A new total synthesis of (±)-isolongifolene involving an aryl participated diazoketone cyclisation strategy

Arnab Roy, Tapas Paul, and Debabrata Mukherjee*

Department of Organic Chemistry, Indian Association for the Cultivation of Science, Jadavpur, Kolkata-700 032, India
E-mail: ocdm@mahendra.iacs.res.in

Dedicated to Professor S. Swaminathan on the occasion of his 80th birthday
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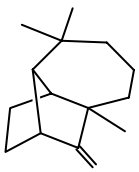
Abstract
A facile total synthesis of (±)-isolongifolene has been successfully accomplished involving aryl participated intramolecular cyclisation of 1,1,4-trimethyl-2-diazoacetyl-6-methoxyindane as the key reaction.

Keywords: Diazoketone, intramolecular cyclisation, conjugate addition, desulfurisation, isolongifolene

Introduction

The bridged tricyclic sesquiterpene longifolene **1** undergoes rearrangement in the presence of acid to provide an isomeric hydrocarbon known as isolongifolene **2**.[1] Isolongifolene **2** incorporates a novel tricyclo[6.2.1.0^{1,6}]undecane skeleton and its structure was confirmed by its synthesis[2] from camphene-1-carboxylic acid **3**. A formal total synthesis of isolongifolene was achieved by Piers and Zbozny[5] involving intramolecular alkylation of an appropriate octalone derivative.



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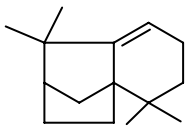

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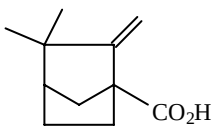

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Besides the construction of the tricyclo[6.2.1.0^{1,6}]undecane framework, the total synthesis of isolongifolene is associated with the difficulty in the generation of *gem*-dimethyl groups in two

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of the three rings and an isolated double bond in ring A. We report herein an aryl participated diazoketone cyclisation strategy to accomplish a very convenient and efficient total synthesis of (±)-isolongifolene. The salient features of our synthesis are (i) facile conversion of the easily accessible[3] ester **4** into the diazomethyl ketone **10** , (ii) aryl participated intramolecular cyclisation[4] of **10** to provide in high yield the tricyclic dienedione **11** as a key intermediate to **2**, and (iii) efficient transformation of **11** into isolongifolene involving regioselective conjugate addition of lithium dimethylcuprate to **11** followed by removal of the two carbonyl groups from the rings A and C of the resulting enedione **12**.

