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# Stereoselective synthesis towards (+)-*trans*-kumausyne employing vinylogous Mukaiyama type reaction on an α-chloro sulfide

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A stereoselective synthesis towards (+)-*trans*-kumausyne is disclosed. The key steps of the synthesis include stereoselective C-C formation employing vinylogous Mukaiyama type reaction of an α-chloro sulfide with 2-trimethylsiloxy furan and base-catalyzed isomerization followed by intramolecular oxa-Michael reaction.

**Keywords:** α-Chloro sulfide, Mukaiyama type reaction, oxa-Michael addition, (+)-*trans*-Kumausyne, 2-trimethylsiloxy furan.

The sea is a source of new compounds belonging to unique structural classes. Laurencia, a genus of red algae produces different compounds, for instance non terpenoid C15 metabolites named lauroxanes that are derived from fatty acid metabolism. Kurosawa isolated enantiomers of *trans*- and *cis*-laurediols **1**[1], and later cyclic compounds, (-)-*trans*-kumausyne **2**, *trans*-(+)-deacetylkumausyne **3**[2], Figure 1, from *Laurencia nippponica*. The cyclic ethers with ring size varying from five to nine are considered to originate biogenetically from laurediols **1** via electrophile mediated cyclization.

Kumausyne is characterized by the presence of a tetrahydrofuran ring with unique enyne and bromohexenyl side chains. It has attracted wide interest from the synthetic community and many total[3] and formal syntheses[4] have been disclosed. As a part of a program to demonstrate the utility of α-chloro sulfides as valuable intermediates for C-C bond formation, we disclose herein the synthesis of an advanced intermediate **6** towards (+)-*trans*-kumausyne, *ent*-**2**.

## Results and Discussion

The retrosynthetic disconnection is depicted in Scheme I. *trans*-Kumausyne was envisioned to be obtained from the opening of epoxide **6** by a nucleophilic alkenyl moiety **7** followed by an Appel reaction to introduce the bromine atom with an inversion of configuration at C10. Compound **6** was imagined to be obtained by intramolecular displacement of a nucleofuge at C10 and chain elongation of the lactol, obtained by reduction of the lactone **8**. The bicyclic compound **8** was envisaged to be obtained through a vinylogous Mukaiyama-type reaction of trimethylsiloxy furan **10** with the chloro sulfide obtained from sulfide **9**.

The synthesis commenced with the sulfide **9** prepared following literature precedent.[5] Treatment of sulfide **9** with *N*-chlorosuccinimide (NCS) afforded the α-chloro sulfide **11** which without isolation was reacted with trimethylsiloxy furan **10** in the presence of catalytic amounts of $ZnBr_2$ to furnish an equimolar inseparable mixture[6] of butenolides **12** and **13**, Scheme II. Deprotection of the diol by cleavage of the acetonide yielded the diols **14** and **15**. The diols on treatment with catalytic amounts of DBU afforded the bicyclic compound **8**[7]. The formation of compound **8** can be rationalized by the initial isomerization at C7 (kumausyne numbering) of *threo*-isomer **14** to the thermodynamically stable *erythro*-isomer **15** followed by oxa-Michael reaction.

Access to the target called for epoxide formation and introduction of enyne side chain. Towards this end, the carbinol **8** was converted to mesylate **16** that on treatment with an excess of Raney-Ni under an atmosphere of hydrogen yielded the alcohol **17**, Scheme III. Attempts at preparation of epoxide prior to elaboration of the enyne side chain were frustrated since C11 alkoxide formation using sodium hydride resulted in a complex mixture of products probably as a

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consequence of β-elimination of the C6-oxygen of the tetrahydrofuran ring. Therefore, the enyne side chain was elaborated first. Alcohol **17** was protected as its silyl ether under standard conditions to afford compound **18** that on reduction with DIBAL-H furnished the lactol **19**. The lactol was immediately employed in the Wittig reaction with the ylide obtained from the phosphonium salt **20**[8] to afford the enyne **21**. Acetylation of the carbinol yielded acetate **22** that on treatment with TBAF furnished the epoxide **6**. With epoxide **6** in hand further elaboration of C12-C15 was attempted. Unfortunately, reaction of epoxide **6** with alkenyl lithium or alkenylmagnesium bromide **7** failed to afford the product, only unreacted starting material

