[CONTRIBUTION FROM THE KEDZIE CHEMICAL LABORATORY, MICHIGAN STATE COLLEGE]

Bromo Derivatives of Benzylphenols. I. Some Monobromo, Dibromo and Tribromo Derivatives of Ortho and Para Benzylphenols

BY R. C. HUSTON, A. NEELEY, B. L. FAYERWEATHER, H. M. D'ARCY, F. H. MAXFIELD, M. M. BALLARD AND W. C. LEWIS

Continuing our studies on the benzylation of phenols, we have prepared bromo derivatives of ortho and para benzyl phenols. A number of the bromo derivatives, of the benzylated cresols, have been described in earlier articles from this Laboratory.[1]

Condensations with Benzyl Chloride

Benzyl chloride was condensed with 2,4-dibromophenol, by the Claisen method,[2] to form 2-hydroxy-3,5-dibromodiphenylmethane[3] and 2,4-dibromophenyl benzyl ether. This phenol was also prepared by the direct bromination (in chloroform) of *o*-benzylphenol.[4]

The benzylation of 2,6-dibromophenol, by means of benzyl chloride (or alcohol) and aluminum chloride, gave a 4-hydroxy-3,5-dibromodiphenylmethane in small yield, most of the original phenol being recovered unchanged. This compound was found to be identical with the dibromo derivative prepared by Zincke and Walter[5] by the direct bromination of *p*-benzylphenol.

The benzylation of *o*-bromophenol by the aluminum chloride method gave 4-hydroxy-3-bromodiphenylmethane and a little 2-hydroxy-3-bromodiphenylmethane. The former was brominated directly to 4-hydroxy-3,5-dibromodiphenylmethane and the latter to 2-hydroxy-3,5-dibromodiphenylmethane.

The benzylation of *p*-bromophenol by the Claisen method gave 2-hydroxy-5-bromodiphenylmethane with some *o*-dibenzyl derivative and 4-bromophenyl benzyl ether. Benzylation of *p*-bromophenol by the aluminum chloride method gave the same diphenylmethane derivatives but no ether. Treatment of this monobenzyl phenol with bromine gave 2-hydroxy-3,5-dibromodiphenylmethane.

In no case did the benzylation of a bromophenol by the aluminum chloride method produce an ether.

Condensation with Bromobenzyl Chlorides

Phenol was condensed with 2-bromobenzyl chloride, 3-bromobenzyl chloride and 4-bromobenzyl chloride by the Claisen and aluminum chloride methods.

(1) Huston and others, THIS JOURNAL, **52**, 4488 (1930); **53**, 2379 (1931); **54**, 1506 (1932).

(2) Claisen, *Ann.*, **442**, 221 (1924).

(3) Rennies, *J. Chem. Soc.*, **49**, 405 (1886).

(4) Prepared by the Claisen reaction or by fractionation of the reaction mixture from the aluminum chloride condensation of phenol and benzyl alcohol (or benzyl chloride).

(5) Zincke and Walter, *Ann.*, **334**, 367 (1904).

As a means of determining the structure of the compounds prepared in these reactions, condensations of each of the three bromo substituted benzyl chlorides were made with 2,4-dibromophenol by the Claisen method and with 2,6-dibromophenol by the aluminum chloride method. The tribromobenzylphenols obtained by these condensations were also prepared by the cold bromination of the corresponding monobromobenzylphenols in chloroform. In no case was it possible to introduce bromine into the benzyl nucleus, the bromine entering only the unoccupied ortho or para position of the phenolic ring.

1. **Condensation by the Claisen Method.**—Phenol with 2-bromobenzyl chloride in toluene yielded 2-hydroxy-2′-bromodiphenylmethane and 2-bromobenzyl phenyl ether; phenol with 3-bromobenzyl chloride yielded 2-hydroxy-3′-bromodiphenylmethane and 3-bromobenzyl phenyl ether; phenol with 4-bromobenzyl chloride yielded 2-hydroxy-4′-bromodiphenylmethane and 4-bromobenzyl phenyl ether.

The treatment of 2,4-dibromophenol in toluene with 2-bromobenzyl chloride gave 2-hydroxy-3,5,2′-tribromodiphenylmethane and 2-bromobenzyl 2,4-dibromophenyl ether; 2,4-dibromophenol and 3-bromobenzyl chloride yielded 2-hydroxy-3,5,3′-tribromodiphenylmethane and 3-bromobenzyl 2,4-dibromophenyl ether; 2,4-dibromophenol with 4-bromobenzyl chloride yielded 2-hydroxy-3,5,4′-tribromodiphenylmethane and 4-bromobenzyl 2,4-dibromo phenyl ether.

