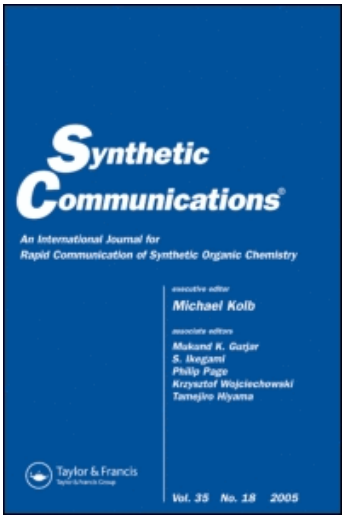

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Synthesis of (±)-2-Methoxy-9a-Carbamorphinan and (±)-2-Methoxy-9a-Carba-14α-Morphinan: Acid Catalyzed Cyclizations of 1-m-Methoxybenzyl-4, 4a,5,6,7,8-Hexahydronaphthalen-2(3H)-ONE and 1 -m-Methox Ybenzyloctalins

Sitaram Pal[a]; Sukumar Ghosh[a]; Bimal K. Banik[a]; Shaikh Khairul Alam[a]; Usha Ranjan Ghatak[a]
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SYNTHESIS OF (±)-2-METHOXY-9a-CARBAMORPHINAN AND (±)-2-METHOXY-9a-CARBA-14α-MORPHINAN: ACID CATALYZED CYCLIZATIONS OF 1-m-METHOXYBENZYL-4, 4a,5,6,7,8-HEXAHYDRONAPHTHALEN-2(3H)-ONE AND 1-m-METHOXYBENZYLOCTALINS

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Abstract : The bridged-ethers,(±)-2-methoxy-9a-carbamorphinan **(1b)** and (±)-2-methoxy-9a-carba-14α-morphinan**(2b)** have been synthesized. The acid-catalyzed cyclizations of 1-m-methoxybenzyloctalone **3b** and 1-m-methoxybenzyloctalins **4b** proceed with high regio-and stereoselectivities leading mostly to the bridged-ketone **14** and ether **1b** respectively, along with o-methoxy-tetracyclic ketone **15** and the ether **17**, in addition to other minor products.

The synthetic methods for (±)-9a-carbamorphinan (**1a**), a strong attractant for the economically important coconut rhinoceros beetle, Oryctes rhinoceros (L) and its inactive epimer, (±)-9a-carba-14α-morphinan (**2a**), reported in an earlier paper[1] in this series through Grew's type cyclizations[2], prompted us to consider the extension of similar approach to the preparation of the respective 2-methoxy analogues **1b** and **2b** for evaluation of the structure-activity

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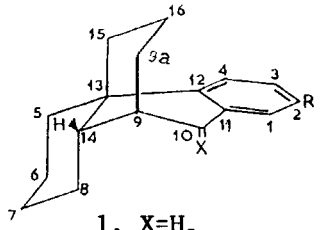
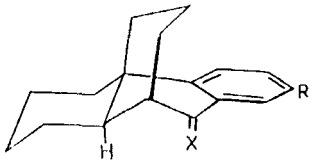
*To whom correspondence should be addressed.



1, X=H_2
5, X=O



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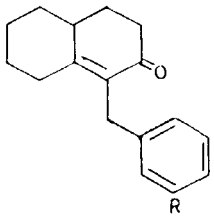
6, X=O



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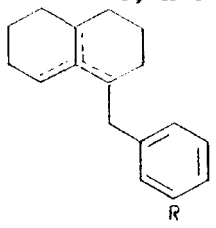
a: R=H
b: R=OMe



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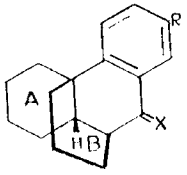
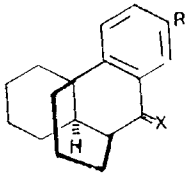
relationship. Unlike the cyclizations of the substrates **3a** and **4a**, used for the synthesis of **1a** and **2a**, in the meta-methoxy analogues **3b** and **4b**, electrophilic attack by a cation in the decalin ring may take place ortho or para to the activating methoxy group in the aromatic moiety resulting in a qualitative and quantitative differences in the nature of the products. Realizing that isolation and identification of the diastereoisomeric bridged compounds could be quite difficult we have also developed unequivocal synthesis of the 2-methoxy hydrocarbones **1b** and **2b** from the previously reported[1] desmethoxy ketones **5a** and **6a**. In this paper we describe the results of these studies.