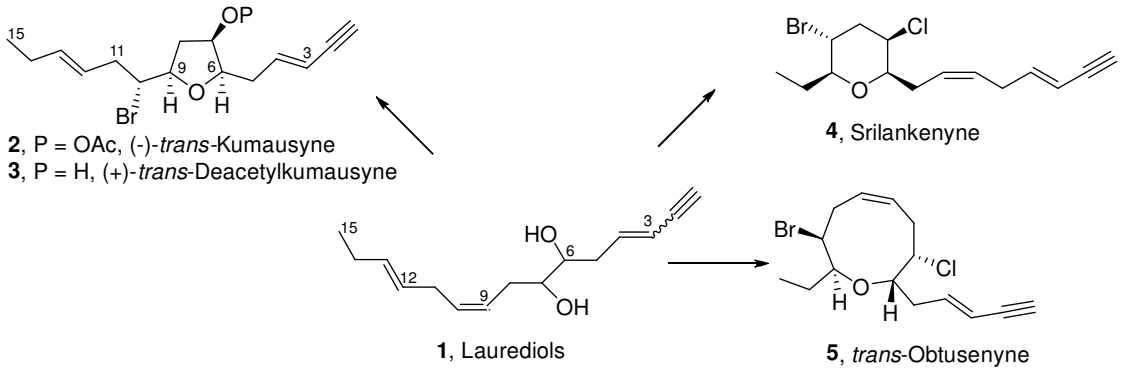
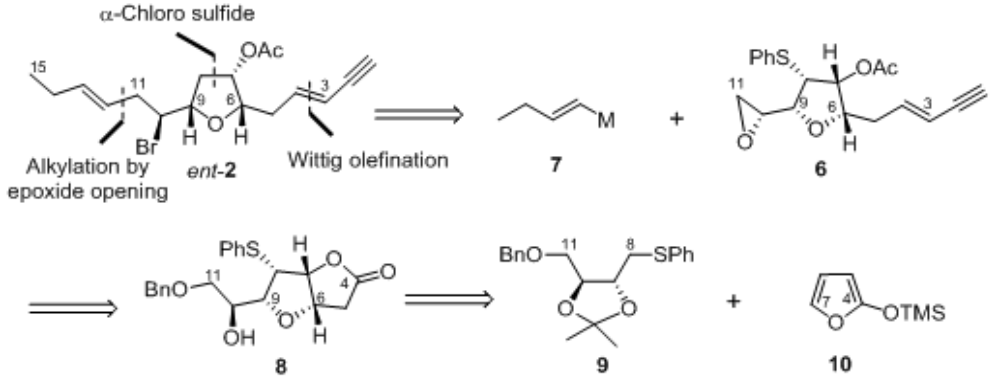
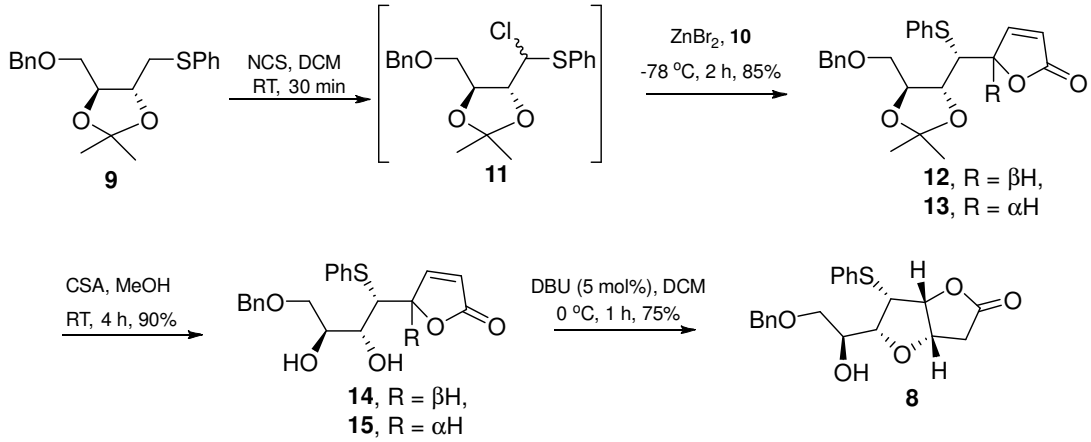


