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Stereocontrolled Approach to Highly Substituted Cyclopentanones. Application in a Formal Synthesis of $\Delta^{9(12)}$- Capnellene

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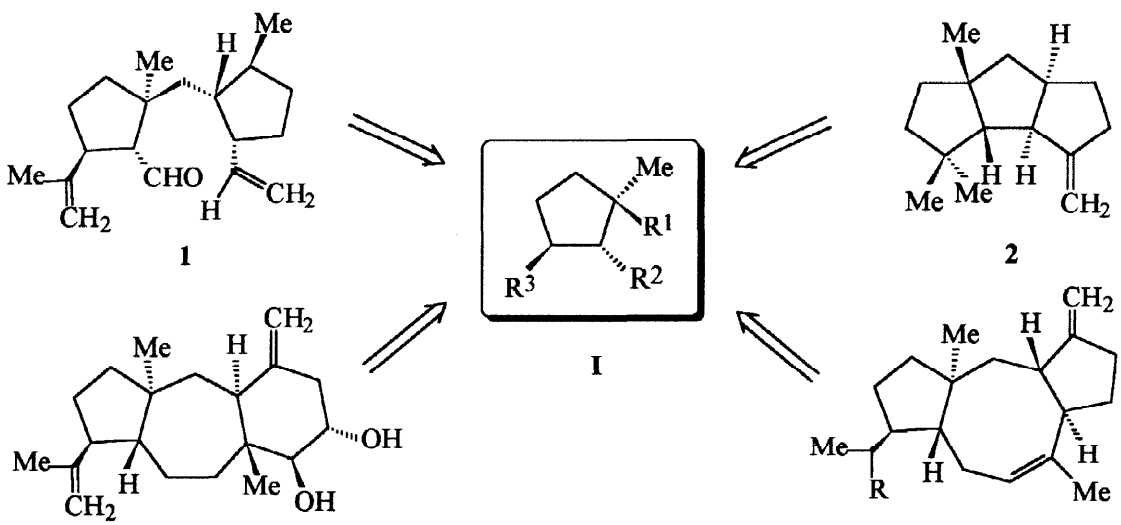
Abstract: A direct stereocontrolled route for the construction of highly substituted cyclopentanones **10a-d** has been developed starting from acyclic ketones **5a,b**. The key step involves copper(I)-catalysed stereoselective photocycloaddition of the dienes **6a-d** followed by stereospecific rearrangement of the cyclobutane derivatives **7a,b, 8** and **9**. Employing this methodology a formal synthesis of the sesquiterpene $\Delta^{9(12)}$-capnellene **2** has been achieved.

A wide range of natural products is represented by the substituted cyclopentanes of the general structure **I**. The diterpene dictymal **1**[1] is a representative example. Several other polycyclic compounds such as $\Delta^{9(12)}$-capnellene **2**,[2] clavularane **3**,[3] ceroplastol **4**,[4] etc. may also be considered to be derived from the cyclopentane **I**. Development of a route for stereoselective construction of the substituted cyclopentanes **I** is of considerable importance for total synthesis of these natural products. Despite the development of many elegant



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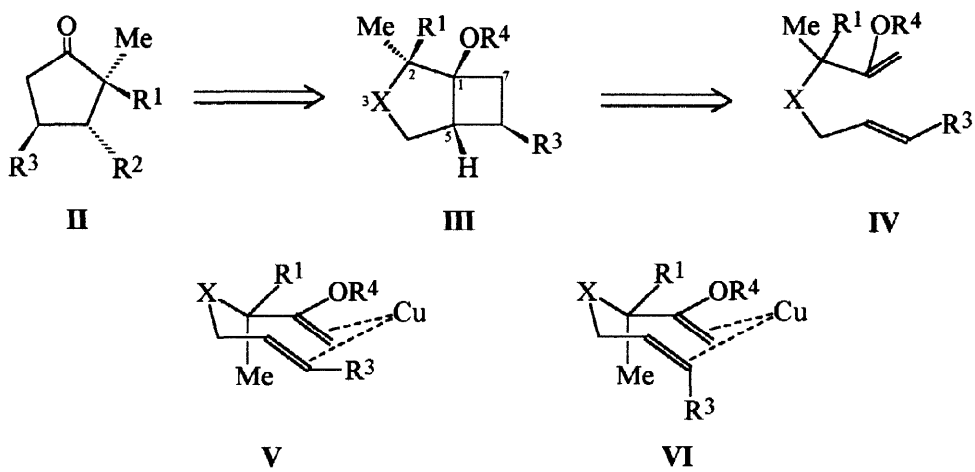
strategies for the synthesis of vicinally substituted cyclopentanes,[5] direct methods for the construction of cyclopentanes[6] with substituents at more than two contiguous centres are rare. Herein, we report[7] a direct stereocontrolled route for the construction of highly substituted cyclopentanones and a formal synthesis of $\Delta^{9(12)}$-capnellene as an application of this route.

Results and Discussion

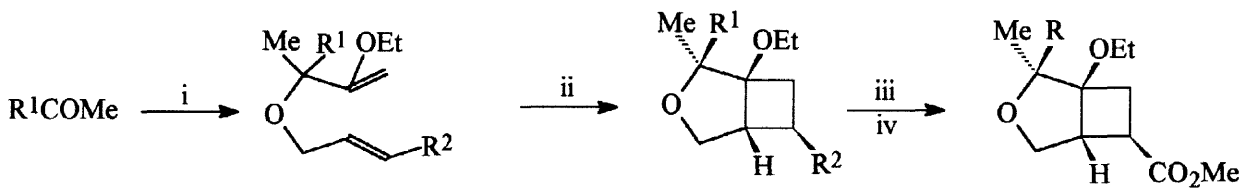
One can imagine that the cyclopentanone **II** (**Scheme 1**) can be the immediate precursor of the cyclopentane **I**. The cyclopentanone **II** can, in principle, be obtained by pinacol-type rearrangement of the cyclobutane derivative **III**. The latter can be derived from copper(I)trifluoromethane sulfonate (CuOTf) catalysed cycloaddition of the diene **IV**. The success of this protocol[8] depends on photocycloaddition of the diene **IV** which plays the pivotal role in determining the stereochemistry of the substituents in the cyclopentanones **II**. As CuOTf catalyses E,Z-olefin isomerisation during irradiation, photocycloaddition of the diene **IV** is expected to produce a mixture of cyclobutane derivatives arising from both E- and Z-olefin. We anticipated that of the two Cu(I)-diene complexes **V** and **VI** formed from E- and Z-olefin prior to photocycloaddition, the complex **VI** would be destabilised due to steric crowding between Me and R^3 inhibiting its formation. Further, of the two groups R^1 and Me, the bulkier one (R^1) would prefer to occupy the less crowded exo position[8c] in the Cu(I)-complexes. Thus photocycloaddition of the diene **IV** would be expected to proceed through the complex **V** to produce the cyclobutane derivative **III**. With this background, execution of the above plan was initiated.