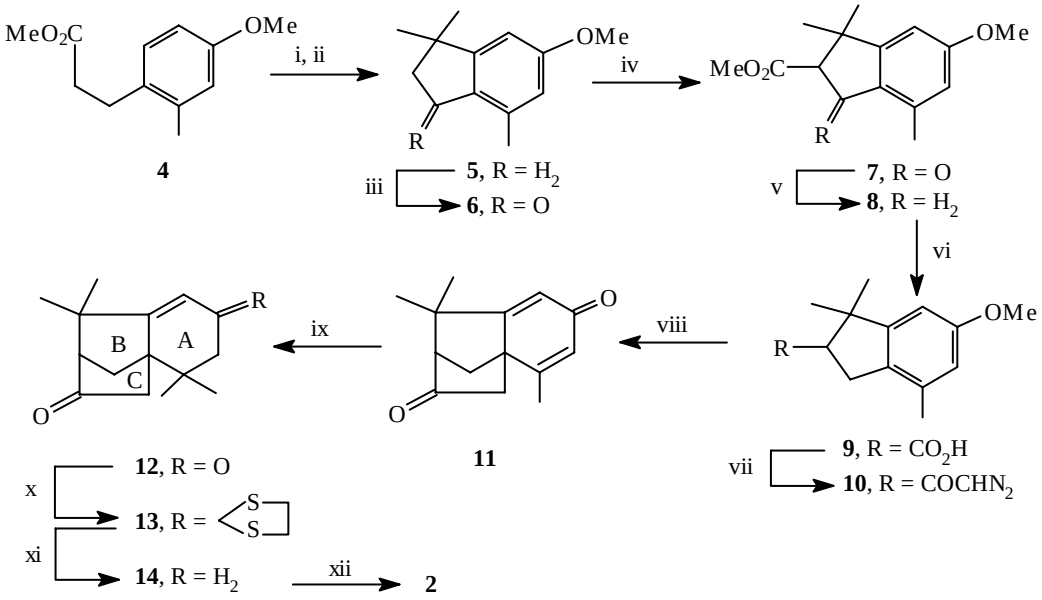
Results and Discussion

Our synthesis of (±)-isolongifolene **2** from methyl 3-(2-methyl-4-methoxyphenyl)propanoate **4** is outlined in Scheme 1. Grignard reaction of the ester **4** with an excess of methyl magnesium iodide followed by intramolecular cyclisation of the resulting carbinol with polyphosphoric acid provided the indane derivative **5** in 72% overall yield. Oxidation of **5** with chromic acid in acetic acid afforded the indanone **6** (73%). Having a convenient route to **6**, we turned our attention to convert **6** into the diazomethyl ketone **10**. The ketone **6** was treated with dimethyl carbonate in the presence of sodium hydride to afford the *β*-ketoester **7** as a crystalline compound in 83% yield. Reduction of **7** with sodium borohydride followed by catalytic hydrogenolysis of the crude product in methanol in the presence of perchloric acid provided the ester **8** in 85% yield. Saponification of **8** furnished the acid **9** which was converted via the corresponding acid chloride into the diazomethyl ketone **10** in excellent yield. The spectral characteristics of the compounds **5-10** as revealed through their ^{1}H and ^{13}C NMR spectra were fully in accord with their structures. Intramolecular cyclisation of the diazoketone **10**, shown in Scheme 2, was effected by treatment with trifluoroacetic acid in dichloromethane at –20^{o}C to afford the crystalline dienedione **11** in 77% yield.

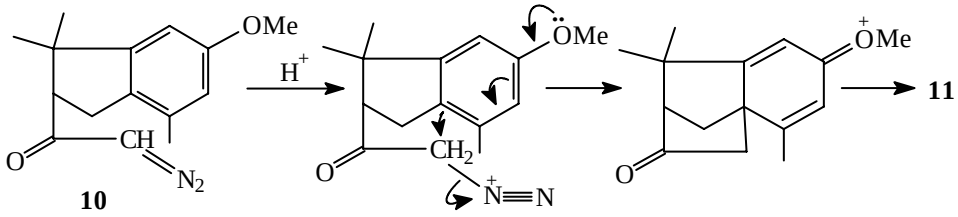
Conjugate addition of lithium dimethylcuprate to **11** in the presence of boron trifluoride etherate furnished the enedione **12** (62%). The construction of the basic tricarbocyclic framework of isolongifolene **2** was thus accomplished in a convenient manner. The IR, ^{1}H NMR and ^{13}C NMR spectra of the dienedione and the enedione were in full accord with the structures **11** and **12**, respectively.

In order to complete a synthesis of isolongifolene **2** from the enedione **12**, it was necessary to remove the two carbonyl groups from the rings A and C of **12**. Treatment of **12** with ethanedithiol and boron trifluoride etherate in methanol at room temperature furnished the monothioacetal **13** as the sole product in 90% yield. Desulfurisation of **13** with sodium and ethanol in liquid ammonia[6] followed by treatment of the crude product with Jones reagent afforded the enone **14** in high yield. The spectral and analytical data of the compound **14** agree with the assigned structure. Huang-Minlon reduction of **14** followed by chromatography of the crude product over neutral alumina and elution with light petroleum afforded pure (±)-

isolongifolene **2** in 76% yield. The identity of synthetic **2** was secured through ^{1}H NMR, ^{13}C NMR, DEPT experiments, and microanalytical data. Also, the spectral data of **2** agreed very well with those reported in the literature.