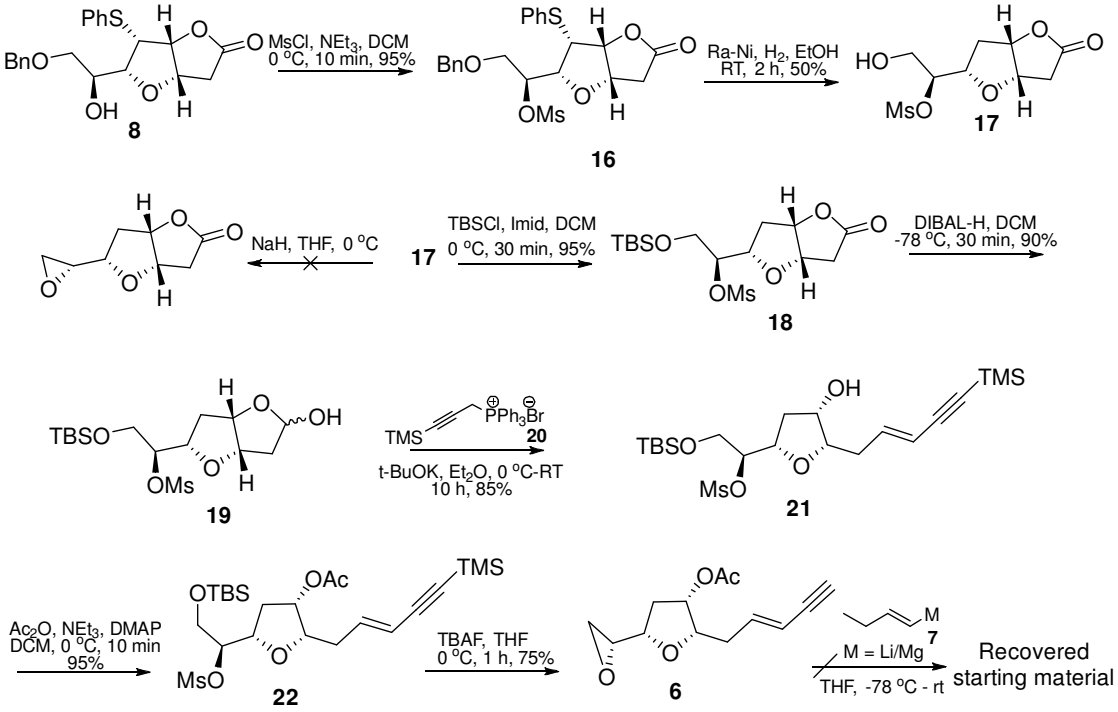

Figure 1 — Representative lauroxanes.




Scheme I — Retrosynthetic analysis of (+)-*trans*-kumausyne.




Scheme II — Synthesis of lactone 8.




Scheme III — Synthesis of advanced intermediate **6**.

was recovered. Since more of epoxide **6** was unavailable and also due to time constraints, the synthesis of (+)-kumausyne could not be completed.

## Experimental Section

### Preparation of lactone 12 and 13

To a solution of sulfide **9** (1.72 g, 5 mmol) in anhydrous DCM (20 mL) was added *N*-chlorosuccinimide (NCS, 750 mg, 5.5 mmol) at rt and stirred for 30 min at the same temperature to afford α-chloro sulfide **11**. The reaction mixture was cooled to -78 °C and $ZnBr_2$ (660 μL, 1 mmol, 1.5 M in THF) followed by 2-trimethylsilyloxyfuran **10** (1.2 mL, 7.5 mmol) were added and the mixture stirred for 2 h at the same temperature. The reaction was quenched by adding saturated aq $NH_4Cl$ (5 mL) and extracted with DCM (3x15 mL). The combined organic layers were washed with brine (10 mL), dried over $Na_2SO_4$ and concentrated under reduced pressure to afford the crude sulfide which was purified by column chromatography using 10% EtOAc/hexanes (v/v) as the eluent to furnish the pure epimeric mixture of sulfide **12** and **13** (*dr* 1:1) as a viscous oil (1.81 g, 4.2 mmol) in 85% yield; TLC, $R_f$ 0.32 (20% EtOAc/hexanes); IR (KBr) 3062, 2924, 2858, 1747, 1573, 1450, 1373, 1259, 1099, 1026, 823, 744 $cm^{-1}$; $^1H$ NMR (500 MHz, $CDCl_3$) δ 7.64 (d, *J* = 5.7 Hz, 1H), 7.43 (d, *J* = 5.7 Hz, 1H), 7.32-7.06 (m, 20H), 6.04 (d, *J* = 5.6 Hz, 1H), 5.96 (d, *J* = 5.7 Hz, 1H), 5.16 (d, *J* = 8.3 Hz, 1H), 5.12 (bs, 1H), 4.5-4.31 (m, 7H), 3.84 (d, *J* = 8.2, 1H), 3.76 (d, *J* = 5 Hz, 1H), 3.73-3.66 (m, 2H), 3.55-3.45 (m, 2H), 3.35 (d, *J* = 8.3, 1H), 1.43 (s, 3H), 1.38 (s, 3H), 1.36 (s, 3H), 1.23 (s, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$): δ 172.6, 172.0, 155.3, 155.2, 137.4, 137.3, 135.0, 133.7, 131.4, 130.5, 129.0, 128.9, 128.1, 127.4, 126.8, 122.0, 121.1, 109.6, 83.9, 82.4, 79.1, 75.9, 75.6, 75.4, 73.3, 70.2, 70.1, 54.6, 51.7, 26.8, 26.64, 26.58, 26.5; MS $[M+Na]^+$ 449; HRMS (ESI) *m/z* calcd for $C_{24}H_{26}O_5SNa$ 449.1398. Found: 449.1382.

