J. Indian Chem. Soc.,
Vol. 66, August—October 1989, pp. 673-680

Model Synthetic Studies for the Construction of 5*H*-Phenanthro[4,5-*bcd*]pyran and pyrone Systems

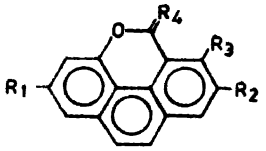
P. L. MAJUMDER* and A. K. SARKAR

Department of Chemistry, University College of Science, 92 Acharya Prafulla Chandra Road, Calcutta-700 009

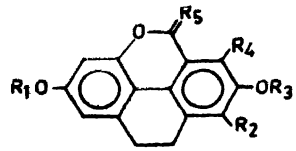
Model synthetic studies for the construction of 5*H*-phenanthro[4,5-*bcd*]pyran and pyrone skeletal systems present in a number of oxygen heterocycles isolated from a series of Indian orchids have been carried out. The synthetic route used for the purpose involved the initial construction of dibenz[*bd*]pyran and pyrone systems with an appropriately substituted suitable two-carbon handle, which on cyclisation afforded the corresponding 5*H*-phenanthro[4,5-*bcd*]pyran and pyrone in reasonably good yields. For the construction of the desired dibenz[*bd*]pyran and pyrone synthones model experiments for the synthesis of the parent dibenz[*bd*]pyran (11) and pyrone (12) have been performed. Reduction of *o*-nitrophenyl benzyl ether (8) to *o*-aminophenyl benzyl ether (9) followed by Pschorr's cyclisation of the corresponding diazonium salt 10 gave dibenz[*bd*]pyran (11) in 62% yield, which underwent facile auto-oxidation to the corresponding pyrone (12). The above synthesis of 11 and 12 provided a new general route to the synthesis of dibenzopyran and pyrone systems. For the synthesis of 5*H*-phenanthro[4,5-*bcd*]pyrans and pyrones following the above route the starting material chosen was the readily available isovanillin (13) which on crossed Cannizzaro reaction with formalin gave isovanillyl alcohol (14) Benzylation of the latter with *o*-nitrobenzyl bromide afforded the *o*-nitrobenzyl aryl ether (15) The hydroxymethyl function of the latter was modified to an acetic acid side-chain which served as the desired two-carbon handle. Treatment of 15 with $SOCl_2$ gave the corresponding chloro derivative (16) which was converted to the nitrile (17) with KCN in acetone. Treatment of 16 with ethanolic KCN, on the other hand, gave the ethyl ether (18). Acid-hydrolysis of 17 afforded the desired acid (19). Interestingly enough, attempted reduction of 19 with Zn/HCl/HOAc or even with milder reducing agent like $FeSO_4/NH_4OH$ led to the total cleavage of the benzyl ether function to give 3-hydroxy-4-methoxyphenyl-acetic acid (20) and *o*-aminobenzyl alcohol (21). On the other hand, the corresponding methyl ester (25), the alcohol (15) and the ethyl ether (18) underwent selective reduction of their nitro group to give the amino compounds 26, 22 and 23 respectively, with the intact benzyl ether function. The above unprecedented hydrolytic cleavage of the acid (19) in course of its reduction was assumed to be due to the formation of a complex of the type 24 through coordination of the benzyl ether oxygen to the metal ions (Zn^{2+} and Fe^{2+}) resulting in considerable weakening of the benzyl carbon – oxygen bond. Diazotisation of the amino methyl ester (26) followed by Pschorr's cyclisation afforded the dibenz[*bd*]pyran derivative (27a) in about 53% yield, which slowly underwent auto-oxidation to the corresponding pyrone (27b). Hydrolysis of the mixture of 27a and 27b followed by cyclisation of the resultant mixture of the corresponding acids with PPA afforded a mixture of the 5*H*-phenanthro[4,5-*bcd*]pyran 28a and pyrone 28b in the ratio of 4 : 1 in about 62% yield. Methylation of the mixture of 28a and 28b with CH_2N_2 gave a mixture of the corresponding methyl ethers 29a and 29b, which were finally separated.

SYSTEMATIC chemical investigation of a series of Indian orchids in our laboratory has resulted in the isolation of a new class of oxygen heterocycles[1-9] having the 5*H*-phenanthro[4,5-*bcd*]pyran and pyrone basic skeletal systems **1a** and **1b**, besides several other compounds of different structural types[10]. These heterocycles are represented by agrostophyllin[1] (**1c**), flaccidinin[2] (**1d**), and a number of their 9,10-dihydro analogues, viz. coelogin[3] (**2a**), coeloginin[3] (**2b**), flavidin[4] (**2c**), oxoflavidin[5] (**2d**), flavidinin[6] (**2e**), oxoflavidinin[6] (**2f**), isoflavidinin[7] (**2g**), isooxoflavidinin[7] (**2h**), imbricatin[8] (**2i**), flaccidin[9] (**2j**) and oxoflaccidin[2] (**2k**). The isolation of these heterocycles prompted us to undertake model synthetic studies for the construction of the basic tetracyclic skeletal systems **1a** and **1b** present in them. The present communication deals with the results of this investigation.

For the construction of the ring systems **1a** and **1b** the feasibility of two different general routes was considered. In one of these routes (route-a, Scheme 1) the synthetic strategy envisaged was to construct first an appropriately substituted phenanthrene like **4** with an alkyl or acyl or ester function at C-4 and a hydroxyl group at C-5 from the corresponding stilbene **3** followed by completing the heterocyclic ring D at the end. But in view of the reported failure to induce cyclisation of the stilbenes like **3** at the desired sites (2,2′) either by Pschorr's method[11] or photochemically[12] due to severe steric interaction of the substituents at 3 and 3′ positions in the transition state, this method seemed to have little general applicability for the construction of the ring systems **1a** and **1b**. In this method cyclisation occurs at the alternative sites (2,6′) through the less crowded transition state to