Scheme 1. Reagents and conditions: (i), MeMgI, Et_2O, reflux; (ii), P_2O_5, H_3PO_4, 90^{o}C; (iii), CrO_3, AcOH, H_2O, 5^{o}C to rt; (iv), $(MeO)_2CO$, NaH, THF, reflux, H_3O^{+}; (v), $NaBH_4$, THF, H_2O, rt; H_2, 10% Pd-C, MeOH, $HClO_4$; (vi), KOH, $(CH_2OH)_2$, H_2O, reflux, H_3O^{+}; (vii), $(COCl)_2$, C_6H_6 , reflux; CH_2N_2, Et_2O, Et_3N, 0^{o}C to rt; (viii), TFA, CH_2Cl_2, -20^{o}C; (ix), $LiMe_2Cu$, Et_2O, THF, $BF_3.Et_2O$, -50 to 0^{o}C; (x), $HSCH_2CH_2SH$, MeOH, $BF_3.Et_2O$, rt; (xi), Na, EtOH, liq. NH_3; (xii) N_2H_4, N_2H_4. 2HCl, $(HOCH_2CH_2)_2O$, 125^{o}C; KOH, 210^{0}C.



Scheme 2

In conclusion, a facile total synthesis of the bridged sesquiterpene artefact isolongifolene has been acomplished involving aryl participated intramolecular cyclisation of an appropriately substituted diazomethyl ketone as the key reaction.

Experimental Section

General Procedures. The compounds described here are all racemates. IR spectra were recorded on Perkin-Elmer model PE 298 and Shimadzu FTIR- 8300 spectrophotometers. Unless otherwise stated, ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ solution at 300 MHz and 75 MHz respectively on a Bruker DPX-300 spectrometer with $SiMe_4$ as internal standard. Moisture sensitive reactions were carried out using standard syringe-septum technique. Anhydrous solvents were obtained by standard procedures. All solvent extracts were dried over anhydrous Na_2SO_4. Product purities were routinely checked by TLC. Ether refers to diethyl ether and light petroleum refers to the fraction of petroleum ether in the boiling point range 60 – 80^{0}C.

1,1,4-Trimethyl-6-methoxyindane (5). To a stirred suspension of MeMgI [prepared from magnesium turnings (5.3 g, 0.22 g-at.) and MeI (32 g, 0.225 mol)] in anhydrous ether (70 mL) was added slowly under nitrogen a solution of the ester **4** (10 g, 0.048 mol) in ether (20 mL). The mixture was stirred at room temperature for 30 min and then refluxed for 5 h. It was then cooled in an ice-bath and decomposed carefully with saturated aqueous NH_4Cl (60 mL). The organic layer was separated and the aqueous phase extracted with ether (2x30 mL). The combined ether solution was washed with water (2x30 mL) and dried. Evaporation of the solvent furnished the crude product as an oil (10 g) [IR (film) 3404, 2968, 1608, 1502 cm $^{-1}$; ^{1}H NMR δ 1.29 (s, 6H, C*Me*$_2$), 1.62-1.70 (m, 2H, ArCH$_2$C*H*$_2$), 2.37 (s, 3H, Ar*Me*), *2*.58-2.64 (m, 2H, ArC*H*$_2$CH$_2$), 3.75 (s, 3H, ArO*Me*), 6.65-6.70 (m, 2H, Ar*H*), 7.04 (d, 1H, *J* = 8.1 Hz, Ar*H*); ^{13}C NMR δ 19.4, 27.2, 29.1, 44.7, 55.1, 70.8, 111.0, 115.8, 129.4, 132.7, 136.9, 157.6] which was cyclised by heating with polyphosphoric acid [prepared by heating at 95-100^{0}C for 2 h a mixture of P_2O_5 (80 g) and H_3PO_4 (89%, 35 mL)] at 90^{0}C for 1 h. The reaction mixture was cooled, decomposed with crushed ice, and extracted repeatedly with ether. The combined ether extract was washed successively with water, saturated aqueous $NaHCO_3$ until alkaline, water again until neutral, and then dried. Removal of the solvent followed by distillation of the residue at 105-108^{o}C (bath temp.) / 0.8 mm Hg furnished the indane **5** (6.58 g, 72%) as a colourless oil; ^{1}H NMR δ 1.23 (s, 6H, C*Me*$_2$), 1.91 (t, 2H, *J* = 7 Hz, ArCH$_2$C*H*$_2$), 2.22 (s, 3H, Ar*Me*), *2*.72 (t, 2H, *J* = 7 Hz, ArC*H*$_2$CH$_2$), 3.77 (s, 3H, ArO*Me*), 6.53 (bs, 2H, Ar*H*); ^{13}C NMR δ 19.2, 27.8, 28.6, 28.7, 41.4, 44.2, 55.3, 105.1, 112.7, 133.5, 134.5, 153.8, 159.1. Anal. Calcd. for $C_{13}H_{18}O$: C, 82.06; H, 9.53. Found: C, 82.22; H, 9.59%.