### Preparation of diol 14 and 15

To a solution of sulfide **12** and **13** (426 mg, 1 mmol) in MeOH (1 mL) was added CSA (5 mol%) and stirred for 4 h. MeOH was evaporated under reduced pressure and the crude compound was purified by column chromatography using 30% EtOAc/hexanes (v/v) as the eluent to afford the pure diols **14** and **15** as a viscous oil (347 mg, 0.9 mmol) in 90% yield; TLC, $R_f$ 0.25 (50% EtOAc/hexanes); IR (KBr) 3446, 3060, 3028, 2923, 2864, 1784, 1754, 1600, 1582, 1478, 1439, 1309, 1160, 1096, 897, 824; $^1H$ NMR (500 MHz, $CDCl_3$) δ 7.71 (d, *J* = 5.6 Hz, 1H), 7.33-7.12 (m, 21H), 6.2-6.1 (m, 2H), 5.68 (d, *J* = 7.6 Hz, 1H), 5.35

(d, *J* = 8.7 Hz, 1H), 4.77-4.64 (m, 2H) 4.52-4.37 (m, 4H), 3.84-3.64 (m, 8H), 3.56-3.41 (m, 4H); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 173.0, 172.4, 155.9, 155.8, 137.3, 137.2, 134.5, 133.9, 132.5, 131.5, 130.2, 129.0, 128.1, 127.8, 127.7, 127.6, 127.5, 127.4, 127.2, 126.7, 121.7, 121.0, 83.5, 82.5, 73.0, 72.9, 71.5, 71.3, 70.9, 70.5, 70.1, 69.7, 54.6, 54.0; MS $[M+Na]^+$ 409; HRMS (ESI) *m/z* calcd for $C_{21}H_{22}O_5SNa$ 409.10802. Found: 409.10761.

**Preparation of bicyclic lactone 8**

To the solution of diol **14** and **15** (386 mg, 1 mmol) in DCM (10 mL) cooled at 0 °C, DBU (46 *μL*, 0.05 mmol) was added and stirred for 1 h at the same temperature. The reaction was quenched by adding 1N HCl (1 mL). The layer was separated and aqueous layer extracted with DCM (3×10 mL). The combined organic layers were washed with brine (5 mL), dried over $Na_2SO_4$ and solvent evaporated under reduced pressure to afford the crude compound which was purified by column chromatography using 20% EtOAc/hexanes (v/v) as the eluent to afford the pure sulfide **8** as white solid (289 mg, 0.75 mmol) in 75% yield; M. P. 82 °C; TLC, $R_f$ 0.32 (50% EtOAc/hexanes); $[\alpha]^{25}_D$ (+) 26.5 (*c* 1, MeOH); IR (KBr) 3448, 2922, 2853, 1782, 1631, 1462, 1290, 1146, 1073, 896, 744, 695; $^1$H NMR (500 MHz, $CDCl_3$) δ 7.31-7.18 (m, 10H), 5.05-4.97 (m, 1H), 4.91 (d, *J* = 4.3,1H), 4.57 (d, *J* = 12.4 Hz,1H), 4.45 (d, *J* = 12.4 Hz,1H), 4.30-4.26 (m, 1H), 4.07 (ddd, *J* = 10.4, 5.5, 4.3 Hz, 1H), 3.67 (d, *J* = 5.1 Hz, 1H), 3.63-3.52 (m, 2H), 2.72-2.62 (m, 2H); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 175.2, 137.6, 133.2, 131.1, 129.4, 128.5, 127.9, 127.8, 127.6, 88.6, 80.2, 76.9, 73.4, 70.6, 70.5, 53.2, 35.9; MS $[M+Na]^+$ 409; HRMS (ESI) *m/z* calcd for $C_{21}H_{22}O_5SNa$ 409.1085. Found: 409.1082.