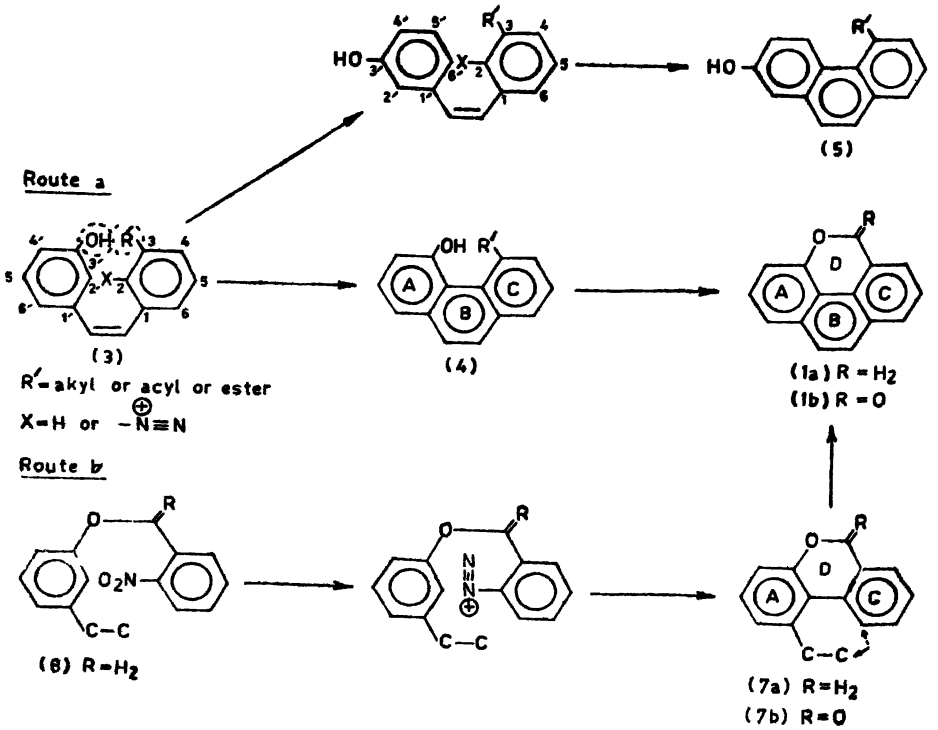
(1a) $R_1=R_2=R_3=H$, $R_4=H_2$
(1b) $R_1=R_2=R_3=H$, $R_4=O$
(1c) $R_1=R_3=OMe$, $R_2=OH$, $R_4=H_2$
(1d) $R_1=R_3=OH$, $R_2=OMe$, $R_4=O$



(2a) $R_1=H$, $R_2=OMe$, $R_3=Me$, $R_4=OH$, $R_5=H_2$
(2b) $R_1=H$, $R_2=OMe$, $R_3=Me$, $R_4=OH$, $R_5=O$
(2c) $R_1=R_2=R_3=R_4=H$, $R_5=H_2$
(2d) $R_1=R_2=R_3=R_4=H$, $R_5=O$
(2e) $R_1=R_2=R_4=H$, $R_3=Me$, $R_5=H_2$
(2f) $R_1=R_2=R_4=H$, $R_3=Me$, $R_5=O$
(2g) $R_1=Me$, $R_2=R_3=R_4=H$, $R_5=H_2$
(2h) $R_1=Me$, $R_2=R_3=R_4=H$, $R_5=O$
(2i) $R_1=R_2=R_3=H$, $R_4=OMe$, $R_5=H_2$
(2j) $R_1=R_2=H$, $R_3=Me$, $R_4=OH$, $R_5=H_2$
(2k) $R_1=R_2=H$, $R_3=Me$, $R_4=OH$, $R_5=O$

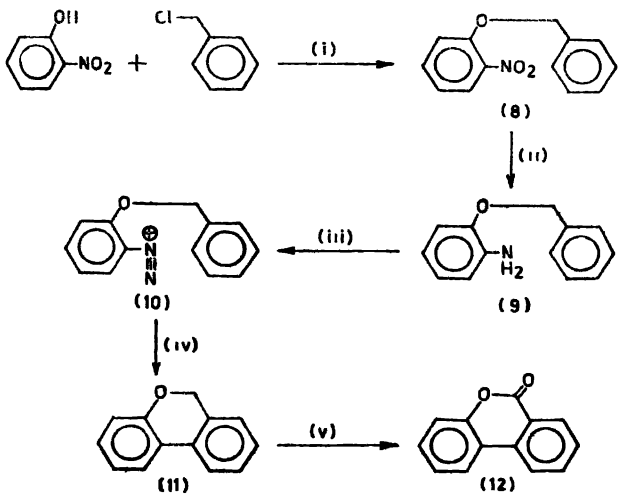
give the phenanthrenes of type **5**, although Sargent and Stanojevic[18] have recently achieved the total synthesis of coeloginin[8] (**2b**) through this route by photochemical cyclisation of 2′-iodostilbene of type **3** which, however, had no other alternative site for cyclisation. The present investigation makes use of an alternative strategy (route-b, Scheme 1) which begins with the construction of a dibenz[*bd*]pyran (**7a**) and pyrone (**7b**) system (constituting the rings A, C and D of **1a** and **1b**) having an appropriately substituted two-carbon handle from a suitable *o*-nitrobenzyl phenyl ether (**6**) through Pschorr's method followed by cyclisation of the two-carbon handle with the neighbouring phenyl ring (ring C).

