



## Synthetic Studies Towards Furosesquiterpenes: Construction of Linearly-fused A/B *trans*- and A/B *cis*- Furo[3,2-b]-and Furo[2,3-b] Decalins

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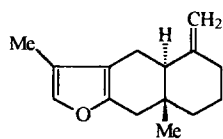
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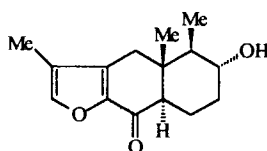
**Abstract:** Linearly fused furo[2,3-b]- and furo[3,2-b] decalin systems with *cis/trans* ring junctions are present in several furosesquiterpenes obtained from marine sponges. A short and efficient synthesis of this ring system is described starting from Hageman's ester (1). The method has been extended for the synthesis of compound 8 and 14 via the diketones 5,6 and 12 respectively.

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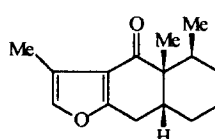
Marine sponges and different plants are rich sources of several furosesquiterpenes.<sup>1</sup> These include compounds like atractylon,<sup>2</sup> furodysin,<sup>3</sup> isoalantolactone,<sup>4</sup> as well as many oxygenated derivatives like ligularone,<sup>5</sup> petasalbin,<sup>5</sup> euryopsonal,<sup>6</sup> septuplinolide,<sup>4</sup> tubipofuran<sup>7</sup> and several other furanoerimophilanes. In all of these compounds a linearly fused furo[2,3-b] or furo[3,2-b] decalin framework, with a *cis* or *trans* ring junction is the key structural feature.



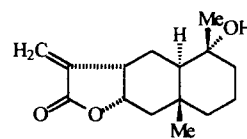
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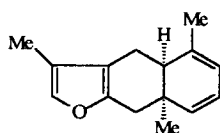
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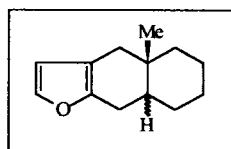
Ligularone



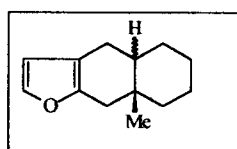
Septuplinolide



Tubipofuran



*cis* or *trans*



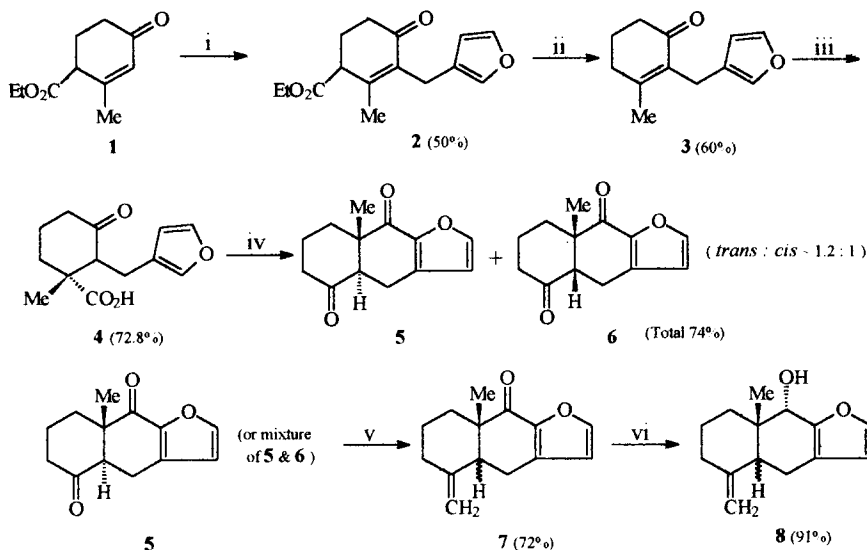
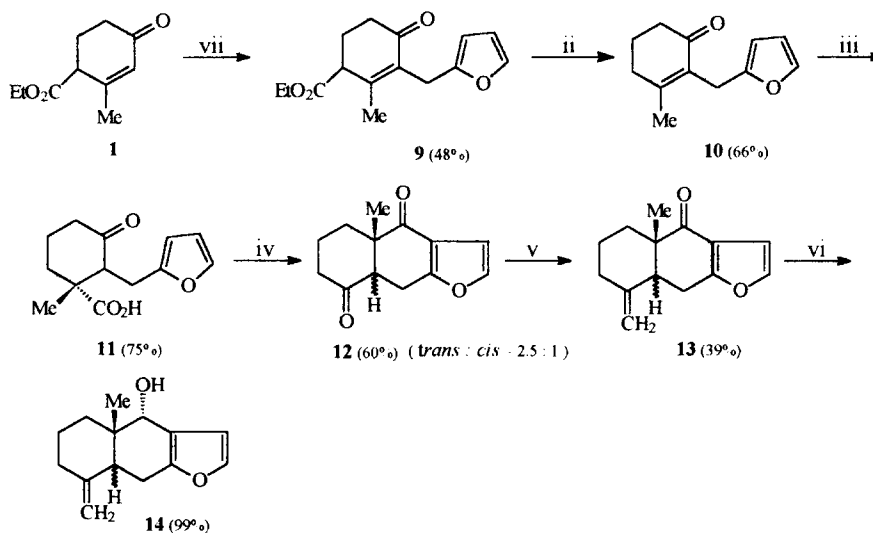
*cis* or *trans*

