Tetrahedron Vol. 49, No. 13, pp. 2767-2782, 1993
Printed in Great Britain

0040-4020/93 $6.00+.00
Pergamon Press Ltd

Convenient Synthesis of Decalin Systems of Bioactive Terpenoids

Vinayak K. Gore, Shailesh R. Desai, T. Mayelvaganan, R. Padmakumar, Shreeshailkumar B. Hadimani and Sujata V. Bhat*

Department of Chemistry, Indian Institute of Technology, Powai, Bombay 400 076, India.

(*Received in UK 9 December* 1992)

ABSTRACT : New analogues of bioactive terpenoids, forskolin, nimbolide, isozonarol and ambrox have been synthesized using general Diels-Alder reaction of 2-formyl-4,4-dimethyl-cyclohexa-2,5-dienone (7) with 1,2-disubstituted-1,3-dienes (8a-k) which yielded endo- & exo-adducts. The deformylation, epimerisation, angular methylation, reduction and oxidation studies on these adducts have been reported.

Several naturally occurring terpenoids having decalin skeleton possess important biological activities which include antifeedant drimane sesquiterpenes warburganal (1) congeners[1]; limonoid triterpenoids, nimbolide (2) analogues[2] ; blood pressure lowering labdane diterpene forskolin (3)[3]; antimicrobial mero sesquiterpenes aureol (4)[4] & isozonarol (5)[5]; and olfactory sesquiterpene ambrox (6)[6] (Figure 1). In addition wide variety of other biological activities are associated with these, as well as, related compounds. Moreover synthetic cis-decalin derivatives also possess antifeedant[7] and olfactory[8] properties. In view of the interesting

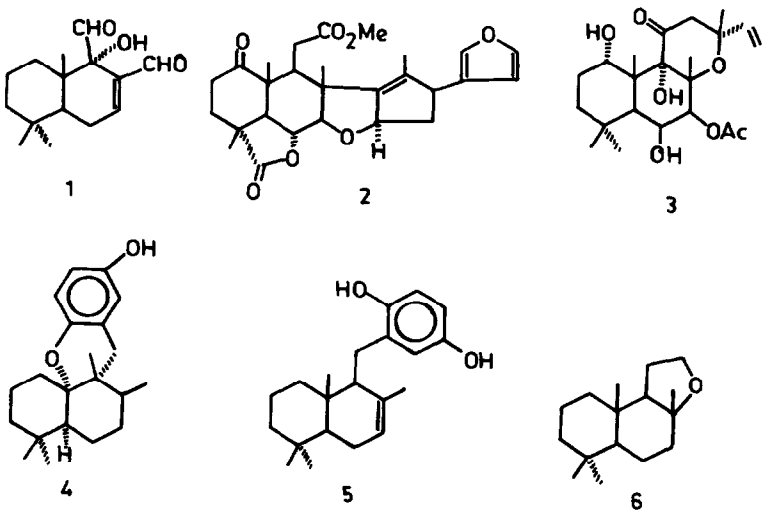


Figure-1

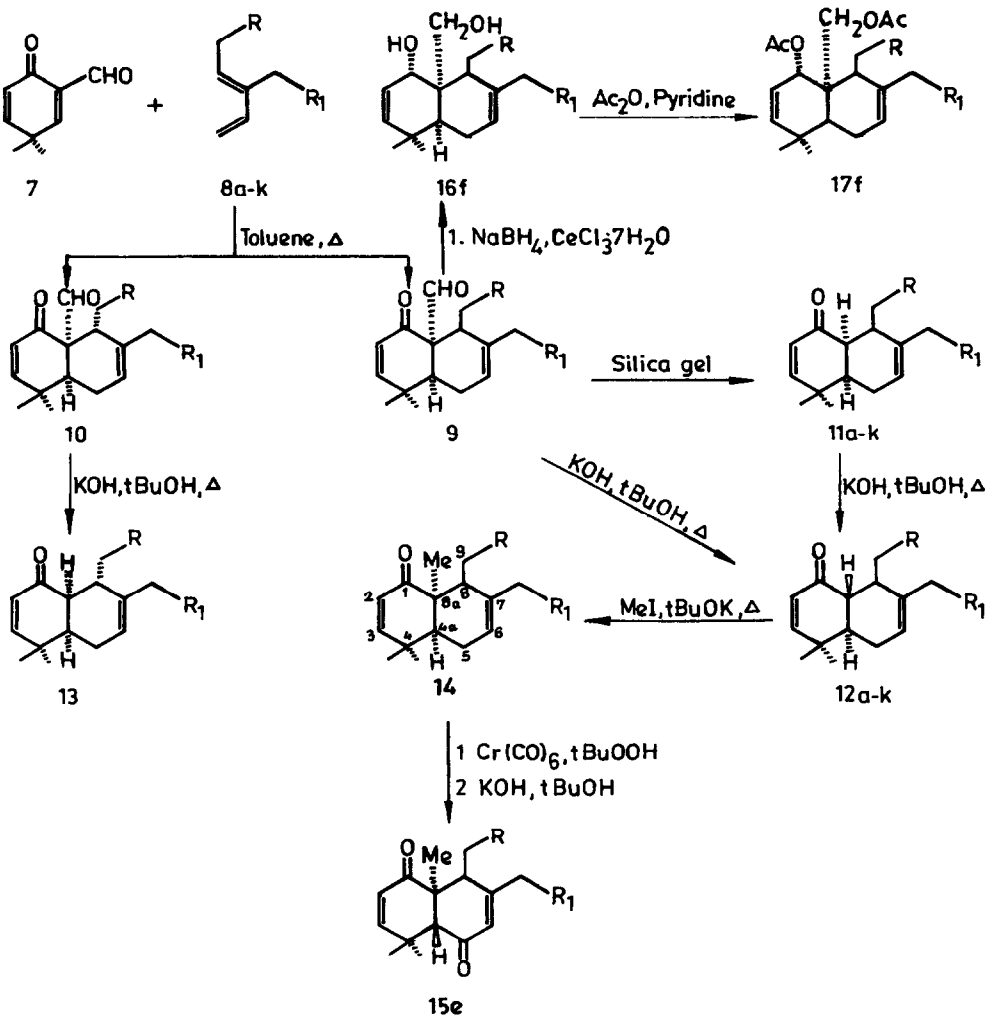
biological activities several synthetic efforts towards drimanes, decalin fragment of 2, forskolin, isozonarol and ambrox have been reported.

Retrosynthetic analysis of decalin moiety involving disconnection across C_{4a}-C_5 and C_8-C_{8a} leads to straightforward Diels-Alder addition of 4,4-dimethyl-cyclohexenone to suitably substituted-1,3-dienes. Early reports of low yields and drastic conditions for thermal additions of 1,3-dienes to substituted cyclohexenones appear to have discouraged continued investigations on the direct generation of their adducts[9]. On the other hand suitably substituted cyclohexadienones undergo facile thermal[9,10], as well as, Lewis acid catalysed additions with 1,3-dienes. Recently Wenkert and coworkers[11] reported a broad study of Diels-Alder reaction of cyclohexenones with various 1,3-dienes under Lewis acid catalysis. However, Welzel and coworkers described[12] unsuccessful attempt of synthesis of A,B-ring system of forskolin through thermal Diels-Alder reaction of 4,4-dimethyl-cyclohexenone with silyloxy dienes. These authors subsequently synthesised A,B-rings of forskolin through Pumerer type reaction of sulfoxide obtained from 4,4-dimethyl-cyclohexenone.

We report herein our studies on Diels-Alder reaction between the dienone **7**[10] and various 1,2-disubstituted -1,3-dienes **8a-k**, subsequent deformylation, epimerisation, angular methylation, oxidation and reduction of the adducts (Figure 2).

