119.8, 119.7, 115.3, 115.0, 60.4, 36.7, 34.8, 33.4, 30.4, 21.6, 16.1, 14.4.

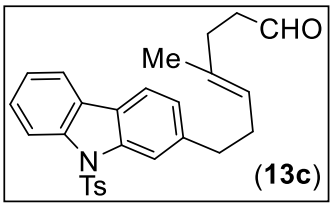
IR (neat) υ_{max} 2980, 2895, 1735, 1660, 1455, 1233, 956, 835 cm^{-1}.

HRMS (ESI-TOF): *m/z*: $[M+H]^+$calcd. for $C_{29}H_{31}NO_4S + H]^+$ 490.2052; found: 490.2033.

Control reduction of γ, δ-unsaturated ester to aldehyde 13c:



An oven-dried round-bottom flask was charged with the γ, δ-unsaturated ester **13b** (4.2 g, 8.578 mmol, 1.0 equiv.) in anhydrous CH_2Cl_2 (40 ml), maintaining inertness with N_2 gas balloon and was cooled to –78 °C, over an acetone bath followed by the addition of a solution of DIBAL-H (1 M in hexanes, 9.0 ml, 9.006 mmol, 1.05 equiv.) in dropwise manner over 10 min. The reaction mixture was stirred at the same temperature for an additional 2 h until the full consumption of the starting material. After complete consumption of the starting material, a saturated aqueous solution of potassium sodium tartrate (25 ml) was added slowly to the reaction mixture, and the resultant mixture was stirred vigorously for another 1 h at 25 °C. The resulting biphasic mixture was then transferred to a separating funnel and the organic layer was separated. The aqueous layer was further extracted with CH_2Cl_2 (25 ml X 2). The combined organic layers were concentrated under reduced pressure and the residue was purified by silica gel column chromatography with a gradient of 10% EtOAc/*n*-hexane afford pure γ,δ-unsaturated aldehyde (**13c**) as a pale yellow liquid (3.52 g, 92% yield).



(*E*)-**4-Methyl-7-(9-tosyl-9*H*-carbazol-2-yl)-hept-4-enal** (**13c**): **13c** was obtained as a yellow oil (8.578 mmol, 3.52 g, 92% yield); R_f = 0.45 (10% EtOAc in *n*-hexane).

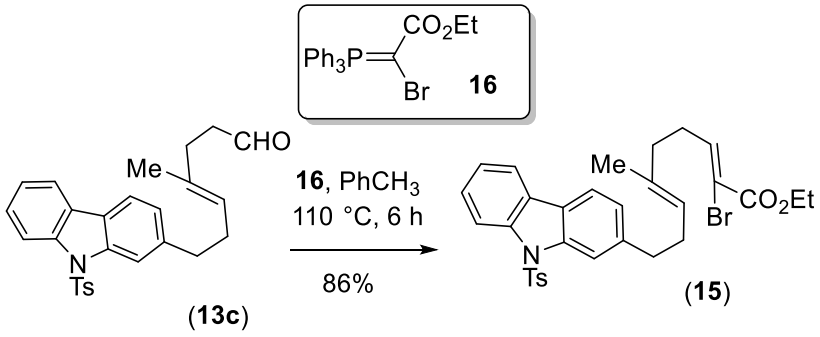
^{1}H NMR (400 MHz, $CDCl_3$): δ 9.74 (t, *J* = 1.8 Hz, 1H), 8.29 (dt, *J* = 8.4, 0.9 Hz, 1H), 8.14 (dd, *J* = 1.4, 0.7 Hz, 1H), 7.84 (ddd, *J* = 7.7, 1.3, 0.7 Hz, 1H), 7.77 (dd, *J* = 7.9, 0.6 Hz, 1H), 7.67 (d, *J* = 8.4 Hz, 2H), 7.46 – 7.41 (m, 1H), 7.32 (td, *J* = 7.5, 1.0 Hz, 1H), 7.16 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.07 (dd, *J* = 8.7, 0.7 Hz, 2H), 5.24 (dddd, *J* = 7.2, 5.8, 2.7, 1.4 Hz, 1H), 2.82 (t, *J* = 7.6 Hz, 2H), 2.51 (tdd, *J* = 6.9, 1.9, 0.7 Hz, 2H), 2.39 (q, *J* = 7.4 Hz, 2H), 2.32 (d, *J* = 7.4 Hz, 2H), 2.24 (s, 3H), 1.55 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 202.7, 144.9, 142.2, 138.8, 138.5, 135.1, 134.2, 129.7, 129.7, 127.0, 126.6, 126.5, 126.5, 124.9, 124.5, 124.5, 124.0, 119.8, 119.7, 115.2, 115.0, 42.3, 36.7, 31.9, 30.4, 21.6, 16.2.

IR (neat) υ_{max} 2980, 2895, 1785, 1660, 1455, 1233, 956, 840 cm^{-1}.

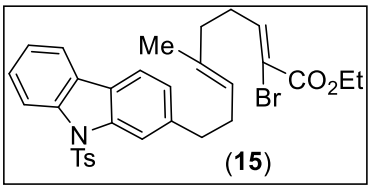
HRMS (ESI-TOF) *m/z*: $[M+Na]^+$ calcd. for $[C_{27}H_{27}NO_3S + Na]^+$ 468.1609, found: 468.1592.

Bromo-Wittig olefination of γ, δ-unsaturated Aldehyde 13c



An oven dried round-bottom flask was charged with a mixture of the aldehyde **13c** (3.6 g, 8.079 mmol, 1.0 equiv.) and ethyl 2-bromo-2-(triphenyl-l5-phosphaneylidene) acetate[1] **16** (4.14 g, 9.695 mmol, 1.2 equiv.) in toluene (30 mL). The reaction mixture was refluxed at 110 °C for 6

h until the complete consumption of the starting material (monitored by TLC). Next, the reaction mixture was cooled to room temperature and all the volatiles were removed under reduced pressure. The crude product was purified by flash column chromatography on silica gel (10% EtOAc in *n*-hexane) to get **15** as a yellowish liquid.



Ethyl (2*Z*,6*E*)-**2-bromo-6-methyl-9-(9-tosyl-9*H*-carbazol-2-yl) nona-2,6-dienoate** (**15**): **15** was obtained as yellowish liquid (8.079 mmol, 4.13 g, 86% yield); R_f = 0.5 (10% EtOAc in *n*-hexane).

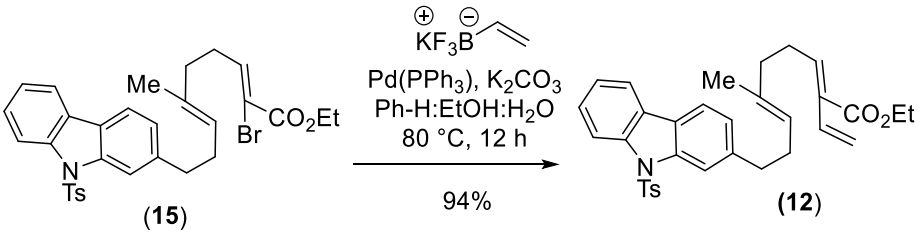
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.32 (dt, *J* = 8.4, 0.9 Hz, 1H), 8.18 (d, *J* = 1.4 Hz, 1H), 7.88 (dt, *J* = 7.7, 1.0 Hz, 1H), 7.81 (d, *J* = 7.9 Hz, 1H), 7.72 – 7.69 (m, 2H), 7.47 (ddd, *J* = 8.4, 7.3, 1.3 Hz, 1H), 7.37 (dd, *J* = 7.5, 1.0 Hz, 1H), 7.31 (d, *J* = 7.0 Hz, 1H), 7.21 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.11 (d, *J* = 8.2 Hz, 2H), 5.32 – 5.27 (m, 1H), 4.29 (q, *J* = 7.1 Hz, 2H), 2.86 (t, *J* = 7.7 Hz, 2H), 2.49 – 2.41 (m, 4H), 2.29 (s, 3H), 2.20 (t, *J* = 7.5 Hz, 2H), 1.58 (s, 3H), 1.35 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 162.6, 145.9, 144.9, 142.3, 138.9, 138.5, 135.1, 134.6, 129.7, 129.7, 127.0, 126.6, 126.6, 126.6, 124.8, 124.8, 124.5, 123.9, 119.8, 119.7, 116.6, 115.3, 115.0, 62.5, 37.2, 36.7, 30.8, 30.5, 21.6, 16.0, 14.3.

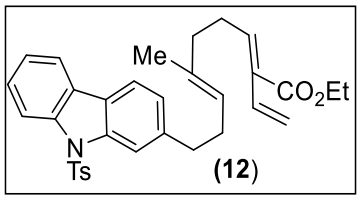
IR (neat) υ_{max} 2980, 2895, 1785, 1660, 1455, 1233, 956, 840 cm^{-1}.

HRMS (ESI) *m/z*: $[M+Na]^+$calcd. for $C_{31}H_{32}BrNO_4S + Na]^+$ 616.1128, found: 616.1093.

Synthesis of triene ester derivative (**12**):



In a flame dried sealed tube, bromoester **15** (2.4 g, 4.036 mmol, 1.0 equiv.) was taken in a mixed solvent of benzene-ethanol-water (25 mL) followed by sequential addition of potassium trifluorovinyl borate (595 mg, 4.439 mmol, 1.1 equiv.) and K_2CO_3 (1.115 g, 8.072 mmol, 2.0 equiv.). The reaction mixture was degassed by purging Argon gas for 15 min. Next, Pd $(PPh_3)_4$ (233 mg, 4.036 mmol, 0.05 equiv.) was added to the solution and the tube was sealed. Then the reaction mixture was allowed to heat to 80 °C on a preheated oil bath for 10 h. After completion of the reaction (monitored by TLC in 10 % EtOAc and hexane) the crude reaction mixture was diluted with water (15 mL). The resulting biphasic mixture was then transferred to a separatory funnel. The organic phase was collected, and the aqueous phase was further extracted with EtOAc (20 mL X 2). The combined organic layer was concentrated under vacuum and the crude product was purified by column chromatography (10% Ethyl acetate in *n*-hexane) to afford **12** .



Ethyl-(*2E,6E*)**-6-methyl-9-(9-tosyl-9*H*-carbazol-2-yl)-2-vinylnona-2,6-dienoate** (**12**): **12** was obtained as colorless gel (4.036 mmol, 2.055 g, 94% yield). R_f = 0.5 (10% EtOAc in *n*-hexane).

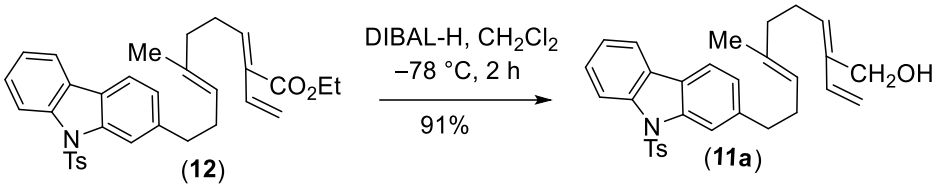
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.32 (d, *J* = 8.3 Hz, 1H), 8.18 (d, *J* = 1.4 Hz, 1H), 7.88 (d, *J* = 7.6 Hz, 1H), 7.80 (d, *J* = 7.9 Hz, 1H), 7.71 – 7.69 (m, 2H), 7.47 (ddd, *J* = 8.5, 7.2, 1.4 Hz, 1H), 7.36 (t, *J* = 7.5 Hz, 1H), 7.21 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.11 (d, *J* = 8.1 Hz, 2H), 6.75 (t, *J* = 7.4 Hz, 1H), 6.50 (dd, *J* = 17.6, 11.5 Hz, 1H), 5.60 (dd, *J* = 17.7, 1.9 Hz, 1H), 5.39 (dt, *J* = 11.5, 1.6 Hz, 1H), 5.30 – 5.27 (m, 1H), 4.25 (q, *J* = 7.1 Hz, 2H), 2.86 (t, *J* = 7.7 Hz, 2H), 2.44 (t, *J* = 7.5 Hz, 4H), 2.28 (s, 3H), 2.17 (t, *J* = 7.7 Hz, 2H), 1.60 – 1.58 (m, 3H), 1.32 (d, *J* = 7.2 Hz, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 167.1, 144.8, 143.4, 142.2, 138.8, 138.5, 135.1, 134.8, 130.6, 129.6, 129.6, 129.2, 126.8, 126.5, 126.5, 126.5, 124.8, 124.4, 123.8, 119.7, 119.6, 119.4, 115.2, 114.9, 60.6, 38.7, 36.7, 30.4, 29.7, 27.4, 21.5, 16.0, 14.3.

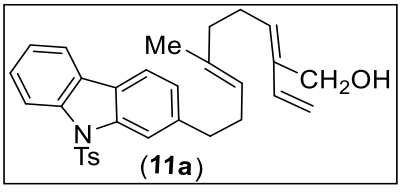
IR (neat) υ_{max} 2980, 2895, 1785, 1660, 1680, 1455, 1233, 956, 840 cm^{-1}.

HRMS (ESI) *m/z*: $[M + Na]^+$ calcd. for $[C_{33}H_{35}O_4NS + Na]^+$ 564.2179, found: 564.2158.

Synthesis of allylic alcohol derivative (11a):



In an oven dried round-bottom long neck flask, α, β-unsaturated ester **12** (2.0 g, 3.692 mmol, 1.0 equiv.) was dissolved in dry CH_2Cl_2 (20 ml), maintaining inertness with N_2 gas balloon and cooled to −78 °C followed by the addition of a solution of DIBAL-H (1 M in hexanes, 3.876 ml, 3.876 mmol, 1.05 equiv.) in dropwise manner over 5 min at −78 °C. The reaction mixture was stirred at the same temperature for an additional 2 h until the full consumption of the starting material. After complete consumption of the starting material (monitored by TLC), a saturated aqueous solution of potassium sodium tartrate (15 ml) was added slowly to the reaction mixture, and the resultant mixture was stirred vigorously for another 1 h at 25 °C. The resulting biphasic mixture was then transferred to a separating funnel and the organic layer was separated. The aqueous layer was further extracted with CH_2Cl_2 (20 ml X 2). The combined organic layers were concentrated under reduced pressure and the residue was purified by silica gel column chromatography with a gradient of 20% EtOAc in *n*-hexane afford the allylic alcohol (**11a**) as pale-yellow liquid (1.68 g, 91% yield).



(2*E*,6*E*)-**6-methyl-9-(9-tosyl-9*H*-carbazol-2-yl)-2-vinylnona-2,6-dien-1-ol**) (**11a**): **11a** was obtained as pale-yellow liquid (3.692 mmol, 1.68 g, 91% yield). $\mathbf{R}_f$ = 0.3 (20% EtOAc in *n*-hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.32 (d, *J* = 8.3 Hz, 1H), 8.18 (s, 1H), 7.88 (d, *J* = 7.6 Hz, 1H), 7.80 (d, *J* = 7.9 Hz, 1H), 7.70 (d, *J* = 8.3 Hz, 2H), 7.48 – 7.44 (m, 1H), 7.36 (t, *J* = 7.5 Hz, 1H), 7.20 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.12 (d, *J* = 8.0 Hz, 2H), 5.88 (dd, *J* = 17.3, 11.3 Hz, 1H), 5.42 (d, *J* = 3.3 Hz, 1H), 5.39 (dd, *J* = 10.8, 1.5 Hz, 1H), 5.28 (t, *J* = 7.1 Hz, 1H), 3.87 (d, *J* = 12.3

Hz, 1H), 3.76 – 3.68 (m, 1H), 3.20 (t, *J* = 6.2 Hz, 1H), 2.86 (t, *J* = 7.7 Hz, 2H), 2.42 (q, *J* = 7.4 Hz, 2H), 2.29 (s, 3H), 2.16 – 2.07 (m, 2H), 1.68 (dt, *J* = 8.8, 6.2 Hz, 2H), 1.58 (s, 3H).

