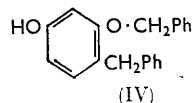
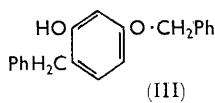
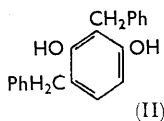
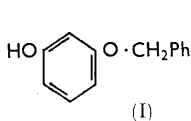


915. *The Benzylation of Resorcinol*

By W. J. HOPWOOD and J. A. STOCK

The reaction of benzyl chloride with resorcinol under various conditions has been studied. In the absence of base, 4- and 2-benzylresorcinol were the major products, but small amounts of resorcinol monobenzyl ether and (probably) 2,4-dibenzylresorcinol were also formed. On the other hand, condensation in acetone in the presence of potassium carbonate gave mainly the mono- and di-benzyl ethers of resorcinol, together with minor quantities of 4- and 2-benzylresorcinol and of *O*¹,4-dibenzylresorcinol, not previously described.

INTEREST in the synthesis of aromatic phosphate polyesters led us to examine methods for the preparation of resorcinol monobenzyl ether, required as an intermediate. Klarmann *et al.*¹ and Gregory and Tomlinson² reported that resorcinol monobenzyl ether (I) may be prepared by the reaction of benzyl chloride with resorcinol in xylene at reflux temperature. Fitton and Ramage³ have challenged this claim, and state, without giving



experimental details, that 4-benzylresorcinol is the main product. We have now studied the reaction in greater detail. The major product was indeed 4-benzylresorcinol (Table I). 2-Benzylresorcinol was also formed, and, in smaller amount, the ether (I). We isolated a fourth substance which did not crystallise, and we believe it to be essentially 2,4-dibenzylresorcinol (II) because it gave a positive reaction with Gibbs's reagent, and was unaffected by ethanolic hydrogen chloride (Table I). A condensation of benzyl chloride and resorcinol carried out under standard Friedel-Crafts⁴ conditions gave a similar spectrum of products.

¹ E. Klarmann, L. W. Gatyas, and V. A. Shternov, *J. Amer. Chem. Soc.*, 1931, **53**, 3397.

² R. A. Gregory and M. L. Tomlinson, *J.*, 1956, 795.

³ A. O. Fitton and G. R. Ramage, *J.*, 1962, 4870.

⁴ E. Klarmann, *J. Amer. Chem. Soc.*, 1926, **48**, 791.

TABLE 1
 Products of condensation in xylene

Fraction no. ^a	Component	R _D (t.l.c.) ^b	% ^c	Identified as
11—15	1 ^d	0.79	2.7	?2,4-Dibenzylresorcinol
16—20	2	0.65	1.2	Resorcinol monobenzyl ether ^e
22—53	3 ^f	0.57	15.8	2-Benzylresorcinol
57—104	4 ^g	0.30	79.8	4-Benzylresorcinol

^a Column and solvent details in Experimental section. ^b Average values, solvent System A. ^c Of material put on column. ^d ν 3400, 1950, 1800; no significant absorption between 1000 and 780 cm.⁻¹. Unaffected (t.l.c.) by 20 hours' exposure to 10N-(1:2) aq.-ethanolic hydrogen chloride. Positive reaction with Gibbs's reagent (λ_{\max} . 525 m μ ; method as in Experimental section). ^e By comparison (t.l.c., m. p.) with authentic sample (Table 2). ^f Rods from benzene-petrol, m. p. 82—84° (lit.,⁵ 82—84°) (Found: C, 77.5; H, 6.2. Calc. for C₁₃H₁₈O₂: C, 78.0; H, 6.0%); dibenzoate, m. p. 138—139° (lit.,⁵ 138—139°); no infrared absorption between 790 and 840 cm.⁻¹ (1,2,3-trisubstitution). ^g Prisms from benzene-petrol, m. p. 78° (lit.,³ 77—78°) (Found: C, 77.6; H, 6.1. Calc. for C₁₃H₁₈O₂: C, 78.0; H, 6.0%); dibenzoate, m. p. 104—105° (lit.,³ 104—105°).

In an attempted condensation in ethanolic hydrogen chloride⁶ only small amounts of 4- and 2-benzylresorcinol were produced. The formation of 2-benzylresorcinol in reactions of the type described above does not appear to have been reported before.

Fitton and Ramage³ have suggested that resorcinol monobenzyl ether (I) may have formed in the Klarmann xylene reaction,¹ and rearranged during the isolation procedure. Freudenberg and Alonso de Lama reported⁷ that the ether (I) rearranged to 4-benzylresorcinol under acid conditions, but we have not been able to confirm this. It seemed possible, though unlikely, that initially formed ether (I) had rearranged to C-benzylresorcinols during the Klarmann synthesis,¹ the hydrogen chloride formed in the reaction acting as catalyst. This possibility was not substantiated.