The stereoselective synthesis of linearly fused furodecalin derivatives is a challenge for synthetic chemists<sup>2,4</sup> and the structural evaluation for biomedical reasons has been pursued.<sup>4,7</sup> We report here a concise route to linearly fused A/B *trans*- and A/B *cis*- furo[3,2-b] and furo[2,3-b] decalin derivatives that contain functionality suitable for preparing the target furanoerimophilanes from Hageman's ester (Scheme 1 & 2).

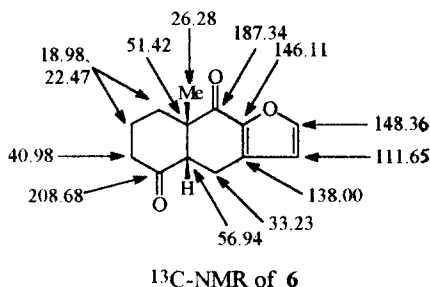
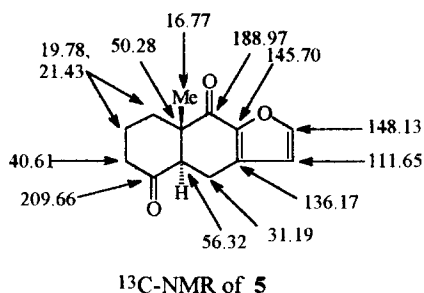
Alkylation of Hageman's ester **1** with 3- or 2- furylmethyl chloride, in the presence of <sup>t</sup>BuOK, afforded the C-3 alkylated product **2** or **9** in 48-50% isolated yield. The compounds were characterized by IR, NMR spectroscopic data as well as by elemental analysis. Alkaline, hydrolytic, decarboxylation of the alkylated Hageman's ester **2** or **9** produced the furylmethylcyclohexenone derivatives (**3** or **10**) as pale yellow oils in 60-66% yield. The <sup>1</sup>H-NMR spectrum of compound **3** has two distinct singlets at 1.97 and 3.43 that correspond to the Me-signal and the furylmethyl group. Three furan protons were observed at  $\delta$  6.22, 7.14 and 7.33. <sup>13</sup>C NMR assignment was made with the aid of DEPT 135 spectrum. These experiments showed four CH<sub>2</sub> carbons at 20.44, 22.19, 32.35 and 37.67, one methyl carbon at 21.32 and three methylene carbons at 111.20, 139.14, 142.49 (C-2, C-4 and C-5 of furan ring). The remaining signals at 198.20, 123.41, 134.26 and 156.25 were assigned as carbonyl and olefinic quaternary carbons respectively. Compound **10** exhibited almost identical spectral data which is in conformity with the assigned structure.