The applicability of route-b (Scheme 1) for the construction of the desired dibenz[*bd*]pyran system was examined by the synthesis of the parent dibenz-[*bd*]pyran (**11**). For this purpose *o*-nitrophenol was benzylated with benzyl chloride in absolute MeOH in presence of anhydrous K_2CO_3 to give *o*-nitrophenyl benzyl ether (**8**), the pmr spectrum of



Scheme 1

which showed a two-proton singlet at δ 5.19 for the methylene protons of the benzyl phenyl ether system, and a one-proton signal at δ 7.81 (dd, J_1 8 Hz and J_2 3 Hz) for an aromatic proton *ortho* to a nitro group. Mild reduction of **8** with Zn/HCl in glacial HOAc below 5° afforded the corresponding amino compound (**9**). The pmr spectrum of the latter lacked signal for the above downfield aromatic proton and showed the signal for the oxymethylene protons at δ 5.03. Diazotisation of **9**, followed by treatment of the resultant diazonium salt (**10**) with copper powder gave dibenz[*bd*]pyran (**11**) as a thick oil in 62% yield (Scheme 2). The structure of



Reagents

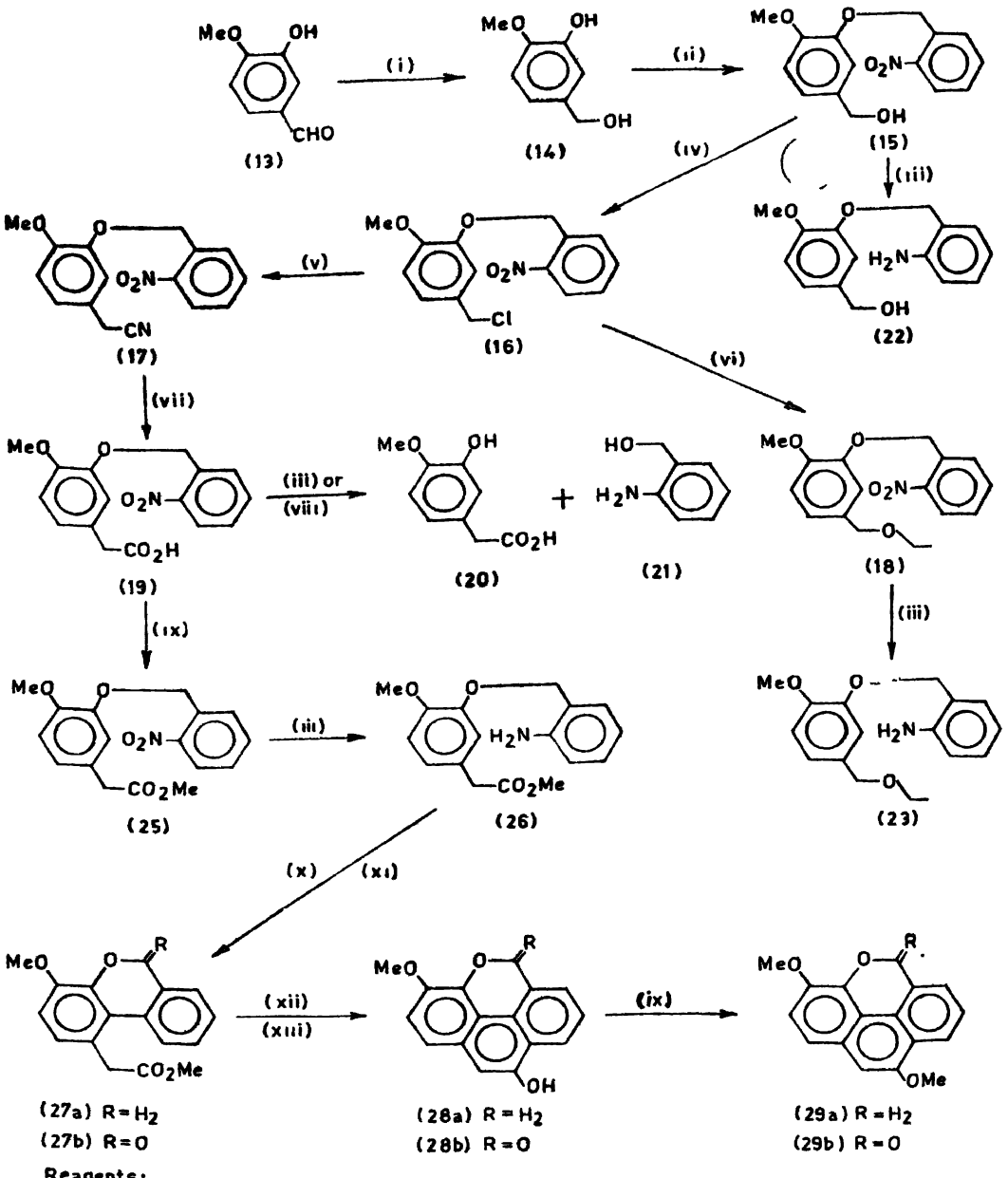
(i) MeOH/K_2CO_3 ; (ii) Zn/HCl/HOAc ; (iii) $NaNO_2$ /H_2SO_4 ; (iv) Cu powder ; (v) air

Scheme 2

the compound was authenticated by its pmr spectrum which showed a two-proton singlet at δ 5.06 for the oxymethylene protons and a multiplet at δ 6.68–7.74 for the eight aromatic protons. Interestingly enough, unlike **8**, **9** and the naturally occurring phenanthropyrans **1c**, **2a**, **2c**, **2e**, **2g**, **2i** and **2j**, the oily dibenz[*bd*]pyran (**11**) when kept in air readily changed to a crystalline mass in about a week. This was found to be a mixture of small amount of **11** and mainly an entirely different compound, m.p. 92°. The latter was shown to be the corresponding dibenz[*bd*]pyrone (**12**) from its ir and pmr spectral data. The ir spectrum of the compound showed band at 1 745 cm^{-1} characteristic of a δ-lactone. Its pmr spectrum lacked the signal at ~δ 5.0 for the methylene protons of the Ar–O–CH_2–Ar system and, instead, showed a relatively downfield signal at δ 7.94 (1H, dd, J_1 8 Hz and J_2 3 Hz) typical of an aromatic proton *ortho* to a carbonyl group. The remaining seven aromatic protons of the compound appeared as a multiplet at δ 7.35–7.49. The driving force for such facile transformation of the pyran (**11**) to the corresponding pyrone (**12**) by triplet oxygen may be attributed to the remarkable tendency of the less stable hydroaromatic dibenzopyran to aromatise to give the more stable planar dibenzopyrone system. Dibenz[*bd*]pyrone (**12**) was earlier obtained[14] in course of transformation study of an appropriately substituted nitrobiphenyl derivative in a low overall yield. The above synthesis of **11** and **12** thus provides a new general method for the construction of dibenz[*bd*]pyrans and pyrones.