Scheme 1

To demonstrate the influence of the size of the vinylic substituent on the stereoselectivity during photocycloaddition, the diene **6a-c** were chosen while the diene **6d** was selected to demonstrate the stereocontrol at three chiral centres on the cyclopentanones to be developed (**Scheme 2**). The dienes **6a-c** were prepared from acetone on reaction with ethoxyvinyl lithium followed by coupling of the resulting alcohol through its sodio salt with crotyl bromide, cinnamyl bromide and sorbyl bromide respectively in overall

excellent yield. The diene **6d** was obtained from the ketone **5d** on reaction with ethoxyvinyl lithium followed by coupling of the resulting alcohol with sorbyl bromide. The dienes were then irradiated in ether solution in the presence of CuOTf as catalyst. While the diene **6a** produced a mixture of the *exo*-adduct **7a** and its corresponding *endo* isomer in ca 2.5:1 ratio (GC) in 41% yield, the diene **6b** with a bulkier Ph group as R^2 produced exclusively the *exo*-adduct **7b** in 53% yield reflecting the attainment of complete stereocontrol with increase in size of R^2 from Me to Ph. The diene **6c** with a propenyl group as R^2, having a size nearly equal to that of Me, gave a mixture of the *exo*-adduct **7c** and its corresponding *endo* isomer in 2.2:1 ratio, while the diene **6d**, with the same substituent, gave a mixture of the *exo*-adduct **7d** and its corresponding *endo* isomer in 3:1 ratio (52% yield). Thus, by increasing the bulk of the vinylic substituent (R^2), photocycloaddition could be made stereoselective. Structural assignment to the photoadducts was based on their spectral data, while the stereochemical assignment was based on their transformation to the cyclopentanones. The mixture of photoadducts obtained from the diene **6c** could, however, be transformed to the exclusive *exo*-cyclobutane derivative **8** as follows. Oxidative cleavage of the propenyl chain of the adduct **7c** and its *endo* isomer with RuO_4 followed by esterification of the resulting carboxylic acid afforded a mixture of the *exo*-methyl ester **8** and its *endo* isomer in 68% yield as evidenced from the presence of two pairs of methyl singlets at δ 1.08, 1.23 (for the major isomer) and 1.2, 1.3 (for minor isomer) in ^1H NMR spectrum. When this mixture was equilibrated with NaOMe-MeOH, the minor isomer with Me signals at δ 1.2 and 1.3 in the product disappeared totally, producing exclusively the thermodynamically more stable[9] *exo*-methyl ester **8**. The mixture of adducts obtained from the diene **6d** was also converted in a similar fashion to the methyl ester **9** in 54% yield.



5a, R^1 = Me
b, R^1 = CH_2Ph

6a, R^1 = R^2 = Me
b, R^1 = Me, R^2 = Ph
c, R^1 = Me, R^2 = CH:CHMe
d, R^1 = CH_2Ph, R^2 = CH:CHMe

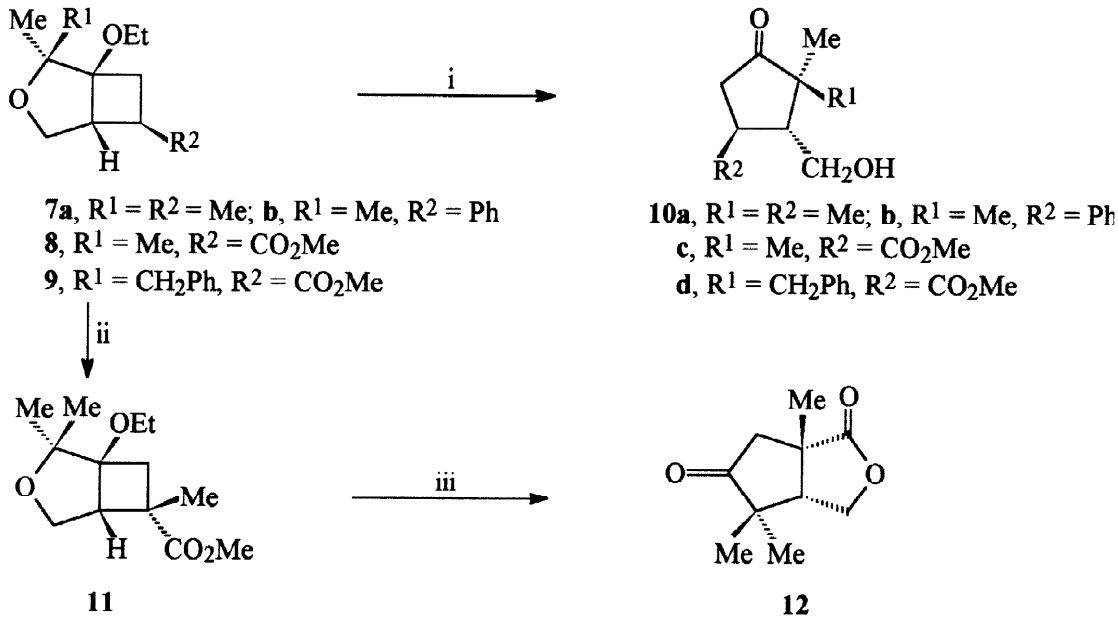
7a, R^1 = R^2 = Me
b, R^1 = Me, R^2 = Ph
c, R^1 = Me, R^2 = CH:CHMe
d, R^1 = CH_2Ph, R^2 = CH:CHMe

8, R = Me
9, R = CH_2Ph

Scheme 2 *Reagents and conditions*: i, a) $EtOCH{:}CH_2$, t-BuLi, THF,-70°C; b) NaH, THF, HMPA, alkenyl bromide; ii) hv, Et_2O, CuOTf; iii, a) $RuCl_3.xH_2O$, CCl_4-CH_3CN-H_2O, b) CH_2N_2, Et_2O; iv) NaOMe-MeOH.