Connection of the cyclohexenone and the furan units was achieved by carbonylation followed by an intramolecular aromatic substitution reaction. The requisite carboxyl was introduced by conjugate addition of cyanide to the unsaturated ketone **3** or **10** followed by in situ alkaline hydrolysis that afforded the keto acids **4** or **11** as colourless solids (72-75% yield). Attempts to cyclise the keto acids (with PPA) or the corresponding acid chlorides (with SnCl<sub>4</sub>) met with failure. However, the keto acids were successfully cyclized with the help of a mixture of trifluoroacetic anhydride and trifluoroacetic acid. Thus, the keto acid **4**, on stirring with a 4:1 mixture of (CF<sub>3</sub>CO)<sub>2</sub>O and CF<sub>3</sub>CO<sub>2</sub>H, produced a mixture of *trans*- and *cis*- 9-methyl-1,5-dioxofuro[3,2-b]decalins (**5** and **6**) in 74% yield. The ratio of *trans*- and *cis*- isomers was 1.2:1 as indicated by <sup>1</sup>H-NMR and G.C. analysis of the crude product. Pure samples of **5** (hexagonal plate) and **6** (needles) were obtained by recrystallization from a mixture of pet. ether-dichloromethane followed by mechanical separation of crystals.

The geometry of the A/B ring junction was established by spectral data, analogy<sup>8</sup> as well as by single crystal X-ray analysis.<sup>9</sup> The <sup>1</sup>H-NMR of the *trans*- decalin **5** showed an upfield shift of  $\delta$  0.33 for the angular Me group compared to that of the *cis*- isomer. Thus while the angular C-Me in *trans*- isomer appeared at  $\delta$  1.05 (singlet), the *cis*- diketone signal was observed at  $\delta$  1.38. The <sup>13</sup>C-NMR of the two isomers also exhibited a marked difference in the chemical shifts of these two methyl groups. The assignment of the carbons of compound **5** and **6** are given below. The comparative stability of the diastereomeric furodiketones was studied. Thus epimerization of a mixture of **5** and **6** with base (DBU) did not significantly increase the amount of *trans* isomer **5**. However, we were able to selectively crystallize *trans* isomer from a dilute solution of the two isomers and with continuous separation, we were able to isolate **5** in ~ 50% yield. Cyclization of the keto acid **11** under identical conditions, produced an oily, nonseparable, mixture of *trans*- and *cis*- diketones (**12**) in ~ 60% yield (*trans*: *cis* ~ 2.5:1).

**SCHEME 1****SCHEME 2**

**Reagents and Conditions :** i)  $t\text{BuOK}$ ,  $t\text{BuOH}$ , 3-Furylmethyl chloride, reflux under  $\text{N}_2$ , 8 hrs  
 ii)  $\text{KOH}$ ,  $\text{H}_2\text{O-EtOH}$  (1:1), reflux under  $\text{N}_2$ , 6 hrs iii)  $\text{KCN}$ ,  $\text{EtOH-H}_2\text{O}$  (2:1),  $\text{HMPA}(\text{cat})$ , reflux under  $\text{N}_2$ , 17 hrs and then 93 hrs after addition of 10%  $\text{KOH}(\text{excess})$  iv)  $(\text{CF}_3\text{CO})_2\text{O}$  +  $\text{CF}_3\text{CO}_2\text{H}$  (4:1), r.t. under  $\text{N}_2$ , 15-16 hrs v)  $\text{Ph}_3\text{P}^+\text{CH}_3\text{I}^-$ ,  $n\text{-BuLi}$ , THF, under argon  $-30^\circ\text{C}$  to r.t., 4 hrs vi)  $\text{LiAlH}_4$ , THF, reflux under argon, 10 hrs vii)  $t\text{BuOK}$ ,  $t\text{BuOH}$ , 2-Furylmethyl chloride, reflux under  $\text{N}_2$ , 8 hrs.



