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Syntheses of 5α, 8aβ-dimethyl and 2, 5α, 8αβ-trimethyl-6β, 7β-O-methylethylidene- 4a, 5, 6, 7, 8, 8a-hexahydro-1(4H)-naphthalenones: AB ring precursors for quassinoid synthesis*

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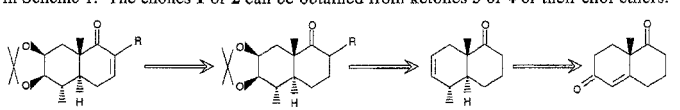
Abstract

Syntheses of title compounds starting from Wieland–Miescher ketone are reported.

Key words: Quassinoids, bruceantin, total synthesis.

1. Introduction

In a project in our laboratory towards the synthesis of quassinoids[1], we were in need of the title compounds **1** and **2** as intermediates. A perusal of literature revealed that Wieland–Miescher (WM) ketone[2] would be the common starting material as shown retrosynthetically in Scheme 1. The enones **1** or **2** can be obtained from ketones **3** or **4** or their enol ethers.



1 R = H
2 R = CH_3

3 R = H
4 R = CH_3

5

WM Ketone

SCHEME 1.

Ketones **3** or **4** can be obtained from **5** which in turn can be obtained from WM ketone. Our first objective was to incorporate the functionality present on the left side portion of **1** or **2** into the cyclohexenone moiety of WM ketone. To begin with, the racemic form of WM ketone was used.

* Taken in part from the Ph.D. thesis of the first author submitted to the University of Hyderabad.
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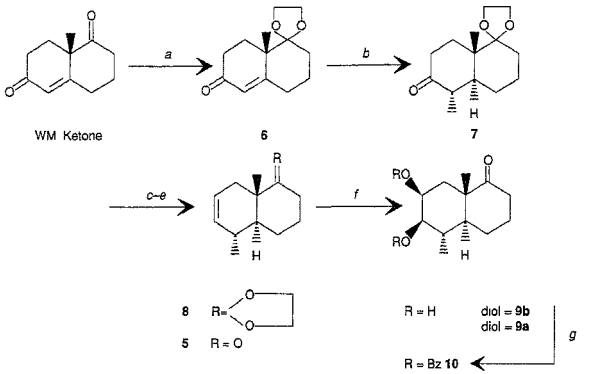
Towards this end, the monoketal **6**[3] was prepared from WM ketone according to the literature procedure using 2-ethyl-2-methyl-1, 3-dioxolane as the *trans*-ketalizing agent(Scheme 2). Generation of the *trans*-ring fusion and α-methylation to the ketal-ketone **7** was accomplished by metal ammonia reduction followed by quenching with iodomethane. Optimum yields of **7** were obtained by the addition of lithium metal to a solution of the ketal-ketone **7** (10 mmol) in THF (20 ml) and dry ammonia (200 ml) followed by quenching with iodomethane (large excess). The yield was reduced when the reaction was scaled up.



(a) 2-Ethyl-2-methyl-1,3-dioxane, $(CH_2OH)_2$, *p*-TsOH, rt; *(b) i.* Li, NH_3, THF, –78°, *ii.* MeI; *(c)* $TsNHNH_2$, THF, reflux, N_2; *(d)* LDA, THF, 0°; *(e)* THF, 1M HCl, reflux; *(f)* OsO_4, NMO, water, acetone, *t*-BuOH, rt, N_2; *(g)* PhCOCl, pyridine, DMAP, rt.

SCHEME 2.

The stereochemistry of ring fusion and the newly introduced methyl group in **7** was assigned by analogy to a similar example in literature[4]. The spectral data (IR and PMR) of **7** were identical to that reported earlier, where it was prepared by a different route[5].

To introduce the double bond at C-6 and C-7 (WM ketone numbering) regioselectively, the Shapiro reaction was sought to be applied to **7**[6]. The *p*-tosylhydrazone of **7** was prepared by modified procedure[5] by refluxing a mixture of **7** and *p*-tosylhydrazide in THF. The IR spectrum of the crude derivative showed the absence of carbonyl band and the presence of characteristic hydrazone bands (3200, 700, and 660 cm^{-1}). The crude *p*-tosylhydrazone of **7** on reaction with LDA in THF at 0° gave the olefin **8** in 75% yield (from the ketone **7**). Spectral data (IR and PMR) of **8** were identical to the reported data[5]. Hydrolysis of **8** using 1M HCl gave the ketone **5** quantitatively. Spectral data (IR, PMR and CMR) of the ketone **5** are in support of its structure. In the IR spectrum, the presence of a carbonyl band (1710 cm^{-1}) and in the PMR spectrum, the absence of ethylene ketal signals at δ 3.87 (br s, 4H) indicated the structure of **5**. Finally, a 12-line CMR spectrum with the carbonyl at 215 ppm is in support of the structure of **5**.