**Preparation of mesylate 16**

To the solution of alcohol **8** (386 mg, 1 mmol) in DCM (4 mL) cooled at 0°C was added DMAP (6 mg), $NEt_3$ (207 µL, 1.5 mmol) and MsCl (89 µL, 1.1 mmol) and the mixture stirred for 10 min at the same temperature. The reaction mixture was diluted with DCM (5 mL), washed with water (5 ml), brine (5 mL), dried over $Na_2SO_4$ and the solvent evaporated under reduced pressure. The crude mesylate was purified by column chromatography using 20% EtOAc/hexanes (v/v) as the eluent to afford the pure compound **16** as a liquid (440 mg, 0.95 mmol) in 95% yield; TLC, $R_f$ 0.4 (50% EtOAc/hexanes); $[\alpha]^{25}_D$ (+) 1.7 (*c* 1, MeOH); IR (KBr) 2923, 2855, 1786, 1586, 1448, 1354, 1172, 1038, 974, 924, 811, 743, 696; $^1$H NMR (500 MHz, $CDCl_3$): δ 7.26 – 7.21 (m, 8H), 7.15 (d, *J* = 8.0 Hz, 2H), 4.98 (t, *J* = 4.8 Hz, 1H), 4.92-4.88 (m, 1H), 4.87 (d, *J* = 4.4 Hz, 1H), 4.63 (d, *J* = 12.1 Hz, 1H), 4.47 (dd, *J* = 8.5, 4.1 Hz, 1H), 4.39 (d, *J* = 12.1 Hz, 1H), 3.85 (dd, *J* = 11.5, 4.1 Hz, 1H), 3.73 (dd, *J* = 11.5, 8.5 Hz, 1H), 3.61 (d, *J* = 3.9 Hz, 1H), 3.00 (s, 3H), 2.70 – 2.58 (m, 2H); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 174.8, 136.9, 131.5, 129.4, 128.4, 128.1, 128.0, 127.9, 127.8, 87.3, 81.5, 77.6, 76.8, 73.2, 68.6, 52.7, 38.6, 35.6; MS $[M+Na]^+$487; HRMS (ESI) *m/z* calcd for $C_{22}H_{24}O_7SNa$ 487.08557. Found: 487.08518.

**Preparation of alcohol 17**

To the solution of benzyl ether **16** (464 mg, 1 mmol) in EtOH (4 mL) was added Raney-Nickel (2 g in EtOH) and stirred for 2 h at rt under an atmosphere of hydrogen. The reaction was filtered through Ceilite, washed with EtOAc and concentrated under reduced pressure to afford the crude compound which was purified by column chromatography using EtOAc as the eluent to afford the pure hydroxy mesylate **17** as a liquid (133 mg, 0.5 mmol) in 50% yield; TLC, $R_f$ 0.2 (EtOAc); $[\alpha]^{25}_D$ + 1.5 (*c* 1, MeOH); IR (KBr) 3448, 2927, 2857, 1739, 1461, 1358, 1244, 1175, 1119, 1031, 926, 842, 770; $^1$H NMR (500 MHz, $CDCl_3$): δ 5.15 (t, *J* = 4.8 Hz,1H), 4.84 (t, *J* = 4.8 Hz, 1H), 4.67 (q, *J* = 4.8 Hz,1H), 4.40 (ddd, *J* = 9.7, 5.9, 4.2 Hz, 1H), 3.90 (d, *J* = 5 Hz, 2H), 3.17 (s, 3H), 2.75 (m, 2H), 2.75 (dd, *J* = 18.6, 5.7 Hz, 1H), 2.66 (d, *J* = 18.6 Hz, 1H), 2.48 (dd, *J* = 14.0, 6.0 Hz, 1H), 2.18 (ddd, *J* = 14.0, 9.1, 5.0 Hz, 1H); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 175.3, 84.1, 83.8, 78.9, 77.8, 62.7, 38.9, 36.6, 34.8; MS $[M+Na]^+$ 289; HRMS (ESI) *m/z* calcd for $C_9H_{14}O_7SNa$ 289.03524. Found: 289.03565.

