

Phenolic structure and colour in Mannich reaction products[†]

John H.P. Tyman* and Mahesh Patel

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

Mannich reactions have been carried out with a variety of model alkylphenols and dimethylamine, methylamine, and diethylenetriamine to trace the origin of persistent coloured products occurring in related reactions with pentadeca(e)nylphenol and 4-*tert*-alkylphenols. It was found to be attributable to the presence of resorcinolic impurities.

Keywords: Mannich reaction, alkylphenol, cardanol

The appearance of a patented procedure¹ with, however, no accompanying separatory nor spectroscopic information, for the synthesis of phenolic Mannich bases useful, notably from diamines, as curing agents for epoxy resins, prompts us to describe our own similar work. This was completed some years ago² although, since then, a study of the reaction conditions³ with 3-pentadecylphenol, the mechanism⁴ and the role of Mannich bases as curing agents⁵ have been reported. In the original work, Mannich bases from 3-pentadecylphenol (1, $n = 0, 2, 4,$ and 6), obtained from cashew nutshell liquid⁵ were compared with those from 4-*tert*-nonylphenol (2), of petrochemical origin and, unexpectedly, a persistent red colour was encountered in the products. Accordingly, to elucidate its origin, the influence of structural features in (1) and (2) with model alkyl phenols and amines was studied. Thus, the role of chain branching in 4-alkylsubstituents, of 3,4,5-trisubstitution, and of side chain unsaturation was investigated resulting in the syntheses of the new Mannich bases, with dimethylamine, **3b–i**, (Scheme 1) and **4**. The use of methylamine and formaldehyde was also examined in the syntheses of **6**, **7**, and **8** (Scheme 2) from phenol (5, R = H) and 3-methylphenol (5, R = Me). The mixed primary/secondary amine, diethylenetriamine, DETA was examined with phenol, 3-methylphenol and **1** (Scheme 3).

The Mannich reaction has been reviewed,⁶ with little mention of primary or mixed primary/secondary amines. It was mainly concerned with the use of secondary amines. Reactions were listed for 3-methylphenol,⁷ 3,5-dimethylphenol,⁸ 2- and 4-methoxyphenol⁹ and the dihydric phenols.⁹ The formation of polymers has also been reported^{10,11} from 1,3-dihydroxybenzene. In the case of primary amines in reactions with only 4- and with 2,4-disubstituted phenols, the formation of an oxazine, a disubstituted and a normal Mannich base has been described.^{12,13}

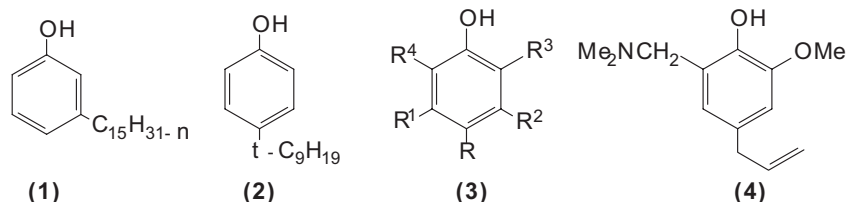
Although colour development did not seem a probable consequence of the Mannich reaction method itself but due to certain impurities in the phenols employed and different from the pink hue attributable to rosolic acid¹⁴ in old samples of phenol, the Mannich bases that were prepared are still novel compounds. Currently the interest in natural as opposed to declining fossil fuel raw material sources adds a topical dimension to this early work. Additionally, recent work¹⁵ has indicated the ready biodegradability of the alk(en)yl side chains in phenolic lipids compared with highly branched types in 4-*tert*-nonylphenol.

Experimental

Chromatography: TLC was effected on microscope slides self coated with Merck Kiesegel G type 60 (analytical plates 0.25 mm and 20 × 20 m preparative plates 1.00 mm) and were visualised by spraying with 0.1% ethanolic rhodamine 6G and viewing under UV light. The solvents were, E (chloroform–ethyl acetate, 95:5), F (80:20), G (93:7) and H (light petroleum–diethyl ether, 95:5). GLC was carried out with a Pye Unicam gas chromatograph (GCD) equipped with FID and an Infotronics GRS 201 programmed integrator. Column chromatography was carried out on Kiesegel G type 60 (mesh 70–230) in glass columns equipped with a zero porosity disc and separations monitored by TLC.

