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## Synthesis of spiro-annulated cyclobutane derivatives through ketene [2+2] cycloaddition and ring-rearrangement metathesis

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Herein is reported a concise synthesis of spiro-annulated cyclobutane tetracyclic and pentacyclic derivatives by ketene addition, and ring-rearrangement metathesis (RRM) as key steps, starting with commercially available norbornadiene and dicyclopentadiene. The tetracyclic spiro-derivative contains a [5/5/4] core unit, which is the key building block to angular triquinanes synthesis. Whereas, the pentacyclic spiro-derivative contains a basic core skeleton of presilphiperfolanes, and other sesquiterpenoids.

**Keywords:** Cyclobutane, spirocyclic, ketene addition, metathesis, dechlorination

Most of the natural products such as alkaloids, terpenoids, lactones, *etc.* contain spirocyclics as a core units. Due to their intrinsic rigidity and complexity, spirocycles draw increasing attention in modern drug design and also in medicinal chemistry<sup>1,2</sup>. Cyclobutane is a highly strained ring system, commonly present in natural products. However, cyclobutane containing spirocyclic compounds are present in limited number of natural products, for example phainanoids, phainanoid **1**, lycopodine derivative **2**. The cyclobutane compound **3** is a highly potent inhibitor of histone methyltransferase. Whereas, the hydroxyl derivatives **4** and **5** are BACE1 ( $\beta$ -site APP-cleaving enzyme 1) inhibitors that lower A $\beta$ -levels in rat (Figure 1)<sup>3</sup>.

Here, we described the synthesis of a rare class of spiro-annulated cyclobutane derivatives by in combination of ketene [2+2] cycloaddition<sup>4</sup> and ring-rearrangement metathesis (RRM)<sup>5</sup> in a concise manner. These derivatives can be useful building blocks to angular triquinanes<sup>6</sup>, sesquiterpenoids, and presilphiperfolane type of compounds.

### Results and Discussion

Our synthesis starts with ketene addition to norbornadiene **6** which involve the reaction of trichloroacetyl chloride in the presence of zinc metal in anhydrous ether at RT for overnight to deliver the [2+2] cycloaddition product **7** in 68% yield<sup>7</sup>. The dichloro compound **7** was exposed to allylation using NaHMDS and LiHMDS and we found that by using LiHMDS condition gave the allylation product to

generate the compound **8** in 57% yield<sup>8</sup>. Subsequently, metathesis of the compound **8** using G-I catalyst in CH<sub>2</sub>Cl<sub>2</sub> at RT gave ring-opening metathesis (ROM) conditions product **9** in 52% yield (Scheme I).

Thereafter, the ROM derivative **9** was subjected to ring-closing metathesis (RCM)<sup>9</sup> using various conditions by changing the catalysts (G-I, G-II, HG-I and HG-II), catalyst loading (5 mol% and 10 mol%), solvent (CH<sub>2</sub>Cl<sub>2</sub>, PhMe) and temperature (RT to reflux temperature). However, we failed to get the desired RCM product **10**<sup>3a</sup>. This may be because of steric factor associated with chlorine atoms present or unfavourable stereochemistry of the unsaturated double bonds present in the compound **9**.

Thereafter, the compound **11** was subjected to dechlorination using Zn/AcOH at 80°C, gave the cyclobutanone derivative **12** in good yield<sup>10</sup>. Using NaHMDS or LiHMDS as a base, the compound **12** was reacted with 4.0 equiv. of allyl bromide at -78°C, and obtained the triallyl derivative **13** in good yield. Finally, the triallyl compound **13** was subjected to metathesis with G-I catalyst (5 mol%) to deliver the spiro-tricyclic derivative **14** *via* ring-rearrangement metathesis (RRM) and RCM in a moderate yields (Scheme II). Later, we have optimized the reaction conditions (Table I) to obtain better yields of metathesis product **14**<sup>11</sup>. The spiro compound **14** has a [5/5/4] tricyclic core. Compounds containing [5/5/4] tricyclic unit were synthetically transformed to angular triquinanes (*e.g.* ventricosene<sup>12a</sup>) by ring expansion of cyclobutane<sup>12</sup>.