Next, the condensation of resorcinol and benzyl chloride in the presence of base was studied. We used the procedure developed by Fitton and Ramage³ for synthesising the monobenzyl ether (I). A number of products was formed and their relative proportions are set out in Table 2. As expected,³ the ether (I) was the main component of the reaction

 TABLE 2
 Products of condensation in presence of base

Fraction no. ^a	Component	R _D (t.l.c.) ^b	R _F B ^c	%	Identified as
4—6	1 ^d	1.00	—	27.6	Resorcinol dibenzyl ether
7—8	2	0.83	—	2.0	O ¹ ,4-Dibenzylresorcinol ^e
10—28	3 ^f	0.65	0.45	36.3	Resorcinol monobenzyl ether
51—62	4 ^g	0.57	0.28	2.3	2-Benzylresorcinol
82—100	5 ^h	0.30	0.05	7.8	4-Benzylresorcinol
102—134	6	0.25	0.03	20.3	Resorcinol ^h

^{a,b} See Table 1. Eluting solvents: fractions 1—70, benzene; 71—77, benzene containing 5% ethyl acetate; 78—119, benzene containing 10% ethyl acetate; 120 onwards, ethyl acetate. ^c Average R_F in solvent system B (t.l.c., triple development). ^d Needles from petrol, m. p. 75—76° (lit.,⁵ 76°) (Found: C, 82.2; H, 6.5. Calc. for C₂₀H₁₈O₂: C, 82.6; H, 6.3%). ^e Needles from petrol, m. p. 75—76° (Found: C, 82.0; H, 6.0. C₂₀H₁₈O₂ requires C, 82.6; H, 6.3%). ^f M. p. 50—51° (lit.,³ 50—51°). ^g As in Table 1. ^h By comparison (t.l.c.) with authentic sample.

mixture. One of the minor products (component 2), whose analysis and infrared spectrum pointed to an O,C-dibenzylresorcinol, gave 4-benzylresorcinol when exposed to ethanolic hydrogen chloride. It was therefore either O¹,4-dibenzylresorcinol (III) or the O¹,6-dibenzyl analogue (IV). Structure (III) seemed more likely on steric grounds, and was confirmed by a positive reaction with Gibbs's reagent.

EXPERIMENTAL

Plates coated with Stahl silica gel G (250 μ) were used for thin layer chromatography (t.l.c.). They were usually developed in 9 : 1 benzene-ethyl acetate (system A), but triple development

⁵ B. Z. Mullaji and R. C. Shah, *Proc. Indian Acad. Sci.*, 1951, **34A**, 173.

⁶ B. R. Brown, W. Cummings, and G. A. Somerfield, *J.*, 1957, 3757.

⁷ K. Freudenberg and J. M. Alonso de Lama, *Annalen*, 1958, **612**, 78.

⁸ H. Schiff and G. Pellizzari, *Annalen*, 1883, **221**, 365.

in 4 : 1 benzene-chloroform (system *B*) was employed occasionally, particularly when a good separation of resorcinol monobenzyl ether and 2-benzylresorcinol was required. Subsequent exposure of the air-dried plates to iodine vapour revealed the compounds as brown or yellow spots whose characteristic hues assisted identification. The R_F values varied somewhat from plate to plate. Mobilities are therefore given as the less variable R_D values, where $R_D = R_F$ compound/ R_F resorcinol dibenzyl ether; the dibenzyl ether was the fastest running of the resorcinol derivatives ($R_F > 0.90$). Benzyl chloride and benzyl alcohol (R_D 1.06 and 0.48 respectively) gave too low a colour yield with iodine to be detected in the reaction mixtures. M. p.s (Kofler) are corrected. Spectra were recorded on Perkin-Elmer model 137 Infracord and UV spectrophotometers.

Reaction of Benzyl Chloride with Resorcinol.—(a) *In xylene.* The procedure of Gregory and Tomlinson² was used. The average yield of final distillate (162–174°/0.1–0.4 mm.; lit.,² 200°/5 mm.) in 4 runs was 25%, monobenylation being assumed. The combined distillates solidified to a wax, m. p. 48–55° (lit.,² 69°). The m. p. and t.l.c. pattern were unchanged by redistillation (182°/0.1 mm.; constant throughout). The redistilled product (1.15 g.) was chromatographed on a silica gel column (19 × 2.2 cm.; 40 g. adsorbent, 200–300 mesh; 10 ml. fractions; elution with benzene to fraction 81, then with 9 : 1 benzene-ethyl acetate). Fractionation was followed by t.l.c. (Table 1).

Two successive recrystallisations of part of the redistilled material (m. p. 48–55°) from benzene gave a crystalline solid, m. p. 72–74°, containing 4- and 2-benzylresorcinol only.

