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

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SYNTHESIS OF (+)-2-METHOXY-9α-CARBAMORPHINAN AND (+)-2-METHOXY-9α-CARBA-14α-MORPHINAN: ACID CATALYZED CYCLIZATIONS OF 1-m-METHOXYBENZYL-4, 4a,5,6,7,8-HEXAHYDRONAPHTHALEN-2(3H)-ONE AND 1-m-METHOXYBENZOLOCTALINS

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Abstract: The bridged-ethers, (+)-2-methoxy-9α-carbamorphinan (1b) and (+)-2-methoxy-9α-carba-14α-morphinan (2b) have been synthesized. The acid-catalyzed cyclizations of 1-m-methoxybenzylctalone 3b and 1-m-methoxybenzoctalins 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 (+)-9α-carbamorphinan (1a), a strong attractant for the economically important coconut rhinoceros beetle, Oryctes rhinoceros (L) and its inactive epimer, (+)-9α-carba-14α-morphinan (2a), reported in an earlier paper1 in this series through Grew's type cyclizations2, 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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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 hydrocarbons 1b and 2b from the previously reported 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. 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 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. 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 involved in changing the hybridization of the carbonyl carbon from sp$^2$ to sp$^3$ in this system. The diazotization 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 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 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-methoxybenzyl octalone 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 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 structure for 16, arising from the cyclodehydration 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 1HNMR 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\textsuperscript{T}AmO, m-OCH\textsubscript{3}C\textsubscript{7}H\textsubscript{6}Cl (ii) NH\textsubscript{2}·NH\textsubscript{2}·H\textsubscript{2}O, KOH, DEG (iii) H\textsubscript{3}PO\textsubscript{4} (iv) CH\textsubscript{3}OH, HCl (v) BF\textsubscript{3}·Et\textsubscript{2}O (vi) H\textsubscript{3}PO\textsubscript{4}·P\textsubscript{2}O\textsubscript{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 borontrifluoride 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\textsuperscript{1,9} of benzyl-
octalones 3a, whereas polyphosphoric acid induced reaction gave cyclodehydrated product similar to 16. In contrast, to the polyphosphoric acid catalyzed cyclization of benzyloctalins, 4a, which gave 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 demethoxy 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 ortho to methoxy aromatic ring. 

**EXPERIMENTAL**

The compounds described are all recemates. IR spectra were recorded on a Perkin-Elmer model PE 298 spectrometer. 1H NMR spectra were recorded on a Varian XL-200 and Jeol FX-100 spectrometers using SiMe4 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 N2 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 (7 ml) was added to the ketone $5a$ (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 ($\text{Na}_2\text{SO}_4$). Evaporation of the solvent gave 7 (400 mg, 90%), m.p. 131 °C (methanol); IR(KBr) 1685, 1605 cm$^{-1}$; $\lambda_{\text{max}}$(EtOH) 238 (logε 4.61), 272 nm (logε 4.26); $^1$H 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: 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 ($\text{Na}_2\text{SO}_4$) and evaporation of solvent gave 8 (250 mg, 80%), m.p. 159 °C (ethanol); IR(KBr) 3640, 3400, 1620 cm$^{-1}$; $\lambda_{\text{max}}$(EtOH) 240 (logε 3.95), 295 nm (logε 3.25); $^1$H 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 added at 0-5°C and the mixture was stirred for 1 h at that temperature. Ice water (30 ml) was added 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 (Na₂SO₄) 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; λmax 226 (logε 4.43), 258 (logε 4.12), 330 nm (log 3.59); 1H NMR (100 MHz, CDCl₃) 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 C₁₇H₂₀O₂: C, 79.65; H, 7.86. Found: C, 79.35; H, 8.02.

