Tetrahedron Letters, Vol.31, No.19, pp 2789-2792, 1990
Printed in Great Britain

0040-4039/90 $3.00 + .00
Pergamon Press plc

FLAVAN AND XANTHENE COMPOUNDS FROM REARRANGEMENT OF PHLOROGLUCINOL POLYMERS

Jonathan White and Lai Yeap Foo
Chemistry Division, DSIR, Private Bag, Petone, New Zealand

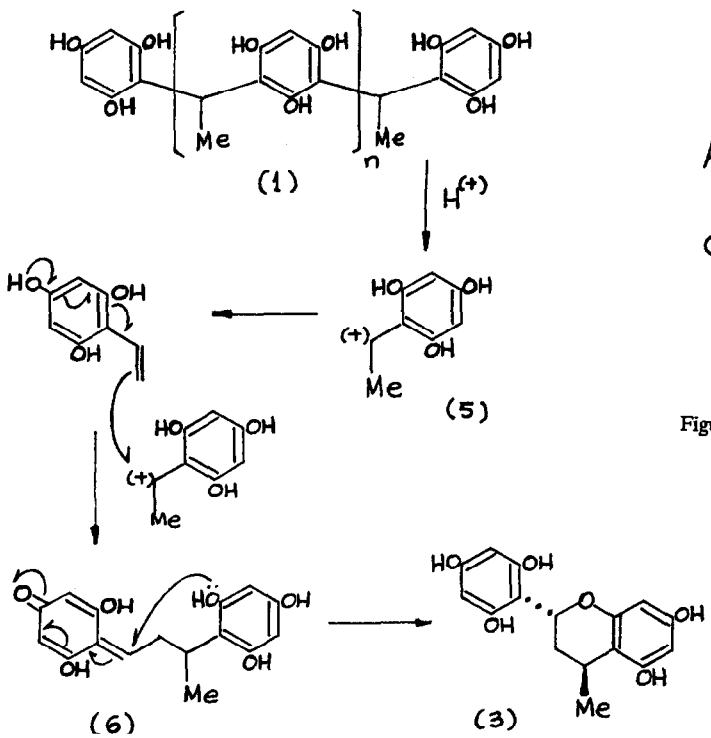
Summary Phloroglucinol reacts with acetaldehyde under acid conditions to give rise to insoluble linear polymeric products which subsequently rearrange to flavan and xanthene compounds.

Condensation of phenols with formaldehyde is an important reaction in the chemical industry which provides a range of well known phenolic resins used for a variety of applications[1]. In recent years much interest in this type of condensation has been directed to generating a range of macrocyclic compounds collectively known as calixarenes which can play hosts to other smaller molecules or metal ions[2,3]. While resorcinol and other phenols react with acetaldehyde to give macrocycles[4-6] in high yields, in contrast phloroglucinol reacts to give rise to rearranged products.

An equimolar mixture of phloroglucinol and acetaldehyde in the presence of EtOH/H_2O/HCl (2:2:1 $^v/_v$) at ambient temperatures polymerises rapidly to form a solid mass within minutes. The material is insoluble in most organic solvents but dissolves slowly in MeOH to enable characterisation by ^{13}C NMR spectroscopy (Figure 2a) which shows broad signals centred at 18, 26, 97, 113 and 155 ppm consistent with a predominantly linear polymer of phloroglucinol units (1) linked together by methyl substituted methylene bridges. On leaving the mixture to stir at room temperature for 48 hours the solid slowly dissolves to give an orange coloured solution which yields 20% by weight of an ether extract. Separation of this extract on Sephadex LH 20 using EtOH-H_2O (1:1 $^v/_v$) as eluant gives among other materials, phloroglucinol, 1,1-di-(2,4,6-trihydroxyphenyl)-ethane (2) and two other novel products (3) and (4) in the proportion of 6:10:1:9 by weight respectively. Microanalytical and MS data indicates (3) to have the elemental composition $C_{16}H_{16}O_6$ which could only be derived from condensation of two molecules each of phloroglucinol and acetaldehyde. This chemical constitution is apparent also from the ^{13}C NMR spectrum with the observation of four high field resonances attributed to a methyl carbon (21.6 ppm), two methine carbons (25.1 and 70.1 ppm) and a methylene carbon (34.8 ppm) together with the downfield resonances accounting for the two phloroglucinol rings. With 2D NMR (H,H-COSY and H,C-COSY) the connectivity of the aliphatic carbons is established as CH_3-CH-CH_2-CH-O. The observation of a degenerate carbon resonance associated with the two protons singlet at δ5.98 indicates the presence of a freely rotating phloroglucinol moiety. In addition, a meta-coupled (J=2.3Hz) proton system (δ5.95 and δ6.09) suggests the presence also of an immobilised phloroglucinol ring possibly involved in a cyclic system. The existence