Most of the earlier methods for preparing furosesquiterpenes depend heavily on setting up of the A/B geometry at the beginning and then introducing the furan ring, whereas our synthetic approach demonstrates that the diastereomeric diketones can be prepared very easily in the presence of furan ring. Thus the method can be used as a direct entry to the furanoerimophilane system and can assemble key intermediates for the synthesis of many furosesquiterpenes.

To demonstrate this approach, we attempted to convert compound **5** to desmethylatractylon. Reduction of **5** with  $\text{Et}_3\text{SiH/TFA}$  reduced the more accessible 5-oxo group, while the 1-oxo group remained intact.  $\text{NaBH}_4/\text{TFA}$  as reducing agent reacted in a similar fashion. We exploited the reactivity difference by installing the exocyclic double bond by selective Wittig methylenation of the 5-oxo group. Thus reaction of **5** with methyltriphenylphosphonium bromide/ $n\text{-BuLi}$  ( $-30^\circ\text{C}$  to r.t.) produced **7** in  $\sim 72\%$  yield. The product, however, was found to be a mixture of *trans* and *cis* isomers (ratio of *trans*:*cis*  $\sim 1.5:1$ ). Compound **12** was also converted to **13** in a similar way. These results demonstrate that the furanoerimophilane system can be assembled by intramolecular aromatic substitution. Differentiation of the resultant diketones is easily achieved and opens the way for elaboration of these intermediates to several sesquiterpenoid natural products.

#### General Method for the preparation of **2** and **9**

Potassium (2.07g, 53 mmol) was dissolved in dry tert butyl alcohol (20 ml) and then the latter was distilled off until a white solid appeared. This was cooled to r.t. and 2-methyl-4-oxocyclohex-2-ene carboxylate (Hagemann's ester) (9.65g, 53 mmol) was added in one portion with stirring under  $\text{N}_2$  atmosphere. The red solution so formed turned into a straw-yellow solid a few minutes after the addition. Furylmethyl chloride (6 g, 52 mmol) was then added and the resultant solution refluxed with stirring for 8 hours. The cooled reaction mixture was then poured onto crushed ice, acidified with cold  $\text{HCl}$  (6N) and extracted with ether. The ether solution was washed thoroughly with water and dried ( $\text{Na}_2\text{SO}_4$ ). Evaporation of the solvent afforded a yellow liquid which was purified by reduced pressure distillation.

Compound **2**, faint yellow oil (7.2 g, 50%), b.p.  $170\text{--}172^\circ\text{C}/12\text{mm}$ ; IR ( $\text{CHCl}_3$ )  $\nu_{\text{max}}$  1678,  $1750\text{ cm}^{-1}$ .  $^1\text{H}$ -NMR( $\text{CDCl}_3$ )  $\delta$ : 1.28(t, 3H,  $J = 7.3\text{ Hz}$ ), 1.98–2.60 (m, 4H), 2.02 (s, 3H), 3.30–3.49 (m, 3H), 4.21(q, 2H,  $J = 7.3\text{ Hz}$ ), 6.23(brs, 1H), 7.17(s, 1H), 7.29(brs, 1H) ppm.  $^{13}\text{C}$ -NMR ( $\text{CDCl}_3$ ) 14.04, 20.51, 20.60, 25.50, 34.39, 47.59,

61.19, 110.94, 122.59, 135.83, 139.16, 142.49, 151.08, 171.90, 196.69. Anal. Calcd. for  $C_{15}H_{18}O_4$ : C, 68.70; H, 6.87; Found: C, 68.35; H 6.51.

