502. *Alkylation of the Aromatic Nucleus. Part III.* The Reaction of Phenols with the n-Butyl Ester of Methanesulphonic Acid.*

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A butyl group is introduced into monohydric phenols when they are heated with n-butyl methanesulphonate. Olefin is not liberated and the n-butyl group is isomerised to s-butyl. There is evidence that phenol is substituted in the *meta*-position as well as in the *ortho*- and *para*-positions.

The earlier work [1] has been mainly concerned with the introduction of alkyl groups into the aromatic nucleus of toluene and its homologues by the thermal decomposition of the arenesulphonic esters of secondary alcohols or of benzyl alcohol. The work now described examined the behaviour of a sulphonic ester of a primary alcohol capable of isomerisation, and determined whether alkylation is accompanied by isomerisation, and to what extent.

The sulphonic esters of primary alcohols, except benzyl, are much more stable than those of secondary alcohols and require inconveniently high temperatures to permit use in alkylation. Phenols were therefore used in this study, advantage being taken of their acidic character to promote decomposition of the sulphonic ester. Butyl methanesulphonate was selected; the n-butyl group fulfils the necessary conditions and the ester can be prepared conveniently in good yield and purified simply by distillation.

The alkylations were smooth with all the monohydric phenols examined except

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* Part II, preceding paper.

[1] (*a*) Földi, *Ber.*, 1928, **61**, 1609; (*b*) Hickinbottom and Rogers, *J.*, 1957, 4124; (*c*) Nenitzescu, Joan, and Teddorescu, *Ber.*, 1957, **90**, 585.

1-naphthol which gave a glass; quinol and resorcinol gave only intractable tars. *p*-Dimethoxybenzene, however, reacted normally to give 2-butyl-1,4-dimethoxybenzene, with some *p*-anisole and butene. It is significant that in all alkylations of monohydric phenols no butene was evolved, although in all other alkylations with butyl esters of sulphonic acids, butene was formed with the expected alkylation products.

It is clear (see Experimental) that the n-butyl group is very largely isomerised to s-butyl and that there is no sure evidence that the *normal* structure survives in these alkylations. Yet an examination of the spectra of liquid products of alkylation reveals small differences; bands are present which do not occur in the spectrum of the corresponding s-butyl compound. Thus the alkylation product of *p*-chlorophenol is a liquid, although both 4-chloro-2-s- and -2-n-butylphenol are solid, and its infrared spectrum shows absorption bands at 8·1, 8·4, 9·58, and 10·8 μ not present in the spectrum of 4-chloro-2-s-butylphenol. Similarly, the liquid portion of the product of alkylation of *p*-cresol, after separation of the bulk of 4-methyl-2-s-butylphenol, has bands at 8·9, 10·8, 11·9 μ not present in the spectrum of 2-s-butyl-*p*-cresol. It would be unwise, in the absence of supporting evidence, to accept this as indicating the presence of n-butyl compounds. Indeed, these bands may arise from the presence of substituted phenols having the butyl group *meta* to the hydroxyl group. This view is supported by examination of the infrared spectrum of a fraction from the product of alkylation of phenol with butyl methanesulphonate. It shows peaks at 10·9, 11·55, 12·5, and 12·8 μ which are not present in the spectra of *o*- and *p*-n- and -s-butylphenols but are present in the spectrum of *m*-s-butylphenol.

If these interpretations are correct, and they find support in the isolation from the mixture of a phenylurethane having the melting point of that from *m*-s-butylphenol, they can be used to provide more evidence of the low selectivity of a carbonium ion in aromatic substitution.[2] An alternative explanation, not yet excluded, is that groups can migrate within the phenol under the influence of methanesulphonic acid.

EXPERIMENTAL

Preparation of Butyl Methanesulphonate.—A stirred mixture of n-butyl alcohol (37 g.) and pyridine (80 g.) was kept at $-5°$ while methanesulphonyl chloride (57·3 g.) was run in slowly and regularly. After 4 hr., the thick mixture was kept overnight in a refrigerator and then treated with about 500 c.c. of water and acidified with hydrochloric acid–crushed ice. The oil was taken up in ether; the ethereal solution was washed with dilute hydrochloric acid till free from pyridine, then with water till neutral, and dried (K_2CO_3). Butyl methanesulphonate (58·5 g.), obtained by distillation, had b. p. 73—75°/1 mm., n_D^{20} 1·4271 (Found: C, 39·9; H, 7·5; S, 21·0. Calc. for $C_5H_{12}O_3S$: C, 39·5; H, 7·9; S, 21·1%) (Sekera and Marvel[3] give b. p. 105°/6 mm., n_D^{20} 1·4319).