**Preparation of silyl ether 18**

To the solution of hydroxy mesylate **17** (266 mg, 1 mmol) in dry DCM (4 mL) maintained at 0 °C was added imidazole (102 mg, 1.5 mmol), TBS-Cl (165 mg, 1.1 mmol) and the mixture stirred for a period of 30 min. The reaction mixture was diluted with DCM (5 mL), washed successively with water (2 mL), brine (4 mL), dried over $Na_2SO_4$ and the solvent evaporated under reduced pressure to yield the crude product which was purified by column chromatography using 10% EtOAc/hexanes (v/v) to furnish the pure product **18** (361mg, 0.95 mmol) in 95% yield as a liquid; TLC, $R_f$ 0.35 (20% EtOAc/hexanes); $[\alpha]^{25}_D$ + 24.8 (*c* 1, $CHCl_3$); IR (KBr) 2933, 2858, 1784, 1741, 1461, 1351, 1257, 1173, 1092, 923, 834, 796; $^1$H NMR

(500 MHz, $CDCl_3$): δ 5.16-5.1 (m, 1H), 4.85-4.78 (m, 1H), 4.60 (dt, *J* = 7.1, 4.0 Hz, 1H), 4.40-4.35 (m, 1H), 3.93 (dd, *J* = 11.0, 7.1 Hz, 1H), 3.83 (dd, *J* = 11.0, 4.0 Hz, 1H), 3.11 (s, 3H), 2.74 (dd, *J* = 18.1, 5.0 Hz, 1H), 2.66 (d, *J* = 18.1 Hz, 1H), 2.46 (dd, *J* = 14.1, 6.0 Hz, 1H), 1H), 2.22 (ddd, *J* = 14.1, 9.1, 5.0 Hz, 1H), 0.90 (s, 9H), 0.09 (s, 3H), 0.08 (s, 3H); $^{13}$C NMR (75 MHz, $CDCl_3$): δ 175.4, 84.3, 84.1, 78.8, 77.5, 63.4, 38.8, 36.7, 34.8, 25.8, 18.2, -5.5; MS $[M+Na]^+$ 403; HRMS (ESI) *m/z* calcd for $C_{15}H_{28}O_7SSiNa$ 403.12172. Found: 403.12170.

**Preparation of enyne 21**

To the solution of lactone **18** (380 mg, 1 mmol) in dry DCM (4 mL) cooled at -78 °C was added DIBAL-H (0.88 mL, 1.1 mmol, 1.25 M in toluene) dropwise and the reaction mixture was stirred for 30 min at the same temperature. The reaction mixture was allowed to warm 0 °C and quenched by adding ice pieces and stirred further for 15 min at the same temperature. The mixture was diluted with DCM (5 mL). The aqueous layer was separated and extracted with DCM (3x5 mL). The combined organic layers were washed with brine (5 mL), dried over $Na_2SO_4$ and concentrated under reduced pressure to afford the lactol **19** as liquid in 90% yield; TLC, $R_f$ 0.3 (50% EtOAc/hexanes). The lactol **19** was used for the next step without purification.

To the suspension of *t*-BuOK (168 mg, 1.5 mmol) in ether (75 mL) was added 3-trimethylsilyl-2-propynyl-triphenylphosphonium bromide **20** (679 mg, 1.5 mmol) at rt. The reaction mixture was stirred for 3 h and then the solution of the lactol **19** (382 mg, 1 mmol) in ether (20 mL) was added and stirring continued for 7 h. The reaction mixture was cooled to 0 °C and quenched with ice, the layers were separated and the aqueous layer extracted with ether (3×10 mL). The combined organic layers were washed with brine (10 mL), dried over $Na_2SO_4$ and the solvent evaporated under reduced pressure to afford the crude product which was purified by column chromatography using 10% EtOAc/hexanes (v/v) as the eluent to afford the pure enyne **21** as oil in 85% yield; TLC, $R_f$ 0.5 (20% EtOAc/hexanes); $[\alpha]^{25}_D$ + 11.4 (*c* 1, $CHCl_3$); IR (KBr) 2925, 2854, 1709, 1460, 1376, 1254, 1175 $cm^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$): δ 6.18 (td, *J* = 15.8, 7.4 Hz, 1H), 5.62 (d, *J* = 15.8 Hz, 1H), 4.55 (q, *J* = 4.7 Hz 1H), 4.44-4.39 (m, 1H), 4.35-4.30 (bs, 1H), 3.97-3.87 (m, 2H), 3.83 (dd, *J* = 11.4, 3.8 Hz, 1H), 3.12 (s, 3H), 2.51-2.37 (m, 2H), 2.14-2.02 (m, 2H), 0.90 (s, 9H), 0.18 (s, 9H), 0.09 (s, 3H), 0.08 (s, 3H);$^{13}$C NMR (75 MHz, $CDCl_3$): δ 141.3, 131.0, 128.9, 112.4, 85.5, 81.7, 76.1, 72.5, 63.6, 39.0, 37.8, 33.1, 26.0, 18.1, 0.1, -5.3; MS $[M+Na]^+$ 499; HRMS (ESI) *m/z* calcd for $C_{21}H_{40}O_6SSi_2Na$ 499.1976. Found: 499.1997.