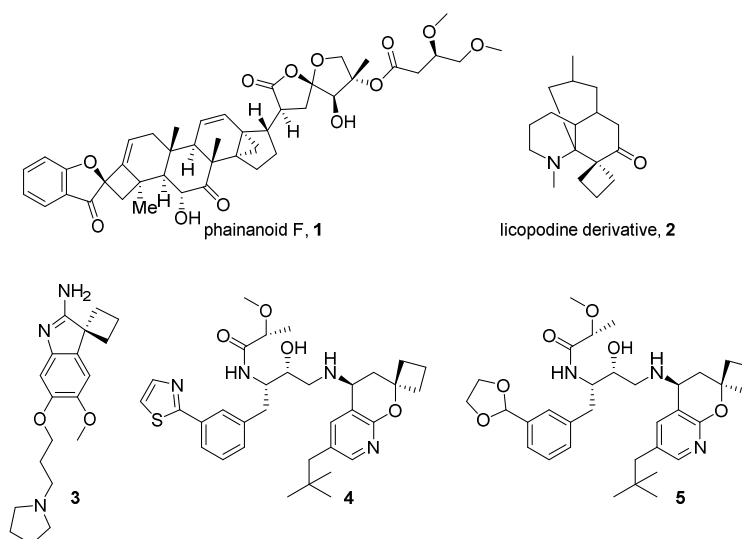
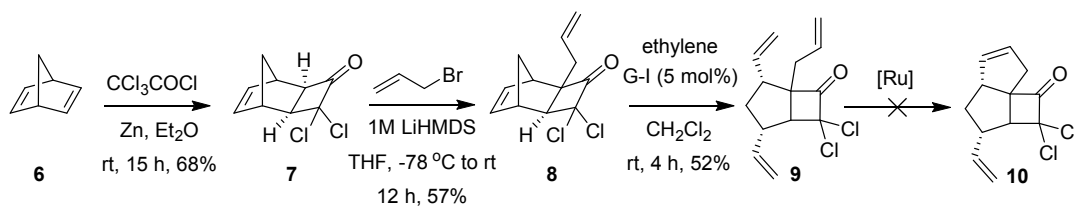
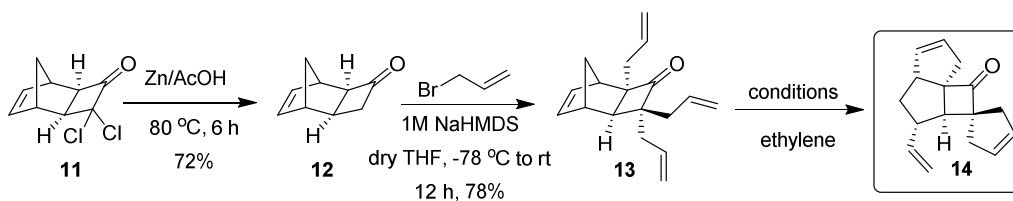


Figure 1 — Cyclobutane containing spirocyclic natural products

Scheme I — Synthesis of the allyl compound **9**Scheme II — Synthesis of the spirocyclic compound **14**Table I — Reaction optimization of RRM of **13** under ethylene gas conditions

Entry	Catalyst (mol %)	Solvent	Temp. (°C)	Time (h)	Yield of <b>14</b>
1	G-I (5)	CH <sub>2</sub> Cl <sub>2</sub>	RT	8	79
2	G-I (10)	CH <sub>2</sub> Cl <sub>2</sub>	RT	6	83
3	G-II (5)	CH <sub>2</sub> Cl <sub>2</sub>	RT	6	80
4	G-II (10)	CH <sub>2</sub> Cl <sub>2</sub>	RT	4	82
5	G-I (5)	PhMe	80	4	68
6	G-II (5)	PhMe	80	4	70

Additionally, the allyl derivative **8** was treated with allyl Grignard reagent at 0°C to synthesize the compound **15** in 78% yields<sup>13</sup>. Subsequent metathesis of **15** by using G-I catalyst, produced the [5/4/6] tricyclic derivative **16** in 75% yield (Scheme III).

Thereafter, we expanded this strategy to synthesize a new class of spiro-compound using dicyclopentadiene

**17** as a starting material using ketene addition. First, the dicyclopentadiene **17** was treated with trichloroacetyl chloride in a suspension of Zn in AcOH to deliver a mixture of ketene addition products **18a** and **18b** in 57% and 25% respectively<sup>7</sup>. Upon dechlorination by using Zn/AcOH method the compound **18a**, delivered the dechlorinated compound **19** in 80% yield<sup>9</sup>. Further, this compound **19** was subjected to allylation by using 4.0 equiv. of allyl bromide in the presence of NaHMDS as a base at -78°C<sup>8</sup>, to produce the triallyl derivative **20**, which was subjected to metathesis to yield the spiro-annulated pentacyclic compound **21** in 82% yields (Scheme IV).