The dienes **8a-g** were synthesised through regioselective alkylation of 3-methyl-3-sulfolene with alkyl halides in the presence of LiHMDS at -90°C in THF, followed by thermolysis in basic solution[13]. Similarly, the diene **8h** was obtained by alkylation of 3-(phenylthiomethyl)-3-sulfolene with bromomethyl methyl ether, followed by thermolysis in refluxing pyridine. Alternatively the dienes **8i-k** were obtained from prenyl benzyl ether, methoxy methyl ethers of linalool and geraniol respectively through oxidation of allylic methyl group, separation of the resulting alcohol and aldehyde by column chromatography over silica gel and Wittig reaction of the aldehyde with methylene triphenyl-phosphorane[14].

The Diels-Alder reaction between the dienophile **7** and diene **8a-k** was achieved by heating in toluene solution (24-96 hrs) to yield a mixture of endo-(**9a-k**, 70-80%) and exo- (**10b-k**, 20-30%) adducts (Table 1) observed from the ^{1}H NMR spectra of the mixture. The formyl proton of endo-adducts appears 0.2 - 0.3 ppm upfield compared with exo-adducts. The column chromatography over silica gel yielded the formylated enones **9**,**10** and deformylated cis-enone **11**. Evidently the endo-formyl enone **9** underwent slow deformylation during the chromatography over silica gel. This was confirmed by repeating the treatment of **9** with silica gel at room temperature for 24 hrs which yielded predominantly cis-enone **11** sometimes



a R = -OMe, R_1 = H

b R = -SPh, R_1 = H

c R = -Ph, R_1 = H

d R = -Ph(OMe)$_2$-2',5'), R_1 = H

e R = $-CH_2OMe$, R_1 = H

f R = $-CH_2CH$(O,O), R_1 = H

g R = $-CH_2-C$(Me)(O,O), R_1 = H

h R = -OMe, R_1 = SPh

i R = $-OCH_2Ph$, R_1 = H

j R = $-CH_2-C(Me)(OCH_2OCH_3)-CH=CH_2$, R_1 = H

k R = $-CH_2-C(Me)=CH-CH_2-OCH_2OCH_3$, R_1 = H

Figure-2

associated with small amount of trans-enone 12 (~ 20%). The epimerisation of cis-enone 11 to trans-enone 12 was achieved by refluxing in basic solution (tBuOH, KOH, 1hr). The endo-adduct 9 on similar basic treatment underwent deformylation followed by epimerisation to give trans-enone 12. On the other hand the exo-adduct 10 on similar basic treatment underwent only deformylation without epimerisation to give cis-enone 13. The resistance of cis hexalone 13 for epimerisation could be attributed to the fact that equatorial C_8-substituent would have more unfavourable axial orientation in the corresponding trans isomer (Figure 3).

^{1}H NMR of enones 9,10,11,12 & 13 are given in tables 2-5 respectively. In the ^{1}H NMR spectra of cis enones 9,10,11 & 13, the 4-bond-w-coupling (1 - 2 Hz) between C_3 and C_{4a} protons was observed which was absent in the trans-enone 12. A w configuration of these two protons is possible only in the cis-enones in which 4a-proton could assume a quasi-equatorial position relative to ring A in the prefered configuration . Such a configuration cannot be achieved in trans-enone 12. The C_{8a}-proton of trans-enones 12

Table 1 Diels-Alder adducts of formyl enone 7:

Entry	Diene (Eq)	Method	Time (hrs)	Yield %	Isomer ratio Endo, 9a-k	Exo, 10a-k
1	8a(2)	B	96	90	100	0
2	8b(00.5)	A	36	72	60[a]	40
3	8c(2)	A	24	71	65	35
4	8d(2)	A	24	72	65	35
5	8e(0.5)	B	10	90	80[a]	20
6	8f(0.4)	A	16	92	80[a]	20
7	8g(2)	A	24	75	80	20
8	8h	C	2	79[b]	-	-
9	8i(0.5)	A	24	83	90	10
10	8j(2.0)	A	24	82	80	20
11	8k(2)	A	24	73	80	20[c]

a) The mixture of enones 9 and 10 (identified by NMR spectra) was inseparable on chromatography over silica gel and hence was allowed to remain on silica gel for 24 hrs, the elution with ethyl acetate: petroleum ether (1 : 9) yielded exo-adduct 10 and endo-deformyl adduct 11.

b) Isolated as deformyl cis-endo adduct 11h and trans-endo adduct 12h.

c) Pure exo isomer could not be isolated.

resonated at δ 2.3 - 2.83 (dd, J = 8 & 13 Hz) whereas the corresponding proton in cis enone 11, it resonated at δ 2.7 - 3.3 (t, J = 3 - 4 Hz).

The olefinic protons at C_2, C_3 and C_6 in trans-enone **12** appear ~0.15 - 0.3 ppm downfield as compared to the corresponding protons in cis-enone **11**.

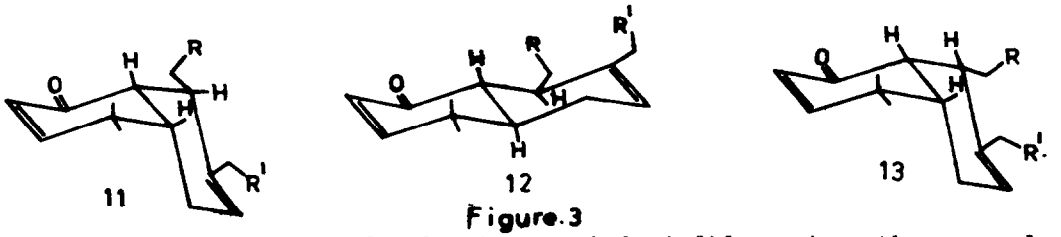


Figure.3

The angular methylation of **12** with methyl iodide using the procedure reported by Ireland and Marshall[15] gave, albeit in low yield (5-45%) (±) cis C_{8a}-methyl enone **14**, the structure of which was supported by ^1H NMR (Table 6). The band due to C_{8a} proton disappeared and the corresponding methyl appeared at δ ~1.3. In the ^{13}C NMR (Table 7) the newly introduced angular methyl group at C_{8a} resonated at δ 26.3 indicating cis stereochemistry of ring junction[16]. This was further supported by 2D-NOESY experiment on compound **14h** (R = OMe, R_1 = SPh) which showed connectivities of C_{8a}-Me protons with C_{4a-H} and C_{8-H}. The structure of **14h** was finally confirmed by single crystal X-ray analysis[17].

The 6-oxo-derivatives **15e** was obtained through oxidation (Cr $(CO)_6$/-tBuOOH in MeCN) of compound **14e**, followed by epimerisation (KOH/tBuOH).[18] On reduction with $NaBH_4/CeCl_3\ 7H_2O$ the enone **9f** gave the diol **16f** which was acetylated (Ac_2O, pyridine) to give the diacetate **17f**.

Thus convenient synthesis of several new (±) Drimane and (±) Labdane derivatives has been achieved. Further applications of these derivatives will be the subject of our subsequent communication.

Acknowledgement : We are grateful to CSIR, New Delhi for granting Senior Research Fellowships (VKG & TM) and research grant 02 (0218) EMR II. We thank, TIFR, and RSIC, Bombay for providing 500 MHz and 300 MHz NMR facility.

EXPERIMENTAL

^1H NMR spectra were recorded with Hitachi R-600 (60 MHz) and Varian XL-300 (300 MHz) NMR spectrometer in $CDCl_3$ using TMS as internal standard, J values are given in Hz. IR spectra were recorded with a Perkin Elmer 681 spectrometer. The microanalysis was done on Carlo Erba Strumentazione 1106 elemental analyser. Usual work-up refers to the extraction with ethyl acetate, washing the organic extracts with water, brine, drying over anhydrous Na_2SO_4 and evaporation of the solvent under reduced pressure. Column chromatography was done on silica gel (100 - 200 mesh), slurry packed, employing increasing amounts of ethyl acetate in petroleum ether (b.p. 60-80°C) as eluting solvent. The dienes **8a-g** were obtained through

alkylation of 3-methyl-3-sulfolene followed by thermolysis[13]. The compounds **9-14**, are viscous oils unless mentioned otherwise. The compounds whose microanalytical data are not given could be detected only by NMR spectra because of difficulty in separating them in pure form.