Spectroscopy: ¹H NMR spectra were recorded on a Varian T60 (60 MHz) and on a Varian FT-80A by courtesy of Varian Associates with TMS as internal standard and ¹³C spectra on a Varian CFT-20. IR spectra were recorded on a Perkin-Elmer 700 and an SP2000 instrument and UV spectra were obtained on a Pye-Unicam SP800. Mass spectroscopy was effected on an AEI modified MS902 and accurate mass measurements by the PCMU Harwell. Microanalyses were carried out by courtesy of the School of Pharmacy, University of London.

Materials: Technical cashew nutshell liquid of Brazilian origin was supplied 3M Research, Harlow, Essex and other phenolic and amine chemicals by Aldrich Chemical Co. diethylenetriamine (99%) was obtained from Kodak Ltd.



3a: R¹ = Me; R = R² = R⁴ = H; R³ = CH₂NMe₂
b: R¹ = R² = R = Me; R⁴ = H; R³ = CH₂NMe₂
c: R¹ = R² = H; R = *i*Pr; R³ = R⁴ = CH₂NMe₂
d: R¹ = R² = H; R = *i*-C₃H₇; R³ = R⁴ = CH₂NMe₂
e: R¹ = R² = H; R = *t*-Bu; R³ = R⁴ = CH₂NMe₂

f: R¹ = C₁₅H₃₁; R = R² = R⁴ = H; R³ = CH₂NMe₂
g: R¹ = C₁₅H₃₁; R = R² = R⁴ = H; R³ = CH₂NEt₂
h: R¹ = C₁₅H_{31-n}; R = R² = R⁴ = H; R³ = CH₂NMe₂
i: R¹ = OH; R = R² = R⁴ = H; R³ = CH₂NMe₂

Scheme 1 Structure and formulae of Mannich bases from secondary amines.

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

[†] Long chain Phenols; part 42a

Procedures for Mannich reactions

Method A: Aqueous formaldehyde (35–40%) was added dropwise over 15 min to a stirred mixture of the phenol and aqueous dimethylamine (25%) (or other water soluble amine) at 10–15°C, the mixture was stirred at 25°C for 1 h and then at 100°C for 2 h. To the hot solution, sodium chloride was added (160 g/mole of the phenol). The cooled mixture was ethereally extracted, the extract was dried (sodium sulfate, anhydrous) and concentrated to give the product.

Method B: The method was as in A except that the solvent was methanol and the mixture was stirred and refluxed for the same period, then concentrated *in vacuo*. The cooled residue in diethyl ether was washed with water, dried and concentrated.

Method C: The same procedure as in A with omission of sodium chloride addition but washing of the mixture in diethyl ether with water, drying and concentration to give the product.

All reactions were monitored by TLC and worked up by crystallisation or prep. TLC.

Mannich reactions with secondary amines

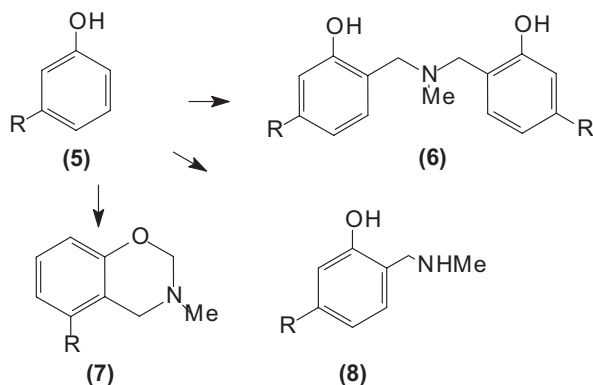
2,4,6-Tri-(dimethylaminomethyl)phenol (Method C): Phenol (9.4 g, 0.10 mol), aqueous dimethylamine (72.0 g, 0.40 mol) and aqueous formaldehyde (28.40 g, 0.350 mol) were reacted to afford a pale yellow-brown oil (80%); ν_{\max} (film, cm^{-1}), 2960, 2800, 1615, 1360, 1300, 1260; δ_{H} (CDCl_3), 2.20 (6H, s, Me_2N), 2.25 (12H, s, $2\text{Me}_2\text{N}$), 3.27 (2H, s, PhCH_2N), 3.50 (4H, s, $2\text{PhCH}_2\text{N}$), 6.98, (2H, s, HAr), 7.76 (1H, s, HOAr, D_2O exch.). This has been described¹⁶ but with no spectral data.