To incorporate the *cis*-isopropylidene unit present in **1** or **2, 5** was *cis*-hydroxylated using osmium tetroxide and 4-methylmorpholine N-oxide[7] to give a stereoisomeric mixture of two *cis*-diols **9a** and **9b** in a ratio of 1:4.8 which were easily separable on a silica gel column. Besides satisfactory elemental analysis, the major stereoisomer **9b** has bands in the IR spectrum at 3425, 3325 and 1710 cm^{-1} for the diol and carbonyl moieties, respectively. The PMR spectrum of **9b** has signals at δ 4.18–4.00 (m, 1H) and 3.20–2.94 (m, 1H) due to the hydroxyl methine protons. Similarly, the minor isomer **9a** was also characterized from its spectral data (IR and PMR).

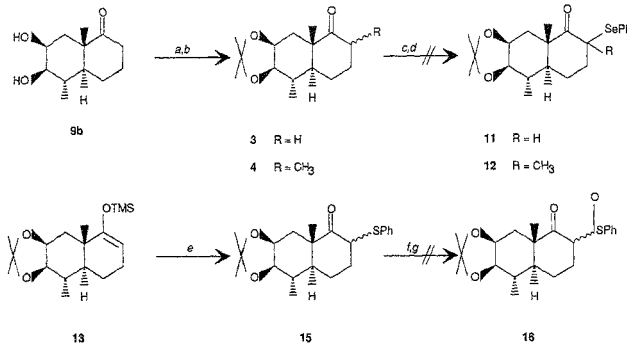
In order to assign the stereochemistry of the *cis*-diol unit in **9a** and **9b, 9b** was converted to its dibenzoate **10** by using the standard procedure (Scheme 2). The PMR spectrum of **10** showed two benzoate methine protons at δ 5.76 (dt appearing as a quartet, *J*=4,8 Hz) and δ 4.87 (dd, *J*=4,12 Hz). Irradiation of the signal at δ 5.76 simplified the signal at δ 4.87 to a doublet at δ 4.86 (*J*=11 Hz). Similarly, irradiation of the signal at δ 4.87 simplified the signal at δ 5.76 to a broad singlet at δ 5.77. These decoupling studies reveal that the doublet at δ 4.86 with coupling constant of 11 Hz is due to the axial orientation of the adjacent methine protons. This is possible between C-5 and C-6 methine protons only. Also, the simplified broad singlet at δ 5.77 is due to the coupling of an equatorial methine proton with the axial and equatorial protons of the adjacent C-8 methylene group. Hence, the decoupling studies indicate that the doublet of doublet resonating at high field (δ 4.87) is due to the axial C-6 benzoate methine proton. This automatically fixes the assignment of C-7 benzoate methine proton as that at δ 5.76 and in the equatorial positions because **10** is derived from a *cis*-diol. The major diol **9b** therefore has the stereochemistry 6β and 7β and consequently the minor diol **9a** is 6α, 7α.

In order to generate the enone double bond present in **1** and **2**, the diol **9b** was converted to its isopropylidene derivative **3** by using acetone and a catalytic amount of sulfuric acid in the presence of anhydrous copper sulfate (Scheme 3). Structure of the isopropylidene derivative **3** was derived from its spectral data (IR, PMR and CMR).

At this stage, the C-2 methyl group present in **2** was introduced by alkylating the ketone **3**. Conditions for optimum yield (95%) of **4** consisted in forming the enolate of **3** using LDA at –15° (ice-salt bath) followed by quenching with iodomethane to give the C-alkylated product. The gross structure of **4** was obtained from its PMR and CMR spectra. In the PMR spectrum, the doublet due to the newly introduced methyl group merged with the existing doublet due to the C-5 methyl group, giving rise to a triplet at δ 0.96. The CMR spectrum of **4** contained all the 14 lines present in the CMR spectrum of **3** along with the newly introduced methyl carbon at 41.2 ppm. The stereochemistry of the C-2 methyl was not worked out as it gets destroyed subsequently in the course of enone formation (see later part).

The conversion of a ketone to an enone is a well-studied transformation in synthetic organic chemistry and many methods are available for this purpose. Some of the procedures used in this work for the conversion of **3/4** to **1/2** include: (i) selenation/oxidation/elimination, (ii) sulfenation/oxidation/elimination, (iii) trimethylsilyl enol ether formation/oxidation, and (iv) halogenation/elimination.

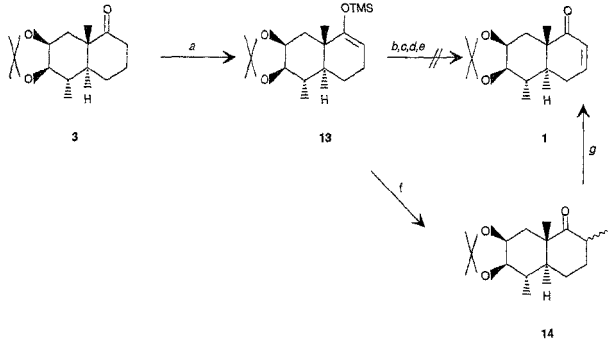
Both the ketones **3** and **4** as well as their enolates (generated by using LDA at –20°) did not react with phenylselenyl chloride or phenylselenyl bromide at room temperature or at –20° (Scheme 3).