The conversions of the epimeric bridged ketones, **5a** and **6a**, to the respective regioisomerically pure methoxy derivatives **1b** and **2b**, were achieved following standard methodologies[3]. However, some unexpected characteristics of

the 9a-carbamorphinan bridged system during these transformations, were uncovered as noted below.

The nitration of the ketone **5a** gave the mononitro derivative **7** in 90% yield which on catalytic hydrogenation in ethanol containing hydrochloric acid in the presence of





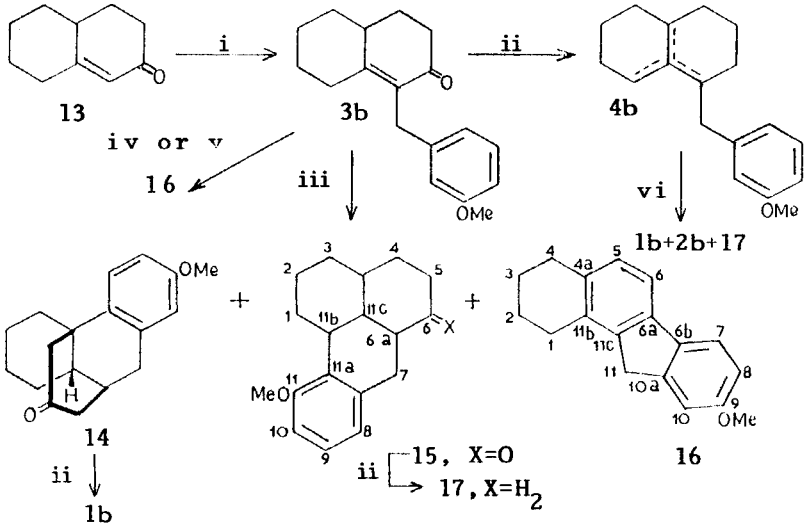
7, R=NO_2, X=O
8, R=NH_2, X=$\langle^{OH}_{H}$
9, R=OH, X=O

10, R=NO_2, X=O
11, R=NH_2, X=$\langle^{OH}_{H}$
12, R=OH, X=O

palladium-on-carbon proceeded rapidly and yielded (74%) the aminoalcohol **8**. The stereochemistry of the newly created chiral centre in benzylic alcohol is uncertain. Attempted hydrogenolysis of **8** under various conditions using perchloric acid in ethyl acetate or acetic acid in the presence of palladium-on-carbon or platinum oxide was unsuccessful. The unusual inertness of the benzylic alcohol group in **8** towards hydrogenolysis clearly indicates that the two bridged-rings (A and B) in this compound prevent its adsorption on the catalyst surface[4]. The initial reduction of the benzylic carbonyl to the alcohol stage in the nitro-ketone **7** is possibly facilitated by the deformation of the bridge-rings allowing adsorption on the catalyst surface and also in the release of strain[5] involved in changing the hybridization of the carbonyl carbon from sp^2 to sp^3 in this system. The diazotization[6] of the aminoalcohol **8** followed by hydrolysis afforded the phenolic ketone **9** in 55% yield. The oxidation

of the secondary benzyl alcohol **8** to **9** possibly arises out of its oxidation[7] with nitric acid or the corresponding oxide produced from the nitrous acid in the diazotization stage. The methylation of **9** gave the oxo-ether **5b** in 96% yield, which on Huang-Minlon reduction[8] afforded the methylether **1b** in 77% yield. In an identical sequence through **10**→**11**→**12**→**2b**, the epimeric ketone **6b** gave the respective methylether **2b**.