Having been successfully prepared, the cyclobutane derivatives **7a, b, 8** and **9** were subjected to rearrangement (**Scheme 3**). Trifluoromethane sulfonic acid (TfOH) between -78°C and rt was found to be the most effective for the rearrangement. The *exo*-cyclobutane derivative **7b** under these conditions afforded a single cyclopentanone derivative **10b** in 55% yield arising from migration of the stereoelectronically disfavoured 1,5-bond.[10] The trans relationship between the C_3- and C_4-hydrogens was established from the

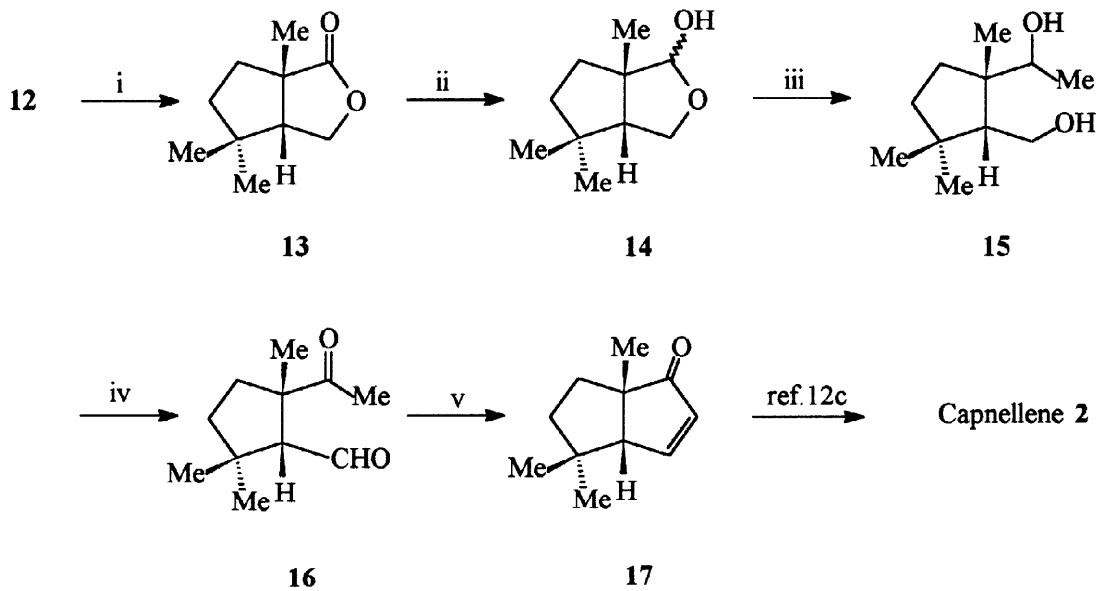
coupling constant (11.6 Hz) in its ^{1}H NMR spectrum. The observed coupling constant is closely comparable to that reported for



Scheme 3 *Reagents and conditions*: i) TfOH, CH_2Cl_2, -78°C to rt; ii) LDA, THF, MeI; iii) TFA, TfOH, 50°C.

trans 1,2-disubstituted cyclopentanes.[6b] Similarly the cyclobutane derivatives **8** and **9** on rearrangement, gave exclusively the single cyclopentanone derivatives **10c** and **10d** in 76% and 55% yields respectively. The trans relationship between the C_3 and C_4 substituents in **10c** and **10d** was similarly ascertained from the coupling constant of the C_4-hydrogen with the C_3 hydrogen as 10.6 and 11.0 Hz respectively. To gain additional support in favour of the trans relationship between C_3 and C_4 substituents in the cyclopentanone derivatives **10**, the rearrangement product of the cyclobutane derivative **8** with a β-carbomethoxy group and that of the cyclobutane derivative **11** with an α-carbomethoxy group were subjected to lactonisation. The cyclobutane derivative **11** with an α-carbomethoxy group was obtained in 74% yield from the cyclobutane derivative **8** on methylation of its lithium enolate. The methylation took place from the least hindered β-face. When the cyclobutane derivative **11** was treated with TFA containing a catalytic quantity of TfOH at 50°C, ring enlargement with concomitant lactonisation of the C_4-CO_2Me with the *syn* C_3-CH_2OH thus generated, took place to afford the lactone **12**, m.p. 70°C in 60% yield. The formation of lactone was confirmed by the lactone carbonyl absorption in IR (1770 cm^{-1}) and ^{13}C NMR (δ 180.9). On the contrary, the cyclopentanone derivative **10c** obtained from rearrangement of the cyclobutane derivative **8** failed to undergo lactonisation through the corresponding acid, thus establishing a *trans* relationship between the C_3- and C_4-substituents. The *cis* relationship of the C_2-Me with C $_3$-CH_2OH in **10d** was based on carbon chemical shift of the Me group. In ^{13}C NMR, the Me *syn* to a vicinal substituent in cyclopentanones is shielded[11] by ~5 ppm more than the one *anti* to

it. Thus, in the cyclopentanone derivatives **10b** and **10c**, the Me's *syn* to CH_2OH appeared at δ 18.7 and 18.6, while the *anti* Me's appeared at δ 24.4 and 23.5 respectively. The chemical shift (δ 18.7) observed for Me in the cyclopentanone derivative **10d** was closely comparable to those for *syn* Me's in **10b** and **10c** establishing the *syn* relationship between Me and CH_2OH. The mixture of the cyclobutane derivative **7a** and its corresponding *endo* isomer, on rearrangement, afforded the cyclopentanone **10a** and its C_4-eipmer in a ratio nearly identical to that of the starting cyclobutanes. Stereochemical assignment to the major isomer of this mixture as **10a** followed from analogy. Thus, the sequence involving photocycloaddition-cyclobutane rearrangement offers an excellent stereocontrolled route for the construction of cyclopentanones with substituents up to three contiguous chiral centres.



Scheme 4 *Reagents and conditions*: i, a) $NaBH_4$, MeOH, rt ; b) NaH, CS_2; c) Bu_3SnH, Toluene, reflux, 61%; ii) DIBALH, Toluene, 0^0C, 56%; iii) MeLi, Et_2O; iv) Oxalyl chloride, DMSO, Et_3N, CH_2Cl_2; v) KOH, MeOH, rt, 56%.