From the successful synthesis of **11** and **12** following route-b (Scheme 2) it may be hopefully expected that similar system with an appropriate two-carbon handle required to build up the fourth ring (ring B) of the desired 5*H*-phenanthro[4,5-*bcd*]-pyrans and pyrones can be readily obtained from a suitable phenolic compound as the starting material. In the present model study the readily available isovanillin (**13**) (Scheme 3) was used as the starting phenolic compound. A cogent reason for this particular choice was that its aromatic methoxyl group would serve to act as a marker in pmr monitoring of the products formed in the subsequent synthetic steps, and its aldehydic function could be readily modified to the required two-carbon handle. A crossed Cannizzaro reaction of isovanillin with formalin gave isovanillyl alcohol (**14**) which was then benzylated with *o*-nitrobenzyl bromide (obtained by reacting *o*-nitrotoluene with *N*-bromosuccinimide) in absolute MeOH in presence of anhydrous K_2CO_3 to give the *o*-nitrobenzyl aryl ether (**15**) in ~87% yield. The pmr spectrum of **15** showing signals at δ 3.93 (ArOMe), 4.58 ($ArCH_2OH$), 5.54 ($ArOCH_2Ar$), 6.93–7.96 (6 aromatic protons) and 8.15 (1 aromatic proton *ortho* to a nitro group) is consistent with its assigned structure.

It is now possible to construct the dibenz[*bd*]-pyran system at this stage and then extend the aliphatic side-chain of the hydroxymethyl group by one carbon atom. But in view of the facile auto-oxidation of **11** to the corresponding pyrone (**12**) it was thought desirable to carry out the Pschorr's cyclisation at the penultimate step to minimise the oxidation of the pyran to pyrone. Keeping this point in mind, **15** was converted to the corresponding chloride (**16**) with $SOCl_2$. Treatment of the latter with KCN in presence of KI in acetone afforded the nitrile (**17**) in 81% yield. The pmr spectrum of **17** is essentially similar to that of **15**, except that the signal at δ 4.58 for $ArCH_2OH$ of the latter is shifted to δ 3.65 for $ArCH_2CN$ in the spectrum of the former. Reaction of the chloride (**16**) with ethanolic KCN, on the other hand, afforded exclusively a different compound which from its pmr spectral data was shown to be the ethyl ether derivative (**18**) of **15**. Hydrolysis of the nitrile (**17**) with aqueous H_2SO_4 (1 : 1) in glacial HOAc gave the corresponding acid **19** (82%) as evident from its pmr spectrum which is strikingly similar to that of **17** except an upfield shift of 0.11 ppm of the signal at δ 3.65 of the latter due to the change, $ArCH_2CN \rightarrow ArCH_2CO_2H$. The acetic

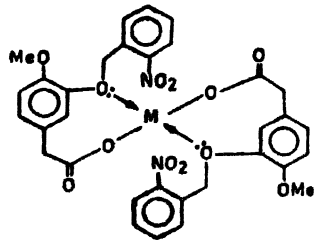


Scheme 3

acid side-chain thus constituted the desired two-carbon handle for building up the fourth ring (ring B) of the final 5*H*-phenanthropyran and pyrone skeleton. Queerly enough, treatment of the acid (**19**) with Zn/HCl/HOAc or even with milder reducing agent like $FeSO_4/NH_4OH$ resulted in the total cleavage of the benzyl ether bond to give 3-hydroxy-4-methoxyphenylacetic acid (**20**) and a basic compound which by comparison with *o*-toluidine appeared to be *o*-aminobenzyl alcohol (**21**). Although from synthetic point of view this unusual cleavage of the benzyl ether system was a

very frustrating observation, it turned out to be an interesting chemical reaction of considerable mechanistic importance. The mechanism of the above cleavage reaction was not quite apparent and became more confusing in view of the fact that *o*-nitrobenzyl phenyl ether (**8**) which is devoid of the acetic acid side-chain underwent smooth reduction of the nitro group with the complete retention of the benzyl ether system. In order to pin-point the factor responsible for this type of hydrolytic cleavage of the benzyl phenyl ether system, both the benzyl alcohol (**15**) and the ethyl ether derivative (**18**) were separately subjected to reduction with either Zn/HCl/HOAc or $FeSO_4/NH_4OH$. Interestingly enough, in either of these reductions, both **15** and **18** underwent smooth reduction to **22** and **23** respectively with intact *o*-aminobenzyl ether moiety.

The above reactions imply that the carboxyl group of the acetic acid side-chain of **19** is somehow responsible for the observed cleavage of its benzyl ether system. A plausible explanation for this unprecedented reaction of **19** may be as follows. The metal ions like Zn^{2+} and Fe^{2+} present in the above reaction media are well-known for their ability to form coordination complexes with a variety of ligands. It is quite likely that these metal ions may also form some kind of complexes involving both the carboxyl group and the benzyl ether oxygen of **19**. One possible form of such coordination complex that can account for the above reaction may be represented by the formulation **24** involving Zn^{2+} or Fe^{2+} and two molecules of **19**. The formation of this type of complex may be assumed to be based on the relative ease of formation of coordination bond between hard and soft acids and bases. While H^+ is unquestionably a hard acid, Zn^{2+} and Fe^{2+} may be regarded as soft acids, and the benzyl phenyl ether oxygen with its lone pair of electrons may be considered to be a soft base. A soft base as above would therefore be expected to form a stronger coordination bond with the soft acids like Zn^{2+} and Fe^{2+} rather than with a hard acid like H^+. The participation of the lone pair of electrons of the oxygen atom of the benzyl phenyl ether moiety in this type of coordination with the metal ions would consequently cause a considerable weakening of the benzyl oxygen bond so that the benzylic carbon atom would become more vulnerable to hydrolytic cleavage. The carboxyl group of the acetic acid side-chain presumably plays the key role in forming normal bonds with the metal ions and thus helps to orient the ether oxygen atoms for an effective intramolecular coordination with the metal ions. The hydroxy and ethoxy groups in **15** and **18** respectively being incapable of forming such normal bond with the metal ions, fail to induce formation of such complexes. As a result, **15** and **18** underwent normal reduction with no such hydrolytic cleavage. It would be interesting to study the effect of the length of the carboxylic acid chain on this type of reaction.