2,4,6-Tri(dimethylaminomethyl-3-methylphenol (3a) (Method A): 3-Methylphenol (10.80 g, 0.10 mol), aqueous dimethylamine (72.0 g, 0.40 mol), and aqueous formaldehyde (28.40 g, 0.35 mol) were reacted during 90 min. The oily product solidified after 3 days and was recrystallised (benzene) to give colourless needles, m.p. 54–57°C (lit.¹⁶ b.p. 200°C/0.50 mm), yield 76%. Found: C, 68.89; H, 10.37; N, 14.63. Reqd. for $\text{C}_{16}\text{H}_{29}\text{N}_3\text{O}$, C, 68.81; H, 10.39; N, 15.05%; ν_{\max} (film, cm^{-1}), 2950, 2860, 2760, 1620, 1595, 1460; δ_{H} (CCl_4), 2.10 (6H, s, Me_2N), 2.20 (12H, s, $2\text{Me}_2\text{N}$), 2.82 (3H, s, MeAr), 3.25 (2H, s, CH_2Ar), 3.43 (2H, s, CH_2Ar), 3.50 (2H, s, CH_2Ar), 6.80 (1H, s, HAr), 10.03, (1H, s, HOAr, D_2O exch.).

2-Dimethylaminomethyl-3,4,5-trimethylphenol (3b) and 2,6-bis(dimethylaminomethyl)-3,4,5-trimethylphenol (Method B): 3,4,5-Trimethylphenol 2.72 g, 0.020 mol, aqueous dimethylamine (9.0 g, 0.050 mol) and aqueous formaldehyde (4.0 g, 0.050 mol) refluxed 6 h (TLC indicated 2 bands). The product solidified on keeping and was separated by prep. TLC (solvent F).

The monosubstituted product (R_f 0.45), m.p. 71–72°C (yield 35%); Found: C, 74.65; H, 9.70. Reqd. for $\text{C}_{12}\text{H}_{19}\text{NO}$, C, 74.61, H, 9.85%. ν_{\max} (KBr disc cm^{-1}) 2850, 1580, 1560, 1440, 1390, 1360, 1320, 1280, 1220; δ_{H} (CCl_4), 2.17 (9H, s, 3MeAr), 2.37 (6H, s, Me_2N), 3.67 (2H, s, ArCH_2N), 6.50 (1H, s, HAr), 10.1, (1H, s, ArOH , D_2O exch.). For the disubstituted product (baseline), m.p. 55–56.5°C (yield 25%); Found: C, 72.54; H, 10.19. Reqd. for $\text{C}_{15}\text{H}_{26}\text{N}_2\text{O}$, C, 72.00; H, 10.40%; ν_{\max} (KBr disc, cm^{-1}), 2950, 2850, 2760, 1720, 1600, 1570, 1450, 1350, 1305, 1285, 1180; δ_{H} (CCl_4) 2.23 (9H, bs, 3MeAr), 2.28 (12H, s, $2\text{Me}_2\text{N}$), 3.57 (4H, s, $2\text{ArCH}_2\text{N}$), 10.18 (1H, s, HOAr, D_2O exch.).

2,6-Bis(dimethylaminomethyl)-4-isopropylphenol (3c) (Method B): 4-Isopropylphenol (2.72 g, 0.020 mol) aqueous dimethylamine (10.8 g, 0.06 mol) and aqueous formaldehyde (4.80 g, 0.06 mol) were refluxed for 6 h, after which work-up gave the product as a pale yellow oil (yield 90%). Found: C, 72.60; H, 10.47; N, 11.17.



Scheme 2 Mannich reaction of phenols with primary amines.