**Preparation of acetate 22**

To the solution of alcohol **21** (476 mg, 1 mmol) in anhydrous DCM (4 mL) cooled at 0°C was added DMAP (6 mg), $NEt_3$ (206 µL, 1.5 mmol) and acetic anhydride (112 µL, 1.1 mmol) and the mixture stirred at rt for 10 min. The reaction mixture was diluted with DCM (5 mL), washed with water (5 mL), brine (5 mL), dried over $Na_2SO_4$ and concentrated under reduced pressure to afford the crude product which was purified by column chromatography using 10% EtOAc/hexanes (v/v) as the eluent to afford the pure acetate **22** as an oil (492 mg, 0.95 mmol) in 95% yield; TLC, $R_f$ 0.42 (20% EtOAc/hexanes); $[\alpha]^{25}_D$ + 2.3 (*c* 1, $CHCl_3$); IR (KBr) 2923, 2853, 2380, 1732, 1627, 1462, 1352, 1251, 1173, 1121, 965, 923, 841, 776; $^1$H NMR (500 MHz, $CDCl_3$): δ 6.13 (td, *J* = 15.9, 6.9 Hz, 1H), 5.56 (d, *J* = 15.9 Hz, 1H), 5.33-5.31 (m, 1H), 4.56 (q, *J* = 4.9 Hz,1H), 4.41-4.35 (m, 1H), 4.05-3.99 (m, 1H), 3.93 (dd, *J* = 11.5, 6.0 Hz, 1H), 3.82 (dd, *J* = 11.5, 2.7 Hz, 1H),3.12 (s, 3H), 2.38-2.32 (m, 2H), 2.22-2.13 (m, 2H), 2.09 (s, 3H), 0.89 (s, 9H), 0.17 (s, 9H), 0.09 (s, 3H), 0.08 (s, 3H); $^{13}$C NMR (125 MHz, $CDCl_3$): δ 170.3, 140.9, 130.8, 128.8, 112.5, 84.9, 80.5, 76.3, 74.9, 63.5, 39.0, 35.4, 33.3, 26.0, 20.9, 18.1, 0.0, -5.3; MS $[M+Na]^+$ 541; HRMS (ESI) *m/z* calcd for $C_{23}H_{42}O_7SSi_2Na$ 541.20820. Found: 541.20955.

**Preparation of epoxide 6**

To the solution of the TBS ether **22** (518 mg, 1 mmol) in THF (10 mL) at 0 °C was added TBAF (3 mL, 3 mmol, 1 M in THF) and the mixture stirred at rt for 1 h. The reaction mixture was cooled to 0 °C and quenched by adding saturated aq $NH_4Cl$ (3 mL). The layers were separated and the aq layer was extracted with EtOAc (3x5 mL).The combined organic layers were washed with brine (5 mL), dried over $Na_2SO_4$ and concentrated under reduced pressure to afford the crude product which was purified by column chromatography using 10% EtOAc/hexanes (v/v) as the eluent to afford the pure epoxide **6** as an oil (177 mg, 0.75 mmol) in 75% yield; TLC, $R_f$ 0.2 (20% EtOAc/Hexanes); IR (KBr) 2924, 2856, 2380, 1736, 1626, 1457, 1381, 1243, 1079, 759; $^1$H NMR (500 MHz, $CDCl_3$): δ 6.21 (td, *J* = 15.9, 7.9 Hz, 1H), 5.55 (d, *J* = 15.8 Hz, 1H), 5.33-5.31 (m, 1H), 4.27-4.20 (m, 1H), 4.10-4.0 (m, 1H), 3.13-3.06 (m, 1H),

2.83-2.76 (m, 1H), 2.62-2.50 (m, 1H), 2.5-2.3 (m, 2H), 2.14-1.96 (m, 5H);$^{13}$C NMR (75 MHz, $CDCl_3$): δ 170.4, 141.7, 140.8, 111.7, 111.1, 80.1, 76.9, 74.8, 52.8, 44.5, 34.0, 33.1, 21.1; MS $[M+Na]^+$ 259.