(a) Acetone, $CuSO_4$, H_2SO_4, –rt; *(b)* LDA, THF, –15°, MeI; *(c)* PhSeCl, EtOAc, rt; *(d)* LDA, PhSeBr, –20°; *(e)* PhSCl, CH_2Cl_2, –78°; *(f)* $^tBu_4NIO_4$, $CHCl_3$, reflux; *(g)* MCPBA, CH_2Cl_2, 0°.

SCHEME 3.

To apply Tsuji's[8] preparation of α,β-unsaturated carbonyl compounds from the corresponding enol ethers, ketone[3] was converted to its enol ether **13** using the procedure of Yamaguchi[9] with a modification in the workup (Scheme 4).



(a) DBU, TMSCl, CH_2Cl_2, 40°, 24 h; *(b)* dppe, diallyl carbonate, $Pd(OAc)_2$, CH_3CN, reflux; *(c)* dppe, allyl methyl carbonate, $Pd(OAc)_2$, CH_3CN, reflux; *(d)* $Pd(OAc)_2$, CH_3CN, reflux; *(e)* NBS, CCl_4, reflux; *(f)* NBS, THF, 0° *(g)* DBU, benzene, reflux.

SCHEME 4.

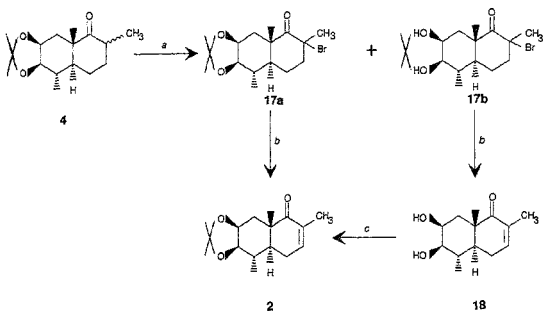
When the enol ether **13** was subjected to Tsuji's conditions (b and c of Scheme 3) no trace of enone **1** was obtained; instead, the saturated ketone **3** was obtained after water workup. Trimethylsilyl enol ethers are also known to give α,β-unsaturated ketones by reaction with palladium (II) acetate alone[10]. However, under these conditions also, recovery of ketone **3** was observed after usual workup. These results indicate that the enol ether **13** is not undergoing any reaction, but getting hydrolyzed during water workup to give the ketone **3**.

Trimethyl silyl enol ethers are known to give α-bromoketones with NBS[11]. Under these conditions, enol ether **13** gave a complex mixture. However, when a solution of the enol ether in THF was reacted with NBS at 0°, bromoketone **14** was obtained in low yield (31%) along with the ketone **3**. Attempts to improve the yield of **14** were unsuccessful. As the bromoketone **14** could not be purified satisfactorily for spectral analysis, it was converted to the enone **1** in 67% yield by treating it with DBU. The IR spectrum of enone **1** showed a strong enone carbonyl band at 1665 cm^{-1}. The PMR spectrum showed two olefinic signals at δ 6.87(ddd, H-3, *J*=3,6,10 Hz) and 5.90 (ddd, H-2, *J*=2,3,10 Hz) along with the other characteristic signals summarized in the experimental section.

As the yield of **14** could not be improved, other methods were sought to achieve the same transformation. The enol ether **13** was converted to the α-phenylsulfenyl ketone **15** in 91% yield (Scheme 3). The presence of aromatic protons at δ 7.46–7.14 (m, 5H) in the PMR spectrum of **15** proved its gross structure incisively. Attempts to oxide the sulfide to sulfoxide, using MCPBA or tetra-*n*-butylammonium periodate so as to eliminate phenylsulfenic acid to obtain the enone **1** were unsuccessful. Both the oxidizing agents gave a complex mixture, from which sulfoxide **16** could not be isolated.

The ketone **4** was subjected to bromination using cupric bromide (Scheme 5)[12]. After usual workup a mixture of two major bromo compounds were noticed from its TLC and IR spectrum. The IR spectrum of the above crude mixture showed hydroxyl band (3450 cm^{-1}) as well as bands due to gem-dimethyl group of the isopropylidene unit (1390 and 1380 cm^{-1}). The presence of a strong hydroxyl band could be due to hydrolysis of the isopropylidene unit by the hydrogen bromide evolved during bromination. As the bromoketones **17a** and **17b** could not be purified satisfactorily, they were subjected to dehydrobromination using DBU to give the enones **2** and **18**, respectively. Both the enones **2** and **18** could be separated on a silica gel column. The structure of **2** was in accordance with its spectral characteristics (IR, PMR and MS). The IR spectrum showed a sharp enone carbonyl band at 1665 cm^{-1}. In the PMR spectrum, the olefinic proton appeared as a multiplet at δ 6.60–6.42. The diol enone **18** could be easily reprotected as its acetonide by applying the previously used methodology to give **2**. The overall yield of the enone **2** obtained from the ketone **4** by this method was 72%.