Reqd. for $\text{C}_{15}\text{H}_{26}\text{N}_2\text{O}$, C, 72.00; H, 10.40; N, 11.19%; ν_{\max} (film, cm^{-1}), 2950, 2860, 2820, 2760, 1610, 1460, 1390, 1350, 1170, 1020; δ_{H} (CCl_4), 1.23 (6H, d, J 6 Hz, Me_2C), 2.30 (12H, s, $2\text{Me}_2\text{N}$), 2.75 (1H, h, J 6 Hz, CHAr), 3.52 (4H, s, ArCH_2N), 6.97 (2H, s, HAr), 9.28, (1H, s, HOAr, D_2O exch.).

2,6-Bis(dimethylaminomethyl-4-tert-pentylphenol (3d) (Method B): 4-tert-Pentylphenol (3.28 g, 0.020 mol), aqueous dimethylamine (19.80 g, 0.06 mol) and aqueous formaldehyde (4.60 g, 0.06 mol) were refluxed for 6 h and the mixture worked up to give a pale yellow oil, (86% yield). Found: C, 73.95; H, 11.25; N, 9.87. Reqd. for $\text{C}_{17}\text{H}_{30}\text{N}_2\text{O}$, C, 73.38, H, 10.79; N, 10.07%; ν_{\max} (film, cm^{-1}), 2950, 2820, 2760, 1610, 1460, 1360, 1260, 1180, 1020, 840; δ_{H} (CCl_4), 0.68 (3H, t, J = 8 Hz, MeC), 1.27 (6H, s, Me_2CAr), 1.67 (2H, q, J = 8 Hz, CH_2CAr), 2.30 (12H, s, $2\text{Me}_2\text{N}$), 3.53 (4H, s, ArCH_2N), 7.03 (2H, s, HAr), 9.70 (1H, s, HOAr, D_2O exch.).

2,6-Bis(dimethylaminomethyl)-4-tert-butylphenol (3e) (Method B): 4-tert-Butylphenol (3.0 g, 0.020 mol), aqueous diethylamine (4.0 g, 0.050 mol) and aqueous formaldehyde (9.0 g, 0.050 mol) were refluxed for 6 h and processed to give colourless crystals, m.p. 40–42°C, (yield 83%). Found: C, 72.20; H, 10.33; N, 10.74. Reqd. for $\text{C}_{16}\text{H}_{28}\text{N}_2\text{O}$, C, 72.73; H, 10.61; N, 10.61%. ν_{\max} (film, cm^{-1}), 2950, 2820, 2760, 1610, 1460, 1360, 1260, 1040, 1040, 840; δ_{H} (CCl_4), 1.33 (9H, s, Me_3CAr), 2.37 (12H, s, $2\text{Me}_2\text{N}$), 3.63 (4H, s, ArCH_2N), 7.17 (2H, s, HAr), 11.07 (1H, s, HOAr, D_2O exch.).

2-Dimethylaminomethyl-5-n-pentadecylphenol (3f) (Method B): 3-Pentadecylphenol (saturated cardanol) (3.0 g, 0.01 mol), aqueous dimethylamine (5.40 g, 0.03 mol) and aqueous formaldehyde (2.43 g, 0.03 mol) were refluxed for 150 min. and the solid product recryst. (light petroleum 40–60°C) as colourless prisms, m.p. 44–47°C, (lit.¹⁷ 47°C). Found: C, 79.73; H, 12.27; N, 3.96. Cald. for $\text{C}_{24}\text{H}_{43}\text{NO}$, C, 79.78; H, 11.91; N, 3.88%; ν_{\max} (KBr disc, cm^{-1}) 2850, 1620, 1580, 1510, 1460, 1380, 1360; δ_{H} (CCl_4), 0.90 (3H, t, Me), 1.27 (26H, m, $(\text{CH}_2)_{13}$), 2.20 (6H, s, Me_2N), 2.20 (2H, t, CH_2Ar), 3.53 (2H, s, ArCH_2N), 6.24 (3H, m, HAr), 9.60 (1H, s, HOAr, D_2O exch.).