(24)

[M = Zn^{2+} or Fe^{2+}]

The above contention gained further credence from the fact that the methyl ester (**25**) of the acid (**19**) obtained by treatment of the latter with CH_2N_2 underwent smooth reduction to the corresponding amine **26** (77.3%) with the intact *o*-aminobenzyl ether moiety (Scheme 3). The structure of **26** was confirmed mainly by its pmr spectrum which showed the expected signals at δ 3.52 and 3.65 ($ArCH_2CO_2CH_3$), 3.79 ($ArOCH_3$), 4.05 ($ArNH_2$), 5.01 ($ArOCH_2Ar$) and 6.60–7.23 (7 aromatic protons). Diazotisation of **26** followed by Pschorr's cyclisation of the resultant diazonium salt afforded the dibenzopyran **27a** (53.1%). The structure of **27a** was confirmed by its pmr signals at δ 3.42 and 3.58 ($ArCH_2CO_2CH_3$), 3.74 ($ArOCH_3$), 5.02 ($ArOCH_2Ar$) and 6.60–7.30 (6 aromatic protons). Like the parent dibenz[*bd*]pyran (**11**), **27a** also underwent gradual auto-oxidation to the corresponding pyrone **27b** so that the starting material for the subsequent steps of hydrolysis and cyclisation was actually a mixture of **27a** and **27b** as evident from its pmr spectrum. The above mixture of **27a** and **27b** was hydrolysed in an atmosphere of nitrogen to give a mixture of the corresponding acids, which on cyclisation with polyphosphoric acid also in nitrogen atmosphere afforded in ~ 62% yield a mixture of the phenanthropyran **28a** and phenanthropyrone **28b** in the ratio of ~ 4 : 1. Because of their very close polarity, **28a** and **28b** could not be separated by conventional chromatography, but their existence was confirmed from the pmr spectrum of the mixture, which showed signals at δ 3.82 ($ArOCH_3$), 4.92 ($ArOCH_2Ar$), 5 87 (ArOH) and 6.60–7.43 (ArH) for **28a**, while a downfield signal at δ 7.58 for an aromatic proton *ortho* to a carbonyl group together with signals at δ 3.91 ($ArOCH_3$), 5.87 (ArOH) and 6.60–7.43 (ArH) indicated the presence of **28b**. Methylation of the mixture of **28a** and **28b** gave the mixture of the corresponding methyl ether derivatives **29a** and **29b**, as evident from the pmr spectrum of the mixture. They could, however, be separated by preparative tlc. It is thus possible to synthesise pure **28b** and **29b** starting from pure **27b** which can be readily obtained if **27a** is kept exposed to air for a longer period. Further work is being carried out for a possible intramolecular Friedel-Craft's alkylation of substrate of the type **27a** or **27b**, in which the $-CH_2CO_2Me$ group is replaced by $-CH_2CH_2Cl$ side-chain to give the 9,10-dihydrophenanthropyrans and pyrones.

The above synthetic studies while providing a very good method for the construction of dibenz-[*bd*]pyrans and pyrones, also formed the basis of a fairly good general method for the synthesis of the 5*H*-phenanthro[4,5-*bcd*]pyrans and pyrones as well as their corresponding 9,10-dihydro derivatives.

Experimental

Melting points were determined in Köfler block and are uncorrected. Ir spectra were run in KBr disc and pmr spectra in a Varian CFT-20 instrument (80 MHz) using TMS as the internal standard. Silica gel (60–120 mesh) was used for column chromatography and silica gel G for tlc. All analytical samples were routinely dried over P_2O_5 under reduced pressure for 24 h. Anhydrous Na_2SO_4 was used for drying organic solvents. Petrol used had b.p. 60–80°.

o-*Nitrophenyl benzyl ether* (**8**) *:* A mixture of *o*-nitrophenol (1.4 g), benzyl chloride (1.2 ml), finely powdered anhydrous K_2CO_3 (0.7 g) and absolute MeOH (10 ml) was refluxed for 5 h. The solution was then filtered to remove K_2CO_3, and MeOH was removed from the filtrate under reduced pressure. The oily residue was treated with water (25 ml) and then extracted with ether. The ether extract was washed twice with 2*N* NaOH solution and then with water. It was dried and removal of solvent left an oily residue which was chromatographed to give pure **8** (1.9 g) as a pale yellow liquid ; δ 5.19 (2H, s, ArOCH_2Ar), 7.81 (1H, dd, J_1 8 Hz and J_2 3 Hz, ArH *ortho* to NO_2 group) and 6.88–7.58 (8H, m, ArH).

o-*Aminophenyl benzyl ether* (**9**) *:* To a stirred mixture of *o*-nitrophenyl benzyl ether (**8** ; 1.5 g), concentrated HCl (35 ml), glacial HOAc (100 ml) and water (25 ml) was added zinc powder[15] (2 g) in small portions at a temperature below 5°. The reaction mixture was then left over for 5 h at the same temperature in stirring condition. Unreacted zinc was then filtered off and the filtrate was washed with $CHCl_3$ and then neutralised with ammonia in the cold. The separated oily layer was extracted with $CHCl_3$, washed with saturated sodium chloride solution, dried and the solvent removed The brown viscous syrupy residue was chromatographed to give pure **9** (1 g, 76.9%) as a light brown semi-solid ; δ 3.65 (2H, s, disappeared on deuterium exchange, NH_2), 5 03 (2H, s, ArOCH_2Ar), 6.65–6.92 (4H, m, protons of the aromatic ring bearing the amino group) and 7.36 (5H, s, protons of the other phenyl ring).

