The synthesis of phenolic propane-1, 2- and 1, 3-diols as intermediates in immobilised chelatants for the borate anion[1]

John H.P. Tyman* and P.B. Payne

Department of Chemistry, Brunel University, Uxbridge, Middlesex UB8 3PH, UK

The isomeric 3-(hydroxyphenyl)propane-1, 2-diols have been synthesised from allylic precursors by epoxidation and cleavage. Several different methods have been examined for obtaining 1-(methoxyphenyl)propane-1, 3-diols. 2-(methoxyphenyl)propane-1, 3-diols and certain hydroxy analogues have been obtained from benzaldoximes converted by oxidation to methoxy- and benzyloxynitromethylbenzenes followed by hydroxymethylation with formaldehyde and catalytic hydrogenation.

Keywords: 3-(hydroxyphenyl)propane-1, 2-diols, 1-(methoxyphenyl)propane-1, 3-diols, 2-(methoxyphenyl)- and 2-(hydroxyphenyl)propane-1, 3-diols.

The interaction between boric acid and polyhydroxy compounds has been recognised since the classical work on the structure of the glucoses[2] and later, that boric acid can form anionic complexes with a resulting increase in acidity.[3] More recently experimental work has involved interest in the solvent extraction of borate complexes by monohydric[4] and lipidic, 3-diols,[5-7] notably from natural water resources. However, the impact of green chemistry, the desirability of elimination of organic solvents and their replacement by aqueous systems has encouraged development of immobilised chelatants for operation in aqueous conditions. Advances in this area have involved complexation of metal ions[8,9] and applications in water technology.[10–12] To our knowledge, this approach has not been used hitherto with the borate anion. In this present work, [13]the synthesis of phenolic-1, 2- and methoxy and phenolic 1, 3-alkane diols is described. The phenolic hydroxyl group in these compounds, bearing substituent mono-1,2- and 1,3-dihydroxyalkyl groups has enabled their conversion to phenol/formaldehyde polymers in work described separately.

Additionally, this present study afforded an opportunity to determine stability constants of the borate complexes of the parent diol monomers. In particular, the role of their progressive conformational mobility from the non-flexible aromatic diols (for example, catechol), 2-hydroxybenzyl alcohols (saligenins, with one flexible OH), to 1, 2 and 1, 3-alkylphenolic diols (with two flexible bonds) has been studied. The work on polymeric diols will be described elsewhere.

The syntheses of the three isomeric 3-(*n*-hydroxyphenyl)propane-1, 2-diols is depicted in Scheme 1 (a, b and c) from the isomeric allylphenols.

In Scheme 2, the preparation of 1-(2-methoxyphenyl) propane-1, 3-diol by the reduction of 2-methoxycinnamaldehyde is shown.

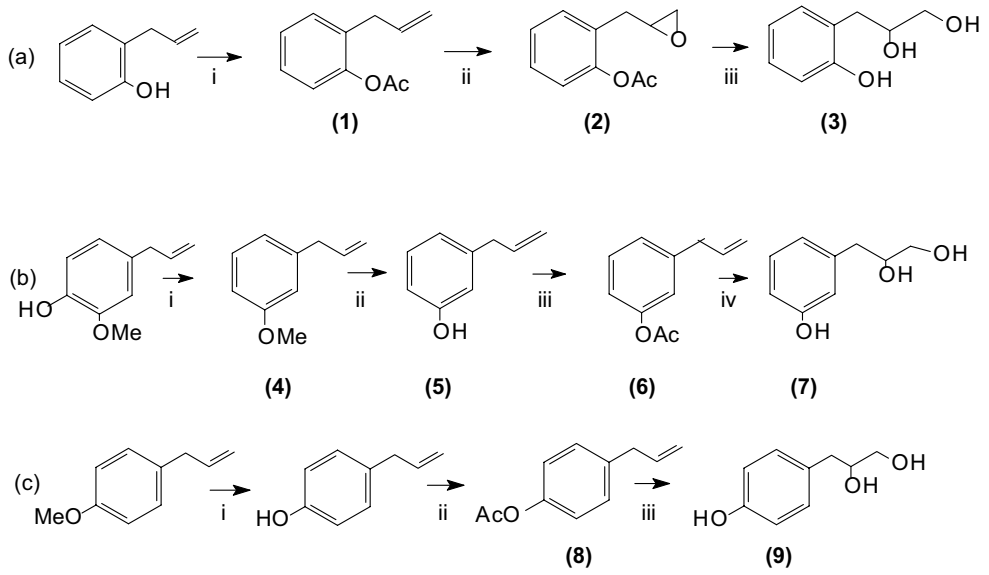
Scheme 3 illustrates the preparation of 2-(4-methoxyphenyl)propane-1, 3-diol from the ethoxycarbonylation of ethyl 4-methoxyphenylacetate and by carboxylation of 4-methoxyphenylacetic acid, with reduction of the resultant diacid. Scheme 4 (a, b and c) gives the preferred route from isomeric benzaldoximes, for syntheses of (a) 2-(4-methoxyphenyl)-propane-1, 3-diol, (b) the 2-methoxy and (c) the 4-hydroxyanalogues, by oxidation, reaction with formaldehyde and reduction.

Experimental

Materials: Chemicals were obtained from Aldrich Chemical Co. All solvents for anhydrous reactions of phenols were dried.

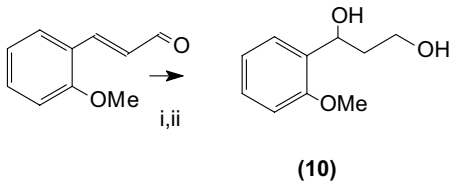
Chromatography: TLC was carried out with silica gel 60A precoated glass plates and visualisations with iodine or under UV light. Column and flash chromatography were carried out on Merck kieselgel 60 (230-400 mesh, ASTM.) and dry flash chromatography on Kieselgel 60H and 60GF.