2-Diethylaminomethyl-5-n-pentadecylphenol (3g) (Method B): 3-Pentadecylphenol 0.30 g, 0.001 mol, aqueous diethylamine (0.15 g, 0.002 mol) and aqueous formaldehyde (0.16 g, 0.002 mol) were refluxed for 5 h and the product purified by prep TLC to give colourless prisms, m.p. 15°C, (yield 29%). Found: C, 80.71, H, 12.60; N, 3.56. Reqd. for $\text{C}_{26}\text{H}_{47}\text{NO}$, C, 80.21; H, 12.08; N, 3.60%; ν_{\max} (film, cm^{-1}), 2920, 2850, 1620, 1580, 1470, 1380; δ_{H} (CCl_4), 1.03 (3H, t, Me), 1.13 (26H, m, $(\text{CH}_2)_{13}$), 1.17 (3H, t, MeCHN), 2.63 (4H, m, CH_2Ar , CH_2N), 3.80 (2H, s, ArCH_2N), 6.63–7.07 (3H, m, HAr), 10.40 (1H, s, HOAr, D_2O exch.).

(8z)-2-Dimethylaminomethyl-5-pentadec-8-enyl and (8z, 11z) – 2-(dimethylaminomethyl) pentadeca-8, 11-dienylphenol were formed by (Method A with omission of NaCl addition) from distilled CNSL with dimethylamine and aqueous formaldehyde. Undistilled CNSL, containing cardol,⁵ when similarly reacted, afforded a red-coloured product.

1,3-Dihydroxybenzene reacted by methods B and C with equimolar proportions of dimethylamine and formaldehyde or with excess of the two reagents afforded a deep red product believed to contain 2,6-bis(hydroxymethyl)-4-(dimethylaminomethyl)-1,3-dihydroxybenzene, with polymeric material, m.p. >300°C, although this product could not be adequately characterised from C/H analysis; ν_{\max} (KBr, cm^{-1}), 2700–3400, 1640, 1480; δ_{H} (DMSO), 2.60 (6H, m, Me_2N), 3.62 (2H, m, CH_2N), 4.95 (4H, bs, D_2O , exch.). By an alternative method for the mono-substituted product (3i), a glass has been obtained.¹⁸ Under basic conditions, we were not able to obtain this compound as described.⁹ The product described was obtained apparently under neutral conditions and a red colour was not mentioned.

6-Dimethylaminomethyl-2-methoxy-4-allylphenol (4) (Method C): 2-Methoxy-4-allylphenol (eugenol) (2.73 g, 0.0170 mol), aqueous dimethylamine (12.20 g, 0.0680 mol) and aqueous formaldehyde (4.860 g, 0.060 mol), were reacted at 70°C during 150 min. to give an orange yellow oil (87% yield), purified by prep. TLC; ν_{\max} (film, cm^{-1}), 3000, 2960, 2850, 2800, 1820, 1680, 1635, 1600, 1490; δ_{H} (CCl_4), 2.28 (6H, s, Me_2N), 3.20 (2H, d, J = 4 Hz, $\text{CH}_2\text{C}=\text{C}$), 3.50 (2H, s, NCH_2Ar), 3.70, (3H, s, MeO), 4.97 (2H, m, $\text{CH}_2=\text{C}$), 5.80 (1H, m, $\text{CH}=\text{C}$), 6.30–6.50 (2H, m, HAr), 9.38 (1H, s, HOAr, D_2O exch.); m/z , M^+ 221.1. Reqd. for $\text{C}_{13}\text{H}_{19}\text{NO}_2$, 221.1415.

Mannich reactions with primary amines

A number of reactions were carried out with primary amines and various phenols

2-Methylaminomethylphenol: (Method C): Phenol (0.70 g, 0.05 mol), 30% aqueous methylamine (20.46 g, 0.20 mol and aqueous

formaldehyde (14.18 g, 0.175 mol) were reacted for 2 h when a white solid separated and was collected, (**8**; R = H), m.p. (partial), 70°C. (lit.¹⁹ 58°C, and lit.²⁰ an oil, both by the same method, from reduction of salicylmethylamine). Found: C, 67.92; H, 7.67; N, 10.31. Reqd. for, C₈H₁₁NO.H₂O, (with possible zwitterion or polymeric impurity; ref.²⁰ commented on the difficulty of complete removal of water), C, 67.84; H, 7.80; N, 9.90%. ν_{\max} (KBr, cm⁻¹), 2950, 2800, 1600, 1460, 1350, 1260, 1020, 890; δ_{H} (CCl₄), 2.0–2.50 (3H, m, MeN), 3.10–3.40 (2H, m, ArCH₂N), 6.80 (4H, HAr, HOAr); ¹H NMR in agreement with lit.²¹ m/z , M⁺ 137.0, Reqd. for C₈H₁₁NO, 137.0841.