The synthetic potential of this protocol was demonstrated by a formal synthesis[12] of the sesquiterpene $\Delta^{9(12)}$-capnellene **2** (**Scheme 4**). To this end, the keto-lactone **12** synthesised as above was chosen. Transformation of the keto-lactone **12** into the lactone **13** was achieved through a three step sequence involving sodium borohydride reduction followed by transformation of the resulting alcohol mixture to xanthates and their reduction with tributyltin hydride in overall good yield. The lactone **13** was then reduced with DIBALH to produce the lactol **14** in 56% yield. Addition of MeLi to the lactol **14** followed by Swern oxidation of the resulting diol **15** gave the keto-aldehyde **16**. Treatment of the keto-aldehyde **16** with 1% aqueous KOH in MeOH at room tempeature effected smooth ring closure to produce the known enone **17**. ^1H NMR spectral data of this sample was found to be identical with those reported in literature.[12d] The enone **17**

has previously been transformed to $\Delta^{9(12)}$-capnellene **2**. Thus, with the synthesis of the enone **17**, a formal synthesis of $\Delta^{9(12)}$-capnellene was achieved.

In conclusion, we have developed a direct stereocontrolled route for the construction of cyclopentanones with substituents up to three contiguous chiral centres. The present approach is a general and flexible one as it begins with easily available acyclic ketones. The protocol creates substituents with chemodifferentiated functional groups which can be employed to annulate a second ring as demonstrated by a formal synthesis of $\Delta^{9(12)}$-capnellene.

Experimental Section

The compounds described are all racemates. Melting points and boiling points are uncorrected. Melting points were taken in open capillary in sulphuric acid bath. Petroleum refers to the fraction of bp 60-80°C. A usual work up of the reaction mixture consists of extraction with an organic solvent, washing with brine, drying over K_2CO_3 (for the ethoxy vinyl ethers) or Na_2SO_4 and removal of solvent in vacuo. Column chromatography was carried out with silica gel (60-120 mesh). Peak positions in ^1H and ^{13}C NMR spectra are indicated in ppm downfield from internal TMS in δ units. NMR spectra were taken in carbon tetrachloride solution at 60 MHz and in $CDCl_3$ solution at 200 and 300 MHz. IR spectra were recorded as neat for liquids and in KBr for solids.

Synthesis of the dienes 6a-d : The general procedure is illustrated by the synthesis of the diene **6a.**

3-(2'-Butenyloxy)-2-ethoxy-3-methyl butene (6a). The ketone **5** was allowed to react with ethoxy vinyl lithium (prepared from ethyl vinyl ether and tert-butyl lithium) according to the procedure[8c] described earlier. The carbinol thus obtained was then transformed to the diene on coupling with appropriate bromide as follows. To a magnetically stirred suspension of NaH (1.5 g, 25 mmol, 40% in oil), freed from adhering oil by repeated washing with petroleum, in THF (20 ml) was added dropwise a solution of the carbinol prepared from acetone **5a** (1.7 g, 13.07 mmol) in THF (10 ml) under N_2 atmosphere. The mixture was gently refluxed for 2h and then cooled to room temperature, and to it was added HMPA (10 ml) followed by crotyl bromide (2.3 g, 17 mmol). After refluxing for 2h, the reaction mixture was cooled to rt and quenched by adding cold water (20 ml). Usual work up of the reaction mixture followed by distillation in presence of 1% (w/w) NEt_3 afforded the diene **6a** as a colourless liquid (1.8 g, 75%); bp 102-103°C (50 mm); IR : 3600-3200 cm^{-1}; ^1H NMR (60 MHz) δ 1.30 (6H, s), 1.33 (3H, t, J = 6 Hz), 1.70 (3H, d, J = 4 Hz), 3.66 (2H, q, J = 3 Hz) partly merged within a multiplet centred at 3.76 (2H), 3.88 (1H, d, J = 2 Hz), 4.15 (1H, d, J = 2 Hz) and 5.16-5.73 (2H, m); ^{13}C NMR (75 MHz) δ 14.3 (CH_3), 17.6 (CH_3), 25.5 (CH_3), 62.6 (CH_2), 63.9 (CH_2), 76.2, 80.9 (CH_2), 128.2 (CH), 128.4 (CH), 164.5. An analytically pure sample of the dienes could not be prepared due to their rapid hydrolysis in the absence of triethyl amine.

2-Ethoxy-3-methyl-3-(3'-phenyl-2'-propenyloxy)-butene (6b). Liquid (61%); bp 145-147°C (0.6 mm); IR : 3600-3200 cm^{-1}; ^1H NMR (60 MHz) δ 1.31 (3H, t, J = 7 Hz), 1.33 (6H, s), 3.69 (2H, q, J = 8 Hz) partly merged within a multiplet centred at 3.93 (3H), 4.17 (1H, d, J = 2 Hz), 5.93-6.70 (2H, m) and 7.06-7.40 (5H, m); ^{13}C NMR

(75 MHz) δ 14.3 (CH_3), 25.6 (CH_3), 62.9 (CH_2), 63.9(CH_2), 81.2 (CH_2), 126.3 (CH), 127.2 (CH), 128.1 (CH), 128.3 (CH), 131.1 (CH), 137.0, 164.4.

2-Ethoxy-3-(hex-2',4'-dienyloxy)-3-methyl butene (6c). Liquid (62%); bp 90-92°C (20 mm); IR : 3600 - 3200 cm^{-1}; ^1H NMR (60 MHz) δ 1.33 (6H, s), 1.36 (3H, t, J = 4 Hz), 1.75 (3H, d, J = 6 Hz), 3.69 (2H, q, J = 8 Hz) partly merged within a multiplet centred at 3.80 (2H), 3.90 (1H, d, J = 2 Hz), 4.16 (1H, d, J = 2 Hz) and 5.26-6.33 (4H, m); ^{13}C NMR (75 MHz) δ 14.3 (CH_3), 17.9 (CH_3), 25.6 (CH_3), 62.9 (CH_2), 63.7 (CH_2), 76.4, 80.9 (CH_2), 127.8 (CH), 128.9 (CH), 131.0 (CH), 131.9 (CH), 164.5.

2-Ethoxy-3-(hex-2',4'-dienyloxy)-3-benzyl butene (6d). Liquid (82%); bp 120-122°C (0.5 mm); IR : 3600-3200 cm^{-1} ; ^1H NMR (60 MHz) δ 1.23 (3H, t, J = 4 Hz), 1.30 (3H, s), 1.75 (3H, d, J = 6 Hz), 2.53-2.96 (2H, m), 3.36-3.93 (5H, m), 4.03 (1H, d, J = 2 Hz), 4.86-6.56 (4H, m) and 7.13 (5H, s) ; ^{13}C NMR (75 MHz) δ 14.5 (CH_3), 18.0 (CH_3), 20.5 (CH_3), 45.9 (CH_2), 62.6 (CH_2), 63.3 (CH_2), 79.5, 83.3 (CH_2), 126.0 (CH), 127.5 (CH), 127.9 (CH), 129.0 (CH), 130.4 (CH), 131.1 (CH), 131.7 (CH), 137.7, 162.4.