Spectroscopy: Infrared spectra were recorded on a Perkin Elmer 1420 instrument as KBr discs or as films for liquids. Proton NMR



Scheme 1 (a,b,c) Reagents: (a) (i) Ac_2O, py.,(ii) m-$ClC_6H_4CO_3H$, (iii) NaOH; HCl. (b), (i) NEt_3, $(EtO)_2P(O)H$,NH_3; EtOH, Na, (ii) 2,4,6-Me_3Py,LiI, (iii)Ac_{2O},py, (iv) 30%H_2O_2,HCO_2H; NaOH.(c) Ac_2O, py., (ii) H_2O_2, HCO_2H; NaOH.

* Correspondent. E-mail: jhptyman@hotmail.com



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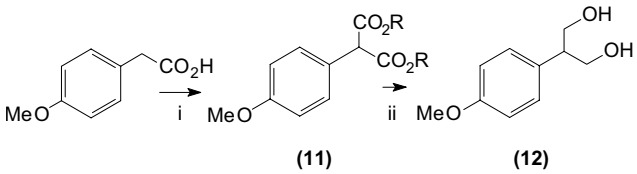
Scheme 2 Reagents: (i) LiH, $(Et)_3B$, (ii) $LiBEt_3H$; $MeSO_3H$, (ii) H_2O_2, NaOH.



(11) **(12)**

Scheme 3 Reagents: (a) (i) nBuLi, CO_2; HCl, (ii) B_2H_6 (R = H). (b) (i) $MeOC_6H_4CO_2Et$, $NaOEt$, $(CO_2Et)_2$; -CO.

spectra were performed on a Varian CFT-20 or a Jeol JNM-FX200 in deuterated solvents with tetramethylsilane as internal standard. Mass spectra were recorded on a modified MS 902 AEI instrument and accurate mass measurements by University of Wales, Swansea, Mass Spectroscopy Centre.

Microanalyses were carried out by Butterrworth Laboratories Ltd, and by Medac Ltd., on a Control Equipment Corporation Model 240 XA and Carlo Erba 1106.

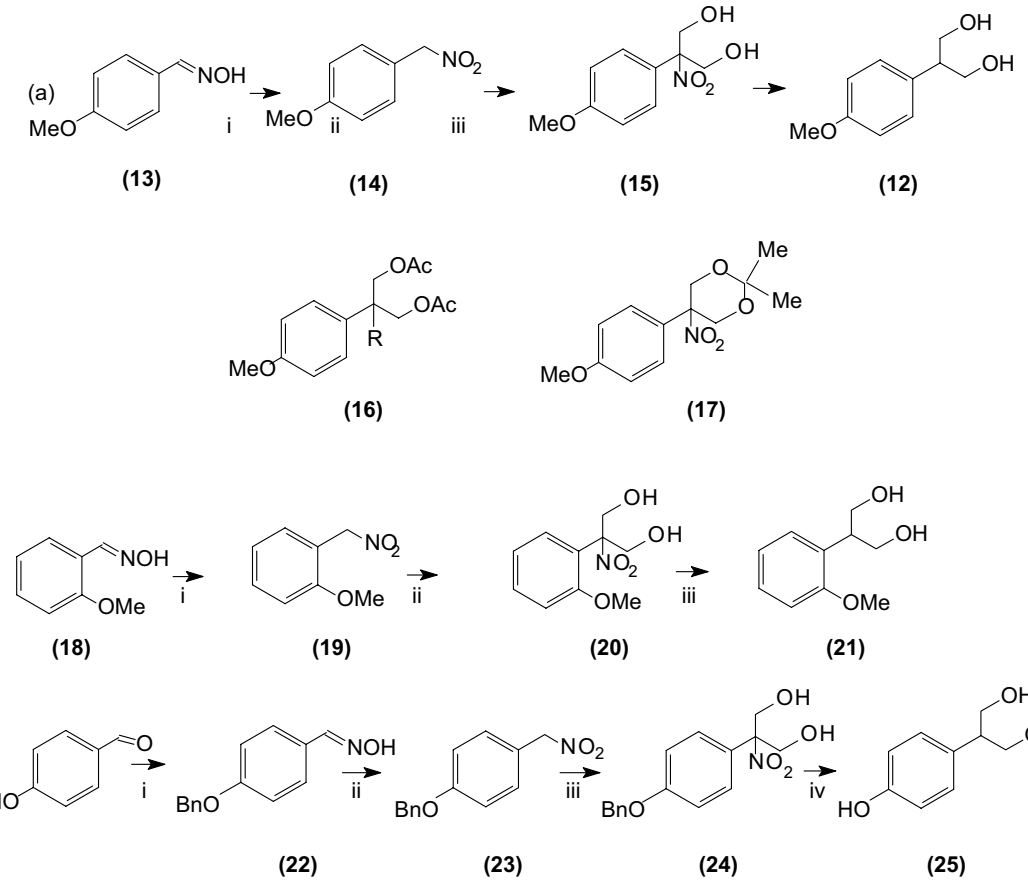
Synthesis of 3-(n-hydroxyphenyl)propane-1, 2-diols 3-(2-hydroxyphenyl)propane-1, 2-diol **(3)** *2-allylphenyl acetate* **(1)**: 2-Allylphenol (20.0 g, 149 mmol), acetic anhydride (140 cm^3, 1.13 mol) and pyridine (280 cm^3) were reacted at 100°C for 2 h. The cooled mixture was diluted with iced water, acidified and extracted to yield the acetate (26.3 g; 92%), R_f 0.73 (chloroform/ethyl acetate, 98 : 2); (Found: C, 74.93; H, 6.90. Cald, for $C_{11}H_{12}O_2$, C, 74.98; H, 6.86%); ν_{max} (cm^{-1}, film), 1760 (C=O); δ_H ($CDCl_3$) 2.26 (3H, s, Me), 3.28 (2H, d, *J* 6.6 Hz, CH_2Ar), 5.10 (2H, m, $=CH_2$), 6.01–5.38 (1H, m, =CH), 7.21–6.99 (4H, m, HAr); *m/z*: M^+, 176.1. Cald. for $C_{11}H_{12}O_2$, 176.1.