Synthesis of diene 8h:

To a mixture of 3-thiomethyl-3-sulfolene (7.2g, 30 mmol) and bromomethyl methyl ether (3.9 ml, 45 mmol) in THF (60 ml) at -98°C was added dropwise a solution of LiHMDS (30 mmol) in THF (20 ml) under the atmosphere of argon. The resulting mixture was allowed to attain 0°C and was subjected to usual workup. The product was purified by chromatography over silica gel to yield 2-methyoxymethyl-3-(phenylthiomethyl)-3-sulfolene (4.5 g, 28%), which was subjected to desulfonylation in refluxing pyridine (100 ml) for 7 hr under atmosphere of argon. The removal of solvent in vacuo and chromatography of the residue over silica gel column yielded the diene **8h** (1.55 g, 83%).

IR (Neat): ν_{max} 1630, 1590, 910, 750 (diene) cm^{-1}. ^1H NMR (300 MHz) δ 7.16-7.42 (5H, m, C_6H_5), 6.59 (1H, dd, J = 11.1, 17.6), 6.5 (1H, t, J = 6.5), 5.43 (1H, d, J = 17.6), 5.30 (1H, d, J = 11.1), 4.05 (2H, d, J = 6.5), 3.24 (3H, S, OCH_3). Anal. Calc. for $C_{13}H_{16}OS$: C, 70.86; H, 7.32%; found: C, 70.58; H, 7.53%.

General Procedure for Synthesis of dienes 8i-k

The dienes **8i-k** were synthesised from prenyl benzyl ether, linalool methoxy methyl ether and geraniol methoxy methyl ether respectively through selenium dioxide oxidation of allylic methyl group followed by Wittig reaction of the resulting aldehydes with methylene triphenyl-phosphorane using the procedures described by Dauben et al.[14]. Dienes **8i-k** were obtained in 60% yield as colourless liquids.

Diene 8i: IR (Neat): ν_{max} 1650, 1610, 910 (diene) cm^{-1}. ^1H NMR (60 MHz) δ 7.33 (5H, bs), 6.35 (1H, dd, J = 11, 17), 5.7 (1H, t, J = 7), 5.16 (1H, d, J = 17), 5.05 (1H, d, J = 11), 4.5 (2H, S), 4.15 (2H, d, J =7), 1.72 (3H, S). Anal. Calc. for $C_{13}H_{16}O$: C, 82.94; H, 8.5%; found: C, 82.65; H, 8.61%.

Diene 8j: IR (Neat): ν_{max} 1650, 1600, 910, 840 (diene) cm^{-1}. ^1H NMR (60 MHz) δ 6.4 (1H, dd, J = 10, 17), 5.9 (1H, dd, J = 10, 17), 4.9-5.15 (4H, m), 5.4 (1H, t, J = 7), 4.6 (2H, S), 3.3 (3H, S), 1.75 (3H, S). Anal. Calc. for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54%; found: C, 74.45; H, 10.72%.

Diene 8k: IR (Neat): ν_{max} 1650, 1620, 910, (diene) cm^{-1}. ^1H NMR (60 MHz) δ 6.35 (1H, dd, J = 11, 17), 5.45 (1H, t, J = 7), 5.35 (1H, t, J = 7), 5.05 (1H, d, J = 17), 4.9 (1H, d, J = 11), 4.6 (2H, S), 4.05 (2H, d, J = 7), 3.35 (3H, S), 1.7 (3H, S). Anal. Calc.for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54%; found: C, 74.54; H, 10.34%.

General Procedures for the Diels-Alder Reaction:

Method A: A mixture of the dienophile **7** (1 mmol) appropriate diene **8a-k** and hydroquinone (10 mg) in toluene was refluxed under an atmosphere of argon for the period mentioned in Table 1. After removal of the solvent *in vacuo* and chromatography of the residue on silica gel gave endo-**9** and exo-**10** hexalones.

Method B: A mixture of appropriate sulfolene (2 mmol), analogue of diene (**8a,e**) and hydroquinone (10 mg) in toluene (10 ml) was refluxed under atmosphere of argon for 2 h. The thermolysis of sulfolene was followed by TLC. After completion of thermolysis dienophile (1 mmol) was added to the cooled reaction mixture and refluxing was continued for 10 h. The solvent was removed *in vacuo* and residue was chromatographed over silica gel to give endo-**9** and exo- **10** hexalones.

Method C: A mixture of the dienophile **7** (4 mmol) and the diene **8h** (2 mmol) in ethylene glycol (8 ml) was heated at 110°C for 2 hr. After cooling the reaction mixture was subjected to the usual workup to give the residue which on chromatography over silica gel column yielded deformyl endo-cis adduct **11h** and trans endo-adduct **12h**.

Hexalone 9a: m.p. 100 - 102°C [Ethyl acetate: hexane (1 : 9)]. IR (Nujol): ν_{max} 1725 (-CHO), 1630 (enone) cm^{-1}. ^{1}H NMR (300 MHz): δ 3.65 (1H, dd, J = 5.9, 10.9, - OCH_2-), 3.51 (1H, dd, J = 3.2, 10.9, -OCH_2-), 3.30 (3H, s, OCH_3). ^{13}C NMR (75.4 MHz): δ 69.94 (-CH_2OCH_3), 57.94 (-OCH_3). Anal Calc. for $C_{16}H_{22}O_3$: C, 73.25; H, 8.45%; found: C, 73.32; H, 8.59%

Hexalone 9c: IR (Neat): ν_{max} 1725 (-CHO), 1660 (enone) cm^{-1}. ^{1}H NMR (300 MHz): δ 7.16 - 7.25 (5H, m, - C_6H_5), 2.87 (1H, dd, J = 3.0, 13.9, -CH_2-Ar), 2.72 (1H, dd, J = 9.1, 13.9, -CH_2 -Ar). ^{13}C NMR (75.4 MHz): 141.54 (C-1'), 127.15 (C-2',6'), 130.44 (C-3', C-5'), 126.54 (C-4'). Anal. Calc. for $C_{21}H_{24}O_2$: C, 81.77; H, 7.85%; found: C, 81.99; H, 7.90%.

Hexalone 9d: IR (Neat): ν_{max} 1730 (-CHO), 1660 (,enone) cm^{-1}. ^{1}H NMR (300 MHz): δ 6.77-6.71 (5H, m, C_6-H_5), 3.77 - 3.75 (3H each, s, -OCH_3x2), 2.95 (1H, dd, J = 9.2, 13.9, -CH_2 Ar). 2.76 (1H, dd, J = 4.0, 13.9, -CH_2 Ar). ^{13}C NMR (75.4 MHz): δ 153.21 & 151.74 (C-5', C-2'), 135.52 (C-1'), 121.27 (C-6'), 111.52 & 111.23 (C-3', C-4'). Anal. Calc. for $C_{23}H_{28}O_4$: C, 74.97; H, 7.67%; found: C, 74.73; H, 7.54%.

Hexalone 9g: IR (Neat): ν_{max} 1730 (-CHO), 1650 (-enone) cm^{-1}. ^{1}H NMR (60 MHz): δ 3.95 (4H, s, -O-CH_2-CH_2-O-), 1.3 (3H, s, C_{11}-Me). Anal. Calc. for $C_{20}H_{28}O_4$: C, 72.26; H, 8.49%; found: C, 72.39; H, 8.53%.

Hexalone 9i: IR (Neat): ν_{max} 1720 (-CHO), 1670 (enone) cm^{-1}. ^{1}H NMR (300 MHz): δ 7.36 - 7.30 (5H, m, C_6H_5), 4.38 (2H, bs, -OCH_2 ph), 3.87 (1H, dd, J = 5.8, 10.1, -CH_2-O-CH_2ph), 3.69 (1H, dd, J = 6.0, 10.1, -CH_2-O-CH_2ph). Anal. Calc. for $C_{22}H_{26}O_3$: C, 78.07; H, 7.75%; found: C, 77.93; H, 7.63%.