Irradiation of the diallyl ether derivatives 6a-d : The general procedure is illustrated by the synthesis of the cyclobutane derivative **7a.**

1-Ethoxy-2,2-dimethyl-6-methyl-3-oxabicyclo[3.2.0]heptane (7a). A solution of the diallyl ether derivative **6a** (0.9 g, 4.9 mmol) in anhydrous ether (250 ml) was irradiated internally in presence of CuOTf (300 mg) through a water cooled quartz immersion well with a medium pressure mercury vapour Hanovia lamp (450W) for 6h. The ether solution was washed with aqueous NH_4OH, water and dried. Removal of ether followed by column chromatography of the residual liquid with petroleum-ether (19:1) as eluent afforded the cyclobutane derivative **7a** (0.37 g, 41%) as a colourless liquid; ^1H NMR (300 MHz) δ 1.15 (3H, s), 1.16 (3H, d, J = 7.2 Hz), 1.18 (3H, t, J = 7.2 Hz), 1.29 (3H, s), 1.61-1.79 (2H, m) 2.28 (1H, t, J = 4.8 Hz), 2.41 (1H, dd, J = 8.4 and 12.6 Hz), 3.29-3.46 (2H, m), 3.54 (1H, d, J = 9.6 Hz), 3.84 (1H, ddd, J = 3.9, 7.2 and 8.7 Hz); ^{13}C NMR (75 MHz) δ 15.7 (CH_3), 21.0 (CH_3), 21.8 (CH_3), 24.1 (CH_3), 26.5 (CH), 31.3 (CH_2), 44.9, 51.3 (CH), 59.1 (CH_2), 63.3 (CH_2), 68.6 (CH_2), 81.8, 85.6. Anal. Calcd. for $C_{11}H_{20}O_2$: C,71.73;H,10.86. Found: C,71.72;H,10.86.

1β-Ethoxy-2,2-dimethyl-6β-phenyl-3-oxabicyclo[3.2.0]heptane (7b). Colourless liquid (53%); ^1H NMR (200 MHz): δ 1.21 (3H, t, J = 7 Hz), 1.24 (3H, s), 1.40 (3H, s), 2.18-2.28 (1H, m), 2.26-2.97 (3H, m), 3.29-3.48 (2H, m), 3.67 (1H, d, J = 10 Hz), 3.92 (1H, dd, J = 4.8 and 9.6 Hz) and 7.12-7.33 (5H, m); ^{13}C NMR (50 MHz) δ 15.8 (CH_3), 21.3 (CH_3), 24.8 (CH_3), 32.1 (CH_2), 36.1 (CH), 52.9 (CH), 59.2 (CH_2), 68.5 (CH_2), 82.2, 85.1, 125.9 (CH), 126.7 (CH), 128.4 (CH) and 145.5; Anal. Calcd. for $C_{16}H_{22}O_2$: C, 78.04; H, 8.94. Found : C, 78.05; H, 9.03.

1β-Ethoxy-2,2-dimethyl-6β-(1'-propenyl)-3-oxabicyclo[3.2.0]heptane (7c) and its corresponding 6α-epimer. Colourless liquid (52%); ^1H NMR (200MHz) (for the major isomer) δ 1.12 (3H, s), 1.14 (3H, t, J = 6 Hz), 1.25 (3H, s), 1.62 (3H, d, J = 5.2 Hz), 1.88 (1H, dd, J = 6.46 and 11.50 Hz), 2.16-2.58 (3H, m), 3.28-3.58 (3H, m), 3.76-3.86 (1H, m) and 5.32-5.62 (2H, m); ^{13}C NMR (75MHz) (for major isomer) δ 15.7 (CH_3), 17.7 (CH_3), 21.2 (CH_3), 24.4 (CH_3), 30.4 (CH_2), 33.7 (CH), 50.7 (CH), 59.3 (CH_2), 68.2 (CH_2), 82.1, 85.4, 123.7 (CH) and 135.0 (CH); Anal. Calcd. for $C_{13}H_{22}O_2$: C, 74.28; H, 10.47. Found : C, 74.31; H, 10.42.

1β-Ethoxy-2β-benzyl-2α-methyl-6β-(1'-propenyl)-3-oxabicyclo[3.2.0]heptane (7d). Colourless liquid (41%); ^{1}H NMR (300 MHz) δ 1.12 (3H, s), 1.23 (3H, t, J = 6 Hz), 1.68 (3H, d, J = 6.1 Hz), 1.95-2.07 (1H, m), 2.43-2.64 (4H, m), 3.09 (1H, d, J = 15 Hz), 3.47-3.54 (2H, m), 3.66-3.74 (1H, m), 4.085 (1H, dd, J = 6 and 15 Hz), 5.41-5.62 (2H, m) and 7.19-7.28 (5H, m); ^{13}C NMR (75MHz) δ 15.9 (CH_3), 17.8 (CH_3), 20.8 (CH_3), 30.8 (CH_2), 34.3 (CH), 37.1 (CH_2), 50.5 (CH), 59.7 (CH_2), 68.5 (CH_2), 83.9, 86.8, 123.9 (CH), 125.9 (CH), 127.8 (CH), 130.8 (CH), 134.9 (CH) and 138.7; Anal. Calcd. for $C_{19}H_{26}O_2$: C, 79.72; H, 9.09. Found : C, 79.50; H, 9.19.

Methyl-2,2-dimethyl-1β-ethoxy-3-oxabicyclo[3.2.0]heptane-6β-carboxylate (8). A solution of the photoadduct **7c** (600 mg, 2.86 mmol) in carbon tetrachloride (3 ml) was added to a solution of RuO_4 generated by adding ruthenium trichloride (5 mg) to a magnetically stirred suspension of sodium metaperiodate in the solvent system containing carbon tetrachloride (4 ml), acetonitrile (7 ml), water (12 ml). The reaction mixture was allowed to stir at rt. for 1.5 h. The white precipitate so formed was then filtered off. The filtrate was extracted with ethyl acetate (3x10 ml). The ethyl acetate extract was washed with saturated $NaHCO_3$ solution (3x2 ml). The $NaHCO_3$ washing was cooled in ice and acidified with concentrated hydrochloric acid. Usual work up of the reaction mixture with ethyl acetate afforded a liquid which was then treated with an ether solution of diazomethane and filtered through a short column of neutral alumina to afford a mixture of the diester **8** and its corresponding *endo* isomer as a liquid (440 mg, 68%); IR : 1735 cm^{-1}; ^{1}H NMR (60 MHz) δ 1.08 (s), 1.16 (t, J = 7 Hz), 1.20 (s), 1.23 (s), 1.30 (s) (total 9H), 2.41 (2H, d, J = 2 Hz) merged within a multiplet at 2.3-2.7 (1H), 2.96 (1H, brt, J = 5 Hz), 3.2-4.2 (4H, m), 3.66 (3H, s).