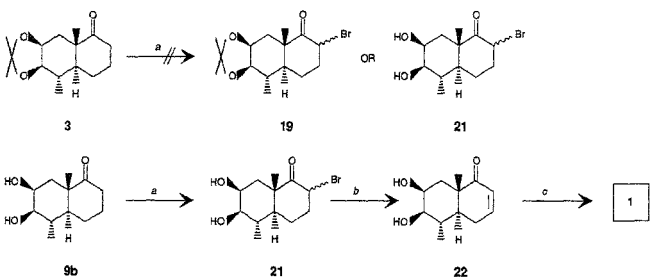
Encouraged by these results, attempts were made to convert the ketone **3** to the enone **1** under similar conditions (Scheme 6). Surprisingly, bromination of **3** with cupric bromide under identical conditions gave a complex mixture which may be due to mono- and dibromination along with hydrolysis of the acetonide group present in **3**. To avoid excess bromination, one equivalent of cupric bromide was used. Also, to prevent hydrolysis of the acetonide functionality, various modifications (addition of potassium carbonate, propylene oxide or bubbling of nitrogen gas through the reaction medium) were attempted. In the presence of



SCHEME 5. *(a)* $CuBr_2$, EtOAc–$CHCl_3$, reflux; *(b)* DBU, benzene, reflux; *(c)* Acetone, $CuSO_4$, H_2SO_4 rt.

potassium carbonate or propylene oxide, no reaction took place to give either **19** or **20**. However, when nitrogen gas was bubbled through the reaction medium only a complex mixture resulted.

When the diol-ketone **9b** was reacted with cupric bromide under normal conditions, fortunately the required bromo compound **21** was obtained (Scheme 6). The IR spectrum of crude **21** showed all the required bands (3400, 1720, 1040 and 710 cm^{-1}). Without further characterization, **21** was converted to the enone **22** using DBU.



SCHEME 6. *(a)* $CuBr_2$, EtOAc–$CHCl_3$, reflux; *(b)* DBU, benzene, reflux; *(c)* Acetone, $CuSO_4$, H_2SO_4, rt.

In the PMR spectrum of **22** two olefinic protons appeared at δ 6.98–6.72 and 5.96–5.76 as multiplets. The diol unit of **22** could be readily protected in its acetonide form to give enone **1**. Once again, the spectral data of this enone were identical with those of that prepared earlier (Scheme 3). The overall yield of the enone **1** obtained by this methodology was 46% from the keto-diol **9b**.

Thus, the enone **1** was obtained from WM ketone in eight steps in an overall yield of 12.6%. Similarly, the enone **2** was obtained in nine steps starting from WM ketone in an overall yield of 17.4%.

2. Experimental

Melting points (°C) were determined using a Büchi 510 capillary melting point apparatus and are uncorrected. IR spectra were recorded on Perkin–Elmer model 1310 spectrophotometer. ^{1}H NMR spectra were recorded at 100 MHz using a Jeol FX-100 instrument. ^{13}CNMR spectra were recorded at 25 MHz using the above instrument. Chemical shifts are reported as δ values in parts per million relative to tetramethylsilane (δ 0.0 ppm) as an internal standard. Data are reported as follows: Chemical shifts (multiplicity, coupling constants, integrated intensity). Elemental analyses were performed using a Perkin–Elmer 240C CHN analyzer.

3. Materials

Unless specified otherwise, reagent-grade reactants and solvents were used as received from chemical suppliers. THF was purified by distillation from sodium-benzophenone. All organic extracts were dried over anhydrous $MgSO_4$. Acme silica gel 100–200 mesh was used for column chromatography.

1,1-Ethylenedioxy-8a-methyl-1,2,3,4,8,8a-hexahydro-6(7H)-naphthalenone(6)[3]

A mixture of WM ketone (5.00 g, 28.09 mmol), 2-ethyl-2-methyl-1,3-dioxolane (18.89 g, 163 mmol) containing 2% ethylene glycol and *p*-TsOH (0.100 g) was stirred at room temperature for 30 h. After neutralisation with triethylamine (0.5 ml), the reaction mixture was diluted with benzene. The organic layer was washed with water, dried and evaporated to give the crude product. Purification over a column of silica gel gave the required monoketal **6** (5.25 g, 84%) as a colourless solid.

mp–64–65° (lit.[3] 65–66); IR(KBr) cm^{-1} 2950, 2875, 1660, 1230, 1110, 1070, 940, 860.