1-Acetoxy-2-(2, 3-epoxypropyl)benzene **(2)**: 2-Allylphenyl acetate (25 g, 142 mM) and 85% m-chloroperbenzoic acid (32 g, 158 mM), in dichloromethane (100 cm^3) were stirred at ambient temperature for 18 h. Excess peracid was removed with aqueous sodium sulfite and worked-up to give the epoxide (19.8g, 73%), b.p. 102°C/0.3 mmHg; R_f 0.55; Found: C, 68.86; H, 6.40. Reqd. for $C_{11}H_{12}O_3$, C, 68.74; H, 6.29%; ν_{max} (cm^{-1}, film), 1750(C=O), 1254 (C–O, epoxide); δ_H ($CDCl_3$), 2.55–2.44 (1H, m, H-epoxy), 2, 76–2.69 (1H, m, H-epoxy), 2.80 (2H, d, *J* = 6.2 Hz, CH_2Ar), 3.03 (1H, m, –$OCHCH_2Ar$), 7.26–7.06 (4H, m, HAr); *m/z*, M^+ 192.1. Reqd. for $C_{11}H_{12}O_3$ 192.2.

3-(2-Hydroxyphenyl)propane-1, 2-diol **(3)**: 1-Acetoxy-2-(2, 3-epoxypropyl)-benzene (18.0 g, 93.8 mM) and 50% (w/w)aqueous sodium hydroxide (75 cm^3, 938 mM) were heated for 30 min, cooled and acidified with 3M HCl to pH1. Work-up gave (11.0 g, 70%), distilled, b.p. 180°C/1.2 mmHg: R_f 0.53 (ethyl acetate/light petroleum, 75 : 25); Found: C, 64.08; H, 7.26, Reqd. for $C_9H_{12}O_3$, C, 64.27; H, 7.19%; ν_{max} (cm^{-1}, film), 3400 (OH); δ_H $(CD_3)_2CO$, 2.80 (2H, d, *J* = 6.4 Hz, CH_2Ar), 3.50 (2H, m, HOCH-CH), 3.96–3.81 (1H, m, $HOCHCH_2$), 7.39–6.64 (4H, m, HAr), 8.62 (1H, s, OH, exch.); *m/z*. M^+ 168.1. Reqd. for $C_9H_{12}O_3$ 168.2.

3-(3-Hydroxyphenyl)propane-1, 2-diol **(7)***: 3-Allylanisole* **(4)**: 3-Methoxyphenylmagnesium bromide with allyl iodide gave a 20% yield of 3-alylanisole and an improved preparation of 3-allylanisole was used from eugenol (3-methoxy-4-allylphenol).

To a stirred ice-cold solution of eugenol (25 g, 156 mM) in carbon tetrachloride (40 cm^3), triethylamine (21 cm^3, 156 mM) and diethyl phosphite (22 cm^3, 169 mM) were added. The mixture was diluted with water, extracted with chloroform, and the extract washed with M sodium hydroxide, water and dried to give the diethylphosphate (44.0 g, 96%), R_f 0.38; (Found: C, 56; 18; H, 7.22. Reqd. for $C_{14}H_{21}PO_5$, C, 56.00; H, 7.05%; ν_{max} (cm^{-1}, film) 1260 (P-O); δ_H ($CDCl_3$), 1.31 (6H, t, *J* = 14.3 Hz, $2(\underline{CH_3}CH_2)$, 3.30 (2H, d, *J* = 6.3 Hz, $Ar\underline{CH_2}CH$), 3.80 (3H, s, OMe), 4.00–4.42 [4H, m,



Scheme 4 (a,b,c) Reagents: (a) (i) $MeCO_3H$, NaOAc, (ii) CH_2O, $NaCO_3$ (iii) EtOH, Pd-C, H_2.(b).(i) $MeCO_3H$, NaOAc, (ii) CH_2O, $NaCO_3$ (iii) EtOH, Pd-C, H_2.(c) (i) BnCl, K_2CO_3; $(NH_2OH)_2SO_4$, NaOH, (ii) $MeCO_3H$, NaOAc (iii) CH_2O, $NaCO_3$,(iv) EtOH, Pd-C, H_2

2(OCH_2CH_3)], 5.01 (2H, d, J = 12.1 Hz, $\underline{CH_2}$=CH), 6.07 (1H, m, CH_2=CH), 6.58–7.21 (3H, m, HAr); *m/z*, M^+, 300, 1. Reqd, for $C_{14}H_{21}PO_5$, 300.3. To stirred eugenol diethyl phosphate (40.0 g, 133 mM) in liquid ammonia (300 cm^3) and ethanol (40 cm^3), sodium (6.5 g, 282 mM) was added over 10 min. After evaporation of the ammonia, work-up gave an oil (18.0 g, 91%), R_f 0.94; δ_H ($CDCl_3$) 3.35 (2H, d, J = 6 Hz, Ar$\underline{CH_2}$CH), 3.76 (3H, s, MeO), 5.03 (2H, d, J = 14.3 Hz, $\underline{CH_2}$=CH), 5.69–6.11 (1H, m, $\underline{CH}$=CH_2), 6.69–7.27 (4H, m, HAr); *m/z*, M^+ 148.1. Reqd. for $C_{10}H_{12}O$, 148.2.

3-Allylphenol (**5**): A mixture of 3-allylanisole (10.0 g, 67 mM), 2, 4, 6-collidine (55 cm^3) and lithium iodide (23.6 g, 176 mM) was refluxed under nitrogen for 22 h. Work-up by acidification and extraction gave the phenol (3.2 g, 35%), R_f 0.34; ν_{max} (cm^{-1}, film), 3600 (OH); δ_H ($CDCl_3$), 3.29 (2H, d, J = 6.6 Hz, Ar$\underline{CH_2}$=CH), 4.98 (2H, m, $\underline{CH_2}$=CH), 5.69–6.19 (1H, m, $\underline{CH}$=CH_2), 6.68–7.09 (4H, m HAr); *m/z*, M^+, 134.1, Reqd. for C_9H_{10} O, 134.2.