This mixture (30 mg, 0.13 mmol) was equilibrated by refluxing it with NaOMe in MeOH (2 ml, 10%). The reaction mixture was diluted with water (1 ml) and extracted with ether (3x5 ml). The aqueous part was then acidified with concentrated hydrochloric acid. Usual work up of this acidic aqueous mixture with ether afforded a yellow liquid (20 mg). Its esterification with an ether solution of diazomethane followed by filtration through a short column of neutral alumina afforded the ester **8** (20 mg, 67%) as a clear liquid; IR : 1735 cm^{-1}; ^{1}H NMR (200 MHz) δ 1.08 (3H, s), 1.10 (3H, t, J = 10 Hz), 1.25 (3H, s), 2.35-2.56 (3H, m), 2.95 (1H, t, J = 4.68 Hz), 3.32-3.46 (2H, m), 3.56 (1H, d, J = 9.85 Hz), 3.65 (3H, s) and 3.81 (1H, dd, J = 4.76 and 9.96 Hz); ^{13}C NMR (50 MHz) δ 15.6 (CH_3), 21.1 (CH_3), 23.9 (CH_3), 26.8 (CH_2), 34.5 (CH), 48.1 (CH), 51.7 (CH_3), 59.8 (CH_2), 68.2 (CH_2), 82.2, 85.6 and 175.1 (CO); Anal. Calcd. for $C_{12}H_{20}O_4$: C, 63.15; H, 8.77. Found : C, 62.81; H, 8.59.

Methyl-2β-benzyl-1β-ethoxy-2α-methyl-3-oxabicyclo[3.2.0]heptane-6β-carboxylate (9). Following the above procedure, the cyclobutane derivative **7d** was transformed to the methyl ester **9** as a liquid in 54% yield; IR : 1735 cm^{-1}; ^{1}H NMR (200 MHz) δ 1.11 (3H, s), 1.24 (3H, t, J = 7.1 Hz), 2.43-2.63 (4H, m), 3.0-3.18 (2H, m), 3.56 (2H, q, J = 6.93 Hz), 3.72 (s, merged within a multiplet at 3.64-3.77, total 4H), 4.13 (1H, dd, J = 4.83 and 10 Hz) and 7.17-7.31 (5H, m); ^{13}C NMR (50 MHz) δ 15.8 (CH_3), 20.4 (CH_3), 27.4 (CH_2), 34.9 (CH), 36.9 (CH_2), 47.9 (CH), 51.9 (OCH_3), 60.2 (CH_2), 68.5 (CH_2), 84.1, 87.0, 126.0 (CH), 127.8 (CH), 130.7 (CH) 138.4 and 175.1 (CO); Anal. Calcd. for $C_{18}H_{24}O_4$: C, 71.05; H, 7.89. Found : C, 70.34; H, 7.64.

Rearrangement of the cyclobutane derivatives 7a, 7b, 8 and 9 : The general procedure is illustrated by the rearrangement of **7a.**

2,2-Dimethyl-3α-hydroxymethyl-4β-methyl cyclopentanone (10a) and its C_4-epimer : Triflic acid (45 μL, 0.5 mmol) was added to a solution of the photoadduct **7a** in dichloromethane (2 ml) at -78°C. The reaction mixture was slowly allowed to warm to rt and stirred for additional 2h (monitored by TLC). It was then diluted with ether (10 ml) and washed with 10% aqueous NaOH solution, brine and dried. Removal of solvent followed by column chromatography of the residual mass with petroleum-ether (3:2) as eluent afforded a mixture of the cyclopentanone derivatives **10a** and its C_4-epimer (40 mg, 52%) as a clear liquid; IR : 3600-3200, 1730 cm^{-1}; ^1H NMR (300 MHz) δ 0.96 (s), 1.11 (d, J = 6 Hz), 1.15 (s) and 1.18 (d, J = 6 Hz) (total 9H), 1.62-1.69 (1H, m), 1.84-2.18 (1H, m), 2.44-2.61 (2H, m) and 3.77-3.92 (2H, m); ^{13}C NMR (75 MHz); δ 16.1 (CH_3), 18.8 (CH_3), 19.2 (CH_3), 19.9 (CH_3), 24.4 (CH_3), 26.6 (CH_3), 29.0 (CH), 30.2 (CH), 44.6 (CH_2), 45.5 (CH_2), 47.6, 48.9, 51.3 (CH), 56.3 (CH), 60.2 (CH_2), 61.9 (CH_2), 222.7 (CO); Anal. Calcd. for $C_9H_{16}O_2$: C, 69.23; H, 10.25. Found : C, 69.81; H, 10.47.

2,2-Dimethyl-3α-hydroxymethyl-4β-phenyl cyclopentanone (10b) : Liquid (55%); IR : 3444-3027, 1735 cm^{-1}; ^1H NMR (200 MHz) δ 1.07 (3H, s), 1.25 (3H, s), 2.23 (partly resolved dt, J = 6, 11.8 Hz, C_3-H), 2.42 (1H, dd, J = 11.7 and 18.8 Hz), 2.80 (1H, dd, J = 8 and 18.8 Hz), 3.07 (1H, dt, J = 8 and 11.6 Hz, C_4-H), 3.71 (2H, d, J = 6.20 Hz) and 6.41-7.56 (5H, m); ^{13}C NMR (75 MHz) δ 18.7 (CH_3), 24.4 (CH_3), 41.9 (CH), 45.7 (CH_2), 48.7, 56.2 (CH), 61.7 (CH_2), 127.0 (CH), 127.2 (CH), 128.8 (CH), 141.9 and 221.0 (CO); Anal. Calcd. for $C_{14}H_{18}O_2$: C, 77.06; H, 8.25. Found : C, 76.76; H, 8.37.