1,1-Ethylenedioxy-5, 8a-dimethyl-1,2,3,4,4a,5,8,8a-octahydro-6(7H)-naphthal enone(7)[5]

Dry ammonia (about 200 ml) was passed into a solution of the monoketal **6** (2.122 g, 9.56 mmol) in THF (20 ml) at –78°C. To this mixture, lithium (0.468 g, 66.9 mmol) was added slowly in small pieces and the contents were stirred for 1.5 h at the same temperature. The reaction was quenched with iodomethane (5.95 ml, 95.6 mmol) and the ammonia allowed to evaporate over a period of 8 h. Water (50 ml) was added and the compound was extracted into ether (3×50 ml) and the organic extract was dried and evaporated. The crude compound on chromatographic purification on silica gel (5% ethyl acetate in hexane as eluant) gave **7** (1.312 g, 57.7%) as a colourless oil.

IR (neat) cm^{-1} 2950, 1700, 1440, 1180, 1120, 1030, 850; PMR δ 3.04–3.81 (m, 4H, $-OCH_2CH_2O$), 2.44–1.40(m, 12H), 1,24 (s, 3H, 8a-CH_3), 0.97(d, 3H, 5-CH_3, J=6).

1,1-Ethylenedioxy-5,8a-dimethyl-1,2,3,4,4a,5,8,8a-octahydronaphthalene(8)[5]

A solution of the ketone **7** (1.865 g, 9.39 mmol) and *p*-toluenesulfonyl hydrazide(1.749 g, 9.39 mmol) in THF (60 ml) was refluxed overnight in a nitrogen atmosphere. The reaction mixture was cooled and poured into water and extracted with dichloromethane. The organic

layer was dried and concentrated to give the crude *p*-toluenesulfonylhydrazone(3.100 g, 97%) of **7**. The IR spectrum of this compound showed no carbonyl band.

To a stirred solution of lithium diisopropylamide (34.0 mmol, prepared from 42.5 mmol of diisopropylamine and 34 mmol of 1.2 M *n*-butyl lithium in hexane) in THF (40 ml) at 0° was added a solution of the above crude *p*-toluenesulfonylhydrazone (3.100 g) in THF (10 ml) and the stirring was continued for another 1 h before quenching with water. Workup as usual with dichloromethane gave the crude olefin **8**. Upon chromatographic purification over a column of silica gel, eluting with 5% ethyl acetate in hexane, the pure olefin **8** (1.306 g, 75%) was obtained.

IR(neat) cm^{-1} 3025, 2950, 2890, 1470, 1380, 1190, 1130, 1090, 1060; PMR δ 5.64–5.22 (m, 2H), 3.87 (br s, 4H), 2.40–1.06 (m, 10H), 0.97 (br s, 3H), 0.93 (s, 3H).

5, 8a-Dimethyl-3,4,4a,5,8,8a-hexahydro-1(2H)-naphthalenone(5)

To a stirred solution of the ketal **8** (2.144 g, 9.66 mmol) in THF (50 ml) was added 1M HCl (8 ml) and the mixture was stirred for 1 h. After dilution with water and extraction with dichloromethane, the organic extract was dried and evaporated to give the crude compound, which was chromatographed over a column of silica gel to give the pure ketone **5** (1.70 g, 99%) as a low melting solid.

IR(neat) cm^{-1} 2950, 2875, 1710, 1450, 1430, 970, 825, 700; PMR δ 5.70–5.22(m, 2H), 2.82–1.18(m, 10H), 1.10(s, 3H, 8a-CH_3), 1.02(d, 3H, 5-CH_3, *J*=6); CMR 215.19, 131.48, 123.71, 48.53, 47.00, 37.47, 32.94, 32.83, 25.41, 24.18, 19.24, 16.70 ppm; Anal. Calcd for $C_{12}H_{18}O$; 80.84, H;10.17. Found: C;80.52, H;10.09.

Preparation of the diols 9a and 9b

To a solution of the olefinic ketone **5** (0.534 g, 3 mmol) in acetone(0.60 ml) were added water (1.5 ml), *t*-BuoH(0.24 ml), N-methyl morpholine-N-oxide dihydrate(0.487 g), osmium tetraoxide(0.005 g), respectively, and the contents stirred for 7 h at room temperature under nitrogen atmosphere. A slurry of sodium hydrosulfite(0.030 g), magnesium silicate or magnesol was filtered. The filtrate was saturated with NaCl and extracted with ethyl acetate. The combined organic layers were dried and evaporated to give the crude compound. Chromatographic purification over a column of silica gel gave the β isomer **9b** as the major component first followed by the α isomer **9a** as the minor component.

5, 8a-Dimethyl-6α,7α-dihydroxy-3,4,4a,5,6,7,8,8a-octahydro-1(2H)-naphthal enone(9a)

Yield 0.084 g, 13%; mp–118°; IR(neat) cm^{-1} 3450, 3400, 2960, 1710, 1380, 1250, 1170, 980; PMR δ 3.81–3.61(m, 1H, 7C*H*OH), 3.00–2.80(m, 1H, 6C*H*OH), 2.64–1.32(m, 10H), 1.10(s, 3H, 8a-CH_3), 0.98(d, 3H, 5-CH_3, *J*=6).