3-Allylphenyl acetate (**6**): 3-Allylphenol (3.0 g, 22 mM), anhydrous pyridine (40 cm^3) and acetic anhydride (20 cm^3) to 100°C. Work-up, as previously, gave the acetate (3.1 g, 80%), R_f 0.75; (Found: C, 74.75; H, 6.94. Reqd. for $C_{11}H_{12}O_2$ C, 74.98; H, 6.86%; ν_{max} (cm^{-1}, film) 1755 (C=O, ester) δ_H ($CDCl_3$) 2.28 (3H, s, $OCOCH_3$), 3.30 (2H, d, J = 6.5 Hz, Ar$\underline{CH_2}$CH), 5.03 (2H, m, $\underline{CH_2}$=CH), 5.72–6.13 (1H, m, $\underline{CH}$=CH_2), 7.15 (4H, m, HAr); *m/z*, M^+, 176.1. Reqd. for $C_{11}H_{12}O_2$, 176.2.

3-(3-hydroxyphenyl)-propane-1, 2-diol (**7**): 3-Allylphenylacetate (2.5 g, 14 mM), was added dropwise to 30% hydrogen peroxide (2.5 cm^3, 22 mM) and formic acid (10 cm^3) at 40–45°C over 30 min, after which the mixture was stirred at ambient temperature overnight. After concentration, the residue was hydrolysed with hot 50% aqueous sodium hydroxide, acidified, extracted and the crude product (1.50 g, 63%), purified by distillation, b.p. 100°C/1.5 mmHg; R_f 0.50 (EtOAc–light petroleum, 75 : 25); (Found: C, 64.20; H, 7.23. Reqd. for $C_9H_{12}O_3$ C, 64.27; H, 7.19%); ν_{max} (cm^{-1}, film), 3350(OH); δ_H ($CDCl_3$), 2.78 (2H, d, J = 6.3 Hz, CH_2Ar), 3.44 (2H, m, CH$\underline{CH_2}$OH), 3.74–3.84 (1H, m, $CH_2\underline{CH}$OH), 7.13 (4H, m, HAr), 8.40 (1H, s, OH, exch.); *m/z*, M^+, 168.2. Reqd. for $C_9H_{12}O_3$, 168.2.

3-(4-Hydroxyphenyl)propane-1, 2-diol (**9**): A mixture of 4-allylanisole (10.0 g, 67 mM), 2, 4, 6-collidine (55 cm^3) and lithium iodide (23.6 g, 176 mM) was refluxed under nitrogen for 22 h. The cooled acidified mixture was worked up as before to afford a brown oil, 4-allylphenol, (3.0 g, 33%), R_f 0.30 (ethyl acetate-light petroleum 75 : 25); δ_H ($CDCl_3$), 3.28 (2H, d, J = 6.4 Hz, ArCH_2CH), 5.00 (2H, m, CH_2=CH), 5.26 (1H, s, OH exch.), 5.75–5.97 (1H, m, CH_2=CH), 6.70 (2H, d, J = 8.7 HAr), 7.01 (2H, d, J = 11.6 Hz, HAr); *m/z*, M^+ 134.2. Reqd. for $C_9H_{10}O$, 134.2.

4-Allylphenyl acetate (**8**): 4-Allylphenol (2.5 g, 14 mM), acetic anhydride (13 cm^3, 109 mM) and pyridine (25 cm^3) were stirred at ambient temperature for 16 h under nitrogen. Work-up of the cooled mixture as before gave the acetate (2.2 g, 89%), which was purified by column chromatography (EtOAc–$CHCl_3$), R_f 0.74; (Found: C, 74.75; H, 6.95. Cald. for $C_{11}H_{12}O$, C, 74.98; H, 6.86%); δ_H ($CDCl_3$), 3.35 (2H, d, J = 6.6 Hz), 5.02(2H, m, $\underline{CH_2}$=CH), 5.68–6.09 (1H, m, CH_2=CH), 6.95 (2H, d, J = 9.0 Hz, HAr), 7.15 (2H, d, J = 9.0 Hz, HAr); *m/z*, M^+ 176.1. Reqd. for $C_{11}H_{12}O_2$, 176.2.

3-(4-Hydroxyphenyl)propane-1, 2-diol (**9**): 4-Allylphenyl acetate (2.0 g, 11 mM) was added dropwise to 30% hydrogen peroxide (2.0 cm^3, 18 mM), and formic acid (8 cm^3) at 40–45°C for 1 h and the mixture then left for 16 h at ambient temperature. Work-up as before, for the isomeric compounds, and hydrolysis at 100°C for 1 h with 50% aqueous sodium hydroxide gave the diol, which was recovered by acidification, extraction with ethyl acetate, concentration and distillation, b.p. 85°C/2 mmHg to give 1.50 g, 60%; R_f 0.54; (Found: C, 64.10; H, 7.30. Reqd. for $C_9H_{12}O_3$, C, 64.27; H, 7.19%; ν_{max} (cm^{-1}, film), 3360(OH); δ_H [$(CD_3)_2CO$], 2.78 (2H, d, J = 6.4 Hz, CH_2Ar), 3.52 (2H, d, $\underline{CH_2}$CHOH), 3.65–3.80 (1H, m, $CH_2\underline{CH}$OH), 6.98 (2H, d, J = 9.0 Hz, HAr), 7.12 (2H, d, J = 9.0 Hz, HAr), 8.45 (1H, s, OH, exch.); *m/z*, M^+ 168.1. Reqd. for $C_9H_{12}O_3$, 168.2.

Synthesis of 1 and 2-(n-methoxyphenyl)propane-1, 3-diols 1-(2-methoxyphenyl)propane-1, 3-diol (10): 2-Methoxycinnamaldehyde (3.70 g, 23 mM), in THF (12 cm^3) was added, under nitrogen, to lithium borohydride[14] (50 cm^3, *ca* 1M solution, 50 mM) and the mixture refluxed for 6 h. Then, to the cooled solution at °C, methanesulfonic acid (4.8 g, 50 mM) was added and. then at ambient temperature after 30 min, 3M sodium hydroxide solution (2 cm^3) and 30% hydrogen peroxide (17 cm^3) were added. After the mixture was stirred for 1 h at 50°C, the aqueous layer was saturated with potassium carbonate and the separated organic material worked-up to afford a yellow oil (2.0 g, 48%). Purification by column chromatography (gradient elution with ethyl acetate-chloroform) gave the diol, R_f 0.34; (Found: C, 65.99; H, 7.80. Reqd. for $C_{10}H_{14}O_3$, C, 65.92; H, 7.74%); ν_{max} (cm^{-1}, film), 3490, δ_H [$(CD_3)_2CO$], 1.89–2.14 (2H, m, CH_2CH_2OH), 2.00 (1H, s, sOH exch.), 3.05 (1H, s, OH, exch.), 3.82 (2H, m, CH$\underline{CH_2}$OH), 3.84 (3H, s, MeO), 5.00–5.25(1H, m, –CH), 6.81–7.44 (4H, m, HAr); *m/z*, M^+, 182.4. Cald. for $C_{10}H_{14}O_3$, 182.2.