Methyl-2,2-dimethyl-3α-hydroxymethyl-cyclopentan-1-one-4β-carboxylate (10c) : Liquid (76%); IR 3600-3200, 1735 cm^{-1}; ^1H NMR (200 MHz) δ 0.90 (3H, s), 1.13 (3H, s), 2.21-2.33 (1H, m), 2.46-2.74 (2H, m), 2.90 (1H, dt, J = 8.2 and 10.6 Hz), 3.69-3.88 (2H, m) and 3.72 (3H, s); ^{13}C NMR (50 MHz) δ 18.6 (CH_3), 23.5 (CH_3), 40.0 (CH_2), 41.4 (CH), 48.0, 52.3 (CH_3), 62.1 (CH_2), 175.4 (CO) and 218.8 (CO); Anal. Calcd. for $C_{10}H_{16}O_4$:C, 59.98; H, 8.05. Found : C, 59.59; H, 8.06.

Methyl-2β-benzyl-2α-methyl-3α-hydroxmethyl-cyclopentan-1-one-4β-carbolxylate (10d) : Liquid (55%); IR : 3480, 1735 cm^{-1}; ^1H NMR (200 MHz) δ 1.03 (3H, s), 2.23 (1H, dd, J = 11.57 and 18.53 Hz) , 2.41-2.54 (1H, m), 2.58-2.71 (2H, m), 2.85 (1H, dt, J = 7.7 and 11 Hz), 3.68 (s, merged within a m at 3.76, 5H), 3.08 (1H, d, J = 13.58 Hz) and 7.08-7.31 (5H, m); ^{13}C NMR (50 MHz) δ 18.7 (CH_3), 41.3 (CH_2), 41.4 (CH), 42.4 (CH_2), 47.0 (CH), 52.2 (OCH_3), 53.1, 62.1 (CH_2), 126.6 (CH), 128.3 (CH), 130.3 (CH), 137.1, 175.2 (CO) and 218.4 (CO); Anal. Calcd. for $C_{16}H_{20}O_4$: C, 69.56; H, 7.24. Found : C, 69.26; H, 7.14.

Methyl-2,2-dimethyl-1β-ethoxy-6β-methyl-3-oxabicyclo[3.2.0]heptane-6α-carboxylate (11) : A solution of the ester (290 mg, 1.27 mmol) in THF (1 ml) was added dropwise to a magnetically stirred solution of LDA [prepared from diisopropyl amine (405 mg, 4 mmol) in anhydrous THF (3.5 ml) and n-BuLi (2 ml, 2 mmol, 1M in hexane)] at -78°C under Ar atmosphere. The reaction mixture was then slowly warmed to -30°C and stirred at that temperature for 1.5 h. The temperature of the reaction mixture was again brought down to -78°C and to it HMPA (1.5 ml) followed by methyl iodide (0.25 ml, 4 mmol) was added dropwise. The reaction mixture was allowed to attain rt and stirred overnight. After quenching with saturated aqueous ammonium chloride

solution, the reaction mixture was worked up to afford a liquid which was chromatographed [petroleum-ether (17:3)] to afford the ester **11** (200 mg, 74%); ^{1}H NMR (200 MHz) δ 1.05 (3H, s), 1.12 (3H, t, J = 7 Hz), 1.17 (3H, s), 1.46 (3H, s), 1.77 (1H, dd, J = 3.4 and 13.2 Hz), 2.39-2.44 (2H, m), 2.68 (1H, d, J = 13.2 Hz), 3.26-3.44 (2H, m), 3.54 (1H, dd, J = 1.24 and 10.97 Hz), 3.61 (3H, s) and 3.74-3.83 (1H, m); ^{13}C NMR (50 MHz) δ 15.7 (CH_3), 19.9 (CH_3), 22.9 (CH_3), 26.7 (CH_3), 31.9 (CH_2), 39.4, 51.6 (CH), 53.6 (OCH_3), 59.3 (CH_2), 65.2 (CH_2), 80.9, 84.9 and 175.8 (CO); Anal. Calcd. for $C_{13}H_{22}O_4$: C, 64.46; H, 9.09. Found : C, 64.44; H, 9.18.

cis-1,6,6-Trimethyl-3-oxabicyclo[3.3.0]octan-2,7-dione (12) : A mixture of the ester **11** (290 mg, 1.2 mmol), TFA (1.5 ml) and triflic acid (50 μl) was heated at 50°C for 1.5 h. The mixture was then cooled in ice and made alkaline with 60% aqueous NaOH. The mixture was extracted with ether and the ether extract was discarded. The alkaline part was acidified with concentrated hydrochloric acid. Usual work up of this mixture with dichloromethane followed by column chromatography [petroleum-ether (4:1)] afforded the lactone **12** as a white crystalline solid (130 mg, 60%); mp 70°C; IR : 1770, 1740 cm^{-1}; ^{1}H NMR (200 MHz) δ 0.99 (3H, s), 1.12 (3H, s), 1.48 (3H, s), 2.33 (1H, d, J = 10 Hz), 2.48 (1H, dd, J = 4 and 8 Hz), 2.91 (1H, d, J = 20 Hz), 4.22 (1H, dd, J = 2 and 10 Hz) and 4.48 (1H, dd, J = 6 and 10 Hz); ^{13}C NMR (50 MHz) δ 19.8 (CH_3), 23.5 (CH_3), 24.8 (CH_3), 43.2, 44.5 (CH_2), 48.6, 54.2 (CH), 66.1 (CH_2), 180.9 (CO) and 217.5 (CO); Anal. Calcd. for $C_{10}H_{14}O_3$: C, 65.93; H, 7.69. Found : C, 65.85; H, 7.80.

cis-1,6,6-Trimethyl-3-oxabicyclo[3.3.0]octan-2-one : $NaBH_4$ (25 mg, 0.66 mmol) was added in small portion to a solution of the keto-lactone **12** (60 mg, 0.33 mmol) in MeOH (1.2 ml) with stirring at rt. Stirring was continued for additional 1h. After diluting with water (0.5 ml), methanol was removed from it and the residue was worked up with ether to afford the corresponding alcohol (40 mg, 66%); IR : 3600-3200, 1760 cm^{-1}; ^{1}H NMR (300 MHz) δ 1.02 (3H, s), 1.03 (3H, s), 1.39 (3H, s), 2.03-2.22 (3H, m), 3.79 (1H, t, J = 3.9 Hz) and 4.26-4.39 (2H, m).