of such a ring system is evidenced by the observation of two separate proton resonances δ1.78 and δ2.43 each as a complex multiplet associated with the methylene carbon. These data are fully consistent with (3) being 2',4',5,6',7-pentahydroxy-4-methyl-flavan, this structure being corroborated further by the NOESY spectrum which shows spatial interactions between the methyl protons and one of the methylene protons (δ1.78) as well as the low field methine proton (Figure 1). This observation indicates the methyl and the aryl substituents are in a trans configuration thus indicating some stereo control in its formation. The proposed mechanism involving the benzylcarbocation[7] (5) from the acid cleavage of the linear polymer is shown in Scheme 1. From the Dreiding model it is apparent that the formation of the trans product is much more favoured as the phenolic oxygen could approach the quinone-methide (6) without hindrance. However, for the cis compound this approach imposes an unfavourable interaction between the quinone-methide moiety and the methyl substituent.

Scheme 1. Proposed mechanism for formation of flavan (3)



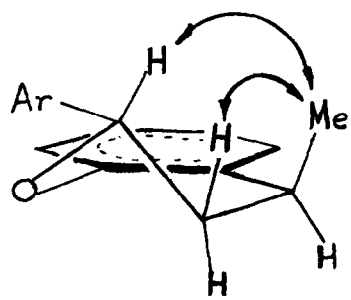
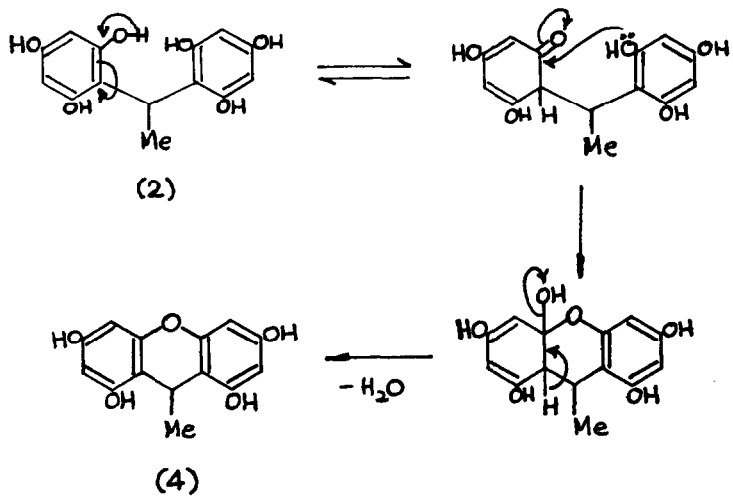


Figure 1. NOEs observed in flavan (3)