With the preparative success of the desired 2-methoxy-9a-carbamorphinans **1b** and **2b** from the respective desmethoxy ketones **5a** and **6a**, the acid catalyzed cyclizations of the m-methoxybenzyloctalone **3b** and the -octalins **4b** were next investigated for a possible direct route for these compounds. The desired monoalkylated octalone **3b**, prepared in 44% yield by alkylation[1] of octalone **13** with m-methoxybenzyl chloride, on cyclization with orthophosphoric acid (Scheme 1) gave a mixture of the isomeric ketones **14**, **15** and the partially aromatized ether **16** along with three other minor compounds of undetermined structures, in a ratio of **ca** 63:24:10:3 in excellent yield. The pure isomeric ketones **14** and **15** and the tetracyclic ether **16** were separated by chromatography. The assigned strcuture for **16**, arising from the cyclodehydration[1] of **3b**, was established by its spectral and elemental analyses. The structure and stereochemistry of the bridged ketone **14** was also conclusively established by its reduction to the ether **1b**. While the structures of the tetracyclic ketone **15** and the corresponding reduced product **17**, resulting from an unusual ortho cyclization to the methoxy group in aromatic ring in **3b** (also in **4b** as shown below), were assigned from the spectral and elemental analyses the stereochemistries of these remain uncertain. The differences in the coupling patterns of the aromatic protons in the ^{1}HNMR spectra of the para-methoxy cyclized product **14** and the ether **1b** with that of the ortho-methoxy product **15** and the



Reagents : (i) K^tAmO, $m\text{-}OCH_3C_7H_6Cl$ (ii) $NH_2\cdot NH_2\cdot H_2O$, KOH, DEG (iii) H_3PO_4 (iv) CH_3OH, HCl (v) $BF_3\cdot Et_2O$ (vi) H_3PO_4-P_2O_5

Scheme-1

corresponding ether **17** (see Experimental) clearly established the relative position of the aromatic methoxy group in these compounds. The reactions of **3b** with hydrogen chloride in methanol or borontrifluride etherate gave the cyclodehydration and partially aromatized ether **16** as the only isolable product in 60% and 35% yields, respectively. The polyphosphoric acid catalyzed reaction of **3b** gave complex mixture of products. It should be noted that (±)-9a-carbamorphinan-16-one was the only product isolated in the orthophosphoric acid catalyzed cyclization[1,9] of benzyl-

octalone **3a**, whereas polyphosphoric acid induced reaction gave cyclodehydrated product[1] similar to **16**. In contrast, to the polyphosphoric acid catalyzed cyclization of benzyloctalins , **4a**, which gave[1] a mixture of the epimeric bridged hydrocarbon **1a**, **2a** and an unknown hydrocarbon in a ratio of **ca** 50:33:17, the m-methoxy benzyloctalins **4b** obtained by Huang-Minlon reduction of **3b**, on cyclization under identical condition gave a mixture of the isomeric ethers **1b**, **2b** and **17** in a ratio of **ca** 89:4:7(GLC) in excellent yield. The high stereoselectivity in the formation of 9a-carbamorphinan ether **1b**, in the cyclization of **4b**, having an activated aromatic ring, with respect to that in desmethoxy substrate **4a** is noteworthy. Similar to the results mentioned above for **3b**, the epimeric bridged ethers **1b** and **2b** in the cyclization of **4b** resulted from the exclusive electrophilic para substitution to the methoxy group in the aromatic ring at the tertiary angular cation, whereas the **peri**-cyclization product **17** originated from the electrophilic attack orhto to methoxy aromatic ring[10].

EXPERIMENTAL

The compounds described are all recemates. IR spectra were recorded on a Perkin-Elmer model PE 298 spectrometer. ^{1}H NMR spectra were recorded on a Varian XL-200 and Jeol FX-100 spectrometers using $SiMe_4$ as an internal standard and the values are expressed in "δ" scale. Analytical GLC was performed on a Shimadzu GC-9A model with a flame ionisation detector employing 1.5% OV-17 (6.5 ft x 0.25 in) column with N_2 as the carrier gas. Elemental analysis was performed by P.P. Bhattacharyya of this laboratory. Column chromatography was performed on neutral alumina (Brockman Grade 1) or silica gel [Glaxo Laboratories (India)]. Petroleum and light petroleum refer to fractions of b.p. 60-80°C and 40-60°C respectively.

(±)-2-Nitro-9a-carbamorphinan-10-one (7) : Concentrated nitric acid (7ml) was aded to the ketone **5a**[1] (375 mg, 1.5 mmol) and the mixture was heated in a boiling water-bath for 30 min. The cold reaction mixture was diluted with ice and extracted with ether. The combined ether extracts were washed with sodium carbonate solution (5%), water and then dried (Na_2SO_4). Evaporation of the solvent gave **7** (400 mg, 90%), m.p. 131°C (methanol); IR(KBr) 1685, 1605 cm^{-1}; λ_{max}(EtOH) 238 (logε4.61), 272nm (logε4.26); ^1H NMR(200 MHz, $CDCl_3$) 1.0-1.96(m,14H), 2.46(brd, 1H, C-14H), 2.64(brs, 1H, C-9H), 7.58(d,J=8Hz, 1H), 8.4(dd,J=8Hz and 3Hz, 1H), 8.90(d, J=3Hz, 1H). Anal. calcd. for $C_{17}H_{19}NO_3$: C, 71.56; H, 6.71. Found : C, 71.42; H, 6.88.