Hexalone 9j: IR (Neat): ν_{max} 1720 (-CHO), 1670 (enone) cm^{-1}. ^{1}H NMR (60

MHz): δ 5.9 (1H, dd, J = 10, 17 H_{12}), 5.1 (1H, d, J = 10 H_{13}), 5.15 (1H, d, J = 17, H_{13}), 4.6 (2H, s, $-OCH_2O-$), 3.4 (3H, s, $-OCH_3$). **Anal.** Calc. for $C_{22}H_{32}O_4$: C, 73.30; H, 8.95%; found: C, 73.43; H, 9.04%.

Hexalone 9k: IR (Neat): ν_{max} 1720 (-CHO), 1670 (enone) cm^{-1}. ^1H **NMR** (60 MHz): δ 5.1 (1H, t, J = 7, H_{12}), 4.05 (2H, d, J = 7 H_{13}), 4.6 (2H, s, $-O-CH_2O$), 3.4 (3H, s, OCH_3). **Anal.** Calc. for $C_{22}H_{32}O_4$: C, 73.30; H, 8.95%; found: C, 73.58; H, 9.14%.

Hexalone 10b: m.p. 99-110°C (Ethyl acetate: hexane (1:9)). IR (Nujol) ν_{max} 1730 (-CHO), 1660 (enone) cm^{-1}. ^1H **NMR** (300 MHz): δ 7.19 - 7.37 (5H, m, $-C_6H_5$), 3.31 (1H, dd, J = 4.8, 13.6, $-CH_2SPh$), 3.12 (1H, dd, J = 5.1, 13.6, $-CH_2SPh$). ^{13}C **NMR** (75.4 MHz) 155.56 (C-1'), 130.58 (C-2', C-6'), 128.90 (C-3', C-5'), 125.53 (C-4'). **Anal.** Calc. for $C_{21}H_{24}O_2S$: C, 74.07; H, 7.12%; found: C, 74.31; H, 7.34%.

Hexalone 10c: IR (Neat): ν_{max} 1730 (-CHO), 1650 (enone) cm^{-1}. ^1H **NMR** (300 MHz): δ 7.14 - 7.18 (5H, m, $-C_6H_5$), 3.01 (1H, dd, J = 4.6, 14.2, $-CH_2$ ph), 2.75 (1H, dd, J = 8.0, 14.2, CH_2ph). ^{13}C **NMR** (125 MHz):140.33 (c-1'), 128.24, 128.77 (C-2', C-3', C-5', C-6'), 126.94 (C-4'). **Anal.** Calc. for $C_{21}H_{24}O_2$: C, 81.77; H, 7.85%; found: C, 81.54; H, 7.55%.

Hexalone 10d: IR (Neat): 1730 (-CHO), 1670 (enone) cm^{-1}. ^1H **NMR** (300 MHz): δ 6.71 - 6.66 (3H, m, C_6H_3-), 3.74 - 3.70 (3H each, s, -OMex2), 3.03 (1H, dd, J = 5.1, 14.0 $-CH_2-Ar$), 2.64 (1H, dd, J = 8.0, 14.0, $-CH_2$ - Ar). **Anal.** Calc. for $C_{23}H_{28}O_4$: C, 74.97; H, 7.67%; found: C, 74.68; H, 7.35%.

Hexalone 10e: IR (Neat) ν_{max} 1715 (-CHO), 1665 (enone) cm^{-1}. ^1H **NMR** δ 3.42 - 3.2 (2H, m, $-CH_2OCH_3$), 3.29 (3H, s, $-OCH_3$). **Anal.** Calc. for $C_{17}H_{24}O_3$: C, 73.88; H, 8.75%; found: C, 73.58; H, 8.62%.

Hexalone 10f: IR (Neat) ν_{max} 1710 (-CHO), 1670 (enone) cm^{-1}. ^1H **NMR** (300 MHz) δ 4.79 (1H, m, H_{11}), 3.80 - 3.98 (4H, m, $-O-CH_2-CH_2-O-$). **Anal.** Calc. for $C_{19}H_{26}O_4$: C, 71.68; H, 8.23%; found: C, 71.48; H, 8.05%.

Hexalone 10g: IR (Neat) ν_{max} 1710 (-CHO), 1670 (enone) cm^{-1}. ^1H **NMR** (60 MHz) δ 3.95 (4H, m, $-O-CH_2CH_2-O-$), 1.3 (3H, s, C_{11}-Me). **Anal.** Calc. for $C_{20}H_{28}O_4$: C, 72.26; H, 8.49%; found: C, 72.48; H, 8.65%.

Hexalone 10i: IR (Neat) ν_{max} 1715 (-CHO), 1670 (enone) cm^{-1}. ^1H **NMR** (300 MHz) δ 7.22 - 7.40 (5H, m, $-C_6H_5$), 4.51, 4.43 (1H each, d, J = 11.9Hz, $-OCH_2Ph$), 3.71 (1H, dd, J = 6.2, 11.0, $-H_9$), 3.60 (1H, dd, J = 3.3, 11.0, H_9).**Anal.** Calc. for $C_{22}H_{26}O_3$: C, 78.08; H, 7.74%; found: C, 78.30;H, 7.86%.

Hexalone 10j: IR (Neat): ν_{max} 1725 (-CHO), 1660 (enone) cm^{-1}. ^1H **NMR** (300 MHz): δ 5.77 (1H, dd, J = 10.2, 17.4, H_{12}), 5.20 (1H, d, J = 10.2, H_{13}), 5.15 (1H, d, J = 17.4, H_{13}), 3.36 (3H, s, OMe). **Anal.** Calc. for $C_{22}H_{32}O_4$: C, 73.30; H, 8.95%; found: C, 73.60; H, 9.18%.

Deformylation of endo-adducts 9a-k on silica gel: A solution of enone **9a-k** was added to silica gel (100 - 200 mesh) column and was left adsorbed for

Table 2 ^{1}H NMR data of Endo-adducts (9)* & Exo-adducts (10)**

Compound	H2 (d)	H3 (dd)	H4a (dt)	H5 (m)	H6 (m)	C7Me (bs)	H8 (bs)	-CHO (s)	C4Me (s)	C4Me (s)
9a	5.80	6.43	2.74	2.26-1.98	5.42	1.76	2.92	9.82	1.24	1.13
9c	6.00	6.71	2.81	2.09-2.30	5.46	1.37	3.19	9.49	1.25	1.99
9d	5.96	6.60	2.74	2.11-2.17	5.41	1.44	3.23	9.53	1.23	1.19
9g	6.0	6.6	2.6	2.1 - 2.3	5.35	1.75	2.6	9.5	1.2	1.1
9i	5.91	6.39	2.52	2.12-2.23	5.34	1.78	2.94	9.66	1.22	1.09
9j	5.96	6.66	2.56	2.01-2.22	5.34	1.74	2.65	9.47	1.21	1.08
9k	6.0	6.6	2.6	2.1 - 2.3	5.35	1.6	2.6	9.5	1.2	1.05
10b	5.78	6.42	2.99	1.96-2.26	5.41	1.77	-	9.83	1.21	1.11
10c	5.82	6.50	2.70	2.07-2.30	5.33	1.42	3.09	9.82	1.17	1.15
10d	5.87	6.46	2.80	2.2 - 2.3	5.27	1.45	3.15	9.84	1.18	1.16
10e	5.88	6.49	2.72	1.95-2.30	5.35	1.73	-	9.79	1.19	1.13
10f	5.87	6.46	2.73	1.92-2.28	5.34	1.73	-	9.87	1.19	1.13
10g	5.9	6.5	2.7	1.95-2.25	5.35	1.7	2.7	9.87	1.2	1.15
10i	5.87	6.43	2.75	2.25-1.97	5.40	1.72	2.97	9.84	1.22	1.12
10j	5.88	6.46	2.66	1.93-2.26	5.33	1.72	2.66	9.82	1.19	1.13

* Coupling constants: J_{2-3} = 10 - 10.2; J_{3-4a} = 0.5 - 1.3; J_{4a-5e} = 3 - 4; J_{4a-5a} = 7 - 8