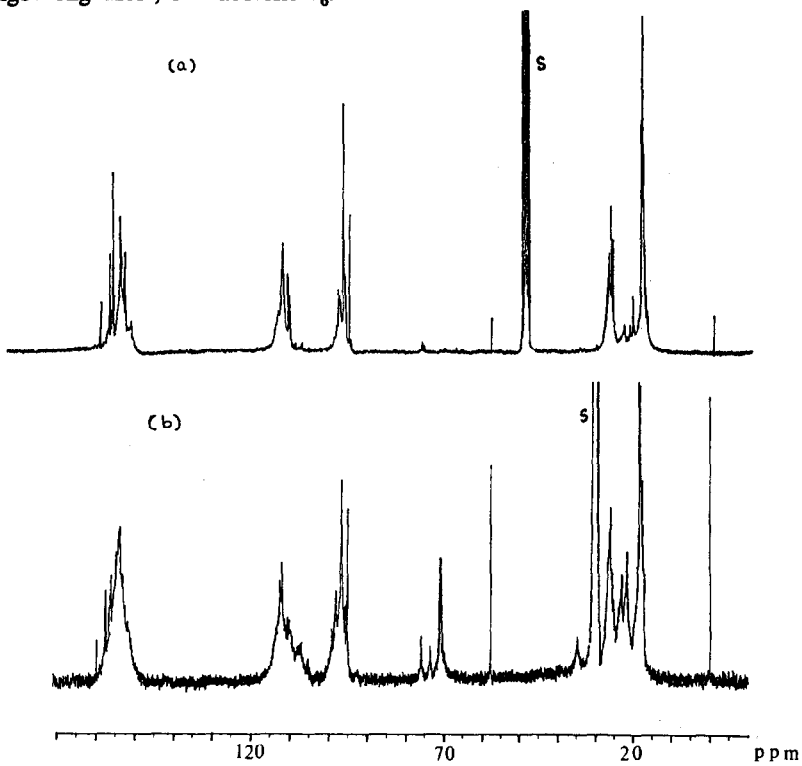
Compound (4) is identified as 9-methyl-xanthene on the basis of its ^1H NMR spectrum which shows four pairs of well resolved doublets at δ1.31 (J = 6.5 Hz, CH_3), δ4.32 (J = 6.5 Hz, CH), δ6.07 (J = 2.3 Hz, 2 x ArH) and δ6.20 (J = 2.3 Hz, 2 x ArH). The ^{13}C resonances observed at 157.5, 157.4, 154.0, 107.1, 98.3, 95.4, 23.4 and 23.3 ppm are fully consistent with the assigned structure which is also corroborated by mass spectral and elemental analytical data. Formation of (4) could be envisaged as arising from cyclization of 1,1-di(2,4,6-trihydroxyphenyl)-ethane (2) via its keto tautomer as shown in Scheme 2.

Scheme 2. Proposed mechanism for formation of (4)



The ^{13}C NMR spectra of the oligomeric fraction from both the ether and the ether insoluble materials (see Figure 2b) show pronounced peaks in the 70 and 23 ppm regions which are identifiable with the flavan and xanthene structures respectively indicating the initial linear polymer had substantially rearranged to a more complex form. This observation contrasts markedly with the reactions of simple phenols and resorcinol with acetaldehyde and may be rationalised on the basis of increased reactivity of the phloroglucinol ring leading to the lability of the inter-phloroglucinol linkages. Phloroglucinol also has the propensity to react like a cyclic ketone[8] thus facilitating nucleophilic cyclization leading to xanthene structures.

Figure 2. ^{13}C NMR spectra of (a) initial polymer, S = MeOH-d_4 and (b) re-arranged oligomers, S = acetone-d_6.



References

1 D.F. Gould, Phenolic Resins, Reinhold Publishing Corporation, New York, 1959.

2 C.D. Gutsche, M. Iqbal and I. Alam, J. Amer. Chem. Soc., 109, 4314 (1987).

3 D.J. Cram, Science, 240, 760 (1988).

4 A.G.S. Hogberg, J. Org. Chem., 45, 4498 (1980).

5 L. Abis, E. Dakanale, A. Du vosel and S. Spera, J. Org. Chem., 53, 5475 (1988).

6 R. Ungaro, A. Pochini, G.D. Andreetti and P. Domiano, J. Chem. Soc. Perkin Trans II, 197 (1985)

7 A.C. Fletcher, L.J. Porter, E. Haslam and G.K. Gupta, J. Chem. Soc. Perkin Trans I, 1628 (1977)

8 R.J. Highet and I.V. Ekhato, J. Org. Chem., 53, 2843 (1988).

(Received in UK 2 March 1990)