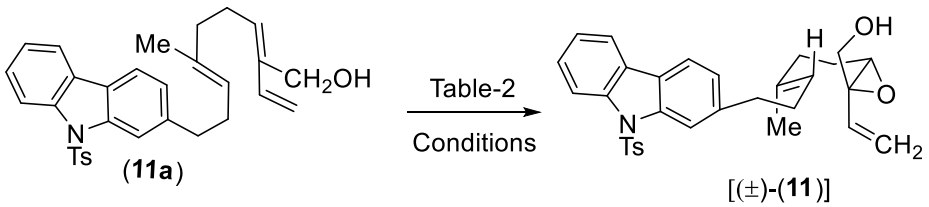
^{13}C NMR (126 MHz, $CDCl_3$): δ 144.8, 142.3, 138.8, 138.5, 135.8, 135.3, 135.1, 132.0, 131.2, 129.6, 129.6, 126.9, 126.5, 126.5, 124.8, 124.4, 124.0, 123.9, 119.7, 119.6, 115.2, 115.2, 114.9, 114.4, 64.8, 39.3, 36.7, 30.3, 25.9, 21.5, 16.1.

IR (neat) υ_{max} 3341, 2980, 2895, 1785, 1660, 1680, 1455, 1233, 1075, 840 cm^{-1}.

HRMS (ESI) *m/z*: $[M + Na]^+$ calcd. for $[C_{31}H_{33}O_3NS + Na]^+$ 522.2073, found: 522.2047.

Racemic epoxidation of 11a:

Table 2: Optimization for Racemic Epoxidation Reaction.

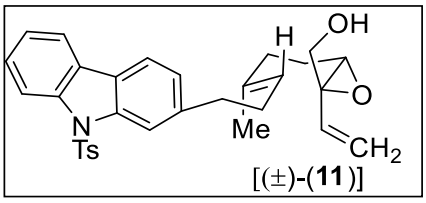


entry	reagent	solvent	temp. (° C)	time (min.)	yield (%)[a,b]
1	*m*-CPBA	CH_2Cl_2	25	10	complex mixture
2	*m*-CPBA	CH_2Cl_2	0	10	complex mixture
3	*m*-CPBA	CH_2Cl_2	–20	10	SM (28%) + 13 (24%) + complex mixture
4	*m*-CPBA	CH_2Cl_2	–60	10	SM (20%) + 13 (53%)

[a]all the reactions are done in 0.10 mmol scale, [b]yields are reported after column chromatography.

An oven dried round-bottom long neck flask, a solution of allylic alcohol **11a** (50 mg, 0.10 mmol, 1.0 equiv.) in CH_2Cl_2 (5 mL) was taken, maintaining inertness with N_2 gas balloon. Next, solid *m*-CPBA (18 mg, 0.102 mmol, 1.02 equiv.) was directly added to the reaction

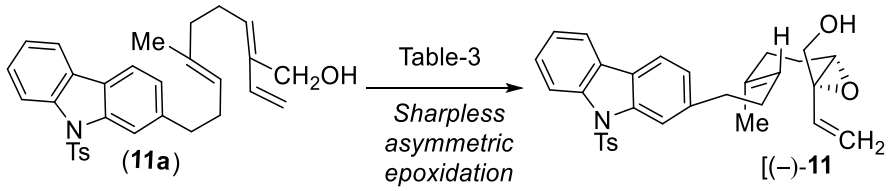
mixture at the same temperature with continuous stirring for additional. The resultant mixture was diluted with 5 mL CH_2Cl_2 and washed with saturated aq. $NaHCO_3$ (5 mL X 2), and brine (5 mL). The organic layer was dried over anhydrous Na_2SO_4, filtered, and concentrated under a vacuum. The residue was purified by flash column chromatography (30% EtOAc in *n*-hexane) to give [(±)-**11**] (27 mg, 0.053 mmol, 53%) as a yellowish liquid.



(2*S*,3*S*)-**3-**((*E*)-**3-Methyl-6-**(**9-tosyl-9*H*-carbazol-2-yl**)**-hex-3-en-1-yl**)**-2-vinyloxiran-2-yl**)**-methanol** [(±)-**11**] : [(±)-**11**] was obtained as yellowish liquid (0.1 mmol, 27 mg, 53% yield).

Sharpless asymmetric epoxidation of 11a:

Table 3: Optimization for Sharpless asymmetric epoxidation.

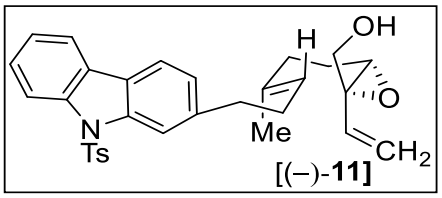


entry	solvent	Ti(O-^{i}Pr)$_4$ (Eq.) : (+)-DET (Eq.)	temp.(° C)	time	yield (%)[a,b]	ee (%)
1	CH_2Cl_2	1:1.2	–20	8 h	92	88
2	$C_2H_4Cl_2$	1:1.2	–20	8 h	83	88
3	Toluene	1:1.2	–20	12 h	86	86
4	CH_2Cl_2	0.5:0.6	–20	14 h	89	91
5	CH_2Cl_2	0.5:0.6	–30	18 h	87	93
6	CH_2Cl_2	0.2:0.3	–30	24 h	88	93
7	CH_2Cl_2	0.1:0.12	–30	32 h	92	93
8	CH_2Cl_2	0.1:0.12	–40	42 h	76	93
9	Toluene	0.1:0.12	–30	42 h	82	91
10	$C_2H_4Cl_2$	0.1:0.12	–30	38 h	73	91

[a]Optimization reactions were carried out on 0.40 mmol of substrate. [b]Yields are isolated after column chromatography.

Procedure for Sharpless asymmetric epoxidation

To a stirred suspension of powdered activated 4Å molecular sieves (500 mg) in CH_2Cl_2 (15 mL) at –30 °C were added (+)-L-diethyl tartrate (62 µL, 0.36 mmol, 0.12 equiv.) and titanium (IV) isopropoxide (107 µL, 0.30 mmol, 0.10 equiv.) sequentially in a flame-dried round-bottom long neck flask, maintaining inertness with N_2 gas balloon. After 10 min of complexation *tert*-butylhydroperoxide (84 µL, 5 M solution in decane, 4.201 mmol, 1.4 equiv.) was added dropwise over 5 min. The resulting mixture was stirred for 40 min followed by the addition of a solution of allyl alcohol **11a** (1.5 g, 3.001 mmol, 1.0 equiv.) in CH_2Cl_2 (15 mL) over 10 min with continuous stirring at –30 °C. After 32 h the reaction mixture was warmed to 0 °C followed by the addition of 10% aqueous solution of NaOH (20 mL), and the mixture was stirred vigorously for 30 min and filtered over a pad of Celite, washed thoroughly with CH_2Cl_2 (30 mL). The organic layer was separated using a separatory funnel. The organic phase was collected, and the aqueous phase was further extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were dried over MgSO4, filtered, and concentrated under a vacuum. The crude product was purified by silica gel column chromatography (30% ethyl acetate in hexane) to afford epoxy alcohol [(–)-**10**] (1.423 g, 92%, 93% ee) as a yellowish liquid.



(2*S*,3*S*)-**3-**((*E*)-**3-Methyl-6-**(**9-tosyl-9*H*-carbazol-2-yl**)-**hex-3-en-1-yl**)-**2-vinyloxiran-2-yl**)-**methanol** [(–)-**11**] : [(–)-**11**] was obtained as colorless gel (3.001 mmol, 1.423 g, 92% yield, 93% ee). R_f = 0.4 (30% EtOAc in *n*-hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.28 (dt, *J* = 8.4, 0.9 Hz, 1H), 8.15 (d, *J* = 0.8 Hz, 1H), 7.84 (ddd, *J* = 7.7, 1.4, 0.7 Hz, 1H), 7.77 – 7.75 (m, 1H), 7.67 (d, *J* = 8.4 Hz, 2H), 7.43 (ddd, *J* = 8.5, 7.3, 1.3 Hz, 1H), 7.32 (td, *J* = 7.5, 1.0 Hz, 1H), 7.17 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.10 – 7.05 (m, 2H), 5.84 (dd, *J* = 17.2, 11.4 Hz, 1H), 5.39 – 5.38 (m, 1H), 5.35 (dd, *J* = 9.5, 1.5 Hz, 1H), 5.27 – 5.22 (m, 1H), 3.84 (d, *J* = 12.3 Hz, 1H), 3.70 (d, *J* = 12.1 Hz, 1H), 3.17 (t, *J* = 6.3 Hz, 1H), 2.82 (t, *J* = 7.7 Hz, 2H), 2.42 – 2.35 (m, 2H), 2.24 (s, 3H), 2.16 – 2.02 (m, 2H), 1.70 – 1.59 (m, 2H), 1.55 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 144.9, 142.3, 138.8, 138.5, 135.1, 135.1, 132.1, 129.7, 129.7, 127.0, 126.6, 126.6, 126.6, 124.8, 124.5, 124.2, 124.0, 119.8, 119.7, 119.4, 115.3, 114.0, 63.8, 63.7, 61.5, 36.8, 36.1, 30.5, 26.1, 21.6, 16.1.

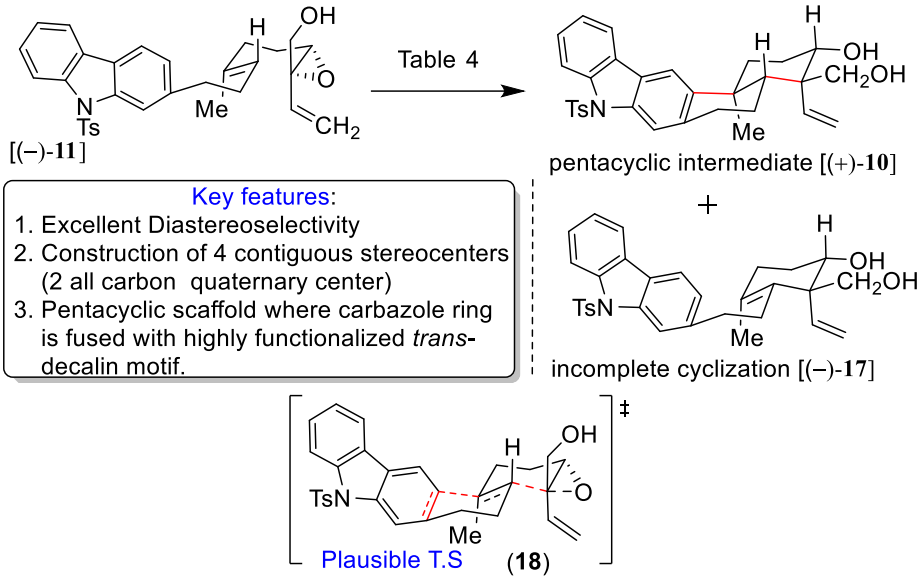
IR (neat) υ_{max} 3341, 2980, 2895, 1785, 1680, 1455, 1280, 1233, 1075, 840 cm^{-1}.

HRMS (ESI) *m/z*: $[M + Na]^+$ calcd. for $[C_{31}H_{33}O_4NS + Na]^+$, 538.2023, found: 538.2036.

$[\alpha]^{25}_{589}$ = – 8.33 (*c* = 0.1, $CHCl_3$).

Lewis Acid mediated epoxy-ene cyclization of [(–)-**11**]**:**

Table 4: Optimization for Epoxy-ene Cyclization Reaction.



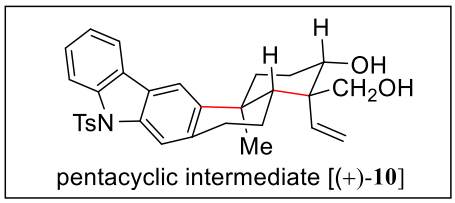
entry	Lewis acid	solvent	temp.	time	product (10:17)%[a,b]
1	$SnCl_4$	$(CH_2Cl)_2$	– 30°C	20 min	58:31
2	$BF_3.OEt_2$	CH_2Cl_2	– 30°C	15 min	51:26
3	Et_2AlCl	CH_2Cl_2	– 30°C	20 min	48:32
4	$Cu(OTf)_2$	toluene	– 30°C	40 min	43:35
5	$SnCl_4$	$(CH_2Cl)_2$	–78 °C	45 min	62:23
6	$SnCl_4$	CH_2Cl_2	–78 °C	45 min	80:12
7	$BF_3.OEt_2$	CH_2Cl_2	–78 °C	40 min	68:16
8	$Ti(O^iPr)_4$	CH_2Cl_2	–78 °C	40 min	71:13
9	Et_2AlCl	CH_2Cl_2	–78 °C	30 min	63:21
10	$TiCl_4$	CH_2Cl_2	–78 °C	30 min	84:7
11	$Cu(OTf)_2$	toluene	–78 °C	45 min	69:18
12	$Cu(OTf)_2$	toluene	– 30°C	40 min	63:22

[a]Optimization reactions were carried out on 0.10 mmol of substrate. [b]Yields are isolated after column chromatography.

Procedure for epoxy-ene cyclization

In an oven dried long-neck round-bottom flask, the epoxy-alcohol [(–)-**11**]**:** (1.2 g, 2.327 mmol, 1.0 equiv.) was taken in anhydrous dichloromethane (20 mL), maintaining inertness with N_2 gas balloon, and was allowed to cool to –78 °C. Then $TiCl_4$ (268 µL, 2.443 mmol, 1.05 equiv.) in DCM (5 mL) was added dropwise manner over a period of 5 min. The reaction mixture was

then allowed to stir at same temperature for 30 min, until the full consumption of the starting material (judged by TLC measurement). The reaction was then quenched by adding saturated $NaHCO_3$ solution (15 mL) and diluted with CH_2Cl_2 (10 mL). The resulting biphasic mixture was then transferred to a separating funnel and the organic layer was separated. The aqueous layer was further extracted with CH_2Cl_2 (20 ml X 2). The combined organic layers were concentrated under reduced pressure and the residue was purified by silica gel column chromatography with a gradient of 40-50% EtOAc in *n*-hexane to give [(+)-**10**] and [(–)-**17**] as a colorless oil.



pentacyclic intermediate [(+)-**10**]

(3*S*,4*R*,4a*R*,13b*S*)**-4-(Hydroxymethyl)-13*b*-methyl-8-tosyl-4-vinyl-2,3,4,4*a*,5,6,8,13*b*-octahydro-1*H*-naphtho-[2,1-*b*]-carbazol-3-ol** [(+)-**10**]: [(+)-**10**] was obtained as colorless gel (2.327 mmol, 1.01 g, 84 % yield). R_f = 0.3 (50% EtOAc in *n*-hexane).

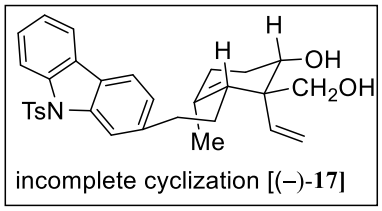
^{1}H NMR (400 MHz, $CDCl_3$): δ 8.23 (d, *J* = 8.3 Hz, 1H), 7.95 (s, 1H), 7.82 (d, *J* = 7.9 Hz, 1H), 7.74 (s, 1H), 7.68 (d, *J* = 8.0 Hz, 2H), 7.41 (t, *J* = 7.9 Hz, 1H), 7.31 (d, *J* = 7.4 Hz, 1H), 7.09 (d, *J* = 8.0 Hz, 2H), 6.13 (dd, *J* = 18.2, 11.5 Hz, 1H), 5.43 (d, *J* = 11.7 Hz, 1H), 5.35 (d, *J* = 18.1 Hz, 1H), 4.25 (d, *J* = 10.9 Hz, 1H), 3.84 (dd, *J* = 11.5, 4.8 Hz, 1H), 3.62 (d, *J* = 10.9 Hz, 1H), 3.16 (d, *J* = 17.8 Hz, 1H), 3.07 (q, *J* = 8.8 Hz, 1H), 2.47 (d, *J* = 13.1 Hz, 1H), 2.26 (s, 3H), 1.97 (d, *J* = 14.0 Hz, 2H), 1.88 – 1.83 (m, 2H), 1.70 – 1.65 (m, 1H), 1.59 – 1.55 (m, 1H), 1.20 (s, 3H).