2-(4-Methoxyphenyl)propane-1, 3-diol (**12**): Diethyl 4-methoxyphenylmalonate. To sodium ethoxide from sodium (2.2 g, 9, 6 mM) and dry ethanol (50 cm^3), diethyl oxalate (14.1 g, 96 mM) was added and then ethyl 4-methoxyphenyl acetate (20.0 g, 103 mM). After 30 min., the solid which separated was filtered and washed with dry diethyl ether and diethyl 2-(4-methoxyphenyl)-3-oxobutanedioate liberated from the sodium salt with ice-cold dilute sulfuric acid and worked-up to give an oil, (17.5 g, J = 58% , (Found: C, 61.18; H, 6.16, Reqd. for $C_{15}H_{18}O_6$, C, 61.22; H., 6.16%); δ_H ($CDCl_3$). 1, 24, 1.21 (6H, 2t, 2Me), 3.77 (3H, s, OMe), 4.17, 4.24 (4H, 2q, $2CH_2$), 5.24 (1H, s, CH), 6.85 (2H. d, J = 9.3 Hz, HAr), 7.20 (2H, d, J = 8.7 Hz, HAr), *m/z*, M^+, 294.2. Reqd for $C_{15}H_{18}O_6$ 294.3. Decarbonylation (over 20 h, TLC monitoring) and distillation *in vacuo* (90°C/0.9 mmHg gave (**11, R = Et**), (1.4 g, 38%); (Found: C, 63.19; H, 6.86. Cald. for $C_{14}H_{18}O_5$, (C, 63, 15; H, 6.81%), R_f 0.50; ν_{max} (cm^{-1}, film), 1725 (C=O, ester); δ_H ($CDCl_3$), 1.23 (6H, 2t, 2Me), 3.75 (3H, s, MeO), 4.51 (4H, 2q, J = 7.2 Hz, $2CH_2$), 6.82 (2 h, d, J = 9.1 Hz, HAr), 7.27 (2H, d, J = 10.9 Hz, HAr); *m/z*, M^+, 266.1. Cald. for $C_{14}H_{18}O_5$, 266.3.

(a) *4-Methoxyphenylmalonic acid* (**11, R = H**) was obtained in 52% yield by carboxylation of 4-methoxyphenylacetic acid, m.p. 141°C (lit.[15] 137–138°C), R_f 0.06. No spectroscopic data were given: ν_{max} (film, cm^{-1}), 2800 (OH), 1700 (C=O); δ_H yield$(CD_3)_2CO$, 3.79 (3H, s, OMe), 4.66 (1H, s, CHAr), 6.90 (2H, d, HAr), 7.40(2H, d, HAr); *m/z*, M^+ 210.2. Cald, for $C_{10}H_{10}O_5$, 210.2.

2-(4-Methoxyphenyl)propane-1, 3-diol **(12):** 4-Methoxyphenylmalonic acid was reduced by diborane in 74% yield, m.p. 85°C, (lit.[12] 83–85°C), R_f 0.36. Spectroscopc data were not given; δ_H ($CDCl_3$), 2.94 (1H, m CH), 3.79 (3H, s, MeO), 3.89 [4H, t, 2(CH_2)], 6.80 (2H, d, HAr), 7.30 (2H, d, HAr); *m/z*, M^+, 182.1. Cald. for $C_{10}H_{14}O_5$, 182.2.

1-Methoxy-4-nitromethylbenzene (**14**): 4-Methoxybenzaldoxime (**13**), m.p. 63–65°C (lit.[16] m.p. 65°C), R_f 0.25; had the following spectroscopic data: ν_{max} (cm^{-1}, film) 3600(OH), δ_H ($CDCl_3$), 3.80 (3H, s, MeO), 6.90 (2H, d, J = 6.5 Hz, HAr), 7.50 (2H, d, J = 8.8 Hz, HAr), 8.10 (H, s, CH); *m/z*, M^+, 151.1. reqd.. 151.2.

(i) To 4-methoxybenzaldoxime (30 g, 246 mM), stirred and heated to 80°C, 32% peracetic acid (63.8 g, 269 mM) and sodium acetate trihydrate (3.0 g, 22 mM) were added and the temperature maintained at 80–90°C during 3–5 h. To the cooled stirred reaction mixture water was added and the separated oil worked-up to give an oil, (28.7 g, 70%), purified by column chromatography (gradient elution with ethyl acetate/chloroform); R_f 0.78; ν_{max} (cm^{-1}, film), 1565 (C–O), 1350 (NO_2); δ_H ($CDCl_3$), 3.81 (3H, s, MeO), 5.35 (2H, s, CH_2Ar), 6.92 (2H, d, J = 6.6 Hz, HAr), 7.36 (2H, d, J = 8.8 Hz, HAr), *m/z*, M^+ 167.1. Reqd. for $C_8H_9O_3N$, 167.2.

(ii) By contrast, oxidation in acetonitrile containing trifluoracetic anhydride with 85% hydrogen peroxide gave a 60% yield of spectroscopically identical material.