*Dibenz[*bd*]pyran* (**11**) *and dibenz[*bd*]pyrone* (**12**) *:* A solution of $NaNO_2$ (0.5 g) in water (10 ml) was added dropwise to a stirred solution of *o*-aminophenyl benzyl ether (**9** ; 0.9 g) in 0.5 *N* H_2SO_4 (70 ml) kept below 0°. To this diazotised solution was added Gattermann copper powder[16] when nitrogen evolved. The mixture was then left overnight. For the completion of the reaction the mixture was then warmed on a water-bath until it showed negative colour reaction with alkaline β-naphthol. It was then filtered and washed with $CHCl_3$. The combined filtrate was then extracted with $CHCl_3$, washed with saturated NaCl solution, dried, concentrated and chromatographed to give pure **11** (0.51 g, 62%) as a colourless oil (Found: C, 85.61 ; H, 5.62. $C_{13}H_{10}O$ requires : C, 85.71; H, 5.49%) ; δ 5.06 (2H, s, ArOCH_2Ar) and 6.68–7.74 (8H, m, ArH).

On keeping the above oily product (**11**) in a desiccator for about a week it changed into a crystalline mass which from its tlc was found to be a mixture of mainly **12** and a small amount of **11**. The mass was chromatographed when pure **12** was obtained. It crystallised from petrol–EtOAc, m.p. 92° (lit.[14] 92.5°) (Found : C, 79.72 ; H, 4.01. $C_{13}H_8O_2$ requires : C, 79.59 ; H, 4.08%) ; ν_{max} 1 745 cm^{-1} (δ-lactone) ; δ 7.94 (1H, dd, J_1 8 Hz and J_2 3 Hz, aromatic proton *ortho* to lactone C=O) and 7.35–7.49 (7H, m, ArH).

o-*Nitrobenzyl bromide :* To freshly purified[17] *N*-bromosuccinimide (18 g) and CCl_4 (150 ml) was added *o*-nitrotoluene (14 g) and the mixture was refluxed after irradiating the solution with uv light[18]. The reaction appeared to be completed in less than 2 h. However, the reaction was continued for another 1 h to ensure completion. After cooling the insoluble succinimide was filtered off, and the filtrate after careful removal of CCl_4 gave a residue which was chromatographed to give pure *o*-nitrobenzyl bromide (17.5 g, 77%), m.p. 45°.

o-*Nitrobenzyl derivative of isovanillyl alcohol* (**15**) *:* A mixture of isovanillyl alcohol (**14**; 8 g) (prepared by crossed Cannizzaro reaction with formalin in the usual manner), *o*-nitrobenzyl bromide (12 g), finely powdered anhydrous K_2CO_3 (4 g) and absolute MeOH (25 ml) was refluxed for 5 h. After cooling, the solution was filtered to remove K_2CO_3. MeOH was removed from the filtrate under reduced pressure. The viscous residue was then treated with 2*N* NaOH solution and the whole mass extracted with ether, washed and dried. After removal of solvent the crude product was crystallised from petrol–EtOAc to give pure **15** (13 g, 86.6%), m.p. 75° ; δ 3.93 (3H, s, ArOCH_3), 4 58 (2H, br s, ArCH_2OH), 5.54 (2H, s, ArOCH_2Ar), 6.93–7.96 (6H, m, ArH) and 8.15 (1H, dd, J_1 8 Hz and J_2 3 Hz, ArH *ortho* to NO_2 group).

*4-Methoxy-3-(*o*-nitrobenzyloxy)benzyl chloride* (**16**) *:* A cold solution of pure $SOCl_2$ (4.1 g) in dry benzene[19] (15 ml) was added slowly to a stirred chilled solution of **15** (10 g) and *N*,*N*-dimethylaniline (4.2 g) in dry benzene (70 ml) in an ice-bath. The stirred reaction mixture was slowly brought to room temperature and then refluxed for 1 h. It was then cooled and washed with 2*N* HCl solution (20 ml). The benzene layer containing the product was freed from acid by successive washing with $NaHCO_3$ and water, dried and the solvent removed to give **16**

(9.5 g, 85%) which was crystallised from petrol–EtOAc, m.p. 104–05°.

4-Methoxy-3-(o-nitrobenzyloxy)benzyl cyanide (**17**) : A mixture of **16** (7 g), finely powdered KCN (2.5 g) and KI (0.4 g) in dry acetone (40 ml) was refluxed with vigorous stirring for 20 h. The reaction mixture was then cooled, filtered and washed with acetone. The combined filtrate was evaporated under reduced pressure to remove acetone. The residue was then taken up in $CHCl_3$, washed with water and dried. The $CHCl_3$ solution on concentration afforded yellow crystals of **17** (5.5 g, 81%), m.p. 145° ; ν_{max} 2 310 (CN) ; δ 3.65 (2H, s, $ArCH_2CN$), 3.90 (3H, s, $ArOCH_3$), 5.53 (2H, s, $ArOCH_2Ar$), 6.84–7.91 (6H, m, ArH) and 8.15 (1H, dd, J_1 8 Hz and J_2 2 Hz, ArH *ortho* to NO_2 group).

4-Methoxy-3-(o-nitrobenzyloxy)benzyl ethyl ether (**18**) : A mixture of **16** (0.5 g), KCN (2 g) in EtOH (15 ml) and water (4 ml) was refluxed for 3 h. The solution was then poured in ice, extracted with Et_2O, washed, dried and the solvent removed. The residue was chromatographed to give **18** (0.5 g, 97%) ; δ 1.19 (3H, t, *J* 7 Hz, CH_3CH_2O), 3.48 (2H, q, *J* 7 Hz, $MeCH_2O$), 3.89 (3H, s, $ArOCH_3$), 4.39 (2H, s, $ArCH_2OR$), 5.54 ($ArOCH_2Ar$), 6.91 (3H, s, ArH), 7.35–8.0 (2H, m, ArH) and 8.15 (1H, dd, J_1 8 Hz and J_2 2 Hz, ArH *ortho* to NO_2 group).