^{13}C NMR (126 MHz, $CDCl_3$): δ 144.9, 142.0, 138.7, 138.6, 136.2, 135.0, 129.7, 129.7, 127.1, 126.5, 126.5, 126.3, 124.6, 124.5, 123.9, 119.9, 119.8, 118.4, 115.2, 115.0, 75.2, 72.2, 64.0, 51.4, 48.1, 41.3, 38.4, 33.5, 31.0, 27.3, 21.5.

IR (neat) υ_{max} 3341, 2980, 2895, 1785, 1680, 1455, 1280, 1233, 1022, 954, 840 cm^{-1}.

HRMS (ESI) *m/z*: $[M + Na]^+$ calcd. for $[C_{31}H_{33}O_4NS + Na]^+$ 538.2028, found: 538.2026.

Optical Rotation: $[\alpha]^{25}_{589}$ = + 23.0 (*c* = 1.0, $CHCl_3$).



incomplete cyclization [(–)-**17**]

(1*S*,2*R***)-2-(hydroxymethyl)-4-methyl-3-(2-(9-tosyl-9*H*-carbazol-2-yl)-ethyl)-2-vinylcyclohex-3-en-1-ol** [(–)-**17**]: [(+)-**17**] was obtained as colorless gel (2.327 mmol, 84 mg, 7% yield); R_f = 0.35 (50% EtOAc in *n*-hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.34 (d, *J* = 8.4 Hz, 1H), 8.16 (s, 1H), 7.89 (d, *J* = 7.7 Hz, 1H), 7.83 (d, *J* = 7.8 Hz, 1H), 7.71 (d, *J* = 8.0 Hz, 2H), 7.49 (t, *J* = 7.8 Hz, 1H), 7.37 (t, *J* = 7.6 Hz, 1H), 7.22 (s, 1H), 7.13 (d, *J* = 8.0 Hz, 2H), 6.57 (dd, *J* = 18.1, 11.6 Hz, 1H), 5.42 (d, *J* = 11.8 Hz, 1H), 5.19 (d, *J* = 18.1 Hz, 1H), 4.14 (t, *J* = 8.4 Hz, 1H), 3.82 (dd, *J* = 12.2, 4.1 Hz, 1H), 3.60 (d, *J* = 10.9 Hz, 1H), 2.96 – 2.86 (m, 2H), 2.29 (s, 3H), 2.19 – 2.14 (m, 1H), 2.07 (s, 1H), 2.02 (d, *J* = 12.6 Hz, 1H), 1.85 – 1.81 (m, 2H), 1.73 (t, *J* = 3.7 Hz, 1H), 1.52 (s, 3H).

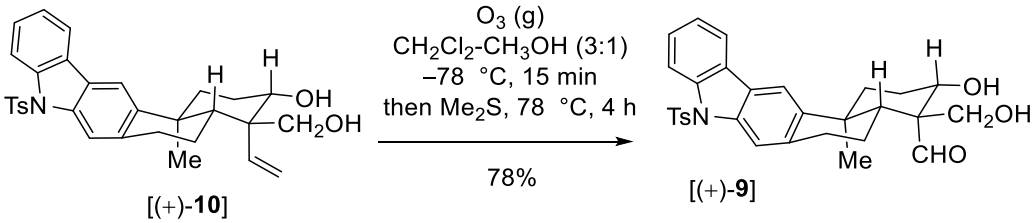
^{13}C NMR (126 MHz, $CDCl_3$): δ 145.0, 142.6, 138.9, 138.7, 137.6, 135.2, 133.6, 129.8, 129.8, 129.2, 127.1, 126.6, 126.6, 126.6, 124.6, 124.4, 124.0, 120.0, 119.8, 118.5, 115.3, 114.7, 73.2, 66.9, 52.9, 36.7, 32.6, 31.4, 29.8, 27.3, 21.6, 20.1.

IR (neat) υ_{max} 3341, 2980, 2895, 1785, 1680, 1455, 1280, 1233, 1022, 950, 890 cm^{-1}.

HRMS (ESI) *m/z*: $[M + Na]^+$ calcd. for $[C_{31}H_{33}O_4NS + Na]^+$ 538.2028, found: 538.2026.

$[\alpha]\ ^{25}_{589}$ = – 26.5 (*c* = 1.0, $CHCl_3$).

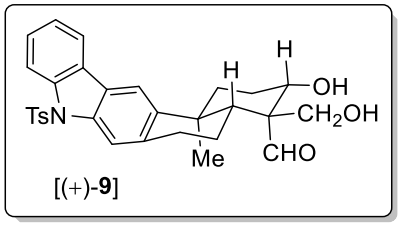
Ozonolysis of diol [(+)-**10**]



[(+)-**10**] [(+)-**9**]

Compound [(+)-**10**] (850 mg, 1.648 mmol, 1.0 equiv.) was dissolved in a solvent mixture of CH_2Cl_2 and CH_3OH (12 mL, 3:1) and was cooled to –78 °C in an acetone bath. O_3 (g) was continuously bubbled through the reaction mixture for 15 min (until the full consumption of

the SM), followed by addition of Me_2S (366 μL, 4.945 mmol, 3.0 equiv.) at the same temperature. The reaction mixture was then allowed to warm to 25 °C and stirred for an additional 4 h. All the volatilities were removed under reduced pressure and the crude product was further purified through column chromatography with a gradient of 50-55% EtOAc/*n*-hexane to afford the aldehyde [(+)-**9**] as a colorless gel (665 mg, 78% yield).



[(+)-**9**]

(3*S*,4*S*,4a*R*,13b*S***)-3-hydroxy-4-(hydroxymethyl)-13b-methyl-8-tosyl-2,3,4,4a,5,6,8,13b-octahydro-1H-naphtho[2,1-b] carbazole-4-carbaldehyde** [(+)-**9**]**: [**(+)-**9**] was obtained as a colorless gel (1.648 mmol, 665 mg, 78% yield). R_f = 0.2 (60% EtOAc in *n*-hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 10.10 (s, 1H), 8.23 (d, *J* = 8.3 Hz, 1H), 7.96 (s, 1H), 7.82 (d, *J* = 7.7 Hz, 1H), 7.76 (s, 1H), 7.68 (d, *J* = 8.4 Hz, 2H), 7.42 (t, *J* = 8.0 Hz, 1H), 7.31 (t, *J* = 7.5 Hz, 1H), 7.10 (d, *J* = 8.2 Hz, 2H), 4.54 (dd, *J* = 10.7, 5.5 Hz, 1H), 3.82 (d, *J* = 11.9 Hz, 1H), 3.74 (d, *J* = 11.0 Hz, 1H), 3.20 (d, *J* = 10.9 Hz, 1H), 3.08 (td, *J* = 10.8, 5.6 Hz, 1H), 2.55 (dd, *J* = 13.6, 3.8 Hz, 1H), 2.26 (s, 3H), 2.16 – 2.13 (m, 2H), 1.95 (dd, *J* = 12.2, 6.6 Hz, 1H), 1.73 – 1.67 (m, 2H), 1.61 (dd, *J* = 14.6, 4.4 Hz, 1H), 1.19 (s, 3H).

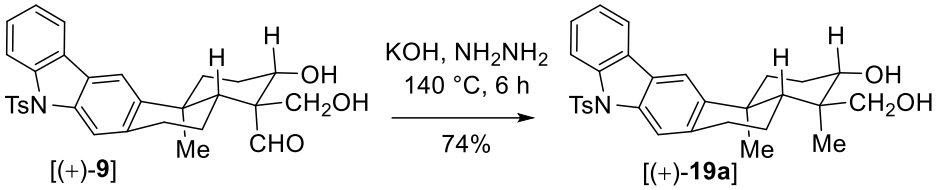
^{13}C NMR (101 MHz, $CDCl_3$) δ 207.1, 144.9, 143.1, 138.6, 137.0, 135.2, 134.5, 129.78, 129.8, 127.2, 126.6, 126.6, 126.5, 124.8, 123.9, 119.7, 115.9, 115.1, 114.8, 68.4, 57.2, 46.7, 37.7, 37.5, 36.9, 31.4, 28.2, 25.5, 21.6, 19.5.

IR (neat) υ_{max} 3572, 2984, 2867, 1753, 1642, 1481, 1368, 1279, 1157, 1042 cm^{-1}.

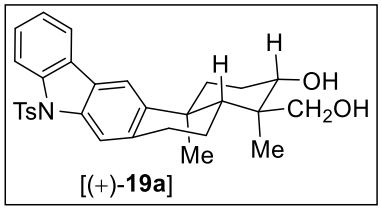
HRMS (ESI) *m/z*: $[M+H]^+$ calcd. for $[C_{30}H_{32}NO_5S]^+$: 518.2001, found: 518.2000.

$[\alpha]^{25}_{589}$ = +67.7 (*c* = 0.18, $CHCl_3$).

Wolff-Kishner reduction of aldehyde [(+)-**9**]**:**



An oven dried round bottom flask was charged with diol aldehyde [(+)-**19a**] (125 mg, 0.241 mmol, 1.0 equiv.) in hydrazine hydrate (6 mL) and the reaction vessel was placed on a preheated oil bath at 140 °C for 1 h for the complete conversion of aldehyde to hydrazone. Then solid KOH (136 mg, 2.414 mmol, 10.0 equiv.) was added at 25 °C. Next, the reaction mixture was refluxed at 140 °C for additional 3 h. The completion of the reaction was confirmed by monitoring TLC. The reaction mixture was then neutralised with 2(N) HCl solution (4 mL). The resulting solution was extracted with EtOAc (8 ml X 3). The combined organic layers were concentrated under reduced pressure, the residue was purified by silica gel column chromatography with a gradient of 40-50% EtOAc in *n*-hexane to give diol [(+)-**19a**] as white foam**.**



(3*S*,4*R*,4a*R*,13b*S*)**-4-(Hydroxymethyl)-4,13b-dimethyl-8-tosyl-2,3,4,4a,5,6,8,13b-octahydro-1H-naphtho** [**2,1-*b***] **carbazol-3-ol** [(+)-**19a**]**:** [(+)-**19a**] was obtained as a white foam (0.241 mmol, 90 mg, 86% yield). R_f = 0.24 (74% EtOAc in *n*-hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.27 (d, *J* = 8.4 Hz, 1H), 7.97 (s, 1H), 7.85 (d, *J* = 7.7 Hz, 1H), 7.76 (s, 1H), 7.71 (d, *J* = 8.2 Hz, 2H), 7.44 (t, *J* = 7.9 Hz, 1H), 7.38 – 7.32 (m, 1H), 7.12 (d, *J* = 8.0 Hz, 2H), 3.83 (d, *J* = 10.4 Hz, 1H), 3.81 – 3.73 (m, 1H), 3.52 (d, *J* = 10.3 Hz, 1H), 3.18 (dd, *J* = 16.9, 6.5 Hz, 1H), 3.08 (dt, *J* = 10.8, 8.2 Hz, 2H), 2.46 (dt, *J* = 13.1, 3.6 Hz, 1H), 2.28 (s, 3H), 1.91 – 1.86 (m, 2H), 1.84 – 1.78 (m, 1H), 1.68 – 1.60 (m, 1H), 1.55 (dt, *J* = 12.0, 4.5 Hz, 1H), 1.29 (s, 3H), 1.04 (s, 3H).

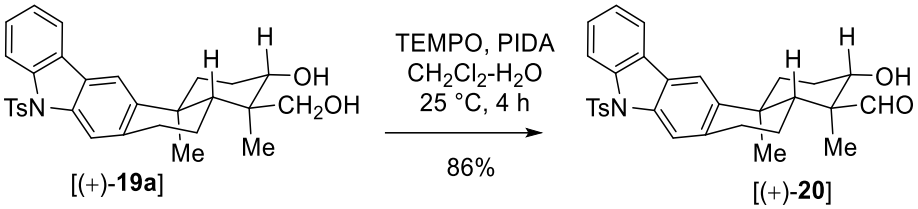
^{13}C NMR (126 MHz, $CDCl_3$): δ 145.6, 144.7, 138.5, 136.7, 135.3, 135.2, 129.7, 129.7, 126.8, 126.7, 126.5, 126.5, 124.4, 123.7, 119.6, 115.4, 115.0, 114.6, 76.2, 71.3, 44.2, 42.2, 37.7, 37.1, 31.1, 27.4, 25.6, 21.5, 19.1, 11.3.

IR (neat) υ_{max} 3658, 3547, 3183, 3061, 2851, 1752, 1521, 1092, 923, 657 cm^{-1}.

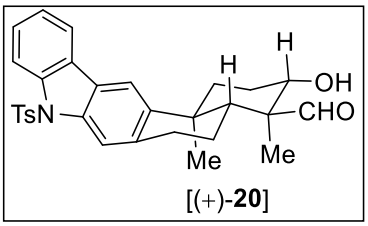
HRMS (ESI) *m/z*: $[M+H]^+$ calcd. for $[C_{30}H_{33}O_4NS + H]^+$ 504.2203, found 504.2191.

$[\alpha]^{25}_{589}$ = +71.5 (*c* = 0.87, CH_3OH).

Synthesis of β-hydroxy aldehyde [(+)-**20**]**:**



In an oven-dried round-bottom flask, diol [(+)-**19a**] (95 mg, 0.188 mmol, 1.0 equiv.) was taken in a mixture of CH_2Cl_2: H_2O (1:1, 4 mL) at 25 °C. To this solution was added TEMPO (38 mg, 0.245 mmol, 1.3 equiv.) and stirred for 5 min. Next, PIDA (79 mg, 0.245 mmol, 1.3 equiv.) was added portion wise to the reaction mixture. The resulting orange-brown mixture was vigorously stirred for an additional 4 h at the same temperature. After completion of reaction (monitored by TLC) saturated aqueous $NaHCO_3$ (4 mL) was added, and excess oxidants were quenched with $Na_2S_2O_3$ (4 mL) and stirred for 5 more min. The mixture was extracted with dichloromethane (8 mL X 2). The organic layers were dried over anhydrous Na_2SO_4 and concentrated in a rotary evaporator under vacuum to afford crude *β*-hydroxy aldehyde [(+)-**20**] as yellow liquid. *β*-hydroxy aldehyde [(+)-**20**] was purified using column chromatography by elute 50% ethyl acetate in *n*-hexane.



(3*S*,4*S*,4a*R*,13b*S*)-**3-Hydroxy-4,13*b*-dimethyl-8-tosyl-2,3,4,4a,5,6,8,13*b*-octahydro-1*H*-naphtho[2,1-*b*] carbazole-4-carbaldehyde** [(+)-**20**]**:** [(+)-**20**] was obtained as a yellow liquid (0.188 mmol, 81 mg, 86% yield), R_f = 0.3 (40% EtOAc in *n*-hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 9.51 (s, 1H), 8.28 (d, *J* = 8.3 Hz, 1H), 8.00 (s, 1H), 7.87 (d, *J* = 7.5 Hz, 1H), 7.78 (s, 1H), 7.72 (d, *J* = 8.0 Hz, 2H), 7.48 – 7.43 (m, 1H), 7.35 (t, *J* = 7.5 Hz, 1H), 7.14 (d, *J* = 7.9 Hz, 2H), 3.90 (dd, *J* = 11.7, 4.6 Hz, 1H), 3.23 – 3.10 (m, 3H), 2.54 (dt, *J* = 13.1, 3.5 Hz, 1H), 2.30 (s, 3H), 2.01 – 1.96 (m, 2H), 1.94 (dd, *J* = 12.4, 2.7 Hz, 1H), 1.77 – 1.69 (m, 1H), 1.51 – 1.47 (m, 1H), 1.31 (s, 3H), 1.25 (s, 3H).