N,N-Bis(2-Hydroxybenzyl)methylamine: With equimolar quantities (0.033 mol) of phenol and methylamine, reaction at ambient temperature during 24 h, the syrupy reaction mixture showed three products (TLC) which were separated by prep. TLC. (solvent E). An oily product was obtained (15% yield), R_f 0.24; δ_{H} (CCl₄), 2.20 (3H, m, NMe), 3.67 (4H, m, (ArCH₂N)₂), 6.83, (8H, m, HAr), 8.93 (2H, s, HOAr, D₂O exch.), representing (**6**, R = H).

3,4-Dihydro-3-methyl-1,3,2H-benzoxazine and 2-methylamino-methyl-5-methylphenol (Method B): 3-Methylphenol (5.4 g, 0.05 mol), aqueous methylamine (5.42 g, 0.05 mol and aqueous formaldehyde (8.10 g, 0.10 mol) were refluxed for 40 min when TLC indicated 3 components (solvent E) which were separated by prep TLC to give (**7**, R = Me), 3,5-dimethyl-3,4-dihydro-3-methyl-2H-1,3-benzoxazine, (17%, R_f 0.72); Found: C, 69.49; H, 7.77; N, 7.55%, Reqd. for C₁₀H₁₃NO 0.5H₂O; 69.77; H, 8.14; N, 8.14%, m.p. 66–69°C; δ_{H} (CDCl₃) 2.33 (3H, s, MeN), 2.63 (3H, MeAr), 3.97 (2H, m, ArCH₂N), 4.83 (2H, m, ArOCH₂N), 6.70–7.0 (3H, m, HAr).

The baseline band, 2-methylaminomethyl-5-methylphenol (**8**, R = Me), a colourless oil (39%); δ_{H} (CDCl₃), 2.33 (3H, s, MeN), 2.60 (3H, s, MeAr), 3.80 (2H, s, ArCH₂N), 6.67–7.15 (3H, m, HAr), 8.90 (3H, m, HOAr and NH, D₂O exch.). m/z , M⁺ 151.0. Reqd. for C₉H₁₃NO, 151.0997.

Phenol, 1,2-diaminoethane, formaldehyde: Phenol (4.70 g, 0.05 mol), 25% aqueous 1,2-diaminoethane (12.0 g, 0.20 mol) and aqueous formaldehyde (14.18 g, 0.17 mol) by Method C gave a yellow rubbery polymer upon cooling the reaction mixture; the product appears to be a 2,6-disubstituted polymer.

Mannich reactions with primary–secondary amines

A number of Mannich reactions were carried out by Method C, as shown in Scheme 3, with diethylenetriamine, (DETA) which contains primary and secondary amino groups. Thus, phenol, 3-methylphenol and 1,3-dihydroxybenzene were reacted with diethylenetriamine (DETA) and aqueous formaldehyde at 80°C and gave amber, orange and reddish pink mixtures of products respectively, which however, could not be fully characterised. Nevertheless, from certain spectroscopic and microanalytical data, we believe that phenol (**5**, R = H) gave (**9** and **10**, R = H), 3-methylphenol (**5**, R = Me) afforded (**9** and **10**, R = Me) and that with 1,3-dihydroxybenzene (**5**, R = OH) a complex mixture resulted containing **9**, **10**, **11**, **12** and **13** (R¹ = (CH₂)₂NH(CH₂)₂NH₂), by analogy with (**6**) from methylamine. Additional hydroxymethyl groups appear possible as well as polymeric structures from reaction at the *o*-, *p*- and *cine* positions. HPLC was not available but now would be more effective than TLC which was used.

Mixed cardanol (distilled, but containing some cardol⁵) (**5**, R = C₁₅H_{31-n}) with aqueous formaldehyde and DETA gave a red oily

product consisting from TLC of a complex isomeric mixture, which we believe to consist of (**9** and **10**, R = C₁₅H_{31-n}), and **13** (R = C₁₅H_{31-n}, R¹ from DETA).