Compound **9**, light yellow liquid, (7.0 g, 48%) b.p. 185-187°C/10mm; IR( $CHCl_3$ )  $\nu_{max}$  1675, 1750  $cm^{-1}$ .  $^1H$ -NMR( $CDCl_3$ )  $\delta$ : 1.30(t, 3H,  $J = 7.3$  Hz), 2.10(s, 3H,  $CH_3$ ), 2.00-2.60(m, 4H), 3.70(s, 2H), 4.20(q, 2H  $J \sim 7.3$  Hz), 6.00(d, 1H), 6.3(m, 1H), 7.30(d, 1H). Anal. Calcd. for  $C_{15}H_{18}O_4$ : C, 68.70; H, 6.87; Found: C, 68.41; H 6.47.

#### General method for the preparation of **3** and **10**

A solution of KOH (4 g, 71.4 mmol) in 10 ml water and 10 ml ethanol was added to the ketoester (**2** or **9**) (4g, 15.3 mmol). The reaction mixture was refluxed with stirring under  $N_2$  atmosphere for 6 hours. Excess alcohol was then removed by distillation under reduced pressure and the residue was diluted with ice water, acidified with 6N HCl, and extracted with ether. The ether extract was washed successively with 5% brine solution, 5%  $NaHCO_3$  solution, and water and then dried ( $Na_2SO_4$ ). Removal of the solvent gave the title compound which was purified by distillation under reduced pressure.

Compound **3**: Pale yellow oil, b.p. 120-122°C/10mm, yield 1.8 g (60%), IR( $CHCl_3$ )  $\nu_{max}$  1675  $cm^{-1}$ ,  $^1H$ -NMR( $CDCl_3$ )  $\delta$ : 1.88-2.04(m, 2H), 1.97(s, 3H), 2.32-2.44(m, 4H), 3.43(s, 2H), 6.22(brs, 1H), 7.14(s, 1H), 7.33(brs, 1H)ppm.  $^{13}C$ -NMR ( $CDCl_3$ ) 20.45, 21.30, 22.19, 32.64, 37.67, 111.20, 123.41, 134.25, 139.13, 142.49, 156.25, 198.20. Anal. Calcd. for  $C_{12}H_{14}O_2$ : C, 75.79; H, 7.37; Found: C, 75.51; H, 7.09.

Compound **10**: light yellow oil b.p. 108-110°C/10mm, yield 2.0 g (66%), IR( $CHCl_3$ )  $\nu_{max}$  1660, 1675  $cm^{-1}$ ,  $^1H$ -NMR( $CDCl_3$ )  $\delta$ : 1.87-2.00(m, 2H), 2.00(s, 3H), 2.34-2.42(m, 4H), 3.65(s, 2H), 5.88(dd, 1H,  $J \sim 0.7$  Hz and 2.5 Hz), 6.20(dd, 1H,  $J \approx 1.6$  Hz and 2.5 Hz), 7.22(dd, 1H,  $J \approx 0.7$  Hz and 0.9 Hz)ppm. MS( $m/z$ ), 190( $M^+$ ) 175, 161, 105, 91, 81, 55. Anal. Calcd. for  $C_{12}H_{14}O_2$ : C, 75.79; H, 7.37; Found: C, 75.58; H, 7.11.

#### General method for the preparation of **4** and **11**

To a solution of the ketone (**3** or **10**) (2.9g, 15 mmol) in 25 ml ethanol and 1.5 ml HMPA, a solution of potassium cyanide (3.3g, 45 mmol) in 15 ml water was added. The solution was then refluxed with stirring under argon atmosphere for 17 hours. It was then cooled to r.t, an aqueous solution(50 ml) of KOH(5.4 g, 96 mmol) was added, and refluxing was continued for another 90 hrs. The solution was then poured into ice-water, acidified with conc. HCl and extracted with ether. After usual work up the keto acid (a brown viscous oil) was redissolved in aqueous sodium bicarbonate solution and extracted with ether to remove any neutral matter. The aqueous part was then cooled in ice, acidified with conc. HCl and extracted with ether. The ether layer was washed with 5% brine solution, dried ( $Na_2SO_4$ ), and concentrated to furnish the keto acid as a brownish yellow oil which solidified on standing.