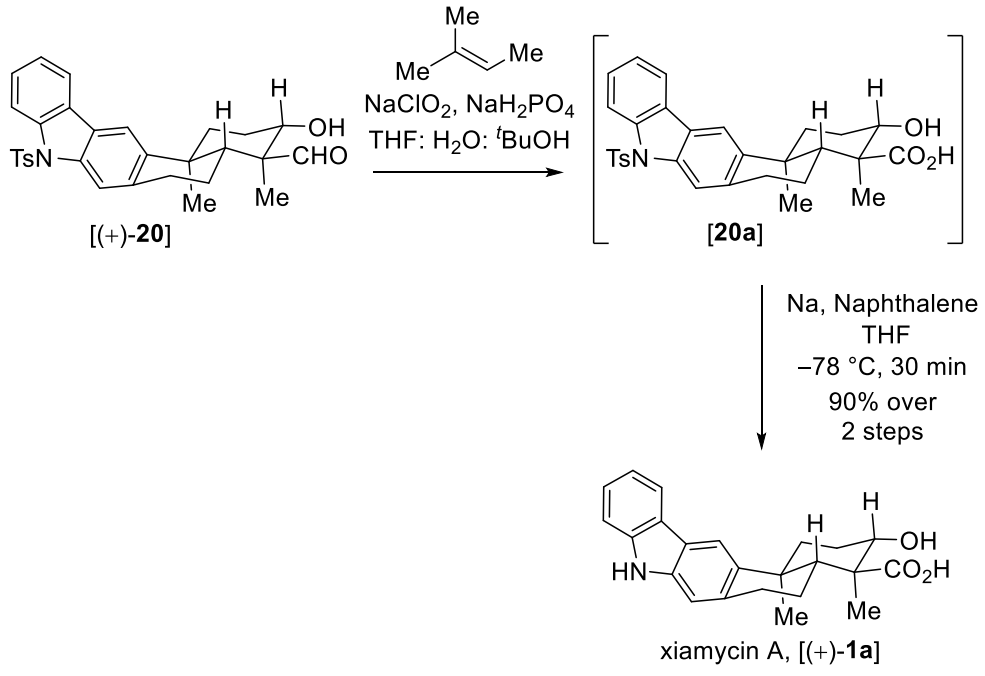
^{13}C NMR (126 MHz, $CDCl_3$): δ 206.6, 144.8, 144.6, 138.5, 136.9, 135.2, 134.8, 129.7, 129.7, 127.0, 126.5, 126.5, 126.5, 124.6, 123.7, 119.6, 115.5, 115.0, 114.8, 71.9, 55.3, 42.9, 36.9, 36.8, 30.7, 27.1, 25.7, 21.5, 20.9, 8.9.

IR (neat)υ_{max}: 3531, 3142, 2981, 2723, 1747, 1499, 883, 758 cm^{-1}.

HRMS (ESI) *m/z*: $[M+H]^+$ calcd. for $[C_{30}H_{31}O_4NS + H]^+$ 502.2052, found 502.2079.

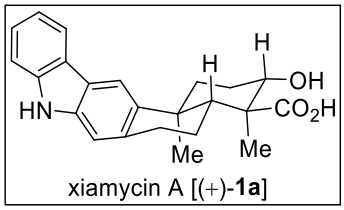
$[\alpha]^{25}_{589}$ = +76.7 (*c* = 0.79, CH_3OH).

Synthesis of xiamycin A [(+)-**1a**]**:**



In an oven dried round bottom flask, the β-hydroxy aldehyde [(+)-**20**] (65 mg, 0.129 mmol, 1.0 equiv.) was taken in a mixture of tetrahydrofuran, tert-butanol and water (4 mL) [THF: H_2O: ^tBuOH (10:10:1)] at 25 °C and 2-methyl-2-butene (137 μL, 1.295 mmol, 10.0 equiv.) was added to the reaction vessel. After 5 min of stirring, NaH_2PO_4 (88 mg, 0.645 mmol, 5.0 equiv.) and $NaClO_2$ (35 mg, 0.387 mmol, 3.0 equiv.) were added sequentially to the reaction mixture. The reaction mixture was allowed to warm to 25 °C with continuous stirring for an additional 2 h. After complete consumption of the starting material (as judged by TLC), it was diluted with water (4 mL) and pH<2 was maintained by addition of 2(*N*) HCl (2 mL). Next, mixture was extracted with EtOAc (8 mL X 3) and organic layer was dried over Na_2SO_4 and concentrated in a rotary evaporator under vacuum to afford *N*-Ts xiamycin A (**20a**) was obtained as white foam, which was taken for the next step without purification.

An over dried round-bottam flask was charged with small pinches of Na-metal (60 mg, 2.58 mmol, 20 equiv.) and naphthalene (331 mg, 2.58 mmol, 20 equiv.) in anhydrous THF (3 mL) at room temperature. The reaction mixture was heated with a hair drier for 3-4 minutes until the solution started turing into greenish color (indicating the formation of Na-naphthalide complex). Next, the reaction mixture was placed into an acetone bath mainting temperature at -78 °C. To this solution was added crude *N*-Ts xiamycin A (**20a**) (0.129 mmol, 1.0 equiv.) obtained from the above step. After the full consumption of the starting material, it was quenched with saturated NH_4Cl solution (3 mL), and the reaction mixture was extracted with EtOAc (10 mL X 3). All organic layers were separated, dried over Na_2SO_4, and concentrated in a rotary evaporator under reduced pressure. The residue was purified by silica gel column chromatography with 70% EtOAc in *n*-hexane to afford naturally occurring xiamycin A [(+)-**1a**] as a white foam (42 mg, 90% over 2 steps).



xiamycin A [(+)-**1a**]

(3*S*,4*S*,4a*R*,13b*S*)-**3-Hydroxy-4,13*b*-dimethyl-2,3,4,4*a*,5,6,8,13*b*-octahydro-1H-naphtho[2,1-*b*] carbazole-4-carboxylic acid** [(+)-**1a**]**:** Natural product xiamycin A [(+)-**1a**]

was obtained as a white foam (0.129 mmol, 42 mg, 90% over 2 steps), R_f = 0.3 (40% EtOAc in *n*-hexane).

^{1}H NMR (500 MHz, CD_3OD): δ 7.97 (d, *J* = 7.7 Hz, 1H), 7.94 (s, 1H), 7.35 (d, *J* = 8.0 Hz, 1H), 7.31 – 7.27 (m, 1H), 7.09 (t, *J* = 7.4 Hz, 1H), 7.07 (s, 1H), 4.13 – 4.07 (m, 1H), 3.14 – 2.98 (m, 2H), 2.63 (dt, *J* = 13.1, 3.4 Hz, 1H), 2.16 (dd, *J* = 12.5, 2.2 Hz, 1H), 2.07 – 1.98 (m, 1H), 1.90 (ddd, *J* = 9.5, 6.4, 3.4 Hz, 2H), 1.78 – 1.71 (m, 1H), 1.55 (ddt, *J* = 12.8, 7.5, 2.2 Hz, 1H), 1.30 (s, 3H), 1.25 (s, 3H).

^{13}C NMR (126 MHz, CD_3OD): δ 181.3, 142.0, 141.8, 140.1, 134.0, 126.0, 124.6, 123.1, 120.5, 119.3, 116.3, 111.4, 110.8, 76.3, 54.9, 47.9, 39.0, 38.3, 32.0, 28.6, 26.3, 22.6, 11.4.

IR (neat) υ_{max} 3321, 2937, 2259, 1675, 1412, 1007, 920, 829 cm^{-1}.

HRMS (ESI) *m/z*: $[M+ Na]^+$ calcd. for $[C_{23}H_{25}O_3N + Na]^+$ 386.1727, found 386.1722.

$[\alpha]^{23}_{589}$ = +109.1 (*c* = 0.52, CH_3OH). lit.[2] $[\alpha]^{21}_D$ = +137.6 (c = 5.3, CH_3OH).

Comparison of **^{1}H-NMR of** (+)-xiamycin A [(+)-**1a**] of this report with natural (+)-**1a** by Hertweck's[2] and with literature by Sarpong[3] and Baran[4]:

Hertweck's isolation report: (+)-xiamycin A [(+)-**1a**] (^{1}H-NMR, 3**00** MHz, CD_3OD) [2]	Sarpong's Total Synthesis of (+)-xiamycin A [(+)-**1a**] (^{1}H-NMR, **700** MHz, CD_3OD) [3]	Baran's Total Synthesis of (+)-xiamycin A [(+)-**1a**] (^{1}H-NMR, **600** MHz, CD_3OD) [4]	This report: (+)-xiamycin A [(+)-**1a**] (^{1}H-NMR, **500** MHz, CD_3OD)
7.96 (dd, *J* = 7.7, 1.1 Hz, 1H)	7.97 (d, *J* = 8.0 Hz, 1H)	7.97 (dt, *J* = 7.8, 1.0 Hz, 1H)	δ 7.97 (d, *J* = 7.7 Hz, 1H)
7.92 (s, 1H)	7.94 (s, 1H)	7.94 (s, 1H)	7.94 (s, 1H)

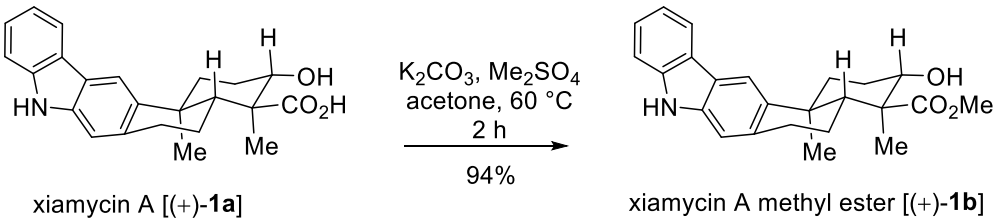
7.34 (dd, *J* = 8.0, 1.1 Hz, 1H)	7.35 (d, *J* = 8.0 Hz, 1H)	7.35 (dt, *J* = 8.1, 0.9 Hz, 1H)	7.35 (d, *J* = 8.0 Hz, 1H)
7.27 (ddd, *J* = 8.0, 7.4, 1.1 Hz, 1H)	7.29 (1H, t, *J* = 7.9 Hz)	7.29 (ddd, *J* = 8.1, 7.1, 1.2 Hz, 1H)	7.31 – 7.27 (m, 1H)
7.08 (ddd, *J* = 8.1, 7.3, 1.1 Hz, 1H)	7.09 (t, *J* = 7.5 Hz, 1H)	7.09 (t, *J* = 7.9, 7.1, 1.0 Hz, 1H)	7.09 (t, *J* = 7.4 Hz, 1H)
7.05 (s, 1H)	7.07 (s, 1H)	7.06 (s, 1H)	7.07 (s, 1H)
4.09 (dd, *J* = 9.1, 7.1 Hz, 1H)	4.10 (dd, *J* = 10.5, 7.5 Hz, 1H)	4.10 (dd, *J* =9.3, 7.1 Hz, 1H)	4.13 – 4.07 (m, 1H)
3.09 (dd, *J* = 16.7, 6.1, 1H)	3.15-3.08 (m, 1H)	3.14 – 3.07 (m, 1H)	3.14 – 2.98 (m, 1H)
3.02 (m, 1H)	3.08-2.99 (m, 1H)	3.06 – 2.98 (m, 1H)	3.14 – 2.98 (m, 1H)
2.61 (td, *J* = 13.1, 3.0 Hz, 1H)	2.64 (d, *J* = 12.8 Hz, 1H)	2.63 (dt, *J* = 13.1, 3.5 Hz, 1H)	2.63 (dt, *J* = 13.1, 3.4 Hz, 1H)
2.15 (dd, *J* = 12.5, 2.0 Hz, 1H)	2.14 (d, *J* = 11.8 Hz, 1H)	2.16 (dd, *J* = 12.6, 2.2 Hz, 1H)	2.16 (dd, *J* = 12.5, 2.2 Hz, 1H)
2.00 (ddd, *J* = 13.4, 12.8, 7.0 Hz, 1H)	2.08-1.98 (m, 1H)	2.01 (tdd, *J* = 12.8, 11.3, 6.9 Hz, 1H)	2.07 – 1.98 (m, 1H)
1.89 (m, 1H)	1.93-1.88 (m, 2H)	1.94 – 1.86 (m, 2H)	1.90 (ddd, *J* = 9.5, 6.4, 3.4 Hz, 2H)
1.74 (m, 1H)	1.78-1.72 (m, 1H)	1.78 – 1.70 (m, 1H)	1.78 – 1.71 (m, 1H)
1.53 (m, 1H)	1.58-1.53 (m, 1H)	1.57 – 1.52 (m, 1H)	1.55 (ddt, *J* = 12.8, 7.5, 2.2 Hz, 1H)
1.29 (s, 3H)	1.30 (s, 3H)	1.29 (s, 3H)	1.30 (s, 3H)
1.23 (s, 3H)	1.25 (s, 3H)	1.24 (s, 3H)	1.25 (s, 3H)

Comparison of ^{13}C-NMR Data:

Hertweck's isolation of (+)-xiamycin A [(+)-**1a**] [^{13}C-NMR, 125.77 MHz, CD_3OD][2]	Baran's Synthesis: (+)-xiamycin A [(+)**1a**] [^{13}C-NMR, 151 MHz, CD_3OD][4]	Sarpong's Synthesis: (+)-xiamycin A [(+)**1a**] [^{13}C-NMR, 176 MHz, CD_3OD][3]	This Synthesis: (+)-xiamycin A [(+)-**1a**] [^{13}C-NMR, 126 MHz, CD_3OD]

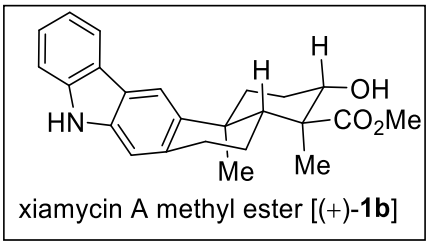
181.3	181.4	181.3	181.3
142.0	142.0	142.0	142.0
141.8	141.8	141.8	141.8
140.1	140.1	140.1	140.1
134.0	134.0	134.0	134.0
126.0	126.1	126.0	126.0
124.7	124.7	124.6	124.6
123.1	123.1	123.1	123.1
120.5	120.6	120.6	120.5
119.3	119.3	119.3	119.3
116.3	116.4	116.4	116.3
111.5	111.4	111.4	111.4
110.8	110.8	110.8	110.8
76.3	76.3	76.3	76.3
54.9	54.9	54.9	54.9
47.9	47.9	47.9	47.9
39.0	39.0	39.0	39.0
38.3	38.3	38.3	38.3
32.0	32.0	32.1	32.0
28.6	28.6	28.7	28.6
26.3	26.3	26.3	26.3
22.6	22.6	22.6	22.6
11.4	11.4	11.4	11.4

Synthesis of xiamycin A methyl ester [(+)-**1b**]**:**



xiamycin A [(+)-**1a**] xiamycin A methyl ester [(+)-**1b**]

In an oven dried round-bottom flask, xiamycin A [(+)-**1a**] (35 mg, 0.096 mmol, 1.0 equiv.) was dissolved in acetone (3 mL) and Me_2SO_4 (11 μL, 0.115 mmol, 1.2 equiv.) was added at 25 °C. Next, K_2CO_3 (16 mg, 0.115 mmol, 1.2 equiv.) was added to the reaction mixture and it was placed on a pre-hated oil bath maintaining temperature at 60 ˚C and stirring was continued for 2 h. After completion of the reaction (monitored by TLC), the reaction mixture was filtered through a celite bed and washed with EtOAc (5 mL X 2). The filtrate was collected, dried over Na_2SO_4 and concentrated in a rotary evaporator under vacuum. The residue was purified by flash column chromatography using 30% EtOAc in *n*-hexane to afford xiamycin A methyl ester [(+)-**1b**] as a white foam (34 mg, 94% yield).



xiamycin A methyl ester [(+)-**1b**]

Methyl (3*S*,4*S*,4a*R*,13b*S*)-**3-hydroxy-4,13b-dimethyl-2,3,4,4a,5,6,8,13b-octahydro-1H-naphtho** [**2,1-b**] **carbazole-4-carboxylate** [(+)-**1b**]**:** Natural product xiamycin A methyl ester [(+)-**1b**] was obtained as a white foam (0.096 mmol, 34 mg, 94% yield), R_f = 0.2 (30% EtOAc in *n*-hexane).