2. **Condensations by the Aluminum Chloride Method.**—Phenol with 2-bromobenzyl chloride in petroleum ether yielded 4-hydroxy-2′-bromodiphenylmethane, 2-hydroxy-2′-bromodiphenylmethane and 2-bromobenzyl phenyl ether; phenol with 3-bromobenzyl chloride yielded 4-hydroxy-3′-bromodiphenylmethane and 3-bromobenzyl phenyl ether; phenol with 4-bromobenzyl chloride yielded 4-hydroxy-4′-bromodiphenylmethane and 4-bromobenzyl phenyl ether.

The combination of 2,6-dibromophenol with 2-bromobenzyl chloride yielded 4-hydroxy-3,5,2′-tribromodiphenylmethane; with 3-bromobenzyl chloride, it yielded 4-hydroxy-3,5,3′-tribromodiphenylmethane; and with 4-bromobenzyl chloride, 4-hydroxy-3,5,4′-tribromodiphenylmethane.

In no case was the ether corresponding to any of the above phenols obtained in the aluminum chloride condensations with 2,6-dibromophenol. It will be noted that the ortho substitution product was obtained along with the para benzylated phenol in the aluminum chloride condensation of phenol and 2-bromobenzyl chloride. The 2-hydroxy-2′-bromodiphenylmethane was separated from the crystals of 4-hydroxy-2′-bromodiphenylmethane as an oil, which later became crystalline upon seeding with a small crystal of the same compound obtained in the Claisen condensation. Evidence of formation of the ortho benzylated phenol was also found in the aluminum chloride condensation of phenol and 3-bromobenzyl chloride as the 4-hydroxy-3,5,3′-tribromodiphenylmethane obtained by the direct bromination of 4-hydroxy-3′-bromodiphenylmethane always melted 4 or 5 degrees lower than the same compound prepared by the condensation of 2,6-dibromophenol and 3-bromobenzyl chloride and was only purified by repeated recrystallizations.

The 2-hydroxy-3′-bromodiphenylmethane and 4-hydroxy-3′-bromodiphenylmethane differ only by 2 or 3 degrees in boiling points and could not be separated by fractional distillation.

3. **Condensations in Methyl Alcohol.**—The 2-bromobenzyl phenyl ether, 3-bromobenzyl phenyl ether and 4-bromobenzyl phenyl ether were prepared by heating phenol and the various monobromobenzyl chlorides in the presence of sodium methylate in

methyl alcohol. These ethers were found to be identical with those obtained in the Claisen and aluminum chloride condensations.

4. Comparison of Yields.—In the Claisen condensations, 2-hydroxy-4-bromodiphenylmethane was obtained in the greatest yield. This amounted to 38% and is not far below the yield of 4-bromobenzyl phenyl ether obtained in the methyl alcohol condensation. The 2-hydroxy-2'-bromodiphenylmethane was obtained in a yield of 14% while the 2-hydroxy-3'-bromodiphenylmethane was obtained in very small amounts, the yields averaging about 4%. It was found, however, in the latter case, that the yields could be greatly increased by adding to the reaction mixture, containing quarter mole quantities, 15 or 20 g. of 3-bromobenzyl phenyl ether. By this means the yield was increased to as high as 20% in several runs. This seems to indicate an equilibrium between the ether and phenol derivative formed in the reaction.

It is interesting to note that the yields of benzylated phenols from para, ortho and meta bromobenzyl chlorides are in the same order and nearly proportional to the rates of hydrolysis of these compounds in acetone or dilute alcohol solution.[6] We expect that continued investigation along this line will throw additional light upon the mechanism of the Claisen reaction.

The yields of 4-hydroxy-2'-bromodiphenylmethane, 4-hydroxy-4'-bromodiphenylmethane and 4-hydroxy-3'-bromodiphenylmethane obtained from the aluminum

TABLE I

BROMO DERIVATIVES OF BENZYLPHENOLS

Compound, -bromodiphenylmethane	Crystalline structure	M. p., °C.	Bromine Calcd.	Bromine Found	Yield, %
2-Hydroxy-3,5-di-	Needles from alc. and water	90–91	46.75	46.82	..
4-Hydroxy-3,5-di-	Needles from pet. ether	56–57	46.75	46.44	..
2-Hydroxy-3-	Liquid	B. p. (2 mm.) 150–153	30.38	30.23	11
4-Hydroxy-3-	Liquid	B. p. (2 mm.) 148–150	30.38	30.05	16
2-Hydroxy-5-	Needles from pet. ether	55–56	30.38	30.36	38
2-Hydroxy-2'-	Plates from pet. ether	47–48	30.38	30.64	14
2-Hydroxy-3'-	Liquid	B. p. (3 mm.) 167–169	30.38	31.06	4
2-Hydroxy-4'-	Needles from pet. ether	72–73	30.38	29.97	38
4-Hydroxy-2'-	Needles from pet. ether	71–73	30.38	31.00	15
4-Hydroxy-3'-	Liquid	B. p. (3 mm.) 169–171	30.38	30.90	17
4-Hydroxy-4'-	Needles from pet. ether	82–83	30.38	29.95	19
2-Hydroxy-3,5,2'-tri-	Needles from gasoline	41.5–42.5	56.97	56.97	5
2-Hydroxy,3,5,3'-tri-	Needles from pet. ether	76–77	56.97	56.96	11
2-Hydroxy-3,5,4'-tri-	Needles from pet. ether	80–81	56.97	56.94	30
4-Hydroxy-3,5,2'-tri-	Needles from pet. ether	78–80	56.97	57.15	12
4-Hydroxy-3,5,3'-tri-	Needles from pet. ether	106–107	56.97	57.46	25
4-Hydroxy-3,5,4'-tri-	Needles from pet. ether	81–82	56.97	56.50	..