This pentacyclic compound **21** containing spiro unit has a [5/5/4] tricyclic scaffold and [5/6/5] tricyclic scaffold. Interestingly, [5/5/4] tricyclic unit is a core structural element present in sesquiterpenoids<sup>14</sup>

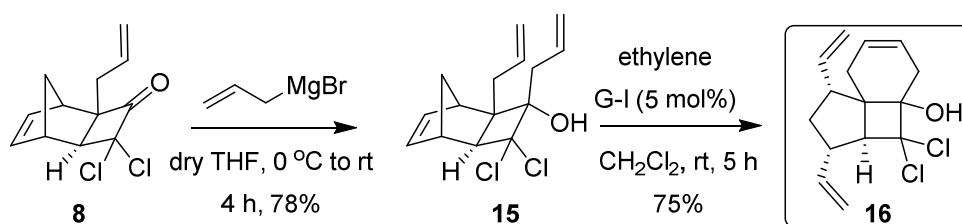
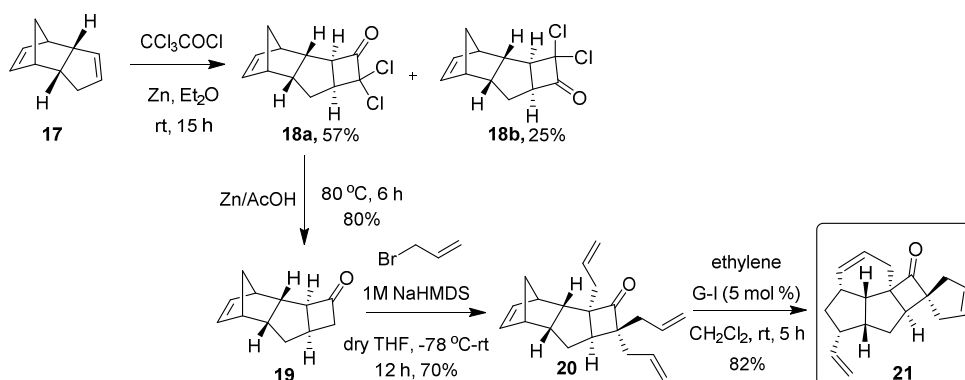
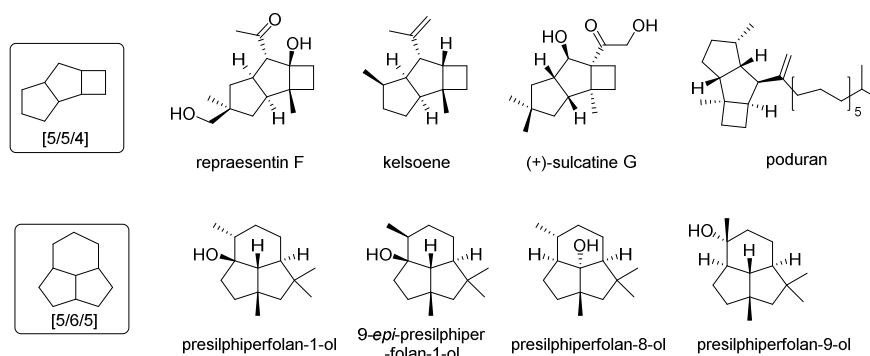
Scheme III — Synthesis of the [5/4/6] tricyclic derivative **16**Scheme IV — Synthesis of the pentacyclic compound **21**

Figure 2 — Natural products containing [5/5/4] tricyclic core and [5/5/6] tricyclic core

such as repraesentin F, kelsoene, (+)-sulcatine G and poduran. While, the [5/5/5] tricyclic unit is a core structure of presilphiperfolanes (Figure 2)<sup>15</sup>.