^{1}H NMR (500 MHz, CD_3OD): δ 7.97 (dt, *J* = 7.8, 0.9 Hz, 1H), 7.90 (s, 1H), 7.36 (dt, *J* = 8.1, 0.9 Hz, 1H), 7.30 (ddd, *J* = 8.1, 7.0, 1.2 Hz, 1H), 7.12 – 7.08 (m, 1H), 7.01 (s, 1H), 4.07 – 4.01 (m, 1H), 3.70 (s, 3H), 3.05 – 2.91 (m, 2H), 2.54 (dt, *J* = 13.2, 3.5 Hz, 1H), 2.10 (dd, *J* = 12.6, 2.4 Hz, 1H), 1.97 – 1.90 (m, 1H), 1.87 – 1.82 (m, 2H), 1.67 (dt, *J* = 13.0, 8.6 Hz, 1H), 1.36 – 1.30 (m, 1H), 1.24 (s, 3H), 1.22 (s, 3H).

^{13}C NMR (126 MHz, CD_3OD): δ 179.6, 142.0, 141.6, 140.1, 133.9, 126.0, 124.6, 123.1, 120.6, 119.4, 116.2, 111.5, 110.8, 76.2, 55.4, 52.5, 48.0, 38.8, 38.3, 31.8, 28.4, 26.2, 22.5, 11.3.

IR (neat) υ_{max} 3371, 2917, 2853, 1699, 1615, 1458, 1253, 899, 798, 541 cm^{-1}.

HRMS (ESI) *m/z*: $[M+ Na]^+$ calcd. for $[C_{24}H_{27}O_3N + Na]^+$ 400.1883, found 400.1905.

$[\alpha]^{23}_{589}$ = +121.3 (*c* = 0.61, CH_3OH). lit.[2] $[\alpha]^{21}_{D}$ = +162.4 (c = 1.3, CH_3OH).

Comparison of ^{1}H-NMR Data:

Comparison of ^{1}H-NMR Data of xiamycin A methyl ester [(+)-**1b**] of this report with natural [(+)-**1b**] by Hertweck's[2] and with literature by Sarpong[3]:

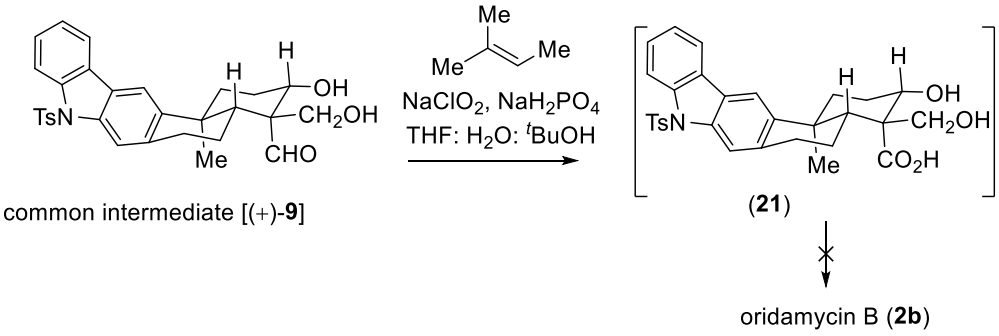
Hertweck's isolation of (+)-xiamycin A methyl ester [(+)-**1b**] (^{1}H-NMR, 300 MHz, CD_3OD)[2]	This report: (+)-xiamycin A methyl ester [(+)-**1b**] (^{1}H-NMR, **500** MHz, CD_3OD)
7.96 (dd, *J* = 7.7, 1.1 Hz, 1H)	7.97 (dt, *J* = 7.8, 0.9 Hz, 1H),
7.92 (s, 1H)	7.90 (s, 1H)
7.34 (dd, *J* = 8.0, 1.1 Hz, 1H)	7.36 (dt, *J* = 8.1, 0.9 Hz, 1H)
7.27 (ddd, *J* = 8.0, 7.4, 1.1Hz, 1H)	7.30 (ddd, *J* = 8.1, 7.0, 1.2 Hz, 1H)
7.08 (ddd, *J* = 8.1, 7.3, 1.1Hz, 1H)	7.12 – 7.08 (m, 1H)
7.05 (s, 1H)	7.01 (s, 1H)
4.05 (dd, *J* = 9.1, 7.1 Hz, 1H)	4.07 – 4.01 (m, 1H)
3.71, (s, 3H)	3.70 (s, 3H)
3.09 (dd, *J* = 16.7, 6.1 Hz, 1H)	3.05 – 2.91 (m, 1H)
2.98 (m, 1H)	3.05 – 2.91 (m, 1H)
2.61 (td, *J* = 13.1, 3.0 Hz, 1H)	2.54 (dt, *J* = 13.2, 3.5 Hz, 1H)
2.13 (dd, *J* = 12.5, 2.0 Hz, 1H)	2.10 (dd, *J* = 12.6, 2.4 Hz, 1H)
2.00 (ddd, *J* = 13.4, 12.8, 7.0 Hz, 1H)	1.97 – 1.90 (m, 1H)
1.88 (m, 2H)	1.87 – 1.82 (m, 2H)
1.74 (m, 1H)	1.67 (dt, *J* = 13.0, 8.6 Hz, 1H)
1.38 (m, 1H)	1.36 – 1.30 (m, 1H)
1.29 (s, 3H)	1.24 (s, 3H)
1.23 (s, 3H)	1.22 (s, 3H)

Comparison of ^{13}C-NMR Data:

Comparison of ^{13}C-NMR Data of Xiamycin A methyl ester [(+)-**1b**] of this report with natural [(+)-**1b**] by Hertweck's[2]

Hertweck's report on isolation of (+) xiamycin A methyl ester [(+)-**1b**] (^{13}C-NMR, 125.76 MHz, CD_3OD)[2]	This Synthesis: (+)-xiamycin A methyl ester [(+)-**1b**] (^{13}C-NMR, 126 MHz, CD_3OD)
179.8	179.6
142.0	142.0
141.8	141.6
140.2	140.1
133.9	133.9
126.1	126.0
124.6	124.6
123.1	123.1
120.5	120.6
119.4	119.4
116.3	116.2
111.5	111.5
110.8	110.8
76.3	76.2
55.4	55.4
52.6	52.5
48.1	48.0
39.0	38.8
38.4	38.3
31.9	31.8
28.5	28.4
26.3	26.2
22.6	22.5
11.3	11.3

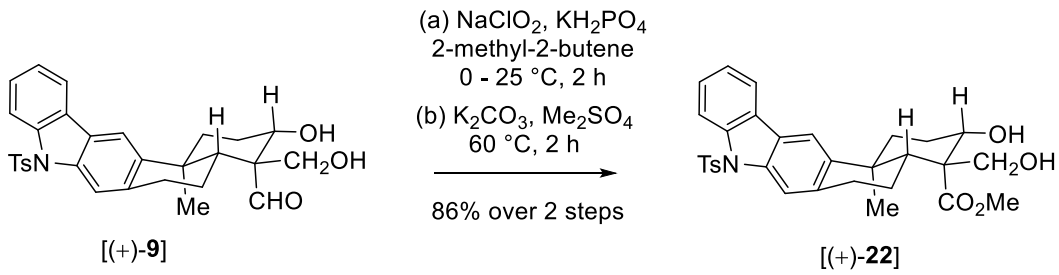
Failure attempt towards oridamycin B [(+)-**2b**]**:**



The aldehyde [(+)-**9**] (120 mg, 0.232 mmol, 1.0 equiv.) was taken in a solvent mixture (5 mL) of tetrahydrofuran, *tert*-butanol and water [THF: H_2O: ^tBuOH (10:10:1)] at 25 °C and 2-methyl-2-butene (246 μL, 2.318 mmol, 10.0 equiv.) was added to the reaction vessel. Followed by KH_2PO_4 (158 mg, 1.159 mmol, 5.0 equiv.) and $NaClO_2$ (63 mg, 0.695 mmol, 3.0 equiv.) were added sequentially. The reaction mixture was allowed to stir for 2 h. After completion of the reaction (as judged by running TLC), it was diluted with water, and pH<2 was maintained by the addition of 2(*N*) HCl (2 mL). Next, the reaction mixture was taken in a separatory funnel and extracted with EtOAc (6 mL X 3) dried over Na_2SO_4 and concentrated in a rotary evaporator under vacuum to afford the acid compound as white foam. The crude acid was charged for the literature-known detosylation reaction conditions (Mg/MeOH and Na/Naphthalene) leading to decomposition.

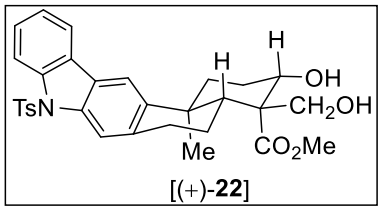
Second Attempt towards oridamycin B:

Synthesis of the *N*-tosyl derivative of oridamycin B methyl ester [(+)-**22**]**:**



The aldehyde [(+)-**9**] (500 mg, 0.966 mmol, 1.0 equiv.) was taken in a solvent mixture (10 mL) of tetrahydrofuran, *tert*-butanol and water [THF: H_2O: ^tBuOH (10:10:1)] at 25 °C and 2-methyl-2-butene (1.0 mL, 9.66 mmol, 10.0 equiv.) was added to the reaction vessel. Followed by KH_2PO_4 (657 mg, 4.829 mmol, 5.0 equiv.) and $NaClO_2$ (262 mg, 2.897 mmol, 3.0 equiv.) were added sequentially. The reaction mixture was allowed to stir for 2 h. After completion of the reaction (as judged by running TLC), it was diluted with water and pH<2 was maintained by addition of 2(*N*) HCl (3 mL). Next, the reaction mixture was taken in a separatory funnel and extracted with EtOAc (8 mL X 3) and dried over Na_2SO_4 and concentrated in a rotary evaporator under vacuum to afford the acid compound as white foam. The crude acid was charged for the next step without further purification.

In an oven-dried round-bottom flask, the crude acid (0.966 mmol, 1.0 equiv.) was dissolved in acetone (8 mL) and Me_2SO_4 (110 μL, 1.159 mmol, 1.2 equiv.) was added at 25 °C. Next, K_2CO_3 (160 mg, 1.159 mmol, 1.2 equiv.) was added to the reaction mixture and the reaction mixture was placed on a preheated oil bath maintaining temperature at 60 °C. The reaction was refluxed for 2 h until the completion of the reaction (monitored by running TLC). After complete consumption of the starting material, the solvent was evaporated, and the residue was dissolved in 8 mL of EtOAc followed by which 8 mL water was added. The resulting biphasic mixture was transferred to a separatory funnel and the organic layer was collected. The aqueous phase was further extracted with EtOAc (8 mL X 2). The combined organic layers were dried over Na_2SO_4 and concentrated in a rotary evaporator under vacuum. The crude product was purified by flash chromatography with a solvent gradient of 40-50% EtOAc in *n*-hexane to furnish the ester [(+)-**22**] as a colorless foam (430 mg, 86% over 2 steps).



[(+)-**22**]

Methyl (3*S*,4*S*,4a*R*,13b*S*)**-3-hydroxy-4-(hydroxymethyl)-13*b*-methyl-8-tosyl-2,3,4,4*a*,5,6,8,13*b*-octahydro-1*H*-naphtho[2,1-b] carbazole-4-carboxylate** [(+)-**22**]**:** [(+)-**22**] was obtained as colorless foam (0.966 mmol, 430 mg, 86% over 2 steps), R_f = 0.2 (50% EtOAc in *n*-hexane).

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.23 (dt, *J* = 8.4, 0.9 Hz, 1H), 7.94 (s, 1H), 7.81 (ddd, *J* = 7.7, 1.3, 0.7 Hz, 1H), 7.75 (s, 1H), 7.68 (d, *J* = 8.4 Hz, 2H), 7.41 (ddd, *J* = 8.5, 7.3, 1.3 Hz, 1H), 7.32 – 7.28 (m, 1H), 7.09 (d, *J* = 8.1 Hz, 2H), 4.35 (t, *J* = 9.4 Hz, 1H), 3.81 (d, *J* = 5.8 Hz, 1H), 3.77 (s, 3H), 3.66 (dt, *J* = 11.8, 5.8 Hz, 1H), 3.16 – 3.10 (m, 1H), 2.99 (ddd, *J* = 17.5, 12.7, 6.0 Hz, 1H), 2.47 (dt, *J* = 13.3, 3.6 Hz, 1H), 2.35 – 2.29 (m, 1H), 2.26 (s, 3H), 2.15 (td, *J* = 9.8, 9.4, 5.0 Hz, 1H), 2.03 – 1.96 (m, 2H), 1.63 (d, *J* = 10.3 Hz, 2H), 1.16 (s, 3H).

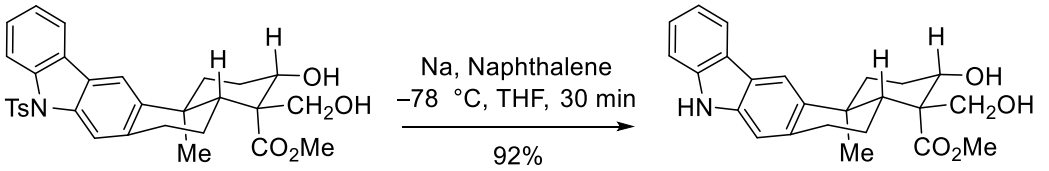
^{13}C NMR (101 MHz, $CDCl_3$): δ 176.3, 144.8, 143.4, 138.6, 136.8, 135.2, 135.1, 129.8, 127.1, 126.6, 126.5, 124.8, 123.8, 119.7, 116.8, 115.1, 114.7, 78.8, 71.1, 53.3, 51.9, 46.8, 38.3, 38.2, 32.8, 29.1, 23.9, 21.6, 21.0.

IR (neat) υ_{max} 3667, 2991, 2885, 2841, 1775, 1481, 1368, 1271, 1093 cm^{-1}.

HRMS (ESI) *m/z*: $[M+H]^+$calcd for $[C_{31}H_{34}NO_6S]^+$: 548.2107, found: 548.2097.

$[\alpha]^{25}_{589}$ = +82.7 (*c* = 0.23, $CHCl_3$).