This experiment was repeated, with (a) a nitrogen atmosphere, (b) an antioxidant, 2,6-di-*t*-butyl-4-methylphenol, present and (c) with cardanol pretreated with 1% of sodium borohydride. In all cases, similar lighter products resulted, although colour partially reverted upon prolonged storage. Hydrogenated CNSL afforded (Method B) a similar red-coloured product. It was concluded that the red colour in products from cardanol (3-pentadecylphenol) was attributable to the presence of cardol (5-pentadec(e)nylresorcinol) probably by way of the keto tautomer.

In experiments on the origin of the red colour, mixtures of (a) DETA and phenol, (b) formaldehyde and phenol, and (c) DETA with formaldehyde, in the hot only resulted in pale yellow but not deep red products. However, each of the dihydric phenols, resorcinol, 5-methyl-, 4-methyl-, 2-methyl-, 5-pentadecyl-, 2-methyl-5-pentadecylresorcinol, in hot ethanolic solution containing bases gave deep red solutions. Formaldehyde was unconnected with the formation of the red colour in their Mannich reactions and indeed the insertion of the methylene group would hinder the conjugation inherent in colour formation. The structural features, chain branching, polyalkylsubstitution and unsaturation in model compounds were thus not influential. The effectiveness of sodium borohydride is considered to be due to radical scavenging and also limitation of autoxidation²² leading to orceinic pigments.

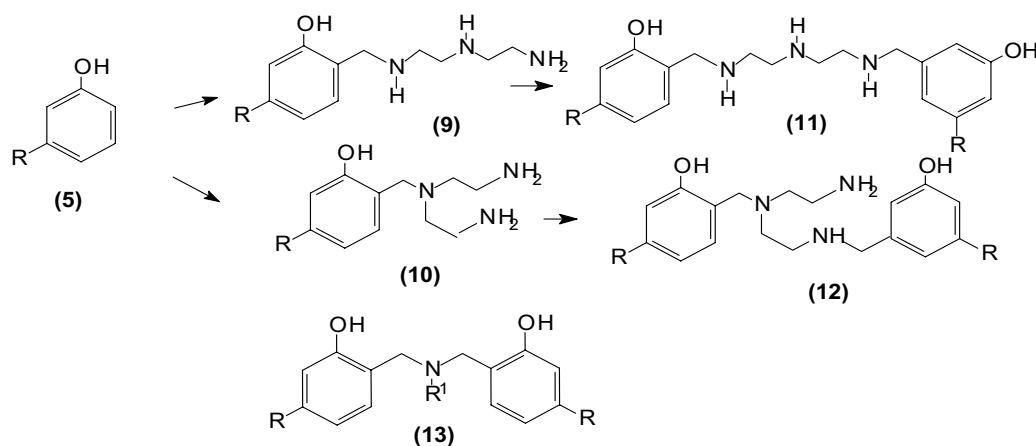
In Mannich reactions, cardol was more reactive than cardanol and this was used subsequently in two methods for the preparation of purer cardanol with a reduced % cardol^{23,24} although a phase separation procedure was later²⁵ found to be more efficient. The patentees¹ do not mention the formation of a red by-product although their raw material is described as 90–92% cardanol and 2–10% of cardol.

An attempt to avoid the basic conditions leading to the red impurity by the use of *N,N*-dimethyl (methylene) ammonium chloride²⁶ was unsuccessful and phenol, unlike indole, was unreactive.

Generally we conclude that short chain alkylphenols with secondary amines readily formed di and trisubstituted dimethylaminomethyl products, whereas the longer chain in 3-pentadecylphenol restricted the reaction to monosubstitution, probably due to steric hindrance, although this was not observed with 3,4,5-trimethylphenol. With primary amines, our work with phenol and 3-methylphenol agrees with previous studies¹³ on 4- and 2,4-disubstituted phenols. DETA appears to lead to reaction at NH₂ and NH groups, giving a complex range of difficultly separable products, and possibly also oxazines. Reactions with longer chain amines were slower than those with dimethylamine^{4,27}

With Mannich bases from cardanol in the subsequent curing reactions with epoxy resins, complex linear and cross-linking reactions ensue. In the isolation of the cardol fraction²⁸ from CNSL we have observed the formation of a blue by-product which does not appear to have noted by the authors and is also reminiscent of resorcinol blue.²⁹ Our general investigation has implicated the formation of phenoxazones and basic xanthenes (dibenzopyrans), which were reported in outline,³⁰ and will be described in another contribution.