To a stirred suspension of NaH (70 mg, 1.14 mmol, 40% in oil) in THF (4.5 ml) was added a solution of the above alcohol (70 mg, 0.38 mmol) in THF (1.5 ml) under nitrogen atmosphere. The mixture was stirred at rt for 2h. Carbon disulphide (575 μl, 9.2 mmol) followed by methyl iodide (185 μl, 2.96 mmol) was added and the mixture was stirred at rt for 18h. Saturated aqueous NH_4Cl (5 ml) and ether (30 ml) were added and the mixture was stirred for additional 10 min. The aqueous layer was extracted twice with ether (10 ml) and the combined ether layer was washed with brine (3 ml), dried and concentrated to afford the corresponding xanthate as yellow oil. It was chromatographed [petroleum-ether (7:3)] to produce pure xanthate (80 mg, 77%); ^{1}H NMR (60 MHz) δ 1.06 (3H, s), 1.13 (3H, s), 1.40 (3H, s), 1.96-2.40 (3H, m), 2.50 (3H, s), 4.25 (2H, d, J = 6 Hz) and 5.56 (1H, t, J = 4 Hz).

A solution of the xanthate (80 mg, 0.29 mmol) as obtained above in dry toluene (2 ml) under nitrogen atmosphere was heated at 100°C with TBTH (127 mg, 0.44 mmol) and AIBN (5 mg). The mixture was refluxed for 4h and toluene was removed from it. To the residue, saturated aqueous solution of potassium fluoride (1 ml) was added and stirred at room temperature for 5h. The precipitated solid was filtered off and the filtrate was extracted with ether (3x5 ml). Removal of solvent followed by column chromatography of the residual liquid with petroleum-ether (4:1) afforded the lactone (**13**) (30 mg, 61%) as a colourless liquid; IR : 1770 cm^{-1}; ^{1}H NMR (300 MHz) δ

0.99 (3H, s), 1.05 (3H, s), 1.39 (3H, s), 1.43-1.59 (2H, m), 1.70-1.80 (1H, m), 2.06-2.21 (2H, m) and 4.19-4.30 (2H, m); ^{13}C NMR (75 MHz) δ 23.5 (CH_3), 23.7 (CH_3), 29.3 (CH_3), 36.0 (CH_2), 40.3 (CH_2), 42.1, 51.1, 56.5 (CH), 66.9 (CH_2) and 183.7 (CO); Anal. Calcd. for $C_{10}H_{16}O_2$: C, 71.42; H, 9.52. Found : C, 71.31; H, 9.49.

cis-1,6,6-Trimethyl bicyclo[3.3.0]oct-3-en-2-one (17) : A solution of DIBALH (1 ml, 1 mmol, 1M in toluene) was added slowly to a solution of the lactone (90 mg, 0.54 mmol) in ether (6 ml) cooled to -16°C under argon atmosphere. The reaction mixture was stirred at this temperature for 1.5 h and then treated with 2 ml of isopropanol. After 20 min the cooling bath was removed and water (0.5 ml) was added to the reaction mixture and stirred vigorously for another 30 min. The aluminium salt was filtered off and the ether solution was washed with brine (2x5 ml), dried and concentrated. Column chromatography of the residue with petroleum-ether (3:1) gave the lactol **14** (50 mg, 56%); ^{1}H NMR (300 MHz) δ 0.95 (s) and 0.96 (s) (total 3H), 1.01 (3H, s), 1.19 (s) and 1.21 (s), (total 3H), 1.36-1.81 (5H, s), 3.76-3.83 (m) and 3.98 (t, J = 8.7 Hz) (total 2H), 4.94 (s) and 5.01 (s), (total 1H); ^{13}C NMR (75 MHz) (for major isomer) δ 22.5 (CH_3), 24.8 (CH_3), 30.0 (CH_3), 37.9 (CH_2), 40.4 (CH_2), 41.7, 55.2, 60.3 (CH), 67.0 (CH_2) and 105.5 (CH).

To a solution of the lactol **14** (50 mg, 0.3 mmol) in dry ether (3 ml), methyl lithium (1 ml, 1 mmol, 1M in ether) was added at -20°C with stirring under argon atmosphere. The mixture was slowly warmed to rt and stirred over night. On quenching with saturated aqueous solution of NH_4Cl (1 ml), the reaction mixture was worked up with ether to afford the diol **15** (40 mg, 73%) as a colourless liquid; ^{1}H NMR (300 MHz) δ 0.70 (3H, s), 1.04 (6H, s), 1.15 (3H, d, J = 3 Hz), 1.21-1.54 (5H, m), 3.57 (1H, dd, J = 3.3 and 11.4 Hz), 3.79 (1H, t, J = 4.5 Hz), 4.00 (1H, q, J = 6.3 Hz) and 4.28 (br, 1H); ^{13}C NMR (75 MHz) δ 18.5 (CH_3), 21.8 (CH_3), 23.8 (CH_3), 29.6 (CH_3), 37.3 (CH_2), 39.9 (CH_2), 42.1, 48.2, 60.3 (CH_2), 61.4 (CH) and 72.2 (CH).

To a sirred solution of oxalyl chloride (0.04 ml, 0.53 mmol) in dichloromethane (1 ml) cooled to -70°C under argon atmosphere, was added a solution of DMSO (0.1 ml, 1.32 mmol) in dichloromethane (1 ml). After stirring for 15 min, a solution of the diol **15** (40 mg, 0.22 mmol) in dichloromethane (1 ml) was added to it. After stirring for 45 min triethyl amine (0.3 ml, 2.2 mmol) was added and the reaction mixture was allowed to warm to room temperature. The mixture was poured in water (2 ml) and worked up with dichloromethane to give the keto aldehyde **16** (30 mg, 77%) as a clear liquid; ^{1}H NMR (300 MHz) δ 1.08 (3H, s), 1.15 (3H, s), 1.46 (3H, s), 1.23-1.64 (4H, m), 2.14 (3H, s), 2.26 (1H, s) and 9.84 (1H, s).

To a solution of the keto aldehyde **16** (20 mg, 0.11 mmol) in methanol (0.5 ml), was added aqueous KOH (0.16 ml, 1%). After stirring for 30 min at rt the reaction mixture was diluted with water (0.5 ml) and worked up with ether to afford the enone **17** (10 mg, 56%) as a clear liquid; ^{1}H NMR (300 MHz) δ 1.02 (3H, s), 1.11 (3H, s), 1.22 (3H, s), 1.15-1.33 (2H, m), 1.65 (3H, m), 1.88 (1H, ddd, J = 13, 7 and 3 Hz) 2.48 (1H, brs), 6.15 (1H, dd, J = 3 and 6 Hz) and 7.58 (1H, dd, J = 3 and 6 Hz) was found to be identical with that reported.[12d]

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