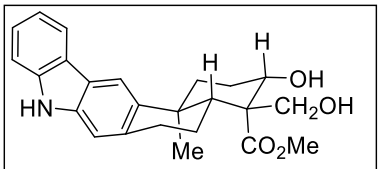
Total synthesis of oridamycin B methyl ester [(+)-**23**]**:**



[(+)-**22**] oridamycin B methyl ester [(+)-**23**]

An oven dried round-bottom flask was charged with small pinches of metallic sodium (approx. 90 mg, 3.651 mmol, 20 equiv.) and naphthalene (468 mg, 3.651 mmol, 20 equiv.) in anhydrous THF (6 mL). The reaction mixture was gently heated with a hair drier for 3-4 min until the solution started turning greenish (indicating the generation of the Na/Naphthalene complex). The greenish solution was then placed at 25 ºC for an additional 15 min (the green color intensifies within the time span). The greenish solution was then added to a cooled solution of hydroxy *N*-tosyl derivative [(+)-**22**] (100 mg, 0.182 mmol, 1.0 equiv.) in anhydrous THF (4 mL) at −78 ºC over a period of 5 min. The reaction mixture was then allowed to stir at the same temperature for an additional 30 min until the full consumption of the starting material. On

completion, the reaction was quenched with saturated NH_4Cl solution (5 mL). The resulting biphasic mixture was then transferred to a separatory funnel and the organic phase was collected. The aqueous phase was further extracted with EtOAc (8 mL X 2). The combined organic layers were collected, dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by flash column chromatography with a solvent gradient of 40-50% EtOAc in *n*-hexane to afford oridamycin B methyl ester [(+)-**23**] as a yellow gel (66 mg, 92% yield).



oridamycin B methyl ester [(+)-**23**]

Methyl (3*S*,4*S*,4a*R*,13b*S***)-3-hydroxy-4-(hydroxymethyl)-13b-methyl-2,3,4,4a,5,6,8,13b-octahydro-1H-naphtho[2,1-b] carbazole-4-carboxylate** [(+)-**23**]**:** [(+)-**23**] was obtained as yellow gel (0.182 mmol, 66 mg, 92% yield); R_f = 0.21 (50% EtOAc in *n*-hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.99 (d, *J* = 7.7 Hz, 1H), 7.95 (s, 1H), 7.85 (s, 1H), 7.37 (dd, *J* = 2.1, 1.0 Hz, 1H), 7.36 (d, *J* = 1.0 Hz, 1H), 7.19 (td, *J* = 5.0, 2.7 Hz, 1H), 7.06 (s, 1H), 4.38 (d, *J* = 10.5 Hz, 1H), 3.82 (d, *J* = 10.5 Hz, 1H), 3.79 (s, 3H), 3.68 (dd, *J* = 12.2, 4.6 Hz, 1H), 3.08 (ddd, *J* = 16.8, 5.3, 2.1 Hz, 1H), 3.03 – 2.93 (m, 1H), 2.59 (dt, *J* = 13.5, 3.6 Hz, 1H), 2.35 (qd, *J* = 13.3, 3.9 Hz, 1H), 2.18 – 2.11 (m, 1H), 2.06 – 1.99 (m, 2H), 1.65 (dd, *J* = 12.1, 2.1 Hz, 2H), 1.22 (s, 3H).

^{13}C NMR (101 MHz, $CDCl_3$): δ 176.4, 140.2, 139.1, 138.3, 133.4, 125.7, 123.5, 122.3, 120.0, 119.3, 117.0, 110.6, 109.7, 79.3, 71.7, 53.3, 51.8, 47.4, 38.7, 38.2, 32.7, 29.3, 24.1, 21.2.

IR (neat) υ_{max} 3652, 3076, 2981, 1887, 1523, 1419, 1273, 1091 cm^{-1}.

HRMS (ESI) *m/z*: $[M+H]^+$calcd for $[C_{24}H_{28}NO_4]^+$: 394.2018, found: 394.2030.

$[\alpha]^{25}_{589}$ = +53.6 (*c* = 0.25, CH_3OH).

Comparison of ^{1}H-NMR Data of (+)-oridamycin B methyl ester [(+)-**23**] of this report with with literature by Trotta[5]:

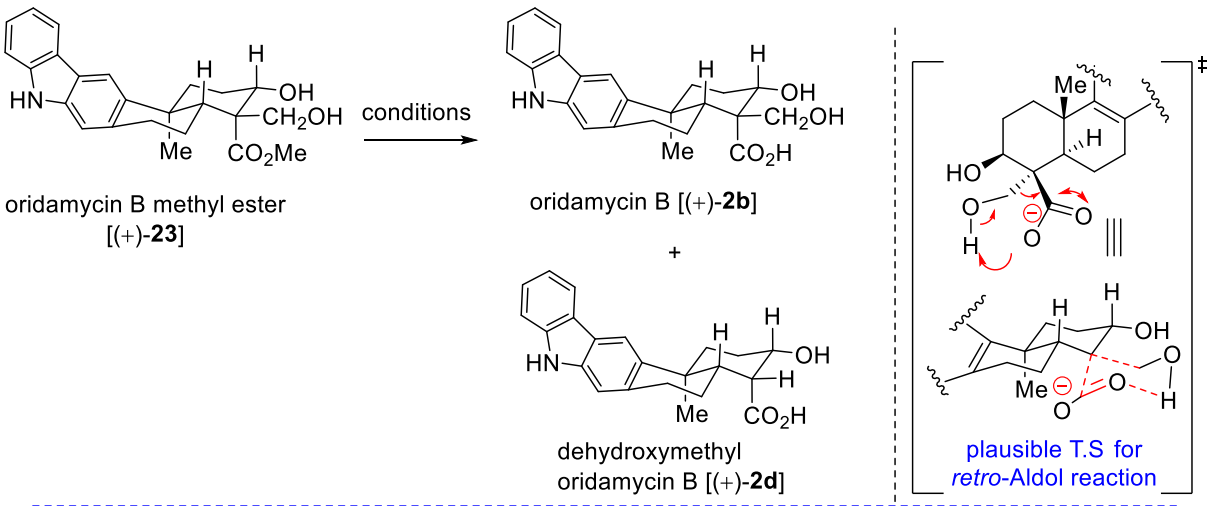
Literature Report by Trotta of (+)-oridamycin B methyl ester [(+)-**23**] (^{1}H-NMR, **600** MHz, $CDCl_3$)[5]	This report: (+)-oridamycin B methyl ester [(+)-**23**] (^{1}H-NMR, **500** MHz, $CDCl_3$)
7.99 (d, *J* = 7.7 Hz, 1H)	7.99 (d, *J* = 7.7 Hz, 1H)
7.95 (s, 1H)	7.95 (s, 1H)
7.83 (s, 1H)	7.85 (s, 1H)
7.37 (d, *J* = 3.9 Hz, 2H)	7.37 (dd, *J* = 2.1, 1.0 Hz, 1H)
7.20 (dq, *J* = 8.0, 4.4 Hz, 1H)	7.19 (td, *J* = 5.0, 2.7 Hz, 1H)
7.07 (s, 1H)	7.06 (s, 1H)
4.38 (t, *J* = 10.6 Hz, 1H)	4.38 (d, *J* = 10.5 Hz, 1H)
3.84 – 3.81 (m, 2H)	3.82 (d, *J* = 10.5 Hz, 1H)
3.80 (s, 4H)	3.79 (s, 3H)
3.69 (td, *J* = 12.0, 4.6 Hz, 1H)	3.68 (dd, *J* = 12.2, 4.6 Hz, 1H)
3.09 (dd, *J* = 16.5, 5.3 Hz, 1H)	3.08 (ddd, *J* = 16.8, 5.3, 2.1 Hz, 1H)
3.05 – 2.95 (m, 1H)	3.03 – 2.93 (m, 1H)
2.59 (dt, *J* = 13.4, 3.6 Hz, 1H)	2.59 (dt, *J* = 13.5, 3.6 Hz, 1H)
2.35 (qd, *J* = 13.2, 3.9 Hz, 1H)	2.35 (qd, *J* = 13.3, 3.9 Hz, 1H)
2.14 (dd, *J* = 14.0, 6.0 Hz, 1H)	2.18 – 2.11 (m, 1H)
2.08 – 1.99 (m, 2H)	2.06 – 1.99 (m, 2H)
1.70 – 1.63 (m, 2H)	1.65 (dd, *J* = 12.1, 2.1 Hz, 2H)
1.22 (s, 3H)	1.22 (s, 3H)

Comparison of ^{13}C-NMR Data of (+)-oridamycin B methyl ester [(+)-**23**] of this report with with literature by Trotta[5]:

Literature Report by Trotta of (+)-oridamycin B methyl ester A methyl ester [(+)-**23**]	This report: (+)-oridamycin B methyl ester A methyl ester [(+)-**23**] (^{13}C-NMR, **101** MHz, $CDCl_3$)

(^{13}C-NMR, **150** MHz, CD_3OD)[5]	
176.4	176.4
140.2	140.2
139.2	139.1
138.3	138.3
133.5	133.4
125.7	125.7
123.6	123.5
122.4	122.3
120.1	120.0
119.4	119.3
117.1	117.0
110.6	110.6
109.8	109.7
79.6	79.3
72.0	71.7
53.4	53.3
51.9	51.8
47.5	47.4
38.8	38.7
38.3	38.2
32.7	32.7
29.4	29.3
24.2	24.1
21.3	21.2

Saponification of oridamycin B methyl ester [(+)-**23**]**:**



entry	conditions	product ratio[a] [(+)-**2b**]:[(+)-**2d**]
1	KOH, THF-H_2O (1:1), 25 °C, 48 h	no reaction
2	KOH, CH_3OH-H_2O (1:1), 25 °C, 48 h	no reaction
3	KOH, THF-H_2O (1:1), 80 °C, 24 h	no reaction
4	KOH, CH_3OH/H_2O/THF(1:1:1), 80 °C, 24 h	conversion in trace
5	LiOH, CH_3OH/H_2O/THF(1:1:1), 80 °C, 24 h	conversion in trace
6	LiOH-KOH, CH_3OH/H_2O/THF(1:1:1), 80 °C, 24 h	**2d** (only **2d**, 72%)[b]
7	LiOH-KOH, CH_3OH/H_2O/THF(1:1:1), 80 °C, 6 h	1:1 + SM[d]
8	LiOH-KOH, CH_3OH/H_2O/THF(1:1:1), 80 °C, 10 h	1:1.2[c,d]

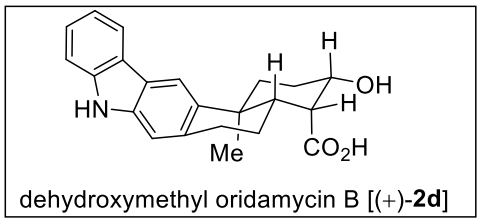
[a]optimization reactions were carried out on 0.04 mmol of substrate.
[b]yields are isolated after column chromatography.
[c]ratio was confirmed from crude NMR.
[d]under silica gel column chromatography [(+)-**2b**] completely decomposes to [(+)-**2d**] *via retro*-Aldol reaction.

General Procedure for Saponification reaction:

In an oven dried round-bottom flask oridamycin B methyl ester [(+)-**23**] (50 mg, 0.127 mmol, 1.0 equiv.) was taken in a solvent mixture of methanol and water (2:1, 3 mL) at 25 °C. Next, KOH (72 mg, 1.27 mmol, 10.0 equiv.) and LiOH (30 mg, 1.27 mmol, 10.0 equiv.) were added sequentially and the reaction mixture was refluxed at 80 ºC. After 10 h (Entry 8, Table 5), the reaction mixture was quenched with 2(*N*) HCl at 0 ºC and the pH of the reaction mixture was adjusted to 2. Then the reaction mixture was extracted with EtOAc (5 mL X 2). The combined

organic layers were collected, dried over Na_2SO_4 and concentrated under reduced pressure. Its crude NMR was taken showing a 1:1.2 ratio of oridamycin B [(+)-**2b**] and dehydroxymethyl oridamycin B [(+)-**2d**].

However, when the crude product was tried for purification by silica gel column chromatography, the mixture of dehydromethyl oridamycin B [(+)-**2d**] and oridamycin B [(+)-**2b**] totally converted to dehydroxymethyl oridamycin B [(+)-**2d**] via retro-Aldol reaction and was collected with a solvent gradient of 2-5% CH_3OH in CH_2Cl_2, affording dehydroxymethyl oridamycin B [(+)-**2d**] as white foam (35 mg, 76% yield). Even purification with neutral or acidic alumina remains unsuccessful. Using the reverse phase HPLC column (Varian Microsorb 300-5 C18 column), as suggested by Trotta[3] and Ang Li et. al[4] turns out to be futile.



dehydroxymethyl oridamycin B [(+)-**2d**]

(3*S*,4*R*,4a*S*,13b*S***)-3-hydroxy-13b-methyl-2,3,4,4a,5,6,8,13b-octahydro-1H-naphtho**[**2,1-b**] **carbazole-4-carboxylic acid** [(+)-**2d**]**:** Dehydroxymethyl oridamycin B [(+)-**2d**] was obtained as white foam (0.127 mmol, 35 mg, 76% yield). R_f = 0.5 (10% CH_3OH in CH_2Cl_2).

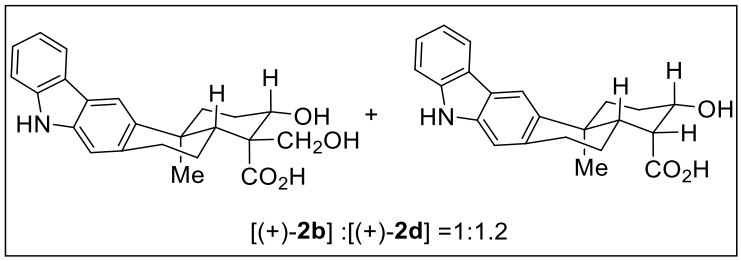
^{1}H NMR (500 MHz, CD_3OD): δ 7.95 (d, *J* = 2.3 Hz, 1H), 7.94 (s, 1H), 7.33 (d, *J* = 8.0 Hz, 1H), 7.28 – 7.24 (m, 1H), 7.07 (d, *J* = 4.1 Hz, 1H), 7.07 – 7.04 (m, 1H), 3.79 (dt, *J* = 10.7, 5.4 Hz, 1H), 3.04 (d, *J* = 3.5 Hz, 1H), 3.03 (d, *J* = 3.5 Hz, 1H), 2.56 (dt, *J* = 13.1, 3.5 Hz, 1H), 2.41 (d, *J* = 10.7 Hz, 1H), 2.05 – 2.01 (m, 1H), 1.81 (d, *J* = 4.3 Hz, 1H), 1.79 (s, 1H), 1.77 – 1.73 (m, 1H), 1.66 (dd, *J* = 6.0, 3.7 Hz, 1H), 1.65 – 1.60 (m, 1H), 1.20 (s, 3H).

^{13}C NMR (101 MHz, CD_3OD): δ 179.6, 141.9, 140.1, 139.1, 134.1, 126.0, 124.5, 122.9, 120.5, 119.3, 116.7, 111.4, 110.6, 73.4, 55.3, 45.0, 37.8, 37.5, 33.0, 31.8, 31.1, 24.2, 23.5.

IR (neat) υ_{max} 3667, 3356, 2991, 2887, 1745, 1551, 1487, 1421, 1068 cm^{-1}.

HRMS (ESI) *m/z*: $[M+ Na]^+$calcd for $[C_{22}H_{23}O_3Na]^+$: 372.1570, found: 372.1561.

$[\alpha]^{25}_{589}$ = +125.8 (*c* = 0.30, CH_3OH).



[(+)-**2b**] :[(+)-**2d**] =1:1.2

Crude NMR data for saponification reaction of oridamycin B methyl ester (**Entry 8, Table 5)** [dehydroxymethyl oridamycin B [(+)-**2d**]: oridamycin B [(+)-**2b**]=(1.2:1)]**:**

^{1}H NMR (500 MHz, CD_3OD): δ 8.01 – 7.93 (m, 4H), 7.41 (dd, *J* = 7.6, 1.9 Hz, 1H), 7.36 (d, *J* = 5.5 Hz, 1H), 7.34 (d, *J* = 5.5 Hz, 1H), 7.30 (t, *J* = 2.3 Hz, 1H), 7.28 – 7.26 (m, 1H), 7.10 (d, *J* = 4.4 Hz, 1H), 7.08 (d, *J* = 5.0 Hz, 1H), 7.06 (s, 1H), 4.10 (d, *J* = 10.9 Hz, 1H), 3.92 (d, *J* = 10.8 Hz, 1H), 3.81 (td, *J* = 10.9, 4.9 Hz, 1H), 3.74 (dd, *J* = 12.3, 4.5 Hz, 1H), 3.04 (td, *J* = 8.4, 7.2, 4.1 Hz, 3H), 2.59 (td, *J* = 10.1, 3.4 Hz, 2H), 2.46 – 2.39 (m, 2H), 2.21 – 2.17 (m, 1H), 2.13 – 2.08 (m, 1H), 2.04 (dt, *J* = 7.8, 3.9 Hz, 1H), 1.98 (d, *J* = 3.8 Hz, 1H), 1.95 – 1.89 (m, 2H), 1.83 (d, *J* = 9.2 Hz, 1H), 1.77 (dd, *J* = 12.4, 3.7 Hz, 1H), 1.67 (dd, *J* = 13.2, 3.9 Hz, 1H), 1.63 – 1.57 (m, 2H), 1.31 (s, 3H), 1.28 (s, 3H).