Reaction of n-Butyl Methanesulphonate with Phenols.—The following general procedure was used; the phenol (~1 mole) was stirred with the sulphonic ester (~0·25 mole) at about 140°. Arrangements were made to collect, in cold traps, the butenes which might be liberated. In general, the onset of alkylation could be recognised by darkening of the mixture.

The product was isolated by diluting the mixture with ether and removing the free methanesulphonic acid with an excess of saturated sodium carbonate solution. The ether solution, after being washed and dried, was distilled to remove the unchanged phenol. Further distillation through a spinning-band column (Haage) under reduced pressure gave a series of fractions of narrow boiling range which were examined for the presence of n- and s-butyl-substituted phenols. It was possible in some preparations to isolate pure material which could be identified by physical constants, by preparation of derivatives, and by infrared spectroscopy.

(a) *With phenol.* The reaction was carried out at 160° for 90 hr. with 39 g. of ester. The product was separated by alkali into diphenyl ether (4·5 g., b. p. 230—240°, m. p. 24—26°;

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[2] Smoot and Brown, *J. Amer. Chem. Soc.*, 1956, **78**, 6245.

[3] Sekera and Marvel, *ibid.*, 1933, **55**, 345.

picrate, m. p. 109—110°; nitro-derivative, m. p. 135°; these m. p.s were unchanged by admixture with authentic specimens) and butyl-phenols, b. p. 124—129°/19 mm., n_D^{20} 1·5289—1·5180 (26·7 g.).

Crystallisation of the phenylurethanes of the butyl-phenols of fractions of b. p. 128—129°/19 mm. gave two main crops: (i) m. p. 101—102° (Found: C, 76·1; H, 7·2; N, 5·2. Calc. for $C_{17}H_{19}O_2N$: C, 75·8; H, 7·1; N, 5·2%) not depressed by admixture with the phenylurethane of *p*-s-butylphenol; (ii) m. p. 71—73° (Found: C, 75·9; H, 7·2; N, 5·4%) depressed to 57—58° by admixture with the phenylurethane of *o*-n-butylphenol (m. p. 71—72°), depressed to 61—64° by admixture with the phenylurethane of *o*-s-butylphenol (m. p. 84—85°), depressed to 68—70° by admixture with the phenylurethane of *m*-s-butylphenol (m. p. 71—72°).

Comparison of the infrared spectrum of the product with that of each of the possible isomeric butylphenols shows that *o*- and *p*-s-butylphenols are present and that the *m*-isomer is almost certainly a constituent of the mixture. There is no clear evidence of the presence of *o*- or *p*-n-butylphenols.

3-*s-Butylphenol*, b. p. 60°/0·1 mm., n_D^{20} 1·5109 (Found: C, 79·4; H, 9·0. $C_{10}H_{14}O$ requires C, 80·0; H, 9·4%) [phenylurethane, m. p. 71—72° (Found: N, 5·3. $C_{17}H_{19}O_2N$ requires N, 5·2%)], was prepared by the demethylation of 3-s-butylanisole [1b] (12 g.) by boiling with concentrated hydriodic acid and acetic acid (equal vols., 200 c.c.) for 4 hr.

(b) *With* p-*chlorophenol.* After 45 hr. at 140°, a crude butyl-4-chlorophenol was obtained, b. p. 140—160°/16 mm., n_D^{20} 1·5362—1·5340. Another distillation gave two fractions: b. p. 140—144°/16 mm., n_D^{20} 1·5362 (2·0 g.) (Found: C, 65·2; H, 7·2. Calc. for $C_{10}H_{13}OCl$: C, 65·0; H, 7·1%), and b. p. 144—155°/16 mm., n_D^{20} 1·5355 (40 g.). No crystalline derivative could be prepared by reaction with either phenyl or 1-naphthyl isocyanate. From the infrared spectra of these fractions, it is apparent that the main constituent is 4-chloro-2-s-butylphenol. 4-*Chloro*-2-*s-butylphenol*, m. p. 49—51°, b. p. 126—128°/12 mm. (Found: C, 65·5; H, 7·0%), was prepared from boron trifluoride and a mixture of 4-chlorophenol and butan-2-ol in light petroleum.

2-*n-Butyl*-4-*chlorophenol*, m. p. 34—36° (Found: C, 65·2; H, 6·9%), was prepared by reduction of 2-n-butyryl-4-chlorophenol [m. p. 52—54°; 2 : 4-*dinitrophenylhydrazone*, m. p. 225—226° (Found: N, 14·4; Cl, 9·6. $C_{16}H_{15}O_5N_4Cl$ requires N, 14·8; Cl, 9·4%)], with amalgamated zinc and hydrochloric acid in acetic acid (Klarmann *et al.*[4] give m. p. 50·5° for the ketone).