## Experimental Section

### Materials and Methods

All commercially available reagents were used without further purification and the reactions involving air-sensitive catalysts or reagents were performed in degassed solvents. Grubbs (G-I, G-II) and Grubbs-Hoveyda (GH-I, GH-II) catalysts were purchased from Aldrich Chemical Company. All metathesis reactions were carried out under ethylene atmosphere. The <sup>1</sup>H NMR (400 and 500 MHz) chemical shifts were reported in parts per million ( $\delta$ ) relative to internal solvent signal ( $\delta$  7.26 in CDCl<sub>3</sub>)

and the coupling constants  $J$  are reported in Hertz (Hz). The <sup>13</sup>C NMR (100 and 125 MHz) chemical shifts were referenced to the internal solvent signals (central peak is  $\delta$  77.16 in CDCl<sub>3</sub>). The high-resolution mass spectrometric (HRMS) measurements were carried out using a Bruker (Maxis Impact) or Micromass Q-ToF spectrometer. Infrared (IR) spectra were recorded on Nicolet Impact-400 FT-IR spectrometer and absorption bands are given in wavenumbers (cm<sup>-1</sup>).

### Synthesis of the allyl derivative **13**

To the solution of the compound **12** (200mg, 1 mmol) in dry THF, 1M solution of LiHMDS (4.0 eq) in THF was added and stirred for 15 min at -78 °C. Later, allyl bromide (0.22 mL, 2.5 eq.) was added

drop-wise at  $-78^{\circ}\text{C}$ , and the reaction mixture was stirred at the same temperature for 1 h. Further, the reaction mixture brought back to RT slowly in 8 h. After completion of reaction, it was quenched with  $\text{H}_2\text{O}$  and extracted with ethylacetate ( $3 \times 30$  mL). The combined organic layer was washed with  $\text{H}_2\text{O}$ , dried over  $\text{Na}_2\text{SO}_4$  and concentrated to get the crude compound **13** which was purified by column chromatography. Yield 57% (136 mg), colourless liquid,  $R_f = 0.75$  (2% EtOAc/hexane). IR (neat): 2931, 2389, 1735, 1627, 1216, 1108, 994, 770  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  6.50 (dd, 1H), 6.33 (dd, 1H), 5.92–5.80 (m, 1H), 5.28–5.18 (m, 2H), 3.19 (s, 1H), 2.90–2.73 (m, 2H), 2.48 (t, 1.46 Hz, 1H), 1.95 (d,  $J = 10.68$  Hz, 1H), 1.65 (qd,  $J = 14.36$  Hz, 1.84 Hz, 1H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  200.4, 140.6, 137.1, 130.3, 120.8, 82.4, 71.4, 56.2, 49.6, 46.3, 44.44, 44.41.

#### General procedure for dechlorination

The chloro compound (**11** or **18a**, 0.5 mmol, 1 equiv) was dissolved in glac. AcOH (0.2 mL) and added to the suspension of Zn in AcOH (1.0 mL) and the resulting mixture was heated to  $80^{\circ}\text{C}$  for 5 h. After completion of reaction, the reaction mixture was brought to RT and quenched with  $\text{H}_2\text{O}$ . Compound was extracted with  $\text{Et}_2\text{O}$  ( $3 \times 40$  mL) from the aqueous reaction mixture. The combined ether layer was washed with  $\text{H}_2\text{O}$  ( $2 \times 30$  mL), dried over  $\text{Na}_2\text{SO}_4$  and evaporated to dry. The crude product was purified by column chromatography to get the desired dechloro compound as a colourless liquid.

**12**: Yield 72% (240 mg), from 500 mg of **11**, Colorless liquid.  $R_f = 0.85$  (2% EtOAc/hexane).  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  6.23 (dd,  $J = 5.63$  Hz, 1H), 6.06 (dd,  $J = 6.62$  Hz, 3.32 Hz, 1H), 2.98 (brs, 1H), 2.94 (brs, 1H), 2.83–2.72 (m, 1H), 2.29–2.19 (m, 2H), 1.48 (d,  $J = 1.48$  Hz, 2H), 1.34–1.32 (m, 1H), 1.14 (t,  $J = 7.02$  Hz, 1H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  211.5, 139.7, 136.0, 66.1, 45.5, 44.0, 43.0, 40.9, 30.1.