5, 8a-Dimethyl-6β,7β-dihydroxy-3,4,4a,5,6,7,8,8a-octahydro-1(2H)-naphthalenone(9b)

Yield 0.401 g, 63%; IR(neat) cm^{-1} 3425, 3325, 2960, 1710, 1435, 1250, 1105, 1050, 960; PMR δ 4.18–4.00(m, 1H, 7C*H*OH), 3.20–2.94(m, 1H, 6C*H*OH), 2.78–1.48(m, 10H), 1.38(s, 3H, 8a-CH_3), 1.04 (d, 3H, 5-CH_3, *J*=6); Anal. Calcd for $C_{12}H_{20}O_3$: C; 67.89, H; 9.497: Found: C;67.68, H;9.530.

*1(2H)-Oxo-5,8a-dimethyl-3,4,4a,5,6,7,8,8a-octahydro-6,7-naphthalenediol dibenzoate(**10**)*

To a solution of the diol **9b** (0.020 g, 0.094 mmol) in pyridine (2 ml) containing DMAP (0.005 g) was added benzoyl chloride (0.044 ml) and the reaction mixture stirred at room temperature overnight. After pouring into ice water, the contents were extracted with ether, the organic layer was washed with water, dried and concentrated to give the crude compound, which was crystallized from hexane–ether to give the ester **10** (0.038 g, 95%) as a colourless solid.

mp–105°; IR(KBr) cm^{-1} 3000, 1720, 1270, 1110, 705; PMR δ 8.02–6.96(m, 10H, Ph), 5.76 (dt appearing as quartet, 1H, H-7, *J*=4, 8), 4.87(dd, 1H, H-6, *J*=4, 12), 2.96–1.52(m, 10H), 1.48(s, 3H, 8a-CH_3), 0.98(d, 3H, 5-CH_3, *J*=6).

*5, 8a-Dimethyl-6,7,-O-methylethylidene-3,4,4a,5,6,7,8,8a-octahydro-1(2H)-naphthalenone(**3**)*

A mixture of the diol **9b** (0.20 g, 0.943 mmol), acetone (5 ml) and anhydrous $CuSO_4$(5.0 g) containing a trace amount of conc. H_2SO_4 was stirred at room temperature for 12 h under nitrogen. The reaction mixture was quenched by adding solid $NaHCO_3$(0.5 g) and filtered. The inorganic salts were repeatedly washed with ethyl acetate and the combined filtrates were evaporated to give an oily material, which was crystallized from hexane to give the ketone **3** (0.221 g, 93%).

mp–90°; IR(KBr) cm^{-1} 2950, 2875, 1710, 1460, 1390, 1380, 1240, 1225, 1060; PMR δ 4.25(dt, 1H, H-7, *J*=6, 2), 3.41(dd, 1H, H-6, *J*=6, 9), 2.70–1.50(m, 10H), 1.44(s, 3H, 8a-CH_3), 1.32(s, 6H, acetonide CH_3), 0.98 (d, 3H, 5-CH_3, *J*=7); CMR 214.5, 107.5, 81.1, 73.1, 47.5, 47.1, 36.5, 34.4, 32.7, 28.6, 26.0, 23.2, 18.4, 15.7 ppm.

*2, 5,8a-Trimethyl-6,7-O-methylethylidene-3,4,4a,5,6,7,8,8a-octahydro-1(2H)-naphthalenone(**4**)*

A solution of diisopropylamine(0.11 ml, 0.8 mmol) in THF (1 ml) was cooled to –5 to –10°. *n*-Butyl lithium(0.5 ml, 6 mmol, 1.2 M in hexane) was injected and the contents stirred at the same temperature for 30 min. A solution of the ketone **3** (0.10 g, 0.4 mmol) in THF (2 ml) was injected slowly. After stirring for another 1 h at the same temperature iodomethane (0.7 ml, 1.2 mmol) was injected and the reaction mixture allowed to reach room temperature. The reaction mixture was poured into water and after usual workup with ethyl acetate the residue was charged over a silica gel column and eluted with 5% ethyl acetate in hexane to furnish the methylated ketone **4** (0.100 g, 95%) as a colourless liquid.

IR(neat) cm^{-1} 3000, 2950, 2875, 1720, 1390, 1250, 1220, 1060; PMR δ 4. 34(dt, 1H, H-7, *J*=4, 2), 3.48(dd, 1H, H-6, *J*=4, 10), 2.86–1.54(m, 9H), 1.46(s, 6H, acetonide CH_3), 1.34 (s, 3H, 8a-CH_3), 1.08(two doublets appearing as a triplet, 6H, 5-CH_3 and 2-CH_3); CMR 214.6, 107.5, 81.1, 73.0, 47.6, 47.2, 41.2, 36.6, 34.5, 32.7, 28.6, 26.0, 23.3, 18.6, 15.8 ppm.