3,3,7-Trimethyl-5-methoxyindan-1-one (6). A solution of CrO_3 (6 g, 0.06 mol) in 80 % aqueous AcOH (30 mL) was added slowly with stirring to a solution of the indane **5** (6.3 g, 0.033 mol) in glacial AcOH (40 mL) at 5^{0}C. After the addition, the mixture was stirred at 10^{0}C for 5 h, allowed to stand at room temperature for 12 h and then diluted with water (70 mL). Solid Na_2CO_3 was added in portions to neutralise most of the acetic acid and the product was extracted with ether (3x50 mL). The combined ether extract was washed with aqueous $NaHCO_3$ and water, dried and concentrated. The residue was distilled to furnish the indanone **6** (4.94 g, 73 %) as a colourless oil, b.p. 138 – 140^{0}C (bath temp.) / 0.6 mm Hg; IR (film) 1697, 1598 cm^{-1}; ^{1}H NMR δ

1.38 (s, 6H, C*Me*$_2$), 2.54 (s, 2H, ArCOC*H*$_2$), 2.60 (s, 3H, Ar*Me*), 3.87 (s, 3H, ArO*Me*), 6.62 (d, 1H, *J* = 2 Hz, Ar*H*), 6.72 (d, 1H, *J* = 2 Hz, Ar*H*); ^{13}C NMR δ 18.6, 30.0 (2C), 37.6, 53.7, 55.4, 104.8, 115.9, 126.5, 140.6, 164.5, 167.6, 204.8. Anal. Calcd. for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.50; H, 8.17%.

2-Methoxycarbonyl-3,3,7-trimethyl-5-methoxyindan-1-one (7). To a stirred suspension of NaH (1.17 g, 0.05 mol) in refluxing dimethyl carbonate (25 mL) was added under nitrogen a solution of the indanone **6** (5 g, 0.024 mol) in THF (40 mL) during 1 h. The mixture was refluxed for 3 h, cooled in an ice-bath and acidified with cold dil. HCl (2N, 30 mL). Water (50 mL) was added and the product extracted with ether (3x70 mL). The combined ether extract was washed successively with aqueous $NaHCO_3$, water and dried. After removal of the solvent, the crude product was purified by chromatography over silica gel (150 g). The solid fractions eluted with ether : light petroleum (1:9) were crystallised from a mixture of ether and petroleum ether to afford the *β*-ketoester **7** (5.33 g, 83%) as colourless plates, m.p. 89-90^{o}C; IR (KBr) 1743, 1687, 1600, 1581 cm^{-1}; ^{1}H NMR δ 1.33 (s, 3H, *Me*), 1.51 (s, 3H, *Me*), 2.61 (s, 3H, Ar*Me*), 3.45 (s, 1H, C*H*CO$_2$Me), 3.74 (s, 3H, CO$_2$*Me*), 3.88 (s, 3H, ArO*Me*), 6.66 (d, 1H, *J* = 2 Hz, Ar*H*), 6.71 (d, 1H, *J* = 2 Hz, Ar*H*); ^{13}C NMR δ 18.7, 25.9, 30.6, 41.6, 51.8, 55.5, 66.0, 104.8, 116.4, 125.4, 141.5, 165.0, 166.0, 169.9, 198.3. Anal. Calcd. for $C_{15}H_{18}O_4$: C, 68.69; H, 6.92. Found: C, 68.77; H, 6.71%.