2-Nitro-2-(4-methoxyphenyl)propane-1, 3-diol (**15**): 1-Methoxy-4-nitromethyl-benzene (10 g, 60 mM), 37% aqueous formaldehyde (10.7 g, 132 mM) and sodium carbonate decahydrate were stirred at ambient temperature and after 1.5 h the mixture warmed at 30–40°C for 20 min. to complete the reaction (TLC monitoring). The mixture was diluted with ice/water, stirred at 10°C for 2 h, filtered and the solid product washed, and dried. The dry solid was stirred with toluene, filtered and dried to give an off-white material, (8.3 g, 61%) which was crystallised (diethyl ether/light petroleum), m.p. 109°C, R_f 0.52; (Found: C, 52.79; H, 5.73; N, 5.99. Reqd. for $C_{10}H_{13}NO_5$, C, 52.86, H, 5.77; N,. 6.16%; ν_{max} (cm^{-1}, KBr disc) 3600 (OH); δ_H ($CDCl_3$), 2.84 (2H, s, 2OH.exch.), 3.80 (3H, s, MeO), 4.42 [4H, s, 2(CH_2)], 6.93 (2H, d, J = 9.1 Hz, HAr), 7.35 (2H, d, J = 8.9, HAr); *m/z*, M^+ 227.4. Reqd. for $C_{10}H_{13}NO_5$, 227.2.

The diacetate and ketal were prepared.

Diacetate: (**16, R = NO_2**) 2-Nitro-2-(4-methoxyphenyl)propane-1, 3-diol (0.200 g, 0.9 mM), pyridine (8 cm^3), and acetic anhydride (4 cm^3) were heated at 100°C during 2 h under nitrogen. Work-up by acidification and extraction gave the product which was purified by vacuum distillation, b.p. 160°C/8 mmHg, R_f 0.72; (Found: C, 54.32; H, 5.55; N, 4.21. Reqd. for $C_{14}H_{17}NO_7$, C, 54.02; H, 5.50; N, 4.50); ν_{max} (cm^{-1}, film), 1740 (C=O, ester), 1350 (NO_2); δ_H ($CDCl_3$), 3.79, (3H, s, MeO), 4.89 [4H, s, 2(CH_2)], 6.87 (2H, d, J = 9.3 Hz, HAr), 7.25 (2H, d, J = 9.1 Hz, HAr); *m/z*, M^+, 265.1(M-NO_2), Reqd. for $C_{14}H_{17}NO_7$, 311.3.

Ketal (**17**): The nitro compd, (0.500 g, 2 mM), in acetone (2 cm^3,

30 mM) containing HCl (1drop) was stirred for 2 h and after recovery the product was purified by vacuum, distillation, b.p. 118–120/ 10^{-3}mm Hg, R_f 0.56; (Found: C, 58.40; H, 6.48; N, 5.40. Reqd. for $C_{13}H_{17}NO_3$, C, 58.42; H, 6.41; N, 5.24%); ν_{max} (cm^{-1}, film), 1555 and 1350 (NO_2); δ_H ($CDCl_3$) 1.39 [3H, s, C–(CH_3)], 1.47 [3H, s, C–(CH_3)], 3.75 (3H, s, MeO), 4.24 (2H, d, J = 12.7 Hz, CH_2), 4.99 (2H, d, J = 13.1 Hz, CH_2), 6.85 (2H, d, J = 9.0 Hz, HAr), 7.22 (2H, d, J = 9.0 Hz, HAr); *m/z*, M^+ 267.0. Reqd. for $C_{13}H_{17}NO_5$, 267.3.

2-(4-Methoxyphenyl)propane-1, 3-diol **(12):** 2-Nitro-2-(4-methoxyphenyl)-propane-1, 3-diol (5.0 g, 22 mM), in ethanol (100 cm^3) containing 5% palladium on calcium carbonate (150 mg) and conc HCl (1 drop) was shaken with hydrogen at ambient temperature and pressure over 16 h. The mixture was filtered, and worked to afford the product (3.1 g, 77%), then purified by column chromatography (gradient elution with diethyl ether/light petroleum), m.p. 84–85°C, R_f 0.36; (Found: C, 65, 77; H, 7.73. Reqd for $C_{10}H_{14}O_3$, C, 65.92; H, 7.74%; ν_{max} (cm^{-1}, KBr disc), 3600 (OH); δ_H ($CDCl_3$), 2.94 (1H, m, CHAr), 3.76 (3H, s, MeO), 3.86[4H, t, 2(CH_2)], 6.78 (2H, d, HAr), 7.28 (2H, d, HAr); *m/z*, M^+, 182.1.Reqd. for $C_{10}H_{14}O_3$, 182.2.

2-(4-Methoxyphenyl)propane-1, 3-diacetate **(16, R = H)**: The diol (1.0 g, 274 mM) in pyridine (56 cm^3) and acetic anhydride (28 cm^3, 274 mM) was heated at 100°C for 2 h under nitrogen After work-up, as before, for the nitro compound, the diacetate was obtained as an oil (0.50 g, 34.2%) purified by distillation, b.p. 110°C/0.4 mmHg; R_f 0.70; (Found: C, 62.91; H, 6.92. Reqd. for $C_{14}H_{18}O_5$ C, 63.14; H, 6.81%; ν_{max} (cm^{-1}, film) 1740 (C=O, ester); δ_H ($CDCl_3$), 2.00 (6H, s, 2CH_3CO), 2.92 (1H, m, CH), 3.76 (3H, s, OMe), 4.27 [4H, d, J = 6.5 Hz, 2(CH_2)], 6.81 (2H, d, J = 9.3, HAr), 7.10 (2H, d, J = 9.0, HAr); *m/z*, M^+, found 207.2, (M^+- OCO). Reqd. for M^+ 266.3.

2-(2-Methoxyphenylpropane-1,3-diol **(21)***:2-Methoxybenzaldoxime* **(18)**: 2-Methoxybenzaldoxime was prepared in 81.3% yield, m.p. 95°C (lit.[16] 95°C, R_f 0.37; ν_{max} (cm^{-1}, film) 3600; δ_H ($CDCl_3$), 3H, s, OMe), 6.86–7.41 (4H, d, HAr), 8.10 (1H, s, OH, exch.); *m/z*, M^+, 151.1. Cald. for $C_8H_9NO_2$, 151.2.

1-Methoxy-2-nitromethylbenzene **(19):** By the general procedure, 2-methoxybenzaldoxime (30 g, 246 mM), 32% peracetic acid (63.8 g, 269 mM) were reacted in glacial acetic acid containing sodium acetate trihydrate (3 g) to give the nitro compound (25.8 g, 62.8%), which was purified by column chromatography (gradient elution with ethyl acetate-chloroform), R_f 0.78; ν_{max}(cm^{-1}, film), 1560, 1350 (NO_2), δ_H ($CDCl_3$) 3.81 (3H, s, OMe), 5.44 (2H, s, CH_2Ar), 6.85–7.39 (4H, m, HAr), *m/z*, M^+, 167.1. Reqd. for $C_8H_9NO_3$, 167.2.