**19**: Yield 80% (265 mg), from 500 mg of **18a**, Colorless liquid.  $R_f = 0.85$  (2% EtOAc/hexane). IR (neat): 2932, 1734, 1439, 1227, 848, 760  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  6.17 (s, 2H), 2.91 (d, 1H,  $J = 3.46$  Hz), 2.66 (s, 1H), 2.62 (d, 1H,  $J = 16.56$  Hz), 2.48 (d, 1H,  $J = 3.47$  Hz), 2.17 (s, 2H), 1.54 (ABq, 1H,  $J = 39.18$  Hz, 9.45 Hz), 1.44 (s, 1H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  211.5, 139.7, 136.0, 66.1, 45.5, 44.0, 43.0, 40.9, 30.1; HRMS (ESI, Q-ToF):  $m/z$  [ $\text{M} + \text{H}$ ] $^+$  Calcd for  $\text{C}_{12}\text{H}_{15}\text{O}$ : 175.1123. Found: 175.1120.

#### General procedure of triallylation

To the solution of the keto compound **12** or **19** (1 eq) in dry THF, 1M solution of NaHMDS (4.0 eq) in THF was added and stirred for 15 min at  $-78^{\circ}\text{C}$ . Later, allyl bromide (4.0 eq.) was added drop-wise at  $-78^{\circ}\text{C}$  and the reaction mixture was stirred at the same temperature for 1 h. Further, the reaction mixture brought back to RT slowly in 8 h. After completion of reaction, it was quenched with  $\text{H}_2\text{O}$  and extracted with ethylacetate ( $3 \times 30$  mL). The combined organic layer was washed with  $\text{H}_2\text{O}$ , dried over  $\text{Na}_2\text{SO}_4$  and concentrated to get the crude triallyl compound (**13** or **20**) which was purified by column chromatography using 2% EtOAc/ hexane.

**13**: Yield 78% (220 mg from 150 mg of **12**) as a colorless liquid.  $R_f = 0.85$  (2% EtOAc/hexane). IR (neat): 2936, 2412, 1765, 1455, 1412, 1117, 915, 761  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  5.95–5.72 (m, 3H), 5.30–4.98 (m, 6H), 3.23–2.78 (m, 5H), 2.26–2.17 (m, 1H), 2.03–1.98 (m, 1H). 14.36 Hz, 1.84 Hz, 1H);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  200.1, 139.8, 135.3, 130.3, 120.9, 118.1, 115.4, 60.7, 51.2, 45.8, 43.8, 40.4; HRMS (ESI, Q-ToF):  $m/z$  [ $\text{M} + \text{Na}$ ] $^+$  Calcd for  $\text{C}_{18}\text{H}_{22}\text{ONa}$ : 277.1563. Found: 277.1567.

**20**: Yield 70% (200 mg from 150 mg of **19**) as a colorless liquid.  $R_f = 0.85$  (2% EtOAc/hexane). IR (neat): 2936, 2405, 1770, 1458, 1117, 759  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 500 MHz):  $\delta$  6.22 (s, 2H), 5.93–5.81 (m, 2H), 5.74–5.63 (m, 1H), 5.17–5.08 (m, 6H), 2.99 (s, 1H), 2.89 (dd, 1H,  $J = 9.70$  Hz, 3.60 Hz), 2.80 (s, 1H), 2.66 (t, 2H,  $J = 6.64$  Hz), 2.50 (d, 1H,  $J = 8.88$  Hz), 2.33–2.25 (m, 3H), 2.20 (dd, 1H,  $J = 14.36$  Hz, 2.21 Hz), 1.78 (dd, 1H,  $J = 14.53$  Hz, 9.22 Hz), 1.72–1.67 (m, 2H), 1.63 (d, 1H,  $J = 8.09$  Hz), 1.48–1.43 (m, 1H), 1.38 (td, 1H,  $J = 14.44$  Hz, 7.28 Hz);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 125 MHz):  $\delta$  220.7 (C), 142.6 (CH), 136.4 (CH), 135.7 (CH), 128.5 (CH), 128.3 (CH), 125.7 (CH), 118.4 ( $\text{CH}_2$ ), 117.8 ( $\text{CH}_2$ ), 117.5 ( $\text{CH}_2$ ), 71.9 (C), 62.5 (C), 55.5 (CH), 54.2 ( $\text{CH}_2$ ), 51.2 (CH), 51.0 (CH), 46.5 (CH), 46.1 (CH), 35.9 ( $\text{CH}_2$ ), 34.4 ( $\text{CH}_2$ ), 31.2 ( $\text{CH}_2$ ), 29.4 ( $\text{CH}_2$ ); HRMS (ESI, Q-ToF):  $m/z$  [ $\text{M} + \text{Na}$ ] $^+$  Calcd for  $\text{C}_{21}\text{H}_{26}\text{ONa}$ : 317.1876. Found: 317.1873.