1,1,4-Trimethyl-2-methoxycarbonyl-6-methoxyindane (8). To an ice-cold stirred solution of the *β*-ketoester **7** (3 g, 11.4 mmol) in THF (20 mL) containing water (2 mL) was added $NaBH_4$ (1 g, 26.3 mmol) in small portions during 30 min. The mixture was stirred at 0^{o}C for 4 h and at room temperature for 15 h. It was then diluted with water (30 mL), acidified carefully with AcOH and extracted repeatedly with ether. The combined ether extract was washed with aqueous $NaHCO_3$, water and dried. The residue remaining upon evaporation of the solvent was dissolved in methanol (20 mL) and hydrogenated over palladium on carbon (10%, 1 g) at room temperature and atmospheric pressure in the presence of a few drops of perchloric acid. Uptake of hydrogen ceased after 2 h. The mixture was filtered, diluted with water (40 mL) and extracted with ether (3x30 mL). The ether extract was washed with water, dried and concentrated. The residue was distilled at 130-132^{o}C (bath temp.) / 0.4 mm Hg to afford the methyl ester **8** (2.41 g, 85%) as a colourless oil; IR (film) 1734, 1610 cm^{-1}; ^{1}H NMR δ 1.04 (s, 3H, *Me*), 1.50 (s, 3H, *Me*), 2.23 (s, 3H, Ar*Me*), 2.86-2.93 (m, 1H), 3.02- 3.08 (m, 1H), 3.14-3.23 (m, 1H), 3.75 (s, 3H, CO$_2$*Me*), 3.78 (s, 3H, ArO*Me*), 6.50 (d, 1H, *J* = 2 Hz, Ar*H*), 6.56 (d, 1H, *J* = 2 Hz, Ar*H*); ^{13}C NMR δ 19.1, 24.9, 27.8, 30.6, 47.1, 51.4, 55.3, 55.7, 105.1, 113.3, 130.6, 134.7, 151.8, 159.3, 173.9. Anal. Calcd. for $C_{15}H_{20}O_3$: C, 72.55; H, 8.12. Found: C, 72.48; H, 7.91%.

1,1,4-Trimethyl-2-carboxy-6-methoxyindane (9). The ester **8** (2.2 g, 8.86 mmol) was hydrolysed by heating under reflux for 12 h with a solution of KOH (2.7 g) in ethylene glycol (12 mL) and water (12 mL). Usual work-up followed by crystallisation of the solid product from a mixture of benzene and light petroleum afforded the acid **9** (1.8 g, 87%) as colourless needles, m.p. 147-148^{o}C; IR (KBr) 1699, 1610 cm^{-1}; ^{1}H NMR δ 1.15 (s, 3H, *Me*), 1.54 (s, 3H, *Me*), 2.24 (s, 3H, Ar*Me*), 2.90-2.96 (m, 1H), 3.08-3.18 (m, 2H), 3.79 (s, 3H, ArO*Me*), 6.52 (d, 1H, *J* =

2 Hz, Ar*H*), 6.57 (d, 1H, *J* = 2 Hz, Ar*H*); ^{13}C NMR δ 19.2, 24.8, 27.7, 30.4, 47.2, 55.4, 55.5, 105.1, 113.4, 130.4, 134.8, 151.8, 159.4, 178.9. Anal. Calcd. for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.93; H, 7.85%.