4-Methoxy-3-(o-nitrobenzyloxy)phenylacetic acid (**19**) : A solution of **17** (5 g) in glacial HOAc was refluxed with aqueous H_2SO_4 (1 : 1 ; 30 ml) for 1 h. The reaction mixture was then poured in crushed ice (100 g). The resulting white solid was washed with a little cold water. The solid was taken in $CHCl_3$ and the $CHCl_3$ solution was extracted with aqueous $NaHCO_3$ to remove the unreacted nitrile. The aqueous bicarbonate extract was neutralised with concentrated HCl in the cold. The liberated white solid was filtered, washed with cold water and crystallised from MeOH to give pure **19** (4.6 g, 82%), m.p. 141° ; δ 3.54 (2H, s, $ArCH_2CO_2H$), 3.88 (3H, s, $ArOCH_3$), 5.52 (2H, s, $ArOCH_2Ar$), 6.87 (3H, s, ArH), 7.35–8.01 (2H, m, ArH) and 8.14 (1H, dd, J_1 8 Hz and J_2 2 Hz, ArH *ortho* to NO_2 group).

Reduction of 4-methoxy-3-(o-nitrobenzyloxy)phenyl acetic acid (**19**) *with Zn/HCl/glacial HOAc* : To a stirred mixture of **19** (0.5 g), concentrated HCl (10 ml), glacial HOAc (30 ml) and water (8 ml) was slowly added powdered zinc (5 g) at a temperature below 5°. The reaction mixture was then stirred for 5 h at the same temperature. It was then filtered and the residue washed with hot $CHCl_3$. The filtrate after addition of sufficient NH_4Cl was basified with NH_4OH in the cold and extracted with $CHCl_3$, and the extract washed, dried and the solvent removed. The gummy residue showed mostly a single iodine staining spot in tlc plate and was found to be different from *o*-toluidine. It was assumed to be *o*-aminobenzyl alcohol (**21**).

The aqueous ammoniacal solution after removal of **21** was then acidified with concentrated HCl in the cold and the resulting solid was extracted with $CHCl_3$, washed with ice-cold water, dried and the solvent removed. The residue was chromatographed to give 3-hydroxy-4-methoxy-phenylacetic acid (**20** ; 0.23 g), which was crystallised from petrol–EtOAc, m.p. 130° ; δ 3.53 (2H, s, $ArCH_2CO_2H$), 3.86 (3H, s, $ArOCH_3$), 6.77 (2H, s, ArH) and 6.86 (1H, s, ArH).

Reduction of 4-methoxy-3-(o-nitrobenzyloxy)-phenylacetic acid (**19**) *with* $FeSO_4/NH_4OH$: A solution of **19** (1 g) in 5*N* NH_4OH (10 ml) was added to a slurry of $FeSO_4$ (7 g) in water (10 ml) and liquor ammonia (18 ml) at 80–90°. After 1 h the product was filtered through a celite bed and the resulting black precipitate was washed with a little 5*N* NH_4OH solution. The filtrate was acidified with concentrated HCl in the cold and the liberated solid was extracted with ether, washed with ice-cold water, dried and the solvent removed. The residue was chromatographed to give **20** (0.5 g).

Reduction of 4-methoxy-3-(o-nitrobenzyloxy)benzyl alcohol (**15**) *and its ethyl ether* (**18**) *with Zn/HCl/HOAc and* $FeSO_4/NH_4OH$: Both **15** and **18** were separately reduced with Zn/HCl/HOAc as well as with $FeSO_4/NH_4OH$ as described above to give, in each case, **22** and **23** respectively (both as semi-solid mass) in about 76% yield. **22** : δ 3.77 (2H, br s, NH_2), 3.77 (3H, s, $ArOCH_3$), 4.49 (2H, s, $ArCH_2OH$), 4.97 (2H, s, $ArOCH_2Ar$) and 6.59–7.18 (7H, m, Ar*H*) ; **23** : δ 1.21 (3H, t, *J* 7 Hz, CH_3CH_2O), 3.48 (2H, q, *J* 7 Hz, CH_3CH_2O), 3.82 (3H, s, $ArOCH_3$), 4.41 (2H, s, $ArCH_2OR$), 5.04 (2H, s, $ArOCH_2Ar$) and 6.62–7.24 (7H, m, ArH).

Methyl ester of 4-methoxy-3-(o-nitrobenzyloxy)-phenylacetic acid (**25**) *and its reduction to the amino derivative* (**26**) *with Zn/HCl/HOAc* : 4-Methoxy-3-(*o*-nitrobenzyloxy)phenylacetic acid dissolved in MeOH was methylated with an etherial solution of CH_2N_2 in the usual manner to give **25**, crystallised from MeOH, m.p. 80°. **25** (2 g) was reduced with Zn dust (20 g) in concentrated HCl (40 ml), HOAc (125 ml) and water (30 ml) by exactly the same manner as described earlier. The product worked up in the usual manner was chromatographed to give pure **26** (77.3%) ; δ 3.52 (2H, s, $ArCH_2CO_2CH_3$), 3.65 (3H, s, CO_2CH_3), 3.79 (3H, s, $ArOCH_3$), 4.05 (2H, s, $ArNH_2$), 5.01 (2H, s, $ArOCH_2Ar$) and 6.60–7.23 (7H, m, ArH).

Pschorr type cyclisation of **26** *to the dibenz[bd]-pyran derivative* (**27a**) *and its conversion to the pyrone* (**27b**) : To a stirred solution of the methyl ester (**26** ; 1 g) in 0 5 *N* H_2SO_4 (75 ml) kept below 0°, was added dropwise a solution of $NaNO_2$ (0.5 g) in water (8 ml). Copper powder was then added to the solution and the mixture left overnight. It was then warmed on a water-bath and extracted with $CHCl_3$, washed with water, dried and the solvent removed. Rapid chromatography of the residue gave **27a** (0.5 g, 53.1%), as an oily mass ; δ 3.42 (2H, s, $ArCH_2CO_2CH_3$), 3.58 (3H, s, CO_2CH_3), 3.74 (3H, s, $ArOCH_3$), 5.02 (2H, s, $ArOCH_2Ar$) and 6.62–7.16 (6H, m, ArH).