Compound **4**, colourless solid, m.p. 181-183°C(ether/0°C), yield 2.6g (73%) IR(KBr)  $\nu_{max}$  1711(br) $cm^{-1}$ .  $^1H$ -NMR( $DMSO-d_6$ )  $\delta$ : 1.17(s, 3H), 1.00-2.75(m, 9H), 6.36(brs, 1H), 7.48(brs, 1H), 7.64(brs, 1H)ppm. MS( $m/z$ )

236( $M^+$ ), 218, 200, 191, 176, 149, 121, 111, 107, 95, 93, 91, 82, 81. Anal. Calcd. for  $C_{13}H_{16}O_4$ : C, 66.10; H, 6.78. Found C, 65.74; H, 6.55.

Compound **11**: Colourless solid, m.p. 157-159°C (benzene-pet. ether), yield 2.7g (75%); IR(KBr)  $\nu_{\max}$  1700, 1708  $\text{cm}^{-1}$ ,  $^1\text{H-NMR}$  ( $\text{CDCl}_3$  +  $\text{DMSO-d}_6$ )  $\delta$ : 1.11(s, 3H), 1.80-2.47(m, 7H), 3.18(dd, 2H,  $J$  = 8.2 and 14.9 Hz) 6.00(d, 1H,  $J$  = 3.0Hz), 6.20(dd, 1H,  $J$  = 1.9, 3.0 Hz), 7.24(d, 1H,  $J$   $\approx$  3.0 Hz)ppm. MS( $m/z$ ) 236( $M^+$ ), 218, 191, 190, 162, 149, 136, 135, 123, 121, 116, 107, 94, 91, 81. Anal. Calcd. for  $C_{13}H_{16}O_4$ : C, 66.10; H, 6.78; Found: C, 65.87; H, 6.67.

#### General method for the preparation of diketone (5 and 6 or 12)

A mixture of the keto acid (**4** or **11**) (0.137g, 0.58 mmol), trifluoroacetic anhydride (3.0 mL), and trifluoroacetic acid(0.6 mL) was stirred overnight at r.t. under argon atmosphere. The brown mixture was then poured onto crushed ice and extracted with ether. The ether extract was then washed successively with ice-cold 5% sodium hydroxide solution, and brine and then dried ( $\text{Na}_2\text{SO}_4$ ) and concentrated. The crude diketone thus obtained was purified by column chromatography (silicagel/benzene-ethylacetate mixture, 8:2).

Compounds **5** and **6**: Colourless solid (*cis:trans*  $\approx$  1:1.2) yield 74%. Pure samples of **5** and **6**, however, were obtained by recrystallization from a pet. ether - dichloromethane solvent mixture followed by mechanical separation of the crystals. [During recrystallization the *cis* isomer was gradually converted to the *trans* isomer (mother liquor) and thus isolable as the major component. Only a small amount of the *cis* isomer could be separated from the reaction mixture].

Compound **5**: Colourless hexagonal plates, m.p. 178-179°C (pet ether-dichloromethane), IR(KBr)  $\nu_{\max}$  1663, 1715  $\text{cm}^{-1}$ ,  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 1.05(s, 3H), 1.81-1.94(m, 2H), 2.08-2.41(m, 4 H), 2.79(dd, 1H,  $J$   $\approx$  4.0 and 16.9 Hz), 2.92(dd, 1H  $J$  = 10.6 and 16.9 Hz), 3.07(dd, 1H,  $J$   $\approx$  4.0 & 10.6 Hz), 6.42(d, 1H,  $J$  = 1.6 Hz), 7.58(d, 1H,  $J$  = 1.6 Hz)ppm.  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 16.77, 19.78, 21.43, 31.19, 40.61, 50.28, 56.32, 111.65, 136.17, 145.70, 148.13, 188.97, 209.66, MS( $m/z$ ) 218( $M^+$ ), 203, 190, 189, 175, 173, 162, 161, 149, 147, 126, 122, 108(B $^+$ ), 105, 93, 91, 81, 80. Anal. Calcd. for  $C_{13}H_{14}O_3$ : C, 71.56; H, 6.42, Found: C, 71.42; H, 6.30. The structure has also been confirmed by X-ray crystallography.