Preparation of the diazoketone (10). A solution of the acid **9** (1.6 g, 6.83 mmol) in dry benzene (15 mL) was refluxed with oxalyl chloride (2.7 g, 21 mmol) for 4 h. Removal of the solvent and excess oxalyl chloride furnished the acid chloride as a pale yellow liquid (1.6 g). The crude acid chloride dissolved in ether (15 ml) was added dropwise with stirring to an ice-cold ethereal solution (150 mL) of diazomethane [prepared from 7.5 g of nitrosomethyl urea] containing Et_3N (0.6 mL). After standing at 0^{o}C for 2 h, the mixture was allowed to reach room temperature overnight. Evaporation of the solvent followed by purification of the residue on a silica gel column (40 g) using ether : light petroleum (1:1) as the eluent furnished the diazoketone **10** (1.59 g, 90%) as a pale yellow viscous liquid [IR (film) 2102, 1637, 1610 cm^{-1}; ^{1}H NMR δ 1.10 (s, 3H, *Me*), 1.46 (s, 3H, *Me*), 2.23 (s, 3H, Ar*Me*), 2.80-3.01 (m, 2H), 3.15-3.23 (m, 1H), 3.78 (s, 3H, ArO*Me*), 5.27 (s, 1H, COC*H*N$_2$), 6.49 (d, 1H, *J* = 2 Hz, Ar*H*), 6.56 (d, 1H, *J* = 2 Hz, Ar*H*); ^{13}C NMR δ 19.1, 24.8, 28.5, 30.5, 47.6, 55.1, 55.3, 61.5, 105.0, 113.3, 130.7, 134.8, 151.8, 159.4, 194.8] which was used for the subsequent intramolecular cyclisation without further purification.

2,7,7-Trimethyltricyclo[6.2.1.0^{1,6}]undec-2,5-diene-4,9-dione (11). A solution of the diazoketone **10** (1.5 g, 5.81 mmol) in dry CH_2Cl_2 (25 mL) was added during 3 min under nitrogen to a stirred solution of trifluoroacetic acid (30 mL) in CH_2Cl_2 (30 mL) at –20^{0}C. The mixture was stirred at – 20^{0}C for another 3 min and then diluted with CH_2Cl_2 (50 mL). The dichloromethane solution was washed with water (3x25 mL), dried and concentrated. The crude product was purified by chromatography over silica gel (30 g). Elution of the column with ether : light petroleum (2:3) furnished the crystalline dienedione which was recrystallised from a mixture of ether and petroleum ether to afford colourless plates of **11** (0.97 g, 77 %), m.p. 179 – 180^{0}C; IR (KBr) 1749, 1668, 1626 cm $^{-1}$; ^{1}H NMR δ 1.23 (s, 3H, *Me*), 1.26 (s, 3H, *Me*), 1.76-1.85 (m, 2H), 2.06 (d, 3H, *J* = 1.5 Hz, vinyl methyl at C-2), 2.16-2.20 (m, 1H), 2.53-2.60 (m, 2H), 6.17 (d, 1H, *J* = 1.5 Hz, vinyl proton), 6.19 (bs, 1H, vinyl proton); ^{13}C NMR δ 19.0, 25.5, 27.3, 38.3, 42.3, 45.8, 53.9, 61.0, 120.5, 129.5, 155.6, 175.3, 187.0, 210.9. Anal. Calcd. for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.51; H, 7.55%.

2,2,7,7-Tetramethyltricyclo[6.2.1.0^{1,6}]undec-5-ene-4,9-dione (12). A solution of $LiMe_2Cu$ was prepared under nitrogen by dropwise addition of MeLi (1.6 M in ether, 15.6 mL, 24.96 mmol) to a stirred suspension of CuI (2.4 g, 12.6 mmol) in anhydrous ether (20 mL) at -30^{0}C. The clear solution of $LiMe_2Cu$ was stirred for 5 min, cooled to -50^{0}C, and 0.7 mL (5.52 mmol) of freshly distilled BF_3. Et_2O was added. After the mixture was stirred for 5 min, a solution of the dienedione **11** (0.9 g, 4.16 mmol) in dry THF (5 mL) was added dropwise. The mixture was stirred at -50^{0}C for 15 min, an additional 0.7 mL (5.52 mmol) of BF_3. Et_2O was added, and the mixture stirred at -40^{0}C for 3 h. The reaction mixture was then allowed to reach 0^{o}C and poured into saturated aqueous NH_4Cl (50 mL). Concentrated NH_4OH solution (12 mL) was added to dissolve the precipitated copper salts and the product was extracted with ether (3x60 mL). The combined ether extract was washed with water (3x40 mL), dried and