(c) *With* 2,4-*dichlorophenol.* This gave after 40 hours at 140°, 2,4-*dichloro*-6-*s-butylphenol*, b. p. 138—140°/22 mm., n_D^{20} 1·5412 (15 g.) (Found: C, 54·2; H, 5·4. $C_{10}H_{12}OCl_2$ requires C, 54·8; H, 5·5%); the *phenylurethane*, m. p. 106—108°, was identical with that, m. p. 107—109° (Found: N, 4·3. $C_{17}H_{17}O_2NCl_2$ requires N, 4·1%), from 2,4-dichloro-6-s-butylphenol [b. p. 136—138°/19 mm., n_D^{20} 1·5381 (Found: C, 54·9; H, 5·4%)], prepared from 2,4-*dichloro*-6-*s-butenylphenol*, b. p. 142—144°/19 mm., n_D^{20} 1·5578 (Found: C, 55·2; H, 4·8. $C_{10}H_{10}OCl_2$ requires C, 55·3; H, 4·6%). The latter was obtained in 40% yield by heating crotyl 2 : 4-dichlorophenyl ether (below) in three times its weight of dimethylaniline for 3 hr.; it had b. p. 142—144°/19 mm., n_D^{20} 1·5578 (Found: C, 55·2; H, 4·8%).

Crotyl 2,4-*dichlorophenyl ether*, b. p. 80—82°/0·1 mm., n_D^{20} 1·5500 (Found: C, 54·9; H, 4·8. $C_{10}H_{10}OCl_2$ requires C, 55·3; H, 4·6%), was prepared in 60% yield by refluxing for 3 hr. 2,4-dichlorophenol (8·2 g.) and crotyl bromide (7 g.) in acetone (100 c.c.) containing potassium carbonate (7·1 g.) after the mixture had been stirred at room temp. for 12 hr.

6-n-Butyl-2,4-dichlorophenol, b. p. 140°/16 mm., n_D^{20} 1·5415, was obtained from Clemmensen reduction of 6-n-butyryl-2,4-dichlorophenol, m. p. 47—48° [2,4-*dinitrophenylhydrazone*, m. p. 226—227° (Found: N, 13·4; Cl, 17·2. $C_{16}H_{14}O_5N_4Cl_2$ requires N, 13·5; Cl, 17·2%)]. Chien and Yin [5] give b. p. 161—163°/11 mm. and m. p. 46—47° for these two compounds respectively.

(d) *With* p-*cresol.* Heating with n-butyl methanesulphonate at 135° for 28 hr. gave a product, b. p. 128°/19 mm., n_D^{20} 1·5215 (supercooled) (13 g.). The m. p. 38—40° was raised to 43—44° by admixture with a specimen of 4-methyl-2-s-butylphenol.

2-n-Butyl-4-methylphenol, b. p. 143°/28 mm., n_D^{20} 1·5181 [phenylurethane, m. p. 79—81° (Rosenwald *et al.* [6] give b. p. 140°/19 mm., n_D^{20} 1·5205, and phenylurethane, m. p. 83—84°)],

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[4] Klarmann, Sliternov, and Gates, *J. Amer. Chem. Soc.*, 1933, **55**, 2576.

[5] Chien and Yin, *J. Chinese Chem. Soc.*, 1939, **7**, 4015.

[6] Rosenwald, Hoalson, and Chenicek, *Ind. Eng. Chem.*, 1950, **42**, 162.

from the Clemmensen reduction of 2-n-butyryl-*p*-cresol, had m. p. 32—34° [semicarbazone, m. p. 159—160° (von Auwers [7] gives m. p. 33—34°; semicarbazone, m. p. 159—160°)].

(e) *With* 2,4-*dimethylphenol.* 28 Hours' reaction at 140° gave butyl-2,4-dimethylphenol, b. p. 116°/14 mm., n_D^{20} 1·5200 (15·4 g.) (Found: C, 81·2; H, 10·3. Calc. for $C_{12}H_{18}O$: C, 80·9; H, 10·2%), which formed a phenylurethane, m. p. 111—112°, identical with that from 2 : 4-dimethyl-6-s-butylphenol. The infrared spectrum showed that the product was substantially the latter phenol.

2,4-*Dimethyl*-6-s-*butylphenol* was prepared for comparison by the reaction of butan-2-ol with 2,4-dimethylphenol in light petroleum with boron trifluoride; it had b. p. 125°/15 mm., n_D^{20} 1·5190; phenylurethane, m. p. 111—113° (Rosenwald *et al.* [6] give b. p. 91—92°/2 mm., n_D^{20} 1·5189; phenylurethane, m. p. 112—113°).