(±)-2-Amino-10-hydroxy-9a-carbamorphinan (8) : A solution of the nitroketone **7** (350 mg, 1.3 mmol) in ethanol (25 ml) and concentrated hydrochloric acid (0.2 ml) was hydrogenated in the presence of 10% palladium on carbon (125 mg) at room temperature and pressure until the uptake of hydrogen ceased (5h). The catalyst was removed by filtration and most of the solvent was removed under reduced pressure. The residue was diluted with 5% sodium carbonate solution (10 ml) and extracted with ether. The organic layer was washed with water and brine, dried (Na_2SO_4) and evaporation of solvent gave **8** (250 mg, 80%), m.p. 159°C (ethanol); IR(KBr) 3640,3400,1620 cm^{-1}; λ_{max}(EtOH) 240 (logε 3.95), 295 nm (logε 3.25); ^1H NMR (100 MHz, $CDCl_3$) 1.01-1.72(m, 14H), 2.0-2.28(m, 5H, methine and NH_2), 5.88(d, J=6Hz, 1H, **OH**), 7.64(dd, J=8Hz and 3Hz, 1H), 7.86-8.04(m, 2H). Anal. Calcd for $C_{17}H_{23}NO$: C, 79.37; H, 9.16. Found : C, 79.31; H, 9.16.

(±)-2-Hydroxy-9a-carbamorphinan-10-one (9) : To a solution of sodium nitrate (0.6 gm, 8.7 mmol) in 80% sulphuric acid (12 ml), the amino alcohol **8** (200 mg, 0.77 mmol) in pyridine

(3 ml) was aded at 0-5°C and the mixture was stirred for 1h at that temperature. Ice water (30 ml) was aded to the reaction mixture followed by urea (0.5 gm). The mixture was stirred for 30 min at room temperature and finally heated on a steam-bath for 2 h. The cooled reaction mixture was extracted with ether. The ether layer was extracted with three portions of 5% potassium hydroxide solution, and the combined basic layers were added to an excess of iced, concentrated hydrochloric acid. The precipitated material was extracted with ether, and the organic layer was washed with brine, dried (Na_2SO_4) and concentrated under reduced pressure to give **9** (137 mg, 69%) as a white solid, m.p. 185°C (Ether); IR (KBr) 1675, 1610 cm^{-1}; λ_{max} 226 (logε 4.43), 258(logε 4.12), 330 nm (log 3.59); 1H NMR (100 MHz, $CDCl_3$) 1.2-1.88 (m, 14H), 2.24-2.56 (m, 2H), 5.6 (brs, phenolic **OH**), 7.12-7.28 (m, 2H), 7.59 (d, J=3Hz, 1H). Anal. calcd. for : $C_{17}H_{20}O_2$: C, 79.65; H, 7.86. Found : C, 79.35; H, 8.02.

(±)-2-Methoxy-9a-carbamorphinan-10-one (5b) : The ketophenol **9** (120 mg, 0.46 mmol) was methylated by refluxing with anhydrous potassium carbonate (1.0 gm) and methyl iodide (1 ml) in dry acetone (5 ml) for 6 h. After distillation of most of the solvent from steam-bath the mixture was diluted with water and extracted with ether. The organic layer was washed with water, dried (Na_2SO_4) and evaporation of solvent gave **5b** (108 mg, 85%), m.p. 68°C (petroleum), homogeneous in GLC (R_t 3.86 min); IR (KBr) 1680,1610 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) 1.2-1.88 (m, 14H), 2.24-2.56 (m, 2H), 3.86 (s, 3H, OCH_3), 7.12-7.28 (m, 2H), 7.59 (d, J=3Hz, 1H). Anal. calcd. for $C_{18}H_{22}O_2$: C, 79.96; H, 8.20. Found : C, 79.71; H, 8.01.