*1-Trimethylsilyloxy-5,8a-dimethyl-6,7-O-methylethylidene-3,4,4a,5,6,7,8,8a-octa hydronaphthalene(**13**)*

To a stirred solution of the ketone **3** (0.073 g, 0.29 mmol) and TMSCl (0.044 ml, 0.347 mmol) in dichloromethane (2 ml) was added DBU (0.056 ml, 0.0375 mmol) and the contents refluxed for 24 h. After removal of the solvent under vacuum, the compound was taken into hexane. Removal of the solvent gave reasonable pure enol ether **13** (0.082 g, 87%). However, chromatographic purification over a column of silica gel led to partial hydrolysis of the enol ether.

IR(neat) cm^{-1} 2950, 1640, 1380, 1240, 1220, 1050, 850; PMR δ 4.50(t, 1H, H-2, *J*=4), 4.22(dt, 1H, H-7, *J*=5, 2), 3.46(dd, 1H, H-6, *J*=5, 10), 2.46–1.48(m, 8H), 1.46(s, 3H, acetonide CH_3), 1.32(s, 3H, acetonide CH_3), 1.18(s, 3H, 8a-CH_3), 0.96(δ, 3H, 5-CH_3, *J*=6), 0.18(s, 9H, $-Si(CH_3)_3$).

*2-Bromo-5,8a-dimethyl-6,7,O-methylethylidene- 3,4,4a,5,6,7,8,8a-octahydro-1(2H)-naphthalenone(**14**)*

A mixture of the enol ether **13** (0.023 g, 0.071 mmol) and NBS (0.014 g, 0.078 mmol) in THF (2 ml) was stirred at 0° for 15 min and quenched by adding saturated $NaHCO_3$. The compound was extracted in dichloromethane and the organic layer was dried and evaporated to give the crude bromo compound. Chromatographic purification over a column of silica gel gave the required bromo ketone **14** (0.004 g) as a syrup.

IR(neat) cm^{-1} 2950, 2875, 1725, 1380, 1390, 1225, 1060.

*5,8a-Dimethyl-6,7-O-methylethylidene-4a,5,6,7,8,8a-hexahydro-1(4H)-naphthalenone(**1**)*

Method 1: To a stirred solution of the bromo ketone **14** (0.006 g, 0.018 mmol) in benzene(1 ml) was added DBU(0.004 ml, 0.029 mmol) and refluxed for 0.5 h. After usual workup with dichloromethane, crude compound was purified over a column of silica gel (eluant 3–5% ethyl acetate in hexane) to give the enone **1** (0.003 g, 67%).

Method 2: A mixture of the enone **22** (0.069 g, 0.329 mmol), anhydrous acetone (5 ml) and $CuSO_4$ (1.00 g), containing a trace amount of conc. H_2SO_4 was stirred under nitrogen for 6 h at room temperature. After neutralization with solid $NaHCO_3$ (0.200 g), the mixture was filtered and the inorganic salts washed with ethyl acetate. The combined organic layers were evaporated to give the crude isopropylidene derivative **1**. Chromatographic purification over a column of silica gel gave **1** (0.060 g, 73%) as a solid.

mp–109–110°; IR(KBr) cm^{-1} 3000, 2950, 1665, 1460, 1380, 1375, 1240, 1060, 850; PMR δ 6.88(ddd, 1H, H-2, *J*=3, 6, 10), 5.90(ddd, 1H, H-3, *J*=2, 3, 10), 4.28(dt, 1H, H-7, *J*=2, 4), 3.48(dd, 1H, H-6, *J*=4, 8), 2.58–1.68(m, 6H), 1.59(br s, 2H, H-4), 1.50(s, 3H, acetonide CH_3), 1.35 (s, 3H, acetonide CH_3), 1.23(s, 3H, 8a-CH_3), 1.03(d, 3H, 5-CH_3, *J*=6). Anal. Calcd for $C_{15}H_{22}O_3$ C;71.96, H;8.86: Found: C; 71.29, H; 8.973.

*2-Phenylsulfenyl-5,8a-dimethyl-6-7-O-methylethylidene-3,4,4a,5,6,7,8,8a octahydro-1(2H)-naphthalenone(**16**)*

The enol ether **13** (0.061 g, 0.18 mmol) was dissolved in dichloromethane (4 ml) and cooled to –78° under nitrogen. To this solution was added phenylsulfenyl chloride (0.030 g, 0.21 mmol) in dichloromethane (2 ml) and the solution stirred at the same temperature for 15 min. The reaction was quenched with water and worked up as usual with dichloromethane. The crude compound was purified over a column of silica gel to give the pure phenylsulfenyl ketone **15** (0. 062 g, 91%) as an oil.