#### Synthesis of compound 15

The compound **8** (150 mg, 0.62 mmol) was dissolved in dry THF under  $\text{N}_2$  atmosphere and cooled to  $0^{\circ}\text{C}$ . To this 1 M allyl Grignard solution (1.2 mL, 2 eq) in THF was added at  $0^{\circ}\text{C}$  and allowed to stir for 4 h at RT under  $\text{N}_2$  atmosphere. After completion of reaction by TLC monitoring, the reaction mixture was quenched with Sat.  $\text{NH}_4\text{Cl}$  solution, extracted with EtOAc ( $3 \times 30$  mL). The combined organic layer was

washed with H<sub>2</sub>O (2 × 20 mL), dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated to give the crude product **15** which was purified by column chromatography using 2% EtOAc/hexane.

Yield 78% (137 mg), colourless liquid. *R<sub>f</sub>* = 0.75 (2% EtOAc/hexane). IR (neat): 3331, 2936, 2410, 1170, 915, 759 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz): δ 6.33 (dd, 1H, *J* = 5.68 Hz, 3.12 Hz), 6.28 (dd, 1H, *J* = 5.60 Hz, 3.00 Hz), 6.19-6.04 (m, 2H), 5.38-5.00 (m, 4H), 3.22 (s, 1H), 2.97 (brs, 1H), 2.88-2.80 (m, 3H), 2.74 (d, 1H, *J* = 1.96 Hz), 1.79 (d, 1H, *J* = 9.84 Hz), 1.59 (qd, 1H, *J* = 9.84 Hz, 1.78 Hz); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz): δ 138.6 (CH), 136.6 (CH), 133.2 (CH), 132.0 (C), 122.0 (CH<sub>2</sub>), 84.2 (C), 82.2 (C), 64.7 (CH), 51.8 (CH), 45.7 (CH<sub>2</sub>), 44.3 (CH), 43.8 (CH<sub>2</sub>); HRMS (ESI, Q-ToF): *m/z* [M + Na]<sup>+</sup> Calcd for C<sub>15</sub>H<sub>18</sub>OCl<sub>2</sub>Na: 307.0632. Found: 307.0635.

**General procedure for metathesis.** The compound (**13**, or **15**, or **20**, 0.2 mmol) was dissolved in CH<sub>2</sub>Cl<sub>2</sub> (7 mM) and degassed with N<sub>2</sub> gas followed by ethylene for about 20 min. To this, the Grubbs catalyst (as mentioned in Table I, 5 mol%) catalyst was added and stirred at RT under ethylene atmosphere. The solvent was removed and the crude product was purified by column chromatography to obtain the pure product.

**14:** Yield 83% (optimized yield (Table I), 44 mg from 60 mg of **13**) as a colorless liquid. *R<sub>f</sub>* = 0.80 (2% EtOAc/hexane). IR (neat): 2936, 2435, 1773, 1455, 1117, 918, 761 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz): δ 5.90-5.78 (m, 1H), 5.70-5.58 (m, 2H), 5.55-5.49 (m, 2H), 4.98 (td, 1H, *J* = 17.08 Hz, 1.32 Hz), 4.89 (td, 1H, *J* = 10.23 Hz, 1.24 Hz), 3.46-3.38 (m, 1H), 2.92-2.78 (m, 2H), 2.73-2.47 (m, 5H), 2.32 (d, 1H, *J* = 3.88 Hz), 2.20 (td, 1H, *J* = 13.14 Hz, 6.60 Hz), 1.67 (td, 1H, *J* = 13.10 Hz, 1.65 Hz), 1.58 (s, 1H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz): δ 221.0 (C), 142.4 (CH), 133.9 (CH), 129.1 (CH), 128.2 (CH), 127.6 (C), 113.4 (CH<sub>2</sub>), 66.3 (C), 58.4 (CH), 56.5 (CH), 47.7 (CH), 44.3 (CH<sub>2</sub>), 40.7 (CH<sub>2</sub>), 40.5 (CH<sub>2</sub>), 35.5 (CH<sub>2</sub>); HRMS (ESI, Q-ToF): *m/z* [M + Na]<sup>+</sup> Calcd for C<sub>16</sub>H<sub>18</sub>ONa: 249.1255. Found: 249.1258.