2-Nitro-2-(2-methoxyphenyl)propane-1, 3-diol **(20):** By the general procedure, 1-methoxyphenyl-2-nitromethylbenzene (10 g, 60 mM) and 37% formaldehyde solution (10.7 g, 132 mM), containing sodium carbonate decahydrate, to give the diol (97 g, 70%) which was crystallised (diethyl ether/light petroleum) m.p. 87–89°C, R_f 0.18; (Found: C, 52.67; H, 5.77; N, 6.20. Reqd. for $C_{10}H_{13}NO_5$, C, 52.86; H, 5.77; N, 6.16%; ν_{max} (cm^{-1}, film), 3600 (OH), δ_H [$(CD_3)_2CO$], 2.85 (2H, s, 2OH.exch.), 3.75 (3H, s, OMe), 4.42 (4H, s, 2CH_2), 6.96–7.36 (4H, m, HAr); *m/z*, M^+, 227.2. Reqd for $C_{10}H_{13}NO_5$, 227.2.

The diacetate was prepared by the general method by reaction of the nitro diol in pyridine with acetic anhydride to give white crystals, R_f 0.72, m.p. 92.5–93.5°C; (Found: 54.30; H, 5.57; N, 4.32. Reqd. for $C_{14}H_{17}NO_7$, C, 54.02; H, 5.50; N, 4.50%; ν_{max} (cm^{-1}, film), 1735 (C=O, ester); δ_H ($CDCl_3$), 1.96 (3H, s, OCOMe), 2.02 (3H, s, OCOMe), 3.75 (3H, s, OMe), 4.76 (2H, d, J = 11.3 Hz, CH_2), 5.08 (2H, d, J = 11.5, CH_2), 6.84–7.09 (4H, m, HAr); *m/z*, M^+, 265.1 (M–NO_2). Reqd. for $C_{14}H_{17}NO_7$, 311.3.

The reduction of the nitro compound (**20**) to (**21**) (Scheme 4a) was not completed.

2-(2-Methoxyphenyl-2-nitroethanol: This mono methylol compound was isolated (TLC monitoring) from the residual solution from crystallisation of the diol from the formaldehyde reaction of 1-methoxy-2-nitromethylbenzene, by prep TLC. Recrystallisation (light petroleum) gave white crystals, m.p. 61–63°C, R_f 0.50; (Found: C, 54.84; H, 5.57; N, 6.99. Reqd. for $C_9H_{11}NO_4$ C, 54.82; H, 5.62; N, 7.10%; ν_{max} (cm^{-1}, KBr disc), 3600(OH); δ_H ($CDCl_3$), 3.86 (3H, s, MeO), 4.33 (2H, d, J = 10.0 Hz, CH_2OH), 6.00–6.16(1H, m, –CH), 6.98–7.51 (4H, m, HAr); *m/z*, M^+, 197.1. Reqd. for $C_9H_{11}NO_4$, 197.2.

2-(4-Hydroxyphenyl)-propane-1, 3-diol **(25)**: 4-Benxyloxybenzaldehyde: 4-hydroxybenzaldehyde (50 g, 410 mM) and benzyl chloride (43 cm^3, 410 mM) in acetone containing potassium carbonate (64 g, 468 mM) were refluxed for 20 h. The cooled mixture was filtered and the filtrate concentrated to an oil which was column chromatographed (ethyl acetate/chlorofirm with gradient elution) to give 71.2 g (82%), (recrystallised light petroleum) as white crystals, m.p. 71–73°C, R_f 0.61 (chloroform); (Found: C, 78.93; H, 5.67. Cald for $C_{14}H_{12}O_2$, C, 79.23; H, 5.705; ν_{max} (cm^{-1}, film) 1700(C=O); δ_H ($CDCl_3$), 5.08 (2H, s, OCH_2Ph), 7.01 (2H, d, J = 8.3 Hz, HAr), 7.34 (5H, s, $PhCH_2$), 7.76 (2H, d, J = 8.3 Hz, HAr), 9.80 (1H, s, CHO); *m/z*, M^+, 212.1. Cald for $C_{14}H_{12}O_2$, 212.1.

4-Benzyloxybenzaldoxime **(22):** 4-Benzyloxybenzaldehyde (30 g, 141 mM), and hydroxylamine sulfate (12.0 g, 73 mM) were reacted in aqueous methanol (1: 20) containing 50% sodium hydroxide (12.3 g, 154 mM) to give the oxime, 24.1 g, (75%), which was purified by column chromatography (ethyl acetate/chloroform, with gradient elution) to afford the product, m.p. 109–111°C, R_f 0.29, (Found: C, 73.73; H. 5.83; N, 5.91. Reqd for $C_{14}H_{13}NO_2$, C, 73.99; H, 5.77; N, 6.16%; ν_{max} (cm^{-1}, film), 3610 (OH), δ_H ($CDCl_3$), 5.05 (2H, s, OCH_2Ph), 6.94 (2H, d, J = 7.8 Hz, HAr), 7.33 (5H, s, OCH_2Ph), 7.47 (2H, d, J = 8.6 Hz, HAr), 8.04 (1H, s, CH); *m/z*, M^+, 227.0. Reqd. for. $C_{14}H_{13}NO_2$, 227.3

1-(4-Benzyloxyphenyl)-4-(nitromethyl)benzene **(23):** 4-Benzyloxybenzaldoxime (20 g, 88 mM), 32% peracetic acid (23 cm^3, 96.8 mM), and sodium acetate trihydrate (0.5 g) were reacted in acetic acid by the general procedure to give the product, 11.8 g (54.6%) which was purified by column chromatography (ethyl acetate/chloroform with gradient elution), recryst. (diethyl ether), R_f 0.67; (Found: C, 69.38; H, 5.38; N, 5.73, Reqd. for $C_{14}H_{13}N\ O_3$, C, 69.12; H, 5.39; N, 5.76%); ν_{max}(cm^{-1}, film (1560, 1340 (NO_2); δ_H ($CDCl_3$), 5.04 (2H, s, OCH_2Ph), 5.31 (2H, s, $ArCH_2NO_2$), 6.85 (2H, d, J = 8.7 Hz, HAR), 7.30 (2H, d, J = 8.1 Hz, HAr), 7.33 (5H, s, OCH_2Ph); *m/z*, M^+, 243.1. Reqd. for $C_{14}H_{13}NO_3$, 243.3.