(±)-2-Methoxy-9a-carbamorphinan (1b) : A suspension of **5b** (80 mg, 0.29 mmol) in 99% hydrazine hydrate (0.5 ml) and

diethylene glycol (2 ml) was heated at 140-145°C for 1 h under N_2, cooled to 100°C and potassium hydroxide (0.35 g) was added. Water was distilled off by heating the reaction mixture until the temperature rose to 200-210°C and maintaining it at the same temperature for 2 h while a slow but constant flow of N_2 was passed through it. The cooled reaction mixture was diluted with water and acidified with 6M-hydrochloric acid and thoroughly extracted with ether. The ethereal extract was washed with water, dried (Na_2SO_4) and evaporated to afford a gummy mass which on chromatography over neutral alumina (2 gm) and elution with petroleum afforded the ether **1b** (57 mg, 75%), as a colourless oil, homogeneous in GLC (R_t 1.99 min); IR (neat) 1605 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) 1.2-2.6 (m, 16H), 2.95-3.26 (m, 2H, benzylic protons), 3.70 (s,3H, OCH_3), 6.47-7.06 (m, 3H). Anal. calcd. for $C_{18}H_{24}O$: C, 84.32; H, 9.44. Found C, 84.04; H, 9.56.

(±)-2-Nitro-9a-carba-14α — morphinan-10-one (10) : Nitration of the 14α-ketone **6a**[1] (200 mg, 0.83 mmol) by an identical procedure to that described for **5a** gave the nitro-ketone **10** (210 mg, 89%), m.p. 166°C (ethanol); IR (KBr) 1685,1605 cm^{-1}; λ_{max} (EtOH) 238 (logε 4.30), 271 nm (logε 3.94); ^1H NMR (200 MHz, $CDCl_3$) 0.97-2.66 (m, 16H), 7.5-8.42 (m, 3H). Anal. calcd. for $C_{17}H_{19}NO_3$: C, 71.56; H, 6.71. Found : C, 71.38; H, 6.90.

(±)-2-Amino-10-hydroxy-9a-carba-14α- ——morphinan (11) : Catalytic reduction of the nitro-ketone **10** (180 mg, 0.63 mmol) in ethanol containing catalytic amount of hydrochloric acid in the presence of 10% palladium-on-carbon by an identical procedure to that described for **7** gave the amino-alcohol **11** (105 mg, 65%), m.p. 188°C (ethanol); IR (KBr) 3600,3380,1605 cm^{-1}; λ_{max} (EtOH) 241 (logε 3.83), 294 nm (logε 3.29); ^1H NMR (200 MHz, $CDCl_3$) 0.88-2.7 (m, 19H),

4.96 (d, J=7Hz, 1H, OH), 6.72 (dd, J=8Hz and 3Hz, 1H), 6.96-7.12 (m, 2H). Anal. calcd. for $C_{17}H_{23}NO$: C, 79.37; H, 9.16. Found : C, 79.11; H, 9.15.

(±)-2-Methoxy-9a-carba-14 α — morphinan-10-one (6a) : The amino alcohol **11** (80 mg, 0.31 mmol) was diazotized by an identical procedure to that described for **8** to give the corresponding keto-phenol **12**, which was directly methylated as described above to give the methoxy-ketone **6b** (65 mg, 77%) m.p. 88°C (petroleum), homogeneous GLC (R_t 5.36 min); IR (KBr) 1685,1605 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) 0.82-2.66 (m, 16H), 3.82 (s,3H), 6.94-7.56 (m, 3H). Anal.calcd. for $C_{18}H_{22}O_2$: C, 79.96; H, 8.20. Found : C, 79.91; H, 8.26.

(±)-2-Methoxy-9a-carba-14α — morphinan (2b) : Huang-Minlon reduction of the ketone **6b** (50 mg, 0.18 mmol) by an identical procedure to that described above, followed by chromatographic purification of the product, afforded the ether **2b** (27 mg, 60%) as a colourless oil, homogeneous in GLC (R_t 2.6 min); IR (neat) 1605 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) 0.9-3.1 (m, 18H), 3.78 (s, 3H), 6.64-7.16 (m, 3H). Anal. calcd. for $C_{18}H_{24}O$: C, 84.32; H, 9.44. Found : C, 84.20; H, 9.59.