concentrated. The residue was purified by chromatography over silica gel (25 g). The fractions eluted with ether : light petroleum (1:3) furnished a crystalline material which was recrystallised from a mixture of ether and petroleum ether to afford the enedione **12** (0.6 g, 62%), m.p. 111-112^{o}C; IR (KBr) 1749, 1666 cm^{-1}; ^{1}H NMR δ 1.06 (s, 3H, *Me*), 1.10 (s, 3H, *Me*), 1.15 (s, 3H, *Me*), 1.22 (s, 3H, *Me*), 1.80-2.05 (m, 3H), 2.15-2.45 (m, 4H), 5.90 (s, 1H, vinyl proton at C-5); ^{13}C NMR δ 23.8, 25.7, 25.8, 26.1, 34.3, 35.4, 42.9, 43.2, 49.6, 56.8, 61.0, 119.5, 177.0, 198.8, 212.8. Anal. Calcd. for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68. Found: C, 77.63; H, 8.89%.

Further elution of the column with ether : light petroleum (1:1) provided the dienedione **11** (0.18 g, 20%), m.p. 177-178^{o}C [^{1}H NMR spectrum was identical with that of the starting dienedione **11**].

4,4-Ethyelenedithio-2,2,7,7-tetramethyltricyclo[6.2.1.0^{1,6}]undec-5-en-9-one (13). To a solution of the enedione **12** (0.5 g, 2.15 mmol) in MeOH (5 mL) were added ethanedithiol (1 g) and BF_3.Et_2O (0.5 mL) and the mixture was stirred at room temperature for 20 h. The reaction mixture was then poured into ice-cold aqueous NaOH (10%, 15 mL) and the product was extracted with ether (3x25 mL). The ether extract was washed with water (2x20 mL), dried and concentrated. The residue was distilled at 162-164^{0}C (bath temp.) / 0.1 mm Hg to give **13** (0.6 g, 90 %) as a colourless oil; IR (film) 1747, 1466, 1387, 1365, 1273 cm $^{-1}$; ^{1}H NMR δ 0.98 (s, 3H, *Me*), 1.07 (s, 3H, *Me*), 1.09 (s, 3H, *Me*), 1.13 (s, 3H, *Me*), 1.62-1.86 (m, 3H), 2.11-2.29 (m, 4H), 3.25-3.45 (m, 4H, S*CH$_2$* *CH$_2$*S), 5.56 (s, 1H, vinyl proton at C-5); ^{13}C NMR δ 24.2, 26.1, 26.4, 26.9, 33.0, 35.6, 38.4, 41.1, 41.4, 44.3, 51.1, 54.2, 61.4, 63.5, 121.6, 149.0, 215.1. Anal. Calcd. for $C_{17}H_{24}OS_2$: C, 66.21; H, 7.84. Found: C, 66.03; H, 8.06%.