** Coupling constants: J_{2-3}=10 -10.2; J_{3-4a}=1-1.5;J_{4a-5e}= 3-4; J_{4a-5a}= 8

Table 3 ^{1}H NMR data of Endo cis compound (11)*

Compound	H2 (d)	H3 (dd)	H5 (m)	H6 (m)	C7Me (bs)	H8 (m)	H8a (t)	C4Me (s)	C4Me (s)
11a	5.70	6.28	1.94-2.08	5.24	1.73	2.5	3.26	1.31	1.06
11b	5.69	6.27	1.94-2.02	5.27	1.79	2.44	3.53	1.30	1.04
11c	5.66	6.16	1.65-1.95	5.28	1.83	2.55	2.70	1.00	1.04
11d	5.68	6.17	2.00-1.97	5.24	1.85	2.63	2.79	1.00	1.09
11e	5.70	6.27	2.00-2.17	5.22	1.73	-	3.14	1.31	1.06
11f	5.68	6.25	2.11-2.28	5.24	1.74	-	3.15	1.29	1.05
11g	5.68	6.25	2.02-2.05	5.25	1.75	2.76	3.12	1.34	1.05
11h	5.70	6.28	1.95-2.25	5.37	-	2.78	3.27	1.31	1.04
11i	5.72	6.30	2.1 -2.25	5.26	1.77	2.58	3.30	1.32	1.07
11j	5.68	6.25	2.1-2.15	5.30	1.74	2.63	3.13	1.30	1.05
11k	5.69	6.26	2.1-2.4	5.24	1.73	2.75	3.15	1.30	1.06

* Coupling constants: J_{2-3} = 10 -10.2; J_{3-4a}= 1.1-2.0;J_{4a-8a}= 3.0 - 3.7

24-48 hrs. The elution of column with petroleum ether: ethyl acetate (9 : 1) yielded endo-cis enone 11a-k (~80%) sometimes containing endo-trans-enone (~20%).

Hexalone 11a: IR (Nujol): 1685 (enone) cm^{-1}. ^1H NMR (300 MHz): δ 3.91 (1H, dd, J = 7.0, 9.2, H_9), 3.81 (1H, dd, J = 6.8, 9.2, H_9), 3.35 (3H, s, $-OCH_3$). Anal. Calc. for $C_{15}H_{22}O_2$: C, 76.89; H, 9.46%; found: C, 77.03; H, 9.59%.

Hexalone 11b: IR (Nujol): 1635 (enone) cm^{-1}. ^1H NMR (300 MHz): δ 7.36 - 7.15 (5H, m, $-C_6H_5$), 3.77 (1H, dd, J = 11.0, 12.8 CH_2Sph), 3.52 (1H, dd, J = 5.3, 12.8, CH_2Sph). Anal. Calc. for $C_{20}H_{24}OS$: C, 76.88; H, 7.74%; found: C, 76.97; H, 7.89%.

Hexalone 11d: IR (Neat): 1675 (enone) cm^{-1}. ^1H NMR (300 MHz): δ 6.74 (1H, d, J = 2.1, Ar-H), 6.70 (1H, dd, J = 2.1, 7.2, Ar-H), 6.68 (1H, d, J = 7.2, Ar-H), 3.75 (3H, s, $-OCH_3$), 3.73 (3H, s, $-OCH_3$), 3.25 (2H, d, J = 8, Ar-CH_2). Anal. Calc. for $C_{22}H_{28}O_3$: C, 77.61; H, 8.29%; found: C, 77.79; H, 8.43%.

Hexalone 11e: IR (Neat): ν_{max} 1690 (enone) cm^{-1}. ^1H NMR (300 MHz): δ 3.42 (2H, m, $-CH_2-OCH_3$), 3.33 (3H, s, $-OCH_3$). Anal. Calc. for $C_{16}H_{24}O_2$: C, 77.38; H, 9.74%; found: C, 77.53; H, 9.82%.

Hexalone 11g: IR (Neat) ν_{max} 1690 (enone) cm^{-1}. ^1H NMR (300 MHz), δ 3.87 - 4.04 (4H, m, $-OCH_2CH_2O-$), 1.30 (3H, s, C_{13}-Me). Anal. Calc. for $C_{19}H_{28}O_3$: C, 74.96; H, 9.27%; found: C, 74.71; H, 9.08%.

Hexalone 11h: IR (Neat): ν_{max} 1680 (enone) cm^{-1}. ^1H NMR (300 MHz): δ 7.28 - 7.18 (5H, m, $-C_6H_5$), 4.05 (1H , dd, J = 6.2, 9.9, H_9), 3.85 (1H, dd, J = 6.7, 9.9, H_9), 3.56 (2H, bs, CH_2-Sph), 3.35 (3H, s, OCH_3). Anal. Calc. for $C_{21}H_{26}O_2S$: C, 73.65; H, 7.65%; found: C, 73.48; H, 7.51%.

Hexalone 11i: IR (Neat): ν_{max} 1685 (enone) cm^{-1}. ^1H NMR (300 MHz): δ 7.26 - 7.36 (5H, m, C_6H_5), 4.52 (2H s, $-OCH_2Ph$). Anal. Calc. for $C_{21}H_{26}O_2$: C, 81.25; H, 8.44%; found: C, 81.38; H, 8.59%.

Hexalone 11j: IR (Neat): ν_{max} 1690 (enone) cm^{-1}. ^1H NMR (300 MHz): δ 5.87 (1H, dd, J = 11.4, 17.2, H_{12}), 5.21 (1H, d, J = 11.5, H_{13}), 5.18 (1H, dd, J = 17.2, H_{13}), 3.38 (3H, s, OCH_3). Anal. Calc. for $C_{21}H_{32}O_3$: C, 75.87; H, 9.71%; found: C, 76.02; H, 9.53%.

Hexalone 11k: IR ν_{max} 1690 (enone) cm^{-1}. NMR (300 MHz): δ 5.39 (1H, dt, J = 10.2, 6.8, H_{12}), 4.63 (2H s, $-O-CH_2-O$), 4.07 (2H, d, J = 6.8, H_{13}), 3.36 (3H, s, $-OCH_3$), 1.70 (3H, s, C_{11}-Me). Anal. Calc. for $C_{21}H_{32}O_3$: C, 75.87; H, 9.71%; found: C, 75.98; H, 9.56%.

Epimerisation of Hexalones 11a-k under basic condition: To a solution of cis cycloadduct 11 (1 mmol) in t-BuOH (5 ml) an aqueous solution of 1N NaOH (3 ml) was added with stirring. The resulting mixture after stirring for 1 hr at room temperature was refluxed for 2 hr and cooled. The reaction mixture was diluted with water, acidified with dil HCL (1N) and

Table 4 ^{1}H NMR data of Endo trans decalones (12)*

Compound	H2 (d)	H3 (d)	H5 (m)	H6 (m)	C7Me (bs)	H8 (m)	H8a (dd)	C4Me (s)	C4Me (s)
12a	5.85	6.59	1.96-2.04	5.63	1.72	2.68	2.68	1.14	1.07
12b	5.83	6.58	2.02-2.07	5.65	1.70	3.08	2.83	1.14	1.03
12c	5.83	6.51	1.80-1.86	5.55	1.79	3.00	2.41	1.05	0.78
12d	5.79	6.46	1.83-1.88	5.54	1.78	3.10	2.49	1.05	0.84
12e	5.83	6.54	1.95-2.1	5.50	1.65	2.75	2.60	1.12	1.03
12f	5.83	6.55	1.80-2.0	5.56	1.65	2.78	2.32	1.13	1.04
12g	5.84	6.56	2.02-2.05	5.57	1.68	2.65	2.30	1.13	1.04
12h	5.85	6.57	1.94-2.01	5.79	-	3.11	2.61	1.09	1.04
12i	5.80	6.58	1.93-2.12	5.64	1.71	2.67	2.73	1.15	1.07
12j	5.84	6.56	1.70-2.01	5.55	1.63	2.73	2.37	1.13	1.04
12k	5.84	6.56	1.70-2.01	5.57	1.64	2.77	2.35	1.13	1.05

* Coupling constants: J_{2-3} = 9.9 - 10.2; J_{8a-4a} = 13 - 14; J_{8-8a} = 7 - 8.2

subjected to the usual work up followed by chromatography over silica gel to yield trans hexalone 12a-k (~90%).