TABLE II

BROMO DERIVATIVES OF BENZYL PHENYL ETHERS

Compound, ether	Crystalline structure	M. p., °C.	Bromine Calcd.	Bromine Found	Yield, %
2,4-Dibromophenyl benzyl	Needles from pet. ether	67–68	46.75	46.78	7.5
4-Bromophenyl benzyl	Needles from alcohol	60–61	30.38	30.00	3
2-Bromophenyl benzyl	Liquid	B. p. (2 mm.) 142–144	30.38	30.17	16
2-Bromobenzyl phenyl	Leaflets from alcohol	34–36	30.4	30.17	8
3-Bromobenzyl phenyl	Flakes from alcohol	36–37	30.4	30.87	12
4-Bromobenzyl phenyl	Flakes from alcohol	92.5–93.5	30.4	31.00	..
2-Bromobenzyl 2,4-dibromophenyl	Needles from alcohol	62–64	56.97	57.3	30
3-Bromobenzyl 2,4-dibromophenyl	Needles from alcohol	49–50	56.97	57.06	9
4-Bromobenzyl 2,4-dibromophenyl	Needles from alcohol	86–87	56.97	56.62	..

(6) Olivier, *Rec. trav. chim.*, **49**, 698, 997 (1930).

chloride condensations averaged about the same, amounting to 15, 19 and 17%, respectively. In the last case, it was found that temperatures below 10° favored the formation of the substituted phenols. In the other cases, the formation of phenol derivatives was found to take place in greatest yields at temperatures between 25 and 30°.

The study of chloro[7] and bromo derivatives of the benzylphenols and benzylcresols is being continued in this Laboratory.

TABLE III

THE FOLLOWING ESTERS OF THE VARIOUS PHENOL DERIVATIVES WERE PREPARED ACCORDING TO THE METHOD OF EINHORN AND HOLLAND[8]

Benzoyl ester of bromodiphenylmethane	Crystalline structure	M. p., °C.	Bromine Calcd.	Bromine Found
2-Hydroxy-3-	Plates from alcohol	89.5– 90	21.77	21.53
4-Hydroxy-3-	Plates from alcohol	63 – 64	21.77	21.44
2-Hydroxy-2′-	Leaflets from pet. ether	39 – 40	21.77	21.60
2-Hydroxy-3′-	Leaflets from pet. ether	69 – 70	21.77	21.99
2-Hydroxy-4′-	Leaflets from pet. ether	50 – 51	21.77	22.19
4-Hydroxy-2′-	Needles from pet. ether	64 – 65	21.77	21.30
4-Hydroxy-3′-	Needles from pet. ether	97 – 98	21.77	22.04
4-Hydroxy-4′-	Leaflets from pet. ether	118 –120	21.77	21.77
2-Hydroxy-3,5,3′-tri-	Needles from pet. ether	90 – 91	45.85	46.32
2-Hydroxy-3,5,4′-tri-	Needles from pet. ether	115 –116	45.85	45.74
4-Hydroxy-3,5,3′-tri-	Needles from pet. ether	131.5–132.5	45.85	46.28
4-Hydroxy-3,5,4′-tri-	Needles from pet. ether	144 –145	45.85	45.84
p-Toluene sulfonyl ester of 2-hydroxy-3	Plates from alcohol	85 – 85.5	19.11	19.16
Benzene sulfonyl ester of 4-hydroxy-3-	Needles from alcohol	56 – 57	19.82	19.36

Summary

Some monobromo, dibromo and tribromo derivatives of the benzylphenols and benzyl phenyl ethers were prepared.

The presence of bromine in the nucleus of benzyl chloride favors the formation of ether in the aluminum chloride condensation.

The presence of bromine in the nucleus of benzyl chloride affects the yield of benzylated phenol in the Claisen reaction. The retarding influence increases in the order—para, ortho, meta.

In certain cases the yield of benzylated phenol by the Claisen reaction is increased several fold by the addition of the corresponding benzyl phenyl ether to the reaction mixture.

EAST LANSING, MICHIGAN

RECEIVED DECEMBER 19, 1932
PUBLISHED MAY 6, 1933

(7) Huston and Eldridge, THIS JOURNAL, **53**, 2260 (1931).

(8) Einhorn and Holland, *Ann.*, **301**, 95 (1898).