6-n-Butyl-2,4-dimethylphenol, m. p. 27—29° [phenylurethane, m. p. 98—100°; α-*naphthylurethane*, m. p. 124—125° (Found: N, 3·7. $C_{23}H_{25}O_2N$ requires N, 4·0%)], was prepared by Clemmensen reduction of 6-n-butyryl-2,4-dimethylphenol (Flynn and Robertson [8]) (Rosenwald [6] gives for 6-n-butyl-2,4-dimethylphenol, b. p. 83°/2 mm.; phenylurethane, m. p. 98—99°).

(f) *With* 2,6-*dimethylphenol.* 48 Hours' heating with n-butyl methanesulphonate at 140° gave a butyl-2,6-dimethylphenol, b. p. 132—138°/18 mm. (18·5 g.), which solidified and from which 2,6-*dimethyl*-4-s-*butylphenol*, m. p. and mixed m. p. 76—77°, was obtained by crystallisation (Found: C, 81·0; H, 9·9. $C_{12}H_{18}O$ requires C, 80·9; H, 10·2%). This compound, m. p. 77—78°, was prepared, for comparison, from 2,6-dimethylphenol, butan-2-ol, and boron trifluoride (Found: C, 80·7; H, 10·1%). It was characterised by its *phenylurethane*, m. p. 106—108° (Found: N, 4·7. $C_{19}H_{23}O_2N$ requires N, 4·7%).

4-n-Butyl-2,6-dimethylphenol, m. p. 30—32°, was prepared from the Clemmensen reduction of 4-n-butyryl-2,6-dimethylphenol, m. p. 124—126° [2,4-*dinitrophenylhydrazone*, m. p. 199—200° (Found: N, 14·8. $C_{18}H_{20}O_5N_4$ requires N, 15·0%)] (von Auwers and Jannsen [9] give m. p. 32—33° for 6-n-butyryl-2,6-dimethylphenol).

(g) *With* p-*dimethoxybenzene.* n-Butyl methanesulphonate (36 g.) was slowly (4 hr.) added to *p*-dimethoxybenzene at 200°. The mixture was stirred during the addition and for 4 hr. more. But-2-ene (9·5 g.) was collected in the cold trap [2,4-dinitrobenzenesulphenyl chloride adduct, m. p. 128—129·5° (Kharasch and Buess [10] give m. p. 128°)]. The reaction mixture, after the usual treatment to free it from sulphonic acid, was distilled to remove unchanged *p*-dimethoxybenzene, and the residue taken up in ether. It was washed with methyl-alcoholic potash (Claisen's solution) to remove *p*-methoxyphenol (5 g.), m. p. and mixed m. p. 54—55° (Found: C, 67·3; H, 6·8; OMe, 24·0. Calc. for $C_7H_8O_2$: C, 67·7; H, 6·5; OMe, 25%).

The neutral product of the reaction had b. p. 80—85°/0·5 mm., n_D^{20} 1·5091 (6·7 g.) (Found: C, 74·2; H, 9·2; OMe, 30·8. $C_{12}H_{18}O_2$ requires C, 74·2; H, 9·3; OMe, 31·9%). Its infrared spectrum indicates that it is essentially 1,4-*dimethoxy*-2-s-*butylbenzene.* A pure sample, b. p. 135°/19 mm., n_D^{20} 1·5100 (Found: C, 74·0; H, 9·3; OMe, 32%), was prepared by bubbling boron trifluoride into butan-2-ol and *p*-dimethoxybenzene in light petroleum till two layers separated. After a further few hours at room temperature, the light petroleum solution was removed, washed, dried, and distilled. 2-n-Butyl-1,4-dimethoxybenzene, b. p. 136—138°/20 mm., n_D^{20} 1·5110 (Found: C, 74·5; H, 9·5; OMe, 31·6%), was prepared by the Clemmensen reduction of 2-n-butyryl-1,4-dimethoxybenzene, a mixture of acetic and hydrochloric acids being used.

2-n-Butyryl-1,4-dimethoxybenzene, b. p. 136—138°/1 × 10^{-3} mm., n_D^{21} 1·5279, was obtained by adding *p*-dimethoxybenzene (9·7 g.) to a homogeneous mixture of aluminium chloride (21·3 g.) and n-butyric anhydride (11·1 g.) in carbon disulphide (150 c.c.) kept at $-5°$. When the addition was complete, the mixture was kept overnight, the solvent distilled off, and the product isolated in the usual way.

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[7] von Auwers, *Annalen*, 1924, **439**, 147.
[8] Flynn and Robertson, *J.*, 1936, 215.
[9] von Auwers and Jannsen, *Annalen*, 1930, **483**, 44.
[10] Kharasch and Buess, *J. Amer. Chem. Soc.*, 1949, **71**, 2724.