Hexalone 12a: IR (Nujol) ν_{max} 1680 (enone) cm^{-1}. ^{1}H NMR (300 MHz) : δ 3.73 (1H, dd, J = 3.1, 9.4 Hz, H_9), 3.62 (1H, dd, J = 2.0, 9.4 Hz, -H_9), 3.32 (3H, s, -OCH_3). Anal. Calc. for $C_{15}H_{22}O_2$: C, 76.89; H, 9.46%; found: C, 77.05; H, 9.61%.

Hexalone 12b: IR (Neat) ν_{max} 1670 (enone) cm^{-1}. ^{1}H NMR (300 MHz) : δ 7.08 - 7.31 (5H, m, Ar-H_5), 3.53 (1H, dd, J = 4.0, 12.0 Hz, -CH_2Sph), 3.47 (1H, dd, J = 3.0, 12.0 Hz, -CH_2Sph). Anal. Calc. for $C_{20}H_{24}OS$: C, 76.88; H, 7.74%; found: C, 77.99; H, 7.58%.

Hexalone 12c: IR (Nujol) ν_{max} 1680 (enone) cm^{-1}. ^{1}H NMR (300 MHz) : δ 7.10 - 7.24 (5H, m, Ar-H_5), 3.14 (1H, dd, J = 3.6, 13.5 Hz, H_9), 2.90 (1H, dd, J = 5.7, 13.5 Hz, H_9). Anal. Calc. for $C_{20}H_{24}O$: C, 85.67; H, 8.63%; found: C, 85.51; H, 8.73%.

Hexalone 12d: IR (Nujol) ν_{max} 1675 (enone) cm^{-1}. ^{1}H NMR (300 MHz) : δ 6.71 (1H, d, J = 8.0 Hz, -Ar-H), 6.67 (1H, dd, J = 2.0, 8.0, -Ar-H), 6.73 (1H, d, J = 2.6, -Ar-H), 3.20 (1H, dd, J = 5.6, 13.7, H_9), 2.70 (1H, dd, J = 4.5, 13.7, H_9). Anal. Calc. for $C_{22}H_{28}O_3$: C, 77.61; H, 8.29%; found: C, 77.80; H, 8.04%.

Hexalone 12e: IR (Neat) ν_{max} 1680 (enone) cm^{-1}. ^{1}H NMR (300 MHz) : δ 3.32 (2H, dd, J = 6.6, 7.2 Hz, H_{10}), 3.27 (3H, s, -OCH_3). Anal. Calc. for $C_{16}H_{24}O_2$: C, 77.37; H, 9.75%; found: C, 77.51; H, 9.88%.

Hexalone 12f: m.p. 61-62°C (n hexane). IR ν_{max}(Neat) 1670 (enone) cm^{-1}. ^{1}H NMR (300 MHz) : δ 3.80 - 3.97 (4H, m, -OCH_2-CH_2-O-), 4.82 (1H, t, J = 4.7 Hz, H_{11}). Anal. Calc. for $C_{18}H_{26}O_3$: C, 74.45; H, 9.03%; found: C,

74.69; H, 8.95%.

Hexalone 12g: IR (Neat) ν_{max} 1675 (enone) cm^{-1}. ^1H NMR (300 MHz) : δ 3.87 - 4.04 (4H, m, $-OCH_2\ CH_2\ O-$), 1.34 (3H, s, $-CH_3$). **Anal.** Calc. for $C_{19}H_{28}O_3$: C, 74.96; H, 9.27%; found: C, 75.12; H, 9.33%.

Hexalone 12h: IR (Neat) ν_{max} 1670 (enone) cm^{-1}. ^1H NMR (300 MHz) : δ 7.13 - 7.33 (5H, m, C_6H_5), 3.73 & 3.63 (1H each, dd, J = 3.3, 9.7 Hz, $-CH_2OMe$), 3.62 (2H, d, J = 1.8 Hz, $-CH_2-S-$), 3.32 (3H, s, $-OCH_3$). **Anal.** Calc. for $C_{21}H_{26}O_2S$: C, 73.65; H, 7.65%; found: C, 73.50; H, 7.52%.

Hexalone 12i: IR (Neat) ν_{max} 1680 (enone) cm^{-1}. ^1H NMR (300 MHz) : δ 7.26 - 7.38 (5H, m, $Ar-H_5$), 4.52 (2H, s, $-O-CH_2Ph$), 3.80 (1H, dd, J = 3.0, 9.6, H_9), 3.67 (1H, dd,, J = 2.5, 9.6, H_9). **Anal.** Calc. for $C_{21}H_{26}O_2$: C, 81.25; H, 8.44%; found: C, 81.41; H, 8.62%.

Table 5 ^1H NMR data of Exo cis decalones (13)*

Compound	H2 (d)	H3 (dd)	H6 (m)	C7 Me (bs)	H8 (bd)	H8a (d)	C4Me (s)	C4Me (s)
13b	5.83	6.38	5.32	1.72	3.00	-	1.26	1.10
13c	5.73	6.29	5.30	1.83	-	2.65	1.18	1.10
13e	5.82	6.37	5.24	1.73	2.78	2.99	1.30	1.10
13f	5.83	6.38	5.23	1.72	2.75	2.86	1.30	1.10
13g	5.80	6.35	5.20	1.75	2.90	2.90	1.30	1.10
13i	5.78	6.33	5.31	1.68	3.15	3.15	1.25	1.04
13j	5. 82	6.37	5.22	1.71	2.85	2.65	1.30	1.10

* Coupling constants: J_{2-3} = 10 - 10.1; J_{3-4a} = 2 - 2.3; J_{4a-8a} = 4.0

Table 6 ^1H NMR data of methyl enones (14)*

Compound	H2 (d)	H3 (d)	H6 (m)	C7 Me (bs)	H8 (m)	C8aMe (s)	C4Me (s)	C4Me (s)	H4a (dd)
14a	5.97	6.44	5.47	1.74	2.07	1.28	1.11	1.00	1.79
14c	6.02	6.64	5.42	1.46	2.34	1.30	1.16	1.13	1.90
14d	5.99	6.61	5.40	1.40	2.40	1.30	1.17	1.15	1.88
14e	6.02	6.59	5.37	1.70	-	1.25	1.11	0.99	-
14h	5.98	6.45	5.66		2.55	1.15	1.08	0.99	1.79
14i	5.92	6.39	5.46	1.79	2.16	1.30	1.11	0.98	1.81
14j	5.98	6.60	5.32	1.71	-	1.28	1.24	1.10	-
14k	6.01	6.58	5.33	1.68	2.22	1.26	1.11	0.99	-

* Coupling constants: J_{2-3} = 10-10.3; J_{4a-5e} = 2-3.5; J_{4a-5a} = 6.5-8.1

Hexalone 12k: IR (Neat) ν_{max} 1680 (enone) cm^{-1}. ^1H NMR (300 MHz) : δ 5.34 (1H, t, J = 6.9 H_{12}), 4.05 (2H, d, J = 6.9, H_{13}), 4.62 (2H, s, $-O-CH_2-O$), 3.36 (3H, s, $-OCH_3$). Anal. Calc. for $C_{21}H_{32}O_3$: C, 75.87; H, 9.71%; found: C, 75.98; H, 9.58%.

Deformylation of Exo-cis-hexalones 10b-k: Exo-cis-hexalones 10b-k were subjected to basic hydrolysis as described above to give deformylated derivatives 13b-k.

Hexalone 13b: IR (Nujol) ν_{max} 1680 (cm^{-1}). ^1H NMR (300 MHz) : δ 7.39 - 7.19 (5H, m, C_6H_5), 3.33 (1H, dd, J = 3.4, 13.3, $-CH_2S-$), 2.67 (1H, dd, J = 11.4, 13.3 $-CH_2S$). Anal. Calc. for $C_{20}H_{24}OS$: C, 76.88; H, 7.74%; found: C, 76.68; H, 7.55%.