IR(neat) cm^{-1} 2950, 1720, 1600, 1390, 1380, 1230, 1060, 740, 690; PMR δ 7.46–7.14(m, 5H), 4.36–4.08 (m, 1H, H-7), 3.52–3.28 (m, 1H, H-6), 2.40–1.52(m, 9H), 1.44(s, 3H, acetonide CH_3), 1.36(s, 3H, acetonide CH_3), 1.30(s, 3H, 8a-CH_3), 0.96(d, 3H, 5-CH_3, *J*=6), 0.18(s, 9H, $-Si(CH_3)_3$).

Preparation of enones 2 and 18 from the ketone 4

(i) Bromination of 4 with $CuBr_2$

Copper (II) bromide (0.178 g, 0.8 mmol) was placed in a 25-ml two-necked RB flask and ethyl acetate (2 ml) was added and brought to reflux. The compound **4** (0.100 g, 0.376 mmol) in chloroform (2 ml) was injected and the refluxing continued for 3 h. At this time all the black copper(II) bromide became green to amber copper(I) bromide. The reaction mixture was brought to room temperature and filtered. Evaporation of the solvent gave two major brominated components (0.112 g) as indicated in TLC. As the products were unstable, no attempt was made to purify them.

(ii) Dehydrobromination

The above crude mixture of bromo compounds was dissolved in benzene (5 ml) and DBU (0.149 ml, 1.0 mmol) was added and refluxed for 8 h. After cooling to room temperature, the reaction mixture was poured into water extracted with ethyl acetate and worked up as usual. The crude residue was charged on a silica gel column and first eluted with 5–10% ethyl acetate in hexane to give the enone **2** (0.058 g, 56% from ketone **4**) as a colourless solid with isopropylidene group intact. Further elution of the column with 20% ethyl acetate in hexane furnished the dihydroxy enone **18** (0.019 g, 19% from ketone **4**) as a colourless syrup.

2,5,8a-Trimethyl-6,7-O-methylethylidene-4a-5,6,7,8,8a-hexahydro-1(4H)-naphthalenone(2)

mp–112–113°; IR(KBr) cm^{-1} 2980, 2950, 1665, 1440, 1360, 1100, 1060, 1000, 710; PMR δ 6.68–6.50(m, 1H, H-3), 4.28(dt, 1H, H-7, *J*=2,4), 3.42(dd, 1H, H-6, *J*=4, 8), 2.48–1.44(m, 9H), 1.74(br s, 2H, H-4), 1.46(s, 3H< 2-CH_3), 1.32(s, 6H, acetonide CH_3), 1.15(s, 3H, 8a-CH_3), 0.98(δ, 3H, 5-CH_3, *J*=6).

2,5,8a-Trimethyl-6,7-dihydroxy-4a-5,6,7,8,8A-hexahydro-1(4H)-naphthalenone(18)

IR(neat) cm^{-1} 3400, 2950, 1665, 1460, 1375, 1240, 1040.

Preparation of the enone 2 from 18

A mixture of the enone **18** (0.019 g, 0.085 mmol), acetone (3 ml) and anhydrous $CuSO_4$ containing a trace amount of conc. H_2SO_4 was stirred at room temperature for 8 h under nitrogen atmosphere and worked up according to the procedure given for the preparation of ketone **3** to give the crude enone **2**. The crude compound was loaded on to a silica gel column and eluted with 5–10% ethyl acetate in hexane to furnish the enone **2** (0.018 g, 80%) as a colourless solid. Spectral data of this compound were identical to the previous enone.

2-Bromo-5,8a-dimethyl-6,7-dihydroxy-3,4,4a,5,6,7,8,8a-octahydro-1(2H)-naphthalenone(21)

Copper (II) bromide (0.316 g, 1.42 mmol) was placed in a 25-ml two-necked RB flask and ethyl acetate (3 ml) was added and brought to reflux. The compound **9b** (0.150 g, 0.70 mmol) in chloroform (3 ml) was injected and brominated as described earlier to give the crude brominated product **21** (0.130 g).

5,8a-Dimethyl-6,7-dihydroxy-4a,5,6,7,8,8a-hexahydro-1(4H)-naphthalenone(22)

The above crude bromo ketone **21**(0.130 g) and DBU(0.204 g, 1.34 mmol) in benzene (10 ml) was refluxed for 5 h, cooled to room temperature and poured into water. Extraction into

ethyl acetate and workup as usual gave the crude compound. Chromatographic purification over a column of silica gel furnished the pure enone **22** (0.069 g, 46.3%) from ketone **21** as a syrup.

IR(neat) cm^{-1} 3400, 2930, 1720, 1665, 1450, 1380, 1250, 1040, 1020; PMR δ 6.98–6.72(m, 1H, H-3), 5.96–5.76(m, 1H, H-2), 4.18–4.00(m, 1H, H-7), 3.22–3.00(m, 1H, H-6), 2.64–1.34(m, 6H), 1.36(s, 3H, 8a-CH_3), 1.00 (d, 3H, J=6).

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