1-m-Methoxybenzyl-4,4a,5,6,7,8-hexahydronaphthalen-2(3H)-one (3b) : The ketone **13** (5.0 g, 33 mmol) was added slowly with stirring to an ice-cold suspesion of dry potassium t-pentyloxide, prepared from potassium metal (1.3 g, 29 mg-atom), in dry thiophene free benzene (30 ml) under N_2 and was refluxed for 1 h. m-Methoxybenzylchloride (6.0 g, 38 mmol) was added dropwise to the ice-cold dark brown solution, and the reaction mixture was allowed to stand at room temperature (ca 25°C) for 15 min, before being heated under reflux for 3h and then acidified with 6M-hydrochloric acid in the cold. The organic layer was separated and the aqueous layer was extracted with benzene; the extract was washed with water,

dried (Na_2SO_4) and the solvent was removed. The residual oil was carefully fractionated to afford **3b** (3.1 g, 31%), b.p. 168-175°C (0.2 mm Hg) (a considerable amount of thick brown by-product, possibly the dialkylated product, was left in the distillating flask); homogeneous in GLC (R_t 5.07 min); IR (neat) 1665,1610 cm^{-1}; λ_{max} 246 nm (logε 4.07); ^1H NMR (200 MHz, $CDCl_3$) 1.10-3.03 (m, 13H), 3.56 (s, 2H), 3.70 (s, 3H), 6.40-7.06 (m, 4H). Anal. calcd. for $C_{18}H_{22}O_2$: C, 79.76; H, 8.20. Found : C, 80.04; H, 8.32.

Acid-catalyzed cyclizations of octalone 3b:

A : With orthophophoric acid : (±)-2-Methoxy-9a-carbamorphinan-16-one (14) ; 11-Methoxy-1,2,3,3a,4,5,6a,7,11b,11c-decahydrobenz[de]anthracen-6-one(15)and 1,2,3,4-tetrahydro-9-methoxybenzo[a] fluorene (16) : The octalone **3b** (500 mg, 1.8 mmol) was treated with orthophosphoric acid (6 ml,89%) and the mixture was heated on a steam-bath for 12 h. The cooled reaction mixture was diluted with water (20 ml)and extracted with ether (4x25 ml). After usual work-up, the residue afforded a colourless liquid (340 mg), b.p. 185-190°C (0.4 mmHg). GLC analysis revealed it to be a mixture of **14 15, 16** and three other minor unknown compounds in a ratio of **ca** 63 (R_t 4.7 min): 24(R_t 3.7 min): 10(R_t 6.4 min): 3(R_ts 2.3,1 and 0.5 min) by co-injection with pure samples of **14, 15** and **16,** obtained after separation of this mixture as described below. The mixture was dissolved in petroleum and chromatographed over activated neutral alumina (25 g). The initial light petroleum elutes (3x100 ml) on standing in a ice-box solidified, which on crystallisation from light petroleum afforded **16** (20 mg), m.p. 142°C, homogeneous in GLC (R_t 6.4 min); IR (KBr) 2850,1610,1460 cm^{-1}; λ_{max} (EtOH) 215 (logε 4.39), 275 (logε 4.41), 305 nm (logε 3.80); ^1H NMR (100 MHz $CDCl_3$) 1.56-1.96 (m, 4H), 2.5-2.9 (m, 4H), 3.5 (brs, 2H), 3.73 (s, 3H), 6.60-7.60 (m, 5H). Anal. calcd.

for $C_{18}H_{18}O$: C, 86.36; H, 7.25. Found : C, 86.32 ; H, 7.30. The middle fraction, with light petroleum (4x40 ml) gave the ketone **14** (100 mg), homogeneous in GLC (R_t 4.7 min); IR (neat) 1705,1600 cm^{-1} ; ^1H NMR (200 MHz, $CDCl_3$) 1.26-2.70 (m, 14H), 3.14-3.30 (m, 2H), 3.80 (s, 3H), 6.72 (brs, 1H), 6.88 (brd, 1H), 7.32 (d,J=8Hz, 1H). Anal. calcd. for $C_{18}H_{22}O_2$: C, 79.76; H, 8.20. Found : C, 79.48; H, 8.21. Further elution with light petroleum (5x15 ml) gave the ketone **15** (35 mg) m.p.120°C, homogeneous in GLC (R_t 3.7 min); IR (KBr) 1700,1610 cm^{-1} ; ^1H NMR (200 MHz, $CDCl_3$) 1.04-2.30 (m, 12H), 2.54-2.70 (m, 2H), 3.22-3.48 (m, 2H, benzylic), 3.82 (s, 3H), 6.80 (d, J=8Hz, 2H), 7.2 (t,J=8Hz, 1H). Anal. calcd. for $C_{18}H_{22}O_2$: C, 79.76; H, 8.20. Found : C, 79.67; H, 8.08.