**Preparation of *trans*-1-iodobutene 7**

1-Butyne gas (8.0 mL, 100 mmol) was collected in a round bottom flask fitted with a Dewar condenser at -78 °C, THF (200 mL) was added followed by DIBAL-H (80.8 mL, 101 mol, 1.25 M in toluene) and the mixture stirred for 4 h at -78 °C. Iodine (25 g, 100 mmol) in THF (100 mL) was added and the mixture gradually allowed to attain rt and stirred for 2 h. The reaction mixture was cooled to 0 °C and quenched by adding aq $Na_2S_2O_3$ (20 mL). The layers were separated and the organic layer was washed with brine, dried over $Na_2SO_4$ and purified by distillation to afford *trans*-1-iodobutene **7** as a colorless liquid in 76% yield.$^1$H NMR (500 MHz, $CDCl_3$) δ 6.55 (dt, *J* = 17.5, 5.2 Hz, 1H), 5.95 (d, *J* = 17.5 Hz, 1H), 2.15 (q, *J* = 6.5 Hz, 2H), 1.02 (t, *J* = 6.5 Hz, 3H).

**Preparation of propargyl bromide**

To the solution of propargyl alcohol (2.8 g, 2.9 mL, 50 mmol) in anhydrous THF (100 mL) was added *n*-butyllithium (58.4 mL, 105 mmol, 1.8 M in hexanes) maintaining the temperature at -78 °C, and the mixture stirred at the same temperature for 30 min. Trimethylchlorosilane (11.4 g, 13.3 mL, 105 mmol) was added and the mixture was allowed to warm to rt and stirred for 30 min to furnish the disilylated compound. Aq hydrochloric acid (3N, 600 mL) was added and the solution was stirred for 1 h to afford the alcohol. Water (30 mL) was added and aq layer was extracted with ether (3x100 mL), the combined organic layers were washed with sodium bicarbonate (20 mL), brine (10 mL) and dried over sodium sulfate. The solvent was evaporated under reduced pressure until the volume was about 70 mL. The mixture was cooled to -78 °C and *n*-butyllithium (30.6 mL, 55 mmol, 1.8 M in hexane) was added and stirred for 30 min at the same temperature. *p*-Toluenesulfonyl chloride (104.8 g, 550 mmol) in THF (300 mL) was added. The mixture was allowed to warm to room temperature during a period of 1 h. The reaction mixture was cooled to 0°C and water (20 mL) was added and aq layers were extracted with ether (3x100 mL). The combined organic layers were washed with brine (20 mL) and dried over sodium sulfate. The solvent was evaporated under vacuum to afford the tosylated compound. To the tosylated compound in acetone (1 L) was added lithium bromide (87.0 g, 1 mol) at room temperature and stirred for 3 h. The reaction mixture was diluted with water (150 mL), the layers were separated and the aq layer extracted with ether (3x100 mL). The combined organic layers were washed with brine (10 mL) and dried over sodium sulfate. The solvent was evaporated under reduced pressure to afford the crude compound which was distilled at 62.5-64.5 °C at 15 mmHg to afford propargyl bromide in in 59% yield (55.88 g) as a colorless liquid. $^1$H NMR (500 MHz, $CDCl_3$): δ 3.88 (s, 2 H), 0.15 (s, 9 H).

**Preparation of Wittig salt 20**

To a solution of 3-bromo-1-trimethylsilylprop-1-yne (20 mmol, 4 g) in benzene (20 mL) was added triphenylphosphine (27 mmol, 7.2 g) and the mixture was stirred at rt for 12 h. The precipitate was filtered off, washed with hexanes and dried under vacuum to yield the pure compound **20** in 76% yield (6,5 g), M. P. 155-159 °C (lit., 154-156 °C); $^1$H NMR (500 MHz, $CDCl_3$): δ 7.89-7.87 (m, 15H), 5.92 (d, *J* = 11.4 Hz, 2H), 0.07 (s, 9 H).

**Conclusion**

In summary, we have disclosed a stereoselective route for the synthesis of an advanced intermediate towards (+)-*trans*-kumausyne, exploiting the C-C forming reaction utilizing the vinylogous Mukaiyama type reaction of trimethylsiloxy furan with an α-chloro sulfide. The butenolides **12** and **13** are converted in a stereoconvergent manner to a single bicyclic lactone **8**. The strategy disclosed herein would be useful for the synthesis of 1,2,5-trisubstituted tetrahydrofuran containing natural products. The synthetic potential of chloro sulfides is elegantly demonstrated.

**Supplementary Information**

Supplementary information is available in the website http://nopr.niscair.res.in/handle/123456789/60.

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