^{13}C NMR (101 MHz, CD_3OD): δ 141.95, 141.90, 140.56, 140.14, 140.02, 139.09, 134.55, 134.07, 125.99, 125.96, 124.51, 124.49, 123.04, 122.93, 120.49, 120.46, 119.30, 119.24, 117.28, 116.72, 111.38, 111.34, 110.58, 73.41, 73.40, 64.47, 46.34, 45.02, 39.74, 39.25, 37.82, 37.50, 33.34, 32.97, 31.91, 31.13, 25.03, 24.23, 23.55, 22.08.

HRMS Data for oridamycin B [(+)-**2b**] from crude saponification reaction (ESI) *m/z*: [M+ Na]$^+$calcd for $[C_{23}H_{25}NO_3Na]^+$: 402.1681, found: 402.1692.

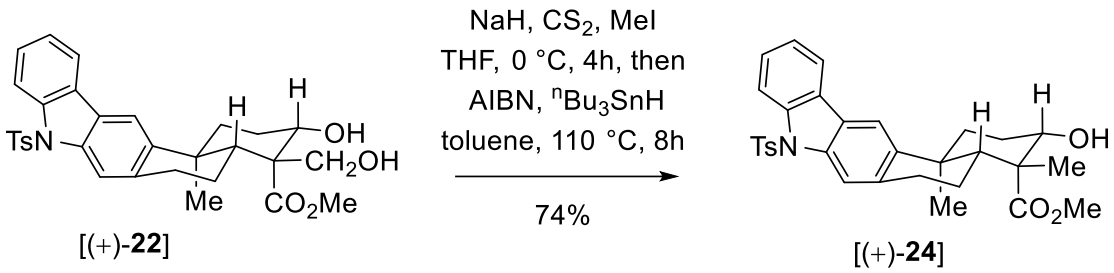
Comparison of ^{1}H-NMR Data: (1). Takada's isolation report[6] of (+)-oridamycin B [(+)-**2b**] (2). This report oridamycin B [(+)-**2b**] from crude saponification reaction (entry 8, Table 5) (3). This report of dehydroxymethyl oridamycin B [(+)-**2d**].

(1). Takada's isolation report for oridamycin B (^{1}H-NMR, 6**00** MHz, CD_3OD)[6]	(2). This report oridamycin B [(+)-**2b**] from crude reaction mixture (^{1}H-NMR, 6**00** MHz, CD_3OD)	(3). This report dehydroxymethyl oridamycin B [(+)-**2d**] (^{1}H-NMR, 5**00** MHz, CD_3OD)
7.95 (d, *J* = 7.9 Hz, 1H)	8.01 – 7.93 (2H)	7.95 (d, *J* = 7.9 Hz, 1H)
7.95 (s, 1H)		7.94 (s, 1H)
7.33 (d, *J* = 7.9 Hz, 1H)	7.41 (dd, *J* = 7.6, 1.9 Hz, 1H)	7.33 (d, *J* = 8.0 Hz, 1H)
7.27 (dt, *J* = 7.9, 1.4 Hz, 1H)	7.36 (d, J = 5.5 Hz, 1H)	7.28 – 7.24 (m, 1H)
7.06 (dt, *J* = 7.9, 1.4 Hz, 1H)	7.10 (d, J = 4.4 Hz, 1H)	7.07 (d, *J* = 4.1 Hz, 1H)
7.05 (s, 1H)	7.08 (d, J = 5.0 Hz, 1H)	7.07 – 7.04 (m, 1H)
4.09 (d, *J* = 11.0, 1H)	4.10 (d, *J* = 10.9 Hz, 1H)	-
3.92 (d, *J* = 11.0, 1H)	3.92 (d, *J* = 10.8 Hz, 1H)	-
3.73 (dd, 12.4, 4.8 Hz, 1H)	3.74 (dd, *J* = 12.3, 4.5 Hz, 1H)	3.79 (dt, *J* = 10.7, 5.4 Hz, 1H)
3.04 (dd, *J* = 10.3, 4.1 Hz, 1H)	3.04 (1H)	3.04 (d, *J* = 3.5 Hz, 1H)
		3.03 (d, *J* = 3.5 Hz, 1H)
2.60 (dt, *J* = 13.0, 3.5 Hz, 1H)	2.46 – 2.39 (1H)	2.56 (dt, *J* = 13.1, 3.5 Hz, 1H)
2.17 (m, 1H)	2.21 – 2.17 (m, 1H)	-
2.08 (m, 1H)	2.13 – 2.08 (m, 1H)	2.05 – 2.01 (m, 1H)
1.95 (m, 1H)	1.98 (d, *J* = 3.8 Hz, 1H)	-
1.92 (dd, 12.2, 2.3 Hz, 1H)	1.95 – 1.89 (1H)	1.81 (d, *J* = 4.3 Hz, 1H)
		1.79 (s, 1H)
		1.77 – 1.73 (m, 1H)
1.59 (m, 1H)	1.63 – 1.57 (1H)	1.66 (dd, *J* = 6.0, 3.7 Hz, 1H)
		1.65 – 1.60 (m, 1H)
1.31 (S, 3H)	1.31 (s, 3H)	1.20 (s, 3H)

Comparison of ^{13}C-NMR Data: (1). Takada's isolation report[6] of (+)-oridamycin B [(+)-**2b**] (2). This report oridamycin B [(+)-**2b**] from crude saponification reaction (entry 8, Table 5) (3). This report of dehydroxymethyl oridamycin B[(+)-**2d**]

(1). Takada's isolation report for oridamycin B[(+)-**2b**] (^{13}C-NMR, 151 MHz, CD_3OD)[1]	(2). This report oridamycin B [(+)-**2b**] from crude reaction mixture (^{13}C-NMR, 101 MHz, CD_3OD)	(3). This report dehydroxymethyl oridamycin B[(+)-**2c**] (^{13}C-NMR, 101 MHz, CD_3OD)
179.2	-	179.6
141.9	141.95	141.90
140.5	140.56	140.14
140.0	140.02	139.09
134.5	134.55	134.07
125.9	125.99	125.96
124.5	124.51	124.49
123.2	123.04	122.93
120.4	120.49	120.46
119.2	119.24	119.30
117.2	117.28	116.72
111.3	111.34	111.38
110.5	110.59	110.58
73.3	73.41	73.40
64.4	64.47	(-CH_2OH group is absent)
55.5	55.48	55.3
46.3	46.34	45.02
39.7	39.74	39.25
39.2	37.82	37.50
33.3	33.34	32.97
29.8	31.91	31.13
25.0	25.03	24.23
22.1	22.08	23.55

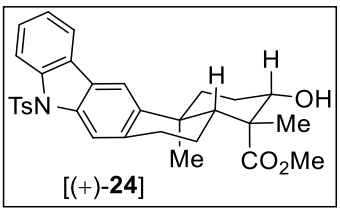
Barton-McCombie deoxygenation of compound [(+)-22]:



An oven dried round-bottom flask was charged with hydroxy tricyclic compound [(+)-**22**] (135 mg, 0.246 mmol, 1.0 equiv.) and CS_2 (16 μL, 0.259 mmol, 1.1 equiv.) in anhydrous THF (5 mL). The reaction mixture was cooled to 0 °C, over an ice-water bath and NaH (12 mg, 0.296 mmol, 1.2 equiv., 60% dispersion in mineral oil) was added. The reaction mixture was allowed to warm to 25 °C with continuous stirring for an additional 4 h and then iodomethane (16 μL, 0.259 mmol, 1.1 eq.) was added. Upon completion of the reaction (as monitored by TLC analysis), the reaction mixture was quenched with saturated NH_4Cl solution (3 mL). The resulting biphasic mixture was transferred to a separatory funnel and the layers that formed were separated. The aqueous phase was further extracted with EtOAc (5 mL X 2). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated in a rotary evaporator under reduced pressure. The crude mono-xanthate derivative (unstable, light-sensitive) was immediately charged for the Barton-McCombie deoxygenation reaction without further purification.

An oven-dried round-bottom flask was charged with the crude mono-xanthate derivative **22a** (0.246 mmol, 1.0 equiv.) and AIBN (4 mg, 0.0246 mmol, 0.10 eq.) in deoxygenated toluene (4 mL) under argon atmosphere. $^{n}Bu_3SnH$ (200 μL, 0.738 mmol, 3.0 eq.) was added to the reaction mixture at 25 °C. Next, the reaction mixture was heated to reflux for 2 h, and upon completion of the reaction (as monitored by TLC analysis), the reaction mixture was diluted with H_2O (10 mL) and EtOAc (10 mL). The resulting biphasic mixture was transferred to a separatory funnel and the layers that formed were separated. The aqueous phase was further extracted with EtOAc (15 mL X 2). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated in a rotary evaporator under reduced pressure. Finally, the crude product was

purified through column chromatography using a solvent gradient of 25-30% EtOAc in *n*-hexane to afford the titled compound [(+)-**24**] as a colorless liquid (97 mg; 74% over 2 steps).



[(+)-**24**]

Methyl (3*S*,4*R*,4a*R*,13b*S*)**-3-hydroxy-4,13*b*-dimethyl-8-tosyl-2,3,4,4a,5,6,8,13*b*-octahydro-1H-naphtho**[**2,1-*b*]** carbazole-4-carboxylate** [(+)-**24**]**:** [(+)-**24**] was obtained as colorless liquid (0.246 mmol, 97 mg, 74% over 2 steps). R_f = 0.3 (30% EtOAc in *n*-hexane).

^{1}H NMR (500 MHz, $CDCl_3$): δ 8.27 (dt, *J* = 8.4, 0.8 Hz, 1H), 7.99 (s, 1H), 7.85 (dt, *J* = 7.5, 1.1 Hz, 1H), 7.79 (s, 1H), 7.72 (d, *J* = 8.4 Hz, 2H), 7.46 – 7.43 (m, 1H), 7.33 (td, *J* = 7.5, 1.0 Hz, 1H), 7.13 (d, *J* = 7.9 Hz, 2H), 3.73 (s, 3H), 3.25 – 3.17 (m, 2H), 3.06 (dd, *J* = 12.4, 5.8 Hz, 1H), 2.48 (dt, *J* = 13.2, 3.6 Hz, 1H), 2.29 (s, 3H), 2.27 – 2.24 (m, 1H), 2.07 – 2.02 (m, 2H), 1.65 – 1.61 (m, 1H), 1.56 (s, 3H), 1.54 (d, *J* = 1.8 Hz, 1H), 1.28 (t, *J* = 2.6 Hz, 1H), 1.15 (s, 3H).

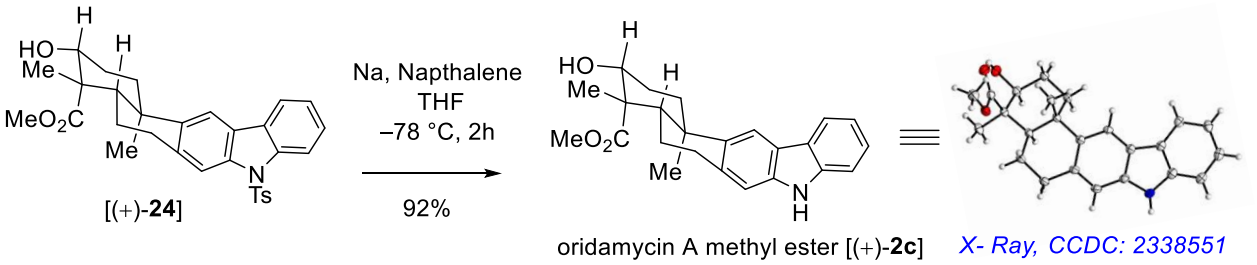
^{13}C NMR (126 MHz, $CDCl_3$): δ 178.5, 144.7, 143.7, 138.5, 136.7, 135.3, 135.2, 129.6, 126.9, 126.5, 126.5, 124.7, 123.7, 119.6, 116.9, 115.0, 114.6, 78.1, 52.4, 51.3, 49.1, 38.6, 38.4, 33.2, 29.1, 23.6, 23.5, 21.5, 21.2.

IR (neat) υ_{max} 3698, 2979, 2868, 1773, 1487, 1389, 1286, 1097 cm^{-1}.

HRMS (ESI) *m/z*: $[M+H]^+$calcd for $[C_{31}H_{34}NO_5S]^+$: 532.2158, found: 532.2143.

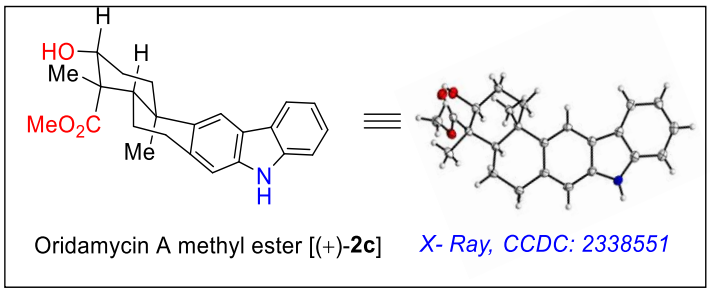
$[\alpha]^{25}_{589}$ = +62.3 (*c* = 0.3, $CHCl_3$).

Total Synthesis of oridamycin A methyl ester [(+)-**2c**]**:**



An oven dried round-bottom flask was charged with small pinches of metallic sodium (approx. 60 mg, 2.63 mmol, 20 equiv.) and naphthalene (338 mg, 2.63 mmol, 20 equiv.) in anhydrous THF (5 mL). The reaction mixture was gently heated with a hair drier for 3-4 min until the solution started turning greenish (indicating the generation of the Na/Naphthalene complex). The greenish solution was then placed at 25 ºC for an additional 15 min (the green color intensifies within the period).

The greenish solution was then added to a cooled solution of hydroxy *N*-tosyl derivative [(+)-**24**] (70 mg, 0.131 mmol, 1.0 equiv.) in anhydrous THF (3 mL) in dropwise manner at –78 ºC over 5 min. The reaction mixture was then allowed to stir at the same temperature for an additional 30 min until the full consumption of the starting material. On completion, the reaction was quenched with saturated NH_4Cl solution (4 mL). The resulting biphasic mixture was then transferred to a separatory funnel and the organic phase was collected. The aqueous phase was further extracted with EtOAc (6 mL X 2). The combined organic layers were collected, dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by flash column chromatography with 25% EtOAc to afford oridamycin A methyl ester [(+)-**2c**] as a white solid (49 mg, 92% yield).



(3*S*,4*R*,4a*R*,13b*S*)**-3-hydroxy-4,13*b*-dimethyl-2,3,4,4a,5,6,8,13*b*-octahydro-1H-naphtho[2,1-*b*] carbazole-4-carboxylic acid** [(+)-**2c**]**:** Oridamycin A methyl ester [(+)-**2c**]

was obtained as white solid (0.131 mmol, 49 mg, 92% yield), R_f = 0.30 (30% EtOAc in *n*-hexane).

Crystallization through slow diffusion with hexane/ethyl acetate affords colorless needle-shaped crystal, which was characterized by single crystal X-ray crystallography.