2-(4-Benxyoxyphenyl)-2-nitropropane-1, 3-diol **(24):** 1-Benzyloxyphenyl-4-nitromethylbenzene (10 g, 41 mM), and 37% aqueous formaldehyde (7.3 cm^3, 90 mM), were reacted by the general procedure with sodium carbonate decahydrate present to give the nitrodiol 7.8 g (63.1%), which was recrystallised (diethyl ether/light petroleum) to give white crystals, m.p. 133–134°C, R_f 0.35; (Found: C, 63.26; H, 5.62; N, 4.32, Reqd for $C_{16}H_{17}NO_5$, C, 63.36; H, 5, 65; N, 4.62%; ν_{max} (cm^{-1}, KBr disc), 3600(OH); δ_H [$(CD_3)_2CO$], 2.80 (2H, s, 2OH, exch.), 4.40 [4H, s, 2CH_2OH], 5.11 (2H, s, OCH_2Ph), 6.99 (2H, d, J = 8.5 Hz, HAr), 7.32 (2H, d, J = 7.8, HAr), 7.39 (5H, s, OCH_2Ph); *m/z*, M^+303.1. Reqd.for $C_{16}H_{17}NO_5$, 303.3.

2-(4-Hydroxyphenyl)propane-1, 3-diol **(25)**: 2-(4-benzyloxyphenyl)-2-nitro-propane-1, 3-diol (5.0 g) hydrogenated in ethanol solution in the presence of Pd–$CaCO_3$ (110 mg) by the general procedure afforded the product 1.50 g (54.2%), m.p. 90–91°C, R_f 0.10: (Found: C, 64.27; H, 7.36. Reqd. for $C_9H_{12}O_3$ C, 64.27; H, 7, 20%; ν_{max} (cm^{-1}, KBr disc), 3600(OH); δ_H [$(CD_3)_2CO$], 2.87 (1H, m, CH), 3.72–3.87 (4H, m, 2CH_2), 6.70 (2H, d, J = 8.6 Hz, HAr), 7.05 (2H, d, J = 8.9, HAr), 8.08 (2H, s. HOAr, exch.); *m/z*, M^+ 168.0. Reqd. for $C_9H_{12}O_3$, 168.2.

Results and discussion

Phenylpropane-1, 2-diols

The dihydroxylation of allylphenolic acetates rather than of the methyl ethers was adopted since their final demethylation proceeded less satisfactorily than alkaline hydrolysis of the acetate. 3-Allylphenol was more readily available from the dehydroxylation of eugenol diethylphosphate[17] than from a Grignard reaction with 3-bromophenylmethyl ether and allyl iodide. Demethylation of the methyl ether with lithium iodide in collidine[18] proved superior to either boron tribromide or trimethylsilyl iodide. Alternative methods for obtaining the precursor, 4-allylphenol, based on selenide chemistry[19] or other approaches[20] afforded low yields.

Phenylpropane-1, 3-diols

For the synthesis of 1-arylpropane-1, 3-diols, the reaction of the dilithio derivative of ethyl hydrogen malonate[21] with 4-methoxybenzoyl chloride to ethyl 4-methoxybenzoyl acetate[22] was effected in 73% yield. Nevertheless, the routes to 1-aryl-1, 3-diols from this and other β-keto ester precursors,[23] by reduction were found less satisfactory than direct lithium borohydride reduction[14,24] of an α, β unsaturated aldehyde as for example in the case of (**10**) obtained from readily available 2-methoxycinnamaldehyde. Its isomers are not readily accessible. An alternative approach to obtain the 4-isomer of (**10**) from the reaction of 4-methoxybenzaldehyde with the tetrahydropyranyl ether of 2-chloroethanol in the presence of lithium failed, probably due to preferential β-eliminationn of the chlorine atom, although the method was successful with 1, 3- related systems and 1, 7-diols.[25,26]

For 2-arylpropane-1, 3-diols, the condensation of ethyl oxalate with ethyl 4-methoxyphenylacetate followed by decarbonylation to give diethyl 4-methoxyphenylmalonate proved less useful than direct carboxylation[27] of the lithio dereivative of 4-methoxyphenylacetic

acid with carbon dioxide and then diborane reduction of the resultant dicarboxylic acid.

However, methoxy or benzyloxyphenylacetic acids (to replace final demethylation by hydrogenolysis) are less available than the methoxy or benzyloxyenzaldehydes (from hydroxybenzaldehydes) and hydroxymethylation of an appropriate derived carbanion for the synthesis of diols (**15**), (**20**) and (**24**) was therefore studied. Formation of a reactive benzylic carbanion was enabled by the presence of a nitro group available through an improved procedure[28] for oxidation of an aldoxime (as the isonitroso tautomer) to the nitromethyl derivative. The nitro compound readily reacted with formaldehyde under alkaline conditions to afford the nitro diol. by adaptation of an earlier method.[29] Methylolation in the aromatic ring did not occur (the subject of part 41a in this series[1]) but only at the carbanion. The hydrogenolysis of the benzyl group in the presence of palladium-calcium carbonate or with palladium/carbon[26] under mildly acidic conditions simultaneously led also to removal of the nitro group to give the final product (**25**).

The complexation properties of the monomers and of formaldehyde polymers has been determined and will be described in full elsewhere. In summary, 1 : 1 and not 2 : 1 (diol/borate) complexation occurs and phenolic-1.3- and propane-1, 2-diols are superior to simple propane diols lacking the phenolic group. Isomeric phenolic diols (**7**) and (**9**) are more effective than (**12**) or (**25**) indicating a preference for 5- rather than 6-membered ring complexes. Steric hindrance impedes complexation in (**3**). The phenolic diols have been polymerised with formaldehyde and found to complex aqueous borate to a high level.

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