**21:** Yield 82% (44 mg from 60 mg of **20**) as a colorless liquid. *R<sub>f</sub>* = 0.80 (2% EtOAc/hexane). IR (neat): 2936, 2438, 1771, 1458, 1119, 760 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 500 MHz): δ 6.08-5.66 (m, 4H), 5.15-4.90 (m, 4H), 3.24-3.13 (m, 2H), 2.96 (s, 1H), 2.91 (dd, 1H, *J* = 15.53 Hz, 7.01 Hz), 2.59-2.56 (m, 1H), 2.43 (d, 1H, *J* = 4.25 Hz), 2.26-2.19 (m, 1H),

2.07-2.00 (m, 1H), 1.82-1.73 (m, 1H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 125 MHz): δ 141.6 (CH), 140.6 (CH), 136.7 (CH), 129.0 (CH), 126.4 (CH), 116.5 (CH<sub>2</sub>), 114.1 (CH<sub>2</sub>), 78.9 (C), 60.1 (CH), 51.7 (CH), 45.0 (CH<sub>2</sub>), 41.2 (C), 39.2 (CH<sub>2</sub>), 38.1 (CH<sub>2</sub>), 34.7 (CH<sub>2</sub>); HRMS (ESI, Q-ToF): *m/z* [M + Na]<sup>+</sup> Calcd for C<sub>15</sub>H<sub>18</sub>OCl<sub>2</sub>Na: 307.0632. Found: 307.0633.

**16:** Yield 75% (30 mg from 40 mg of **15**) as a colorless liquid. *R<sub>f</sub>* = 0.80 (2% EtOAc/hexane). IR (neat): 3330, 2936, 2433, 1170, 915, 760 cm<sup>-1</sup>; <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz): δ 5.86-5.72 (m, 2H), 5.71-5.65 (m, 1H), 5.64-5.53 (m, 2H), 5.03 (td, 1H, *J* = 17.16 Hz, 1.56 Hz), 4.97 (td, 1H, *J* = 10.33 Hz, 1.34 Hz), 2.84 (td, 1H, *J* = 16.86 Hz, 2.10 Hz), 2.68 (dd, 2H, *J* = 11.46 Hz, 6.64 Hz), 2.63-2.47 (m, 4H), 2.41 (td, 1H, *J* = 17.11 Hz, 2.04 Hz), 2.37-2.29 (m, 2H), 2.10-1.99 (m, 1H), 1.69 (dd, 1H, *J* = 14.16 Hz, 7.04 Hz), 1.39 (d, 1H, *J* = 10.56 Hz), 1.54-1.47 (m, 2H); <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz): δ 224.6 (C), 139.5 (CH), 133.2 (CH), 129.0 (CH), 128.0 (CH), 121.9 (CH), 114.6 (CH<sub>2</sub>), 77.3 (CH), 70.2 (C), 65.7 (C), 53.2 (CH), 50.8 (CH), 48.1 (CH), 45.8 (CH), 45.4 (CH<sub>2</sub>), 36.2 (CH<sub>2</sub>), 35.7 (CH<sub>2</sub>), 35.3 (CH), 29.4 (CH<sub>2</sub>), 27.2 (CH<sub>2</sub>); HRMS (ESI, Q-ToF): *m/z* [M + Na]<sup>+</sup> Calcd for C<sub>19</sub>H<sub>22</sub>ONa: 289.1563.

## Conclusion

Cyclobutane containing spiro compounds are rare class of spiro compounds, and a limited number of natural products are present. Here, we have synthesized [5/5/4] spiro-compound **14** and [5/6/5/4] spiro compound **21** starting with commercially available norbornadiene and dicyclopentadiene respectively *via* ketene addition, dechlorination followed by triallylation and metathesis sequence in good yields. Additionally, we have also synthesized [5/4/6] tricyclic derivative **16** by Grignard addition followed by metathesis. The core structures of these derivatives are present in natural products and bioactive compounds. This methodology has a potential application in natural and non-natural products synthesis