B : With dry hydrogen chloride in methanol : Compound 16 : The octalone **3b** (130 mg, 0.48 mmol) was dissolved in anhydrous methanol(4 ml) and cooled in an ice-salt bath (ca 10°C). The reaction mixture was then saturated with dry hydrogen chloride and left overnight at room temperature and finally refluxed for 1 h. After removal of most of the solvent under reduced pressure the mixture was diluted with water and extracted with ether. The ethereal extract was washed with 2% sodium hydroxide solution, followed by brine and dried (Na_2SO_4). The residue after the removal of the solvent was chromatographed over neutral alumina (5 g) and eluted with petroleum to afford **16** (60 mg, 50%) m.p. and mixed m.p. 142°C ; GLC (R_t 6.4 min) identical with the sample described above.

C : With boron trifluoride-etherate : Compound 16 : The octalone **3b** (50 mg, 0.18 mmol) in dry benzene (2 ml) was refluxed for 9 h with boron trifluoride-etherate (0.5 ml). After usual work-up, the chromatography of the product on neutral alumina using petroleum gave **16** (15 mg, 34%), m.p. and mixed m.p. 142°C.

Reduction of 14 to 1b : Huang-Minlon reduction of **14** (75 mg, 0.27 mmol) by an identical procedure to that described for **6b** followed by chromatographic purification of the product, afforded the ether **1b**, as a colourless oil identical GLC, IR and ^{1}H NMR with the sample described above.

Reduction of 15 to 11-methoxy-1,2,3,3a,4,5,6,6a,7,11b-dodecahydro-11c(H)-benz [de]anthracene (17) : Huang-Minlon reduction of the ketone **15** (20 mg, 0.074 mmol) by an identical procedure as described above, followed by chromatographic purification of the product afforded the ether **17** (10 mg, 53%) homogeneous by GLC (R_t 1.6 min); IR (neat) 1600 cm^{-1} ; ^{1}H NMR (200 MHz, $CDCl_3$) 1.04-2.0 (m, 15H) 2.46-2.58 (m, 1H), 3.12-3.26 (m, 2H, benzylic), 3.78 (s, 3H, OCH_3), 6.70 (d, J=8Hz, 1H), 6.76 (d, J=8Hz, 1H), 7.1 (t, J=8Hz, 1H). Anal. calcd. for $C_{18}H_{24}O$: C, 84.32; H, 9.44. Found : C, 84.08; H, 9.40.

1-m-Methoxybenzyloctahydronaphthalenes (4b) : The reduction of the ketone **3b** (2.0 g, 7.4 mmol) in hydrazine hydrate (2.0 ml,99%) and distilled diethylene glycol (25 ml) was carried out under identical condition as described for **5b** to afford the m-methoxy-benzyloctalins (**4b**), as a colourless liquid (1.5 g, 80%), b.p. 140-150°C (0.2 mm Hg); GLC showed the presence of tnree components in a ratio of **ca 80**:5:15 with R_t values 2.8, 2.4 and 3.3 min respectively; IR (neat) 1610 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) 0.97-3.5 (m, 17H), 3.79-3.80 (m, 3H), 6.71-7.60 (m, 4H).

Cyclization of m-methoxy-benzyloctalins 4b with polyphosphoric acid : The aforementioned mixture of m-methoxy-benzyloctalins **4b** (500 mg, 1.9 mmol) was added to a well stirred solution of plyphosphoric acid [prepared from phosphorus pentoxide (5.0 g) and orthophosphoric acid (2.5 ml, 89%)] and heated in oil bath at 150°C for 1 h. After usual work-up, the residue was distilled to afford a colourless liquid (425

mg, 85%), b.p. 138-145°C (0.2 mm Hg). GLC analyses showed it to be a mixture of **1b,2b** and **17** in a ratio of **ca** 89:4:7 by co-injection with the respective pure samples.

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