We thank Minnesota 3M Research Ltd. for sponsorship and Brunel University for some postgraduate financial assistance.



Scheme 3 Mannich reactions of phenols with a secondary/primary amine.

Received 19 October 2006; accepted 11 January 2007
Paper 06/4265

References

- H. Tien, R. Li, X. Zhao and Q. Zhang, Faming Zhuanli Shenqing Gonghakai Shuomingshu CN 1374292, April 5 2002.
- M. Patel, M Phil thesis, Brunel University, 1978.
- J.H.P. Tyman and V. Tychopoulos, *Synth. Commun.*, 1986, **16**, 1402.
- E.L. Short, J.H.P. Tyman and V. Tychopoulos, *J. Chem. Tech. Biotech.*, 1992, **53**, 389.
- J.H.P. Tyman, *Synthetic and natural phenols*, Elsevier Science, Amsterdam, 1996, Chap. 13, p.538.
- F.F. Blicke, *Organic Reactions*, Vol.1, Chap.10, 303.
- H.A. Bruson and C.W. Macmullen, *J. Am. Chem. Soc.*, 1941, **63**, 1765.
- W.T. Caldwell and T.R. Thompson, *J. Am. Chem. Soc.*, 1939, **61**, 765.
- J. Decombe, *Compt. Rend.*, 1933, **197**, 258.
- E.S. Ebers, US Patent, 2417975, (1942), *Chem. Abs.*, 41, 4003.
- G.E. van Gils, *Divn. Poly. Chem. Preprints. Am. Chem. Soc.*, 1967, (8), 1508.
- W.J. Burke, *J. Am. Chem. Soc.*, 1949, **71**, 609.
- W.J. Burke, R.P. Smith and G. Weathrbee, *J. Am. Chem. Soc.*, 1952, **74**, 602.
- R.L.M. Allen, *Colour Chemistry In Studies in modern chemistry*, Nelson, 1971, Chap.7, p.112.
- J.H.P. Tyman and I.E. Bruce, *J. Surfactants Deterg.*, (2004), **7**, 167.
- H.A. Bruson and C.W. Macmullen, *J. Am. Chem. Soc.*, 1941, **63**, 270.
- A.S. Gulati, V.S. Krishnamachar and B.C. Subba Rao, *Ind. J. Chem.*, 1963, **2**, 114.
- L. Mangoni, *Ann. Chim.*, 1958, **48**, 930.
- L. Cazaux and P. Tisnes, *J. Heterocycl. Chem.*, 1976, **13**, 665.
- T.M. Kitson and G.H. Freeman, *Biorg. Chem.*, 1993, **21**, 354.
- P. Maroni, L. Cazaux, P. Tisnes and M. Zambeti, *Bull. Soc. Chim. Fr.*, 1980, 185.
- H. Musso and D. Maassen *Chem. Ber.*, 1962, **95**, 2831.
- M. Patel, J.H.P. Tyman and A. Manzara, UK Application, 8100208, 6th Jan 1981.
- J.H.P. Tyman, UK Application, GB 2152925A, 24th Oct. 1983.
- J.H.P. Tyman, I.E. Bruce and P. Payne, *Nat. Prod. Lett.*, 1992, **1**, 117.
- G. Kinast and L.F. Tietze, *Angew. Chem. Int. Edn.*, 1976, **15**, 239.
- A.J. Revukas, US Patent 2489672 (Nov. 29, 1949).
- R. Paramashivappa, P.P. Kumar, P.J. Vithayatvil and A.S. Rao, *J. Agric. Food Chem.*, 2001, **49**, 2548.
- H. Musso, I. Seeger and U.I. Zahorszky, *Angew. Chem.*, 1961, **73**, 434.
- J.H.P. Tyman, M. Patel and R.N. Tanner, Abstract C67, 12th IUPAC Symp. on the Chemistry of Natural Products, Tenerife, 1980.