(±)-2-Methoxy-9a-carbamorphinan-10-one (5b): The keto-phenol 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 (Na₂SO₄) and evaporation of solvent gave 5b (108 mg, 85%), m.p. 68° C (petroleum), homogeneous in GLC (RI 3.86 min); IR (KBr) 1680,1610 cm⁻¹; 1H NMR (200 MHz, CDCl₃) 1.2-1.88 (m, 14H), 2.24-2.56 (m, 2H), 3.86 (s, 3H, OCH₃), 7.12-7.28 (m, 2H), 7.59 (d, J=3Hz, 1H). Anal. calcd. for C₁₈H₂₂O₂: 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 N₂, 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 N₂ 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 (Na₂SO₄) 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 (Rₜ 1.99 min); IR (neat) 1605 cm⁻¹; ¹H NMR (200 MHz, CDCl₃) 1.2-2.6 (m, 16H), 2.95-3.26 (m, 2H, benzylic protons), 3.70 (s, 3H, OCH₃), 6.47-7.06 (m, 3H). Anal. calcd. for C₁₈H₂₄O: 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 (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, CDCl₃) 0.97-2.66 (m, 16H), 7.5-8.42 (m, 3H). Anal. calcd. for C₁₇H₁₉N0₃: C, 71.38; H, 6.90. 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, CDCl₃) 0.88-2.7 (m, 19H),
4.96 (d, J=7 Hz, 1H, OH), 6.72 (dd, J=8 Hz and 3 Hz, 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-9α-carba-14α-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, CDCl₃) 0.82-2.66 (m, 16H), 3.82 (s, 3H), 6.94-7.56 (m, 3H). Anal. calcd. for C_{18}H_{22}O₂: C, 79.96; H, 8.20. Found: C, 79.96; H, 8.20.

(±)-2-Methoxy-9α-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, CDCl₃) 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 suspension of dry potassium t-pentyloxide, prepared from potassium metal (1.3 g, 29 mg-atom), in dry thiophene free benzene (30 ml) under N₂ 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 (Na₂SO₄) 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 distilling flask); homogeneous in GLC (Rₜ 5.07 min); IR (neat) 1665,1610 cm⁻¹; λₘₐₓ 246 nm (logε 4.07); ¹H NMR (200 MHz, CDCl₃) 1.10-3.03 (m, 13H), 3.56 (s, 2H), 3.70 (s, 3H), 6.40-7.06 (m, 4H). Anal. calcd. for C₁₈H₂₂O₂: C, 79.76; H, 8.20. Found: C, 80.04; H, 8.32.

Acid-catalyzed cyclizations of octalone 3b:

A : With orthophosphoric 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 (Rₜ 4.7 min): 24 (Rₜ 3.7 min): 10 (Rₜ 6.4 min): 3 (Rₛ 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 (Rₜ 6.4 min); IR (KBr) 2850,1610,1460 cm⁻¹; λₘₐₓ (EtOH) 215 (logε 4.39), 275 (logε 4.41), 305 nm (logε 3.80); ¹H NMR (100 MHz CDCl₃) 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\textsubscript{18}H\textsubscript{18}O: C, 86.36; H, 7.25. Found: C, 86.32; H, 7.30. The middle fraction, with light petroleum (4×40 ml) gave the ketone 14 (100 mg), homogeneous in GLC (R	extsubscript{t} 4.7 min); IR (neat) 1705, 1600 cm\textsuperscript{-1}; \textsuperscript{1}H NMR (200 MHz, CDCl\textsubscript{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\textsubscript{18}H\textsubscript{22}O\textsubscript{2}: C, 79.76; H, 8.20. Found: C, 79.48; H, 8.21. Further elution with light petroleum (5×15 ml) gave the ketone 15 (35 mg) m.p. 120 °C, homogeneous in GLC (R	extsubscript{t} 3.7 min); IR (KBr) 1700, 1610 cm\textsuperscript{-1}; \textsuperscript{1}H NMR (200 MHz, CDCl\textsubscript{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\textsubscript{18}H\textsubscript{22}O\textsubscript{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 over night 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\textsubscript{2}SO\textsubscript{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	extsubscript{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 lb: 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 lb, 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 three 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-benzylctalins 4b with polyphosphoric acid: The aforementioned mixture of m-methoxy-benzylctalins 4b (500 mg, 1.9 mmol) was added to a well stirred solution of polyphosphoric 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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