Compound **6**: Colourless needles, m.p. 156-157°C (pet. ether- dichloromethane), IR(KBr)  $\nu_{\max}$  1663, 1715  $\text{cm}^{-1}$ ,  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 1.38(s, 3H), 1.49-1.95(m, 2H), 2.28-2.40(m, 2H), 2.62-2.69(m, 3H), 2.81(dd, 1H,  $J$   $\approx$  5.8 and 21.2 Hz), 3.37(dd, 1H,  $J$   $\approx$  5.8, and 21.2 Hz), 6.44(d, 1H,  $J$   $\approx$  1.7 Hz), 7.54(d, 1H,  $J$   $\approx$  1.7 Hz)ppm.  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 18.98, 22.47, 26.28, 33.23, 40.98, 51.42, 56.94, 111.65, 138.00, 146.11, 148.36, 187.34, 208.68. MS( $m/z$ ) 218( $M^+$ ), 203, 190, 189, 175, 173, 162, 161, 149, 147, 126(B $^+$ ), 122, 108, 105, 93, 91, 81, 80. Anal. Calcd. for  $C_{13}H_{14}O_3$ : C, 71.56; H, 6.42. Found: C, 71.40; H, 6.31.

Compound **12**: Viscous yellow oil (solidified to a colourless solid on standing for a prolonged period, m.p. 62-65°C) yield 60% (*cis:trans*  $\approx$  1:2.5). IR(KBr)  $\nu_{\max}$ : 1678, 1709  $\text{cm}^{-1}$ ,  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 1.0(s) and 1.36(s) (total 3H, due to *trans* and *cis*-Me. ratio 2.5 : 1), 1.50-2.65(m, 6H), 2.80-3.20(m, 3H), 6.58 and 6.66

(d,  $J \approx 2.5$  Hz, total 1H), 7.3 and 7.36(d,  $J \approx 2.5$  Hz, total 1H)ppm. MS(m/z): 218(M) 126, 108, 93, 80. Anal. Calcd. for  $C_{13}H_{14}O_3$ : C, 71.56; H, 6.42. Found C, 71.21; H 6.19.

### General method for the preparation of 7 and 13

A 1.6M solution of n-butyllithium (0.053 ml) was injected slowly to a cold ( $-30^\circ\text{C}$ ) stirred suspension of methyltriphenylphosphonium iodide (39 mg, 0.096 mmol) in dry THF(0.5 ml), under argon atmosphere. After 35-40 minutes a THF solution(0.5 ml) of the diketone (**5**, **11** or a mixture of **5** & **6**) (14 mg, 0.064 mmol) was injected dropwise. The stirring was continued at  $-30^\circ\text{C}$  for about 30 minutes and then allowed to attain r.t. It was further stirred at room temperature (3-3.5 hours) before quenching with ice water. Extraction with ether followed by the usual work up afforded the crude product which is purified by column chromatography (silicagel/benzene-pet ether, 4:1).