2,2,7,7-Tetramethyltricyclo[6.2.1.0^{1,6}]undec-5-en-9-one (14). A solution of the thioacetal **13** (0.55 g, 1.78 mmol) in dry ether (15 mL) and EtOH (1 mL) was added under nitrogen to distilled liquid ammonia (80 mL). To this mixture was added Na metal (0.8 g, 0.035 g-at.) with stirring during 2 min. After 5 min, EtOH was added dropwise until the blue colour disappeared. The ammonia was allowed to evaporate. The residue was diluted with water (25 mL) and extracted with ether (3x30 mL). The combined ether extract was washed with water (2x25 mL), dried, and concentrated. The residue, dissolved in acetone (25 mL), was treated with dropwise addition of Jones reagent at 10^{o}C until the colour of the reagent persisted for 2 min. A few drops of methanol were added to destroy the excess reagent. The reaction mixture was diluted with water (50 mL) and extracted repeatedly with ether. The combined organic extract was washed with water, aqueous $NaHCO_3$, water and dried. The residue remaining upon evaporation of the solvent was purified by chromatography on silica gel (10 g). Elution of the column with ether : light petroleum (1: 9) furnished the enone **14** (0.32 g, 82%) as a colourless oil; IR (film) 1749, 1461 cm $^{-1}$; ^{1}H NMR δ 0.90 (s, 3H, *Me*), 0.97 (s, 3H, *Me*), 1.04 (s, 3H, *Me*), 1.09 (s, 3H, *Me*), 1.25-1.38 (m, 3H), 1.63-1.84 (m, 3H), 2.01-2.26 (m, 3H), 5.40 (t, 1H, *J* = 3.6 Hz, vinyl proton at C-5); ^{13}C NMR δ 22.5, 22.7, 26.3, 26.8, 27.7, 31.1, 33.6, 35.6, 41.2, 45.3, 54.6, 61.7, 114.5, 150.6, 216.8. Anal. Calcd. for $C_{15}H_{22}O$: C, 82.52; H, 10.16. Found: C, 82.39; H, 10.25%.

(±)-Isolongifolene (2). A mixture of the ketone **14** (0.28 g, 1.28 mmol), hydrazine hydrate (4 mL, 99%), hydrazine dihydrochloride (1.1 g) and diethylene glycol (14 mL) was heated to

125°C in an atmosphere of nitrogen and kept at that temperature for 2 h. The reaction mixture was then cooled to 80°C and solid pellets of potassium hydroxide (2 g) were added. The temperature was gradually raised to 210°C by distilling off low boiling materials. The reaction mixture was maintained at 210-220°C for 3 h, then cooled, poured into water (25 mL), and extracted with ether (3x30 mL). The distillate containing the low boiling materials was also diluted with water (20 mL) and extracted with ether (3x20 mL). The combined ethereal extract was washed with cold dilute hydrochloric acid (20 mL, 3N), water (2x30 mL), and dried. After removal of ether, the residue was purified by chromatography on neutral alumina (10 g). Elution with light petroleum furnished (±)-isolongifolene (**2**) (0.2 g, 76%) as a colourless oil; ^{1}H NMR δ 0.84 (s, 3H, *Me*), 0.93 (s, 3H, *Me*), 0.95 (s, 3H, *Me*), 1.04 (s, 3H, *Me*), 1.03-1.25 (m, 6H), 1.38-1.47 (m, 2H), 1.63-1.77 (m, 2H), 1.93-1.99 (m, 1H), 5.14 (t, 1H, *J* = 3.6 Hz, vinyl proton); ^{13}C NMR δ 22.9, 24.2, 24.9, 25.6, 26.5, 28.9 (2C), 31.1, 33.8, 36.7, 41.9, 46.7, 56.0, 110.6, 155.6. Anal. Calcd. for $C_{15}H_{24}$: C, 88.16; H, 11.84. Found: C, 88.31; H, 11.95%.

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References

1. Ranganathan, R.; Nayak, U. R.; Santhanakrishnan, T. S.; Dev, S. *Tetrahedron* **1970**, *26*, 621.
2. Sobti, R. R.; Dev, S. *Tetrahedron* **1970**, *26*, 649.
3. Chatterjee, A.; Hazra, B. G. *Tetrahedron* **1977**, *33*, 1983.
4. Ye, T.; McKervey, M. A. *Chem. Rev.* **1994**, *94*, 1091 and references therein.
5. Piers, E.; Zbozny, M. *Can. J. Chem*. **1979**, *57*, 2249.
6. Ireland, R. E.; Wrigley, T. I.; Young, W. G. *J. Am. Chem. Soc.* **1958**, *80*, 4604.