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.98 (d, *J* = 6.5 Hz, 2H), 7.36 (d, *J* = 8.1 Hz, 1H), 7.30 (ddd, *J* = 8.1, 7.0, 1.2 Hz, 1H), 7.12 – 7.08 (m, 1H), 7.07 (s, 1H), 3.26 (dd, *J* = 12.2, 4.5 Hz, 1H), 3.10 (ddd, *J* = 16.7, 5.4, 2.0 Hz, 1H), 3.02 – 2.94 (m, 1H), 2.61 (dt, *J* = 13.3, 3.6 Hz, 1H), 2.36 – 2.30 (m, 1H), 2.27 – 2.23 (m, 1H), 2.19 – 2.11 (m, 1H), 1.94 (dt, *J* = 13.0, 3.8 Hz, 1H), 1.62 (dd, *J* = 13.7, 9.7 Hz, 1H), 1.56 – 1.54 (m, 1H), 1.52 (s, 3H), 1.29 (s, 3H).

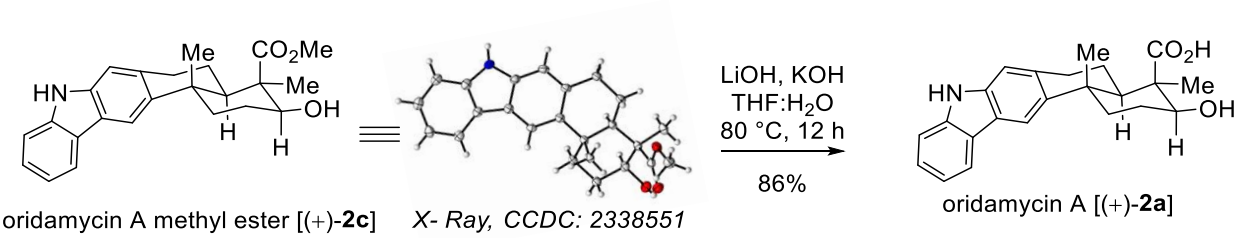
^{13}C NMR (126 MHz, $CDCl_3$): δ 178.6, 140.1, 139.5, 138.2, 133.7, 125.5, 123.5, 122.3, 120.0, 119.2, 117.1, 110.5, 109.7, 78.2, 52.9, 51.3, 49.1, 39.0, 38.4, 33.1, 29.3, 23.8, 23.7, 21.4.

IR (neat) υ_{max} 3380, 2964, 2847, 1732, 1667,1539, 1464, 1234, 791 cm^{-1}.

HRMS (ESI) *m/z*: $[M+ Na]^+$ calcd for $[C_{24}H_{27}O_3NNa]^+$: 400.1883, found: 400.1879.

$[\alpha]^{25}_{589}$ = +87.9 (*c* = 0.20, $CHCl_3$).

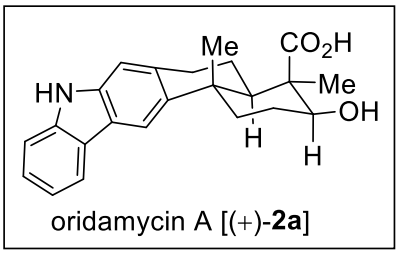
Total synthesis of oridamycin A [(+)-**2a**]**:**



oridamycin A methyl ester [(+)-**2c**] *X- Ray, CCDC: 2338551* oridamycin A [(+)-**2a**]

In an oven dried round-bottom flask oridamycin A methyl ester [(+)-**2c**] (28 mg, 0.074 mmol, 1.0 equiv.) was taken in a mixture of methanol and water (2:1, 3 mL) at 25 °C. Next, LiOH (18 mg, 0.74 mmol, 10 equiv.) was added and the reaction mixture was heated to reflux at 80 ºC. After completion of the reaction as confirmed by TLC analysis (12 h), the reaction mixture was cooled to 25 ºC and quenched with 2(*N*) HCl (3 mL) and the pH of the reaction mixture was

adjusted to 1-2. Then the whole reaction mixture was extracted with EtOAc (8 mL X 2). The combined organic layers were collected, dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by flash column chromatography with 80-90% EtOAc to afford the naturally occurring oridamycin A [(+)-**2a**] as a white foam (24 mg, 86% yield).



oridamycin A [(+)-**2a**]

(3*S*,4*R*,4a*R*,13b*S*)**-3-hydroxy-4,13*b*-dimethyl-2,3,4,4a,5,6,8,13*b*-octahydro-1*H*-naphtho[2,1-*b*] carbazole-4-carboxylic acid** [(+)-**2a**]**:** Oridamycin A [(+)-**2a**] was obtained as white foam (0.074 mmol, 24 mg, 86% yield), R_f **=** 0.20 (70% EtOAc in *n*-hexane).

^{1}H NMR (500 MHz, CD_3OD): δ 7.97 (d, *J* = 8.0 Hz, 1H), 7.96 (s, 1H), 7.35 (d, *J* = 8.1 Hz, 1H), 7.30 (td, *J* = 7.9, 1.1 Hz, 1H), 7.09 (td, *J* = 7.9, 1.1 Hz, 1H), 7.06 (s, 1H), 3.26 (dd, *J* = 12.2, 4.5 Hz, 1H), 3.09 (ddd, *J* = 16.7, 5.4, 2.0 Hz, 1H), 3.01 – 2.93 (m, 1H), 2.60 (dt, *J* = 13.3, 3.6 Hz, 1H), 2.35 – 2.29 (m, 1H), 2.26 – 2.22 (m, 1H), 2.18 – 2.10 (m, 1H), 1.93 (dt, *J* = 13.0, 3.8 Hz, 1H), 1.61 (dd, *J* = 13.7, 9.7 Hz, 1H), 1.55 – 1.53 (m, 1H), 1.51 (s, 3H), 1.29 (s, 3H).

^{13}C NMR (101 MHz, CD_3OD): δ 181.0, 142.1, 140.4, 140.1, 134.5, 126.1, 124.6, 123.2, 120.6, 119.3, 117.5, 111.4, 110.7, 79.1, 54.0, 49.8, 40.0, 39.6, 34.0, 30.3, 24.8, 24.6, 22.5.

IR (neat) υ_{max}: 3366, 2939, 2216, 1655, 1439, 1033, 931, 871 cm^{-1}.

HRMS (ESI) *m/z*: $[M+H]^+$calcd for $[C_{23}H_{26}O_3N]^+$: 364.1913, found: 364.1915.

$[\alpha]^{20}_{589}$ = +68.7 (*c* = 0.12, MeOH); Isolation $[\alpha]^{22.4}_{D}$ = + 73.3 (c = 0.07, MeOH)[6]

Comparison of **^{1}H-NMR** of (+)-oridamycin A [(+)-**2a**] of this report with natural [(+)-**2a**] by Takada[6] and with literature by Sarpong[3]:

Takada's isolation report (^{1}H-NMR, 3**00** MHz, CD_3OD) [6]	Sarpong's Synthesis of (+)-oridamycin A [(+)-**2a**] (^{1}H-NMR, 700 MHz, CD_3OD)[3]	This report: (+)-oridamycin A [(+)-**2a**] (^{1}H-NMR, 500 MHz, CD_3OD)
7.93 (d, *J* = 8.0 Hz, 1H)	7.96 (d, *J* = 8.0 Hz, 1H)	7.97 (d, *J* = 8.0 Hz, 1H)
7.93 (s, 1H)	7.96 (s, 1H)	7.96 (s, 1H)
7.32 (d, *J* = 8.0 Hz, 1H)	7.34 (d, *J* = 8.0 Hz, 1H)	7.35 (d, *J* = 8.1 Hz, 1H)
7.25 (dt, *J* = 8.1, 1.4 Hz, 1H)	7.28 (t, *J* = 7.6 Hz, 1H)	7.30 (td, *J* = 7.9, 1.1 Hz, 1H)
7.05 (dt, *J* = 8.1, 1.4 Hz, 1H)	7.08 (d, *J* = 7.6 Hz, 1H)	7.09 (td, *J* = 7.9, 1.1 Hz, 1H)
7.03 (s, 1H)	7.07 (s, 1H)	7.06 (s, 1H)
3.22 (dd, *J* = 12.2, 4.6 Hz, 1H)	3.26 (d, *J* = 11.5 Hz, 1H)	3.26 (dd, *J* = 12.2, 4.5 Hz, 1H)
3.06 (ddd, *J* = 16.3, 5.4, 2.3 Hz, 1H)	3.10 (dd, *J* = 16.2, 4.6 Hz, 1H)	3.09 (ddd, *J* = 16.7, 5.4, 2.0 Hz, 1H)
2.94 (ddd, *J* = 16.3, 5.4, 2.3 Hz, 1H)	2.98 (dd, *J* = 16.5, 4.6 Hz, 1H)	3.01 – 2.93 (m, 1H)
2.57 (dt, *J* = 13.6, 3.6 Hz, 1H)	2.60 (dd, *J* = 13.2, 2.0 Hz, 1H)	2.60 (dt, *J* = 13.3, 3.6 Hz, 1H)
2.30 (dq, *J* = 12.6, 2.3 Hz, 1H)	2.38 – 2.31 (m, 1H)	2.35 – 2.29 (m, 1H)
2.23 (m, 1H)	2.25 (dd, *J* = 13.9, 6.0 Hz, 1H)	2.26 – 2.22 (m, 1H)
2.09 (dt, *J* = 12.7, 5.4 Hz, 1H)	2.20 – 2.15 (m, 1H)	2.18 – 2.10 (m, 1H)
1.90 (qd, *J* = 13.6, 3.6 Hz ,1H)	1.98 – 1.92 (m, 1H)	1.93 (dt, *J* = 13.0, 3.8 Hz, 1H)
1.58 (dt, *J* = 13.6, 4.1 Hz, 1H)	1.65 – 1.60 (m, 1H)	1.61 (dd, *J* = 13.7, 9.7 Hz, 1H)
1.56 (m, 1H)	1.57 – 1.45 (m, 4H)	1.55 – 1.53 (m, 1H)
1.48 (s, 3H)		1.51 (s, 3H),
1.26 (s, 3H)	1.29 (s, 3H)	1.29 (s, 3H)

Comparison of **^{1}H-NMR** of (+)-oridamycin A [(+)-**2a**] of this report with natural (+)-**2a** by Takada[6] and by Sarpong[3]:

Takada's Isolation of (+)-oridamycin A [(+)-**2a**] (^{13}C-NMR, 151 MHz, CD_3OD)[6]	Sarpong's Synthesis of (+)-oridamycin A [(+)-**2a**] (^{13}C-NMR, 176 MHz, CD_3OD)[3]	This Synthesis: (+)-oridamycin A [(+)-**2a**] (^{13}C-NMR, 101 MHz, CD_3OD)
181.0	181.0	181.0
142.0	142.0	142.1
140.3	140.3	140.4
140.1	140.1	140.1
134.5	134.5	134.5
126.1	126.0	126.1
124.6	124.6	124.6
123.2	123.2	123.2
120.5	120.6	120.6
119.3	119.3	119.3
117.5	117.5	117.5
111.4	111.4	111.4
110.7	110.7	110.7
79.1	79.0	79.1
54.1	54.0	54.0
49.8	49.8	49.8
40.0	39.9	40.0
39.6	39.6	39.6
34.0	34.0	34.0
30.3	30.2	30.3
24.8	24.8	24.8
24.6	24.5	24.6
22.5	22.5	22.5

Crystal Data and Structure Refinement of Compound oridamycin A methyl ester [(+)-2c]

A colorless block 0.22 × 0.19 × 0.14 mm in size was mounted on a Cryoloop with Paratone oil. Data were collected in a nitrogen gas stream at 100(2) K using omega scans. Crystal-to-detector distance was 43.92 mm and exposure time was 0.50 seconds per frame at low angles and 2.00 seconds at high angles, using a scan width of 0.5°. 2Θ range for data collection/° 7.438 to 136.266. A total of 16632 reflections were collected covering the indices $-8 \leq h \leq 8$, $-13 \leq k \leq 13$, $-14 \leq l \leq 12$. 3340 reflections were found to be symmetry-independent, with a R_{int} of 0.0557. Indexing and unit cell refinement indicated a primitive, monoclinic lattice. The space group was found to be P21/c (No. 14). CrysAlis^{Pro} 1.171.41.115a (Rigaku Oxford Diffraction, 2021) Empirical absorption correction using spherical harmonics, implemented in SCALE3 ABSPACK scaling algorithm. Solution by intrinsic phasing (SHELXT-2018/2) produced a heavy-atom phasing model consistent with the proposed structure. All non-hydrogen atoms were refined anisotropically by full-matrix least squares (SHELXL-2018/3). All hydrogen atoms were placed using a riding model. Their positions were constrained relative to their parent atom using the appropriate HFIX command in SHELXL-2018/3.

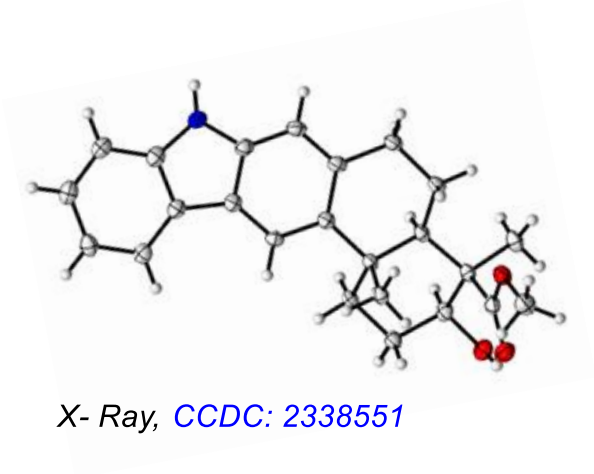


Figure S3. Single crystal XRD structure of compound [(+)-**2c**]. ORTEP drawn at a 50% probability level.

Table 1: Crystal data and structure refinement for SK29 [(+)-**2c**].

Identification code	SK29
Empirical formula	$C_{24}H_{27}NO_3$
Formula weight	377.46
Temperature/K	100(10)
Crystal system	monoclinic

Space group	$P2_1$
a/Å	7.44500(10)
b/Å	10.94740(10)
c/Å	11.98780(10)
α/°	90
β/°	97.5050(10)
γ/°	90
Volume/Å^3	968.676(18)
Z	2
ρ_{calc}g/cm^3	1.294
μ/mm^{-1}	0.673
F(000)	404.0
Crystal size/mm^3	0.22 × 0.19 × 0.14
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	7.438 to 136.266
Index ranges	$-8 \leq h \leq 8$, $-13 \leq k \leq 13$, $-14 \leq l \leq 12$
Reflections collected	12042
Independent reflections	3340 [R_{int} = 0.0557, R_{sigma} = 0.0356]
Data/restraints/parameters	3340/1/258
Goodness-of-fit on F^2	1.048
Final R indexes [I>=2σ (I)]	R_1 = 0.0306, wR_2 = 0.0793
Final R indexes [all data]	R_1 = 0.0312, wR_2 = 0.0801
Largest diff. peak/hole / e Å^{-3}	0.20/-0.14
Flack parameter	-0.11(11)

References:

1. D. B. Denny, S. T. Ross, *J. Org. Chem*. 1962, **27**, 998-1000.

2. a) L. Ding, J. Münch, H. Goerls, A. Maier, H.-H. Fiebig, W.-H. Lin, C. Hertweck, *Bioorg. Med. Chem. Lett.* 2010, **20**, 6685-6687; b) L. Ding, A. Maier, H.-H. Fiebig, W.-H. Lin, C. Hertweck, *Org.Biomol. Chem*. 2011, **9**, 4029-4031; c) Z., Xu, M., Baunach, L., Ding, C., Hertweck, *Angew. Chem. Int. Ed*. 2012, **51**, 10293-10297.

3. M. Pfaffenbach, I. Bakanas, N. R. O'Connor, J. L. Herrick, R. Sarpong, *Angew. Chem. Int. Ed.*, 2019, **58**, 15304-15308.

4. B. Rosen, E. Werner, A. O'Brian, P. Baran, *J. Am. Chem. Soc*. 2014, **136**, 5571-5574.

5. A. H. Trotta, *Org. Lett.* 2015, **17**, 3358-3361.

6. K. Takada, H. Kajiwara, N. Imamura, *J. Nat. Prod*. 2010, **73**, 698-701.