When kept exposed to air, **27a** was slowly oxidised to the corresponding pyrone **27b** which was separated by chromatography ; δ 3.46 (2H, s, $ArCH_2CO_2CH_3$), 3.58 (3H, s, CO_2CH_3), 3.79 (3H, s, $ArOCH_3$), 6.80–7.16 (5H, m, ArH) and 7.56 (1H, br, ill-resolved, ArH *ortho* to lactone C=O).

5H-Phenanthropyran (**28a**) *and pyrone* (**28b**) *and their methyl ethers* (**29a** *and* **29b**) *:* The mixture of the methyl esters of the dibenzo-pyran **27a** and pyrone **27b** (1 g) was hydrolysed with 25% aqueous ethanolic NaOH (10 ml) on a boiling water-bath for 1 h in an atmosphere of nitrogen. MeOH was then removed under reduced pressure and the residue neutralised with concentrated HCl in the cold. The liberated crude acids were filtered, dried and then heated with polyphosphoric acid (5 g) on a steam-bath for a few minutes with constant stirring. The reaction mixture was cooled and poured in ice-water, extracted with ether, washed successively with dilute $NaHCO_3$ and water, dried and the solvent removed. The residue (0.55 g, 62.5% ; assuming the starting material to be only **27a** and the final product only **28a**) contained a mixture of **28a** and **28b** in a ratio of ~4 : 1, which could not be separated by conventional column chromatography ; the mixture of **28a** and **28b** : δ 3.82 (s, $ArOCH_3$ of **28a**), 3.91 (s, $ArOCH_3$ of **28b**), 4.92 (s, $ArOCH_2Ar$ of **28a**), 5.87 (br s, ArOH of both **28a** and **28b**), 6.60–7.43 (m, ArH of both **28a** and **28b**) and 7.54 (dd, ill-resolved, ArH *ortho* to lactone C=O of **28b**).

The mixture of **28a** and **28b** in MeOH was methylated with an ethereal solution of CH_2N_2 in the usual manner to give a mixture of **29a** and **29b** ; the mixture : δ 3.65, 3.82 and 3.88 (each s, $ArOCH_3$), 4.92 (s, $ArOCH_2Ar$ of **29a**), 6.73–7.25 (m, ArH) and 7.58 (dd, ill-resolved, ArH *ortho* to lactone C=O of **29b**). **29a** and **29b** were separated in small amounts by preparative tlc.

Acknowledgement

The authors thank C. S. I. R., New Delhi, for financial assistance.

References

1. P. L. Majumder and E. Sabzabadi, *Phytochemistry*, 1988, **27**, 1899.
2. P. L. Majumder and D. C. Maiti, *Phytochemistry*, 1989, **28**, 887.
3. P L Majumder, D Bandyopadyay and S Joardar *J Chem Soc, Pekkin Trans 1*, 1982, 1131
4. P L Majumder, N Datta, A K Sarkar and J Chakraborti, *J Nat Prod*, 1982, **45**, 730
5. P L Majumder and N Datta, *Phytochemistry* 1984 **23**, 671
6. P L Majumder and N Datta, *Indian J Chem Sect B* 1982, **21**, 534
7. P L Majumder, A K Sarkar and J Chakraborti *Phytochemistry*, 1982, **21**, 2713
8. P L Majumder and A K Sarkar, *Indian J Chem Sect B* 1982, **21**, 829
9. P L Majumder and D C Maiti, *Phytochemistry*, 1988 **27**, 899
10. P. L Majumder and S Lahiri *Indian J. Chem Sect B*, 1989, **28**, 771 , *Phytochemistry*, 1989 28, 000 , P L Majumder and M Joardar *Indian J. Chem., Sect B*, 1984 **23**, 1040 , 1985, **24**, 1192 , P L Majumder and R C Sen, *Phytochemistry*, 1987, **26**, 2121 , *Indian J. Chem., Sect B*, 1987, **26**, 18 ; P L Majumder and S Chatterjee *Phytochemistry* 1989, **28**, 1986 S R Bhandari, A H Kapadi, P L Majumder, M Joardar and J. N. Shoolery, *Phytochemistry*, 1985 **24**, 801 , P L Majumder, A Kar and J N Shoolery, *Phytochemistry*, 1985, **24**, 2083 P L Majumder and A Kar, *Phytochemistry*, 1987 **26** 1127 , 1989, **28**, 1487 ; P L Majumder and S Banerjee *Phytochemistry*, 1988, **27**, 245 , *Tetrahedron* 1988, **44**, 7303 , *Indian J. Chem.*, in press P L Majumder, A. Pal and M. Joardar *Phytochemistry* 1989, **28**, 000 , P L Majumder, S. Laha and N Datta, *Phytochemistry*, 1982, **21**, 478 , P L Majumder and M Basak, *Phytochemistry*, 1989 **28**, 000 , P L Majumder and J Chakraborti, *Tetrahedron*, 1985, **41**, 4973 *J. Indian Chem Soc.*, 1989 **66** 834 , P L Majumder and A Pal, *Phytochemistry* 1985, **24**, 2120 , P L Majumder, A Pal and S Lahiri, *Indian J. Chem , Sect. B*, 1987, **26**, 297
11. E Hardegger, M Schellenbaum and H Corrodi *Helv Chim Acta*, 1963, **46**, 1171
12. R M Letcher and L R M Nhamo, *J. Chem. Soc Perkin Trans 1*, 1973, 1263
13. M. V Sargent and E Stanojevic, *J Chem Soc, Perkin Trans. 1*, 1984, 1919
14. I Heilborn and H M Bunburry, ' Dictionary of Organic Compounds", Eyre and Spottiswoode, London, 1953, Vol 2, p 758
15. T Kametani R Charubala, M Ihara, M Koizumi and K Fukomoto, *J. Chem. Soc. (C)*, 1971, 3315
16. R. M. Elovson and F F Gadallah, *J. Org. Chem* 1971, **36**, 1769
17. K B Wiberg and L H Slangh, *J. Am. Chem Soc* 1959, **81**, 4871
18. K. B Wiberg and L H Slangh, *J Am Chem. Soc* 1958, **80**, 3034
19. N. L. Drake and W B Tuhmmler, *J Am. Chem. Soc* 1955, **77**, 1204