Compound **7**: Colourless solid, m.p.  $98-101^\circ\text{C}$ , yield 72%, IR(KBr)  $\nu_{\text{max}}$   $1659\text{ cm}^{-1}$ .  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 1.00(s, *trans*  $\text{C}_9\text{-Me}$ ), 1.25(s, *cis*  $\text{C}_9\text{-Me}$ ) [two methyl singlets equivalent to 3H], 1.35-3.04(m, 9H), 4.60 & 4.70 (both brs, due to vinylic H's of *cis* isomer), 4.74 & 4.96 (d,  $J \approx 1.3$  and 1.2 Hz respectively, due to two vinylic H's of *trans* isomer), 6.38 & 6.40 (both d,  $J \approx 1.8$  Hz and 1.7 Hz respectively, total 1H,  $\text{C}_3\text{-H's}$  of furan ring for *cis* and *trans* isomer)(*cis: trans*  $\approx 1:1.5$ ), 7.56(d, 1H,  $J \approx 1.8$  Hz,  $\text{C}_2\text{-H's}$  of furan ring) ppm.

Compound **13**: Viscous pale yellow oil (sweet smelling), yield 39%, IR (KBr)  $\nu_{\text{max}}$   $1675\text{ cm}^{-1}$ .  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 0.97(s, *trans*  $\text{C}_9\text{-Me}$ ), 1.23 & 1.25(s, *cis*,  $\text{C}_9\text{-Me}$ ), 1.29-3.15(m, 9H), 4.59 & 4.76(s, vinylic H's due to *trans* isomer), 4.73 & 4.97(d,  $J \approx 1.2$  Hz & 1.3 Hz respectively, vinylic H's due to *cis* isomer), 6.64 & 6.66(d,  $J \approx 2.1$  Hz, total 1H,  $\text{C}_3\text{-H's}$  of furan ring due to *trans* and *cis* isomer), 7.31 and 7.32(d,  $J \approx 2.1$  Hz,  $\text{C}_2\text{-H's}$  of furan ring due to *trans* and *cis* isomer) (*Ratio of trans: cis*  $\approx 1:2.7$ ).

### Reduction of the ketone (7 or 13): General method for the preparation of alcohols (8 and 14)

A mixture of the ketone (**7** or **13**) (25 mg, 0.115 mmol) and LAH  $\sim 20$  mg (excess) in dry THF (2 ml) was refluxed with stirring under argon atmosphere for 10 hours. After decomposing with saturated sodium sulphate solution (few drops), ether was added and after brief stirring the ether layer was decanted, and the process was repeated 4-5 times. The combined ether extract was washed with brine solution, dried ( $\text{Na}_2\text{SO}_4$ ) and concentrated to furnish the alcohols as highly viscous oil (23-25 mg) (91-99%).

Compound **8**: Viscous pale yellow oil, yield 23 mg (91%), IR(neat)  $\nu_{\text{max}}$   $1650, 3396\text{ cm}^{-1}$ .  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 0.76 and 1.19(s, 3H total, *trans* and *cis*  $\text{CH}_3$ ), 0.84-2.74(m, 9H), 3.65-3.75(m, 1H,  $-\text{OH}$ ), 4.40(brd, 1H,  $\text{CHOH}$ ), 4.60-4.90(m, 2H), 6.22(d, 1H,  $J \approx 1.5$  Hz), 7.32(d, 1H,  $J \approx 1.5$  Hz) ppm.

Compound **14**: Viscous pale yellow oil, yield 25 mg(99%), IR(neat) $\nu_{\text{max}}$   $1639, 3396\text{ cm}^{-1}$ .  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 0.70 and 1.08(s, total 3H, *trans* and *cis*  $\text{CH}_3$ ) (ratio of *trans: cis*  $\approx 5:3$ ), 0.83-2.61(m, 9H), 3.64-3.69(br, m, 1H,  $-\text{OH}$ ), 4.35-4.39(brd, 1H,  $-\text{CHOH}$ ), 4.68-4.90(m, total 2H, vinylic H's of *cis* and *trans* isomer), 6.37 and

6.38(d, total 1H J = 1.8 Hz)(due to *cis* and *trans* isomer), 7.26(d, 1H, J = 1.8 Hz). (Compounds **7** and **13**, and **8** and **14** are *cis*- and *trans* mixtures that are only characterized by <sup>1</sup>H-NMR and IR).

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