(b) *In nitrobenzene (Friedel-Craft).* The method of Klarmann⁴ was used. The oil obtained on acidification of the ether-washed alkaline extract showed a t.l.c. pattern similar to that described under (a), except that resorcinol monobenzyl ether was not detected. Unchanged resorcinol was present. 4-Benzylresorcinol (0.79 g.) and 2-benzylresorcinol (0.24 g.) were obtained as the major components by chromatography of the oil (1.27 g.) on silica gel as in (a).

(c) *In acetone in presence of potassium carbonate.* The procedure of Fitton and Ramage³ was followed. In a typical experiment, carried out on a 0.66 molar scale, t.l.c. of a few μ l. of the filtered acetone reaction solution revealed at least 8 components. Isolation of the major products was achieved by chromatography on silica gel as in (a), and details are given in Table 2. Traces of two very minor components (R_D 0.52, 0.43) were also observed.

Characterisation of O¹,4-Dibenzylresorcinol.—(a) *Action of hydrogen chloride.* A little (ca. 5 mg.) of component 2, Table 2, was dissolved in 10N-(1 : 2) aqueous-ethanolic hydrogen chloride (1 ml.) and set aside for 3 hr. in a stoppered tube. Only 4-benzylresorcinol and a slight trace of 2-benzylresorcinol were detected (t.l.c.).

(b) *Reaction with Gibbs's reagent (2,6-dichlorobenzoquinone chloroimide).*⁹ A crystal (<1 mg.) of the dibenzyl compound was dissolved in a fresh solution (ca. 1 ml.) of 2,6-dichlorobenzoquinone chloroimide in pyridine (90 mg./50 ml.), and 0.05M pH 9.2 borate buffer (ca. 10 ml.) added. A very intense blue colour developed (λ_{\max} 595 μ).

Reaction of Benzyl Alcohol and Resorcinol in Ethanolic Hydrogen Chloride.^{cf.6}—Resorcinol (1.38 g.) and benzyl alcohol (1.08 g.) were dissolved in 8.5N-ethanolic hydrogen chloride (10 ml.) and the solution set aside in a stoppered flask for 7 days at room temperature. T.l.c. of the red solution revealed unchanged resorcinol as main component. 4- and 2-Benzylresorcinol were also present in relatively small amounts, the former predominating.

Action of Hydrogen Chloride.—(a) *On resorcinol monobenzyl ether (I).* (i) The ether (ca. 5 mg.) was dissolved in a mixture (ca. 1 ml.) of 10N-aqueous hydrochloric acid (1 vol.) and ethanol (2 vol.). The solution was heated on a steam-bath for 1 hr. T.l.c. of the reaction mixture showed resorcinol as major component, with minor amounts of 4- and 2-benzylresorcinol, and traces of other unidentified substances. A substantial amount of unchanged ether was also present. When the reaction was carried out at 61° (boiling chloroform temperature), conversion was slower and a trace of ether remained even after 48 hr. heating. The only reaction product formed in substantial quantity was resorcinol; 4- and 2-benzylresorcinol were also detected, but only in trace amounts.

(ii) The ether (ca. 5 mg.) was dissolved in a mixture (ca. 1 ml.) of saturated (10.3N) ethanolic hydrogen chloride (2 vol.) and 10.4N-aqueous hydrochloric acid (1 vol.) at room temperature. Cleavage was complete within 2 hr. Resorcinol was the only product detected (t.l.c.).

(iii) As in (ii), but with 10.3N-ethanolic hydrogen chloride only. Ether fission proceeded

⁹ F. E. King, T. J. King, and L. C. Manning, *J.*, 1957, 563.

more slowly than in the medium described in (ii), but was complete in less than 24 hr. Resorcinol was again the only product.

(iv) A solution of the ether (200 mg.; 1.0 mmole) in xylene (5 ml.) containing 8.6N-ethanolic hydrogen chloride (0.12 ml.; *ca.* 1 equiv.) was heated for 6 hr. under reflux. Starting material was the only substance present in significant amount (t.l.c.).

(b) *On 2- and 4-benzylresorcinol.* Small quantities of the 2- and 4-benzyl derivatives were separately dissolved in 10.3N-aqueous or aqueous-ethanolic hydrogen chloride as in (a, ii) and (a, iii) above and set aside for 6 days at room temperature. T.l.c. of each of the four solutions revealed the presence of starting material only.

Heating 2-benzylresorcinol in 3N-aqueous-ethanolic hydrogen chloride as in (a, i) gave starting material and a trace of resorcinol. 4-Benzylresorcinol under these conditions gave starting material, with traces of 2-benzylresorcinol and resorcinol.

We thank Professor F. Bergel, F.R.S., for interest, Dr. R. Wade for help in the interpretation of the infrared spectra, Miss V. Lewis for experimental assistance, and Mr. P. D. Regan for an early experiment on t.l.c. This investigation was supported by grants to this Institute from the Medical Research Council, the British Empire Cancer Campaign for Research and by the U.S. Public Health Service.

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[Received, January 5th, 1965.]