## Supplementary Information

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

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## References

- (a) Kotha S, Panguluri N R & Ali R, *Eur J Org Chem*, 5316 (2017); (b) Kotha S, Deb A Ch, Lahari K & Manivannan E, *Synthesis*, 2 (2009) 0165; (c) Ding A, Meazza M, Guo H, Yang J W & Rios R, *Chem Soc Rev*, 47 (2018) 5946.
- (a) Smith L K & Baxendale L R, *Org Biomol Chem*, 13 (2015) 9907; (b) Putatunda S, Alegre-Requena J V, Meazza M, Franc M, Rohal'ova D, Vemuri P, Cisorova I, Herrera R P, Rios R & Vesely J, *Chem Sci*, 10 (2019) 4107; (c) Carreira E M & Fessard T S, *Chem Rev*, 114 (2014) 8257.
- (a) Wang M & Lu P, *Org Chem Front*, 5 (2018) 254; (b) Miesch L, Welsch T, Rietsch V & Miesch M, *Chem Eur J*, 15 (2009) 4394; (c) Sergeiko A, Poroikov V V, Hanus L O & Dembitsky V M, *Open Med Chem J*, 2 (2008) 26.
- Mehta G & Kotha S, *J Org Chem*, 50 (1985) 5537.
- (a) Kotha S, Meshram M, Khedkar P, Benerjee S & Deodhar D, *Beilstein J Org Chem*, 11 (2015) 1833; (b) Kotha S, Mesharam M & Aswar V R, *Tetrahedron Lett*, 60 (2019) 151337; (c) Arjona O, Csaky A G & Plumet J, *Eur J Org Chem*, 611 (2003).
- Kotha S, Kubiak G, Lannoye G & Cook J M, *J Org Chem*, 53 (1988) 2327.
- (a) Mehta G & Rao H S P, *Synth Commun*, 15 (1985) 991; (b) Ghosez L, Montaine R, Roussel A, Vanlierde H & Mollet P, *Tetrahedron*, 27 (1971) 615; (c) Surendra K, Rajendar G & Corey E J, *J Am Chem Soc*, 136 (2014) 642.
- (a) Kotha S & Pulletikurti S, *RSC Adv*, 8 (2018) 14906; (b) Kiss L, Kardos M, Forró E & Fülöp F, *Eur J Org Chem*, 1283 (2015).
- (a) Bose S, Ghosh M & Ghosh S, *J Org Chem*, 14 (2012) 6345; (b) Handore K L & Reddy D S, *Org Lett*, 16 (2014) 4252; (c) Kotha S, Sreenivasachary N, Mohanraja K & Durani S, *Bioorg Med Chem Lett*, 11 (2001) 1421.
- Kishali N H, Dogan D, Sahin E, Gunel A, Kara Y & Balci M, *Tetrahedron*, 67 (2011) 1193.
- (a) Kotha S & Pulletikurti S, *Synthesis*, 51 (2019) 3981; (b) Kotha S, Pulletikurti S & Dommaraju Y, *Heterocycles*, 98 (2019) 79.
- (a) Sethofer S G, Staben S T, Hung O Y & Toste D, *Org Lett*, 10 (2008) 4315; (b) Wu Y-J, Zhu Y-J & Burnell D J, *J Org Chem*, 59 (1994) 104; (c) Franck-Neumann M, Miesch M & Gross L, *Tetrahedron Lett*, 33 (1992) 3879; (d) Kotha S & Aswar V R, *Org Lett*, 18 (2016) 1808.
- (a) Kotha S & Ravikumar O, *Eur J Org Chem*, 3900 (2016); (b) Kotha S, Chinnam A K & Shirabate M, *Beilstein J Org Chem*, 11 (2015) 1514.
- (a) Mehta G & Sreenivas K, *Chem Commun*, 1892 (2001); (b) Cheng S-Y, Dai Ch-F & Duh Ch-Y, *J Nat Prod*, 70 (2007) 1449; (c) Rinkel J, Lauterbach L & Dickschat J S, *Angew Chem Int Ed*, 56 (2017) 16385; (d) Ferrer S & Echavarren A M, *Org Lett*, 20 (2018) 5784; (e) Bach T & Hehn J P, *Angew Chem Int Ed*, 50 (2011) 1000.
- (a) Radulovic N, Mladenovic M Z, Stojanovic N M, Randjelovic P J & Blagojevic P D, *J Nat Prod*, 82 (2019) 1874; (b) Hong A Y & Stoltz B M, *Angew Chem Int Ed*, 51 (2012) 9674; (c) Pepper H P, Lam H C, Bloch W M & George J H, *Org Lett*, 14 (2012) 5162; (d) Hu P & Synder S A, *J Am Chem Soc*, 139 (2017) 5007.