Hexalone 13c: IR (Nujol) ν_{max} 1675 cm^{-1}. ^1H NMR (300 MHz) : δ 7.30 - 7.15 (5H, m, $-C_6H_5$), 3.09 (2H, bd, J = 14.5, H_9). Anal. Calc. for $C_{20}H_{24}O$: C, 85.67; H, 8.63%; found: C, 85.88; H, 8.82%.

Table 7 ^{13}C NMR data of selected compounds

carbon No.	9a	9c	9d	10b	10c	12a	12f	14a	14h
1	195.40	197.09	197.55	196.05	196.96	201.38	201.4	202.95	202.62
2	125.65	128.92	127.27	126.65	126.07	125.99	126.18	127.15	127.08
3	155.40	157.32	157.27	156.12	156.92	159.23	159.06	155.59	155.89
4	36.89	35.79	35.89	36.84	37.30	35.79	35.91	35.39	32.29
4a	39.41	39.32	40.02	39.50	38.70	39.76	37.31	44.24	44.04
5	25.46	25.13	25.81	25.14	25.92	24.82	25.03	23.54	23.38
6	122.27	120.66	116.97	122.22	121.37	122.10	121.84	121.14	125.12
7	131.17	138.71	130.67	133.16	136.00	133.73	135.42	131.93	131.93
8	42.64	44.88	42.55	41.06	43.94	43.46	44.49	45.23	44.16
8a	63.47	66.76	66.35	64.23	65.04	44.02	45.86	47.90	44.94
4Me	25.46	23.80	24.02	21.65	22.87	21.05	21.22	22.89	--
4Me	25.94	26.39	23.26	25.56	25.85	20.15	20.14	23.40	23.38
7Me	30.00	30.54	30.46	30.05	31.06	27.89	28.02	32.40	32.27
8aCHO	201.97	200.18	200.67	201.18	201.62	--	--	--	--
8aMe	--	--	--	--	--	--	--	26.31	26.36

Hexalone 13e: IR (Neat) ν_{max} 1675 (enone) cm^{-1}. ^1H NMR (300 MHz) : δ 3.39 - 3.48 (2H, m, $-CH_2-O-$), 3.32 (3H, s, $-OCH_3$). Anal. Calc. for $C_{16}H_{24}O_2$: C, 77.38; H, 9.74%; found: C, 77.17; H, 9.55%.

Hexalone 13f: IR (Neat) ν_{max} 1680 (enone) cm^{-1}. ^1H NMR (300 MHz) : δ 4.87 (1H, m, H_{11}), 3.80 - 3.99 (4H, m, $-O-CH_2-CH_2-O-$). Anal. Calc. for $C_{18}H_{26}O_3$: C, 74.45; H, 9.03%; found: C, 74.25; H, 9.23%.

Hexalone 13g: IR (Neat) 1675 cm^{-1} (enone). ^1H **NMR** (60 MHz) : δ 4.0 (4H, bs, $-O-CH_2-CH_2-O-$), 1.35 (3H, s, $C_{11}Me$). **Anal.** Calc. for $C_{19}H_{28}O_3$: C, 74.96; H, 9.27%; found: C, 74.68; H, 9.53%.

Hexalone 13i: IR (Neat) ν_{max} 1680 (enone) cm^{-1}. ^1H **NMR** (300 MHz) : δ 7.72 - 7.31 (5H, m, $-C_6H_5$), 4.56, 4.43 (1H each, d, J = 12.5 H, $-OCH_2ph$), 3.55 (1H, dd, J = 4.0, 9.5, H_9), 3.34 (1H, t, J = 9.5, H_9). **Anal.** Calc. for $C_{21}H_{26}O_2$: C, 81.25; H, 8.44%; found: C, 81.09; H, 8.24%.

Hexalone 13j: IR (Neat) ν_{max} 1685 (enone) cm^{-1}. ^1H **NMR** (300 MHz) : δ 5.80 (1H, dd, J = 11.2, 17.4, H_{12}), 5.19 (1H, d, J = 11.2, H_{13}), 5.17 (1H, d, J = 17.4, H_{13}), 4.70 (1H, d, J = 7, OCH_2O), 4.61 (1H, d, J = 7, OCH_2O), 3.37 (3H, s, OCH_3), 1.32 (3H, s, $C_{11}CH_3$). **Anal.** Calc. for $C_{21}H_{32}O_3$: C, 75.87; H, 9.71%; found: C, 75.58; H, 9.51%.

Angular Methylation of Hexalone 12

To a solution of potassium metal (480 mg, 12.3 mmol) in t-BuOH (16 ml) under the atmosphere of argon was added hexalone 12 (0.85 mmol) in benzene (10 ml) after stirring for 5 minutes at room temperature the reaction mixture was cooled (0-5°C) and methyl iodide (1 ml, 2.28 g, 16.1 mmol) was added. The mixture was stirred at room temperature for 1/2 hr refluxed for 2 hr and was subjected to the usual work up to give residue which was chromatographed over silica gel, elution with ethyl acetate: petroleum ether (1 : 9) gave methyl derivatives **14a-k**, and unreacted hexalone 12.

Hexalone 14a: IR (Nujol) ν_{max} 1680 (enone) cm^{-1}. ^1H **NMR** δ 3.46 (1H, dd, J = 7.3, 9.9, $-CH_2-O-$), 3.39 (1H, dd, J = 4.1, 9.9, $-CH_2O$), 3.16 (3H, s, $-OCH_3$).**Anal.** Calc. for $C_{16}H_{24}O_2$:C,77.38;H,9.74%; found:C,77.14;H, 9.91%.

Hexalone 14c: IR (Neat) ν_{max} 1680 cm^{-1}. ^1H **NMR** δ 7.14 - 7.22 (5H, m,$-C_6H_5$), 2.85 (1H, dd, J = 3.4, 14.1, $-CH_2ph$), 2.50 (1H, dd, J = 7.5, 14.1, $-CH_2-ph$). **Anal.** Calc. for $C_{21}H_{26}O$: C, 86.26; H, 8.27%; found: C, 85.84; H, 8.77%.

Hexalone 14d: IR (Neat) ν_{max} 1680 (enone) cm^{-1}. ^1H **NMR** (300 MHz) : δ 6.76 (1H, d, J = 2.1, ArH), 6.70 (1H, dd, J = 2.1, 7.2, Ar-H), 6.68 (1H, d, J = 7.2, ArH), 3.74 (3H, s, $-OCH_3$), 3.77 (3H, s, $-OCH_3$). **Anal.** Calc. for $C_{23}H_{30}O_3$: C, 77.93; H, 8.53%; found: C, 77.78; H, 8.39%.

Hexalone 14e: IR ($CHCl_3$) ν_{max} 1670 (enone) cm^{-1}. ^1H **NMR** (300 MHz) : 3.27 (3H, s, OCH_3), 3.17 (2H, m, $-CH_2OMe$). **Anal.** Calc. for $C_{17}H_{26}O_2$: C, 77.82; H, 9.99%; found: C, 77.67; H, 9.71%.

Hexalone 14h: IR (Nujol) ν_{max} 1670 (enone) cm^{-1}. ^1H **NMR** (300 MHz) : 7.33 - 7.19 (5H, m, C_6H_5), 3.63 (2H, bs, $-CH_2Sph$), 3.47 (1H, dd, J = 5.8, 8.9, $-CH_2-O-$), 3.42 (1H, dd, J = 3.7, 8.9, $-CH_2-O-$), 3.17 (3H, s, $-OCH_3$). **Anal.** Calc. for $C_{22}H_{28}O_2S$: C, 74.12; H, 7.92%; found: C, 74.38; H, 7.78%.

Hexalone 14i: IR (Neat) ν_{max} 1670 (enone) cm^{-1}. ^1H **NMR** (300 MHz) : δ 7.23 - 7.36 (5H, m, C_6H_5), 4.38, 4.31 (1H, d, J = 12 , $-O\ CH_2$ ph), 3.59 (1H,

dd, J = 7, 9.9, $-CH_2Oph$), 3.50 (1H, dd, J = 4, 9.9, $-CH_2Oph$). **Anal.** Calc. for $C_{22}H_{28}O_2$: C, 81.95; H, 8.13%; found: C, 81.56; H, 8.43%.

Hexalone 14k: IR (Neat) ν_{max} 1690 (enone) cm^{-1}. ^1H **NMR** (300 MHz) : δ 5.26 (1H, bt, J = 6.8, H_{12}), 4.61 (2H, s, $-O-CH_2O$), 4.03 (2H, d, J = 6.8, H_{13}), 3.36 (3H, s, $-OCH_3$), 1.59 (3H, bs, $C_{11}-CH_3$). **Anal.** Calc. for $C_{22}H_{34}O_3$: C, 76.26; H, 9.89%; found: C, 76.44; H, 10.04%.

Synthesis of Hexalones 15e

Hexalone **14e** (19mg, .00766 mmol), Cr $(CO)_6$ (7.3 mg, .032mmol) and 80% t-BuOOH (0.05 ml, 0.04 mmol) were refluxed in dry acetonitrile (3 ml) for 15 hrs. The reaction mixture was cooled to room temperature and diluted with ether (10 ml). The organic layer was washed with water (5 ml x 2) and brine (2 ml x 2) and dried over Na_2SO_4. The solvent was removed and the residue was purified by chromatography over silica gel. The product was epimerised by stirring with KOH (4mg) in dry t-butanol (0.5 ml) for 3 hrs and the reaction mixture was subjected to usual workup to yield 1,6-dioxo-derivative **15e**.

IR ($CHCl_3$): ν_{max} 1675 and 1685 (enones) cm^{-1}. ^1H **NMR** 300 MHz δ 6.76 (1H, d, J = 10.0 Hz, H_3), 6.27 (1H, d, J = 10 Hz, H_2), 5.84 (1H, s, H_6), 3.44 (3H, s,$-OCH_3$), 2.44 (3H, s, C_7-CH_3), 1.46 (3H, s, CH_3), 1.24 (3H, s, $-CH_3$), 1.26 (1H,s,CH_3).**Anal.**Calc. for $C_{17}H_{24}O_3$;C,73.88;H,8.74%;found:C,73.61; H, 8.54%.

Reduction of Hexalone 9f with $NaBH_4.CeCl_3.7H_2O$

To a stirred and cooled mixture of **9f** and **10f** (1 g, 3.14 mmol), $CeCl_3.7H_2O$ (1.12 g, 3.14 mmol) in methanol (20 ml) was added sodium borohydride, (120 mg, 3.16 mmol), and stirring continued for 2 hrs, the solvent was removed in vacuo and the residue was extracted with ethyl acetate. The extract on drying over sodium sulphate and evaporation gave a liquid which after silica gel column chromatography gave hexalone **16f** (230 mg, 23%).

Hexalone 16f: **m.p.** 124-125°C (hexane : benzene, 1:1). IR (Nujol) 3250 cm^{-1} (-OH). ^1H **NMR** (300 MHz) δ 5.49 (1H, dd, J = 1.9, 10.2), 5.4 (1H, bs), 5.33 (1H, dd, J = 2.6, 10.2), 4.90 (1H, m) 4.43 (1H, bs), 4.03 (1H, d, J = 11), 3.84 - 4.03 (4H, m) , 3.62 (1H, d, J = 11), 3.45 (1H, bs, D_2O exchangeable), 1.68 (3H, bs), 0.96 (3H, s), 0.77 (3H, s). **Anal.** Calc. for $C_{19}H_{30}O_4$: C, 70.78; H, 9.38%; found: C, 70.86; H, 9.43%.

Acetylation of Hexalone (16f)

To a stirred solution of **16f** (200 mg, 0.62 mmol) in dry pridine (1 ml) was added acetic anhydride (127 mg, 0.12 mL,1.24 mmol) and the stirring wascontinued for 12 hrs. The solvent was removed in vacuo and the residue was subjected to usual workup to yield viscous liquid which after silica gel column chromatography afforded **17f** (228 mg, 90%)

Diacetate 17f: IR (Neat) ν_{max} 1740 (ester), cm^{-1}. ^1H **NMR** (300 MHz) δ 5.53

(1H, t, J = 2.14, H_1), 5.41 (1H, dd, J = 10, 2.14, H_2), 5.39 (1H, bs, H_6), 5.31 (1H, dd, J = 10, 1.68, H_3), 4.79 (1H, t, J = 4.58, -CH ), 4.28, 3.99 (1H each, d, J = 11.6, C_{8a}-CH_2-O-), 3.81-3.95 (4H, m, -OCH-CH_2O-), 2.13, 2.07 (3H each, s, -$COCH_3$x2) 1.68 (3H, bs, C_7-CH_3), 1.0, 0.8 (3H each, s, CH_3x2) **Anal.** Calc. for $C_{23}H_{34}O_6$: C,67.96; H,8.43%; found: C,67.84;H,8.36%.

REFERENCES

1) Groot, A.D. ; Van Beck, T.A., Recl. Trav. Chim. Pays-Bas 1987, **106**, 1 and references cited therein.

2) Siddiqui, S. ; Siddiqui, B.S. ; Faisi, S. ; Mahamood, T., J. Nat. Prod., 1988, **51**, 30.

3) Colombo, M.I. ; Zinczuk, J. ; Bacigaluppo, J.A. ; Somoza, C. ; Ruveda, E.A., J. Org. Chem., 1990, **55**, 5631.

4) Djura, P. ; Stierle, D.B. ; Sullivan, B. ; Faulkner, D.J. ; Arnold, E. ; Clardy, J., J. Org. Chem., 1980, **45**, 1435.

5) Welch, S.C. ; Prakash Rao, A.S.C., J. Org. Chem., 1978, **43**, 1957.

6) Paquette, L.A. ; Maleczka, R.E., J. Org. Chem., 1991, **56**, 912.

7) Jackson, W.P., Ley, S.V., J. Chem. Soc., Perkin Trans. I, 1981, 1516.

8) Escher, S. ; Giersch, W. ; Niclass, Y. ; Berhardinelli, G. ; Ohloff, G., Helv. Chim. Acta, 1990, **73**, 1935.

9a) Liu, H.J. ; Browne, E.N.C., Can. J. Chem., 1987, **65**, 1262.

b) Liu, H.J. ; Ramani, B., Tetrahedron Lett., 1988, 6721.

10) Liotta, D., Saindane, M., and Barnum, C., J. Am. Chem. Soc., 1981, 103, 3224.

11) Angell, E.C. ; Fringuelli, F. ; Guo, M. ; Minuti, L.; Taticchi, A.; Wenkert, E., J. Org. Chem., 1988, **53**, 4325 and references cited therein.

12) Neunert, D. ; Klein, H. ; Welzel, P., Tetrahedron, 1989, **45**, 661.

13) Desai, S.R. ; Gore, V.K. ; Mayelvaganan, T. ; Padmakumar, R. ; Bhat, S.V., Tetrahedron, 1992, **48**, 481.

14) Dauben, W.G. ; Saugier, R.K. ; Fleischhauer, I., J. Org. Chem., 1985, **50**, 3767.

15) Ireland, R.E. ; Marshall, J.A., J. Org. Chem., 1962, **27**, 1615.

16a) Breitmaier, E. ; Voelter, W., ^{13}C NMR spectroscopy, Verlag Chemie, Weinheim, New York, 1978, pp219-299.

b) Goswami, A. ; Barua, R.N. ; Sharma, R.P. ; Baruah, J.N. ; Kulanthaivel, P. ; Herz, W., Phytochemistry 1984, **23**, 837.

17) Kalyan Das ; Sinha, U.C. ; Desai, S.R. ; Bhat, S.V. ; Tavale, S.S. ; Puranik, V.G., Acta Cryst, 1992, **C48**, 525.

18) Ji, Y. ; Moog, C. ; Schmitt, G. ; Bishoff, P. ; Luu, B., J. Med. Chem., 1990, **33**, 2264.