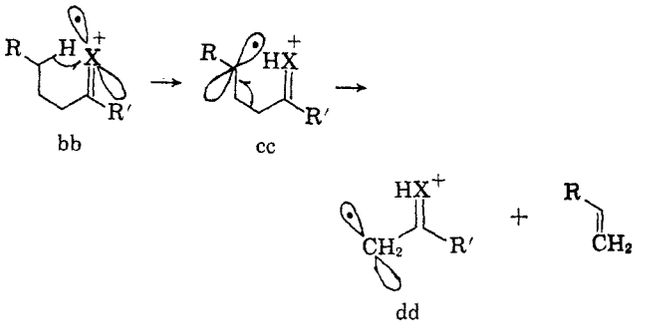
transfer of a hydrogen atom. In addition it has been suggested[19b] that mass spectrometric reactions occurring *via* radical intermediates will be characterized by *site-specific* transfer reactions to form new bonds to the original radical site, and on this basis the McLafferty rearrangement might be written as the stepwise process bb → dd. This mechanism clearly suggests that the nature of the radical species produced at the γ carbon (as in cc) will strongly influence the feasibility of this fragmentation mode; *i.e.*, the more stabilized a radical can be at the γ position the more easily will the rearrangement occur, and the more abundant will be the fragment resulting from such a process. The clear prediction is then that a hydrogen atom on a secondary atom will be transferred more readily than one on a primary carbon atom since the usual order of radical stabilities is 3° > 2° > 1°.[20] As noted earlier, ketones,[6] aldehydes,[12] esters,[12] azomethines,[7] semicarbazones,[8] aldehyde DNP's,[9] and oximes[11] show γ-hydrogen specificity and with the exception of only the last class of compounds they all show in their mass spectra a striking preference for transfer of a secondary hydrogen. We have shown in this paper that the same specific hydrogen transfers occur with ketone dimethylhydrazones and dinitrophenylhydrazones. It seems, therefore, that the trigger for the type of fragmentation exemplified by the McLafferty rearrangement may be the localization of both charge and radical



character at specific atomic sites in ions produced by electron impact.

(20) See, for example, J. Hine, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, p 422.

Experimental Section

The mass spectra and the high-resolution mass measurements were determined with an AEI MS-9 mass spectrometer operating with an ionizing voltage of 70 ev and with a source temperature of 200°. The samples were admitted into the ion source through an all-glass heated inlet system operating at 80°.

The dimethylhydrazones were prepared according to a modification of a published procedure[21,22] using commercially available aldehydes or ketones and N,N-dimethylhydrazine. In a typical preparation the carbonyl compound was dissolved in a large excess of dimethylhydrazine and the solution was heated under reflux for 2 hr. After cooling, the excess reagent was removed *in vacuo* and ice and saturated salt solution were added to the residue. The organic phase was isolated and purified by gas liquid partition chromatograph on an Apiezon L column operating at 150° and 15 psi of helium.

(21) R. H. Wiley, S. C. Slaymaker, and H. Krauss, *J. Org. Chem.*, **22**, 204 (1957).

(22) See also G. R. Newkome and D. L. Fishel, *ibid.*, **31**, 677 (1966).

Selective Mono-O-alkylation of 2,6-Dibromohydroquinone

LINNEAUS C. DORMAN

Edgar C. Britton Research Laboratory, The Dow Chemical Company, Midland, Michigan

Received May 12, 1966

It was demonstrated that 2,6-dibromohydroquinone can be selectively mono-O-alkylated at either the 1 or 4 oxygen depending on whether the monoanion or dianion is being alkylated. The monoanion alkylates preferentially at the 1 oxygen and the dianion at the 4 oxygen. The selectivity in each case is increased on changing from water to dimethyl sulfoxide and this difference in selectivity is attributed mainly to solvation effects. 2,6- and 3,5-dibromophenols were employed as model compounds and their relative rates of methylation provide support for the rationalization of the 2,6-dibromohydroquinone O-alkylation reactions.

In connection with some work in this laboratory, it was of interest to prepare several 3,5-dibromo-4-alkoxyphenols (II). 2,6-Dibromohydroquinone appeared to be a suitable intermediate for this purpose. At first inspection, it appeared that this hydroquinone would preferentially mono-O-alkylate at the unhindered 4 oxygen. Therefore, the projected synthetic route to II (Scheme I) was first to alkylate the 4 oxygen with a benzyl group, followed by an alkylation of the 1 oxygen with the desired R group, and finally removal of the benzyl group by hydrogenolysis.

Proceeding in this manner, 2,6-dibromohydroquinone was alkylated with benzyl bromide in dimethyl sulfoxide (DMSO) with potassium carbonate as base. Near-equimolar quantities of each reagent were used. The mono-O-alkylated product, isolated in 62% yield, had ν_{OH} (0.5% CCl_4) at 3430 (broad) and 3610 (sharp) cm^{-1} characteristic of intermolecularly hydrogen bonded and free phenolic absorptions, respectively.[1,2] This product was, therefore, 3,5-dibromo-4-benzyloxyphenol (III) and not the anticipated isomer, 2,6-dibromo-4-benzyloxyphenol (I).[3,4] In order to clarify the factors which lead to this result, the mono-O-alkylation reactions of 2,6-dibromohydroquinone monoanion and dianion and of model compounds, 2,6- and 3,5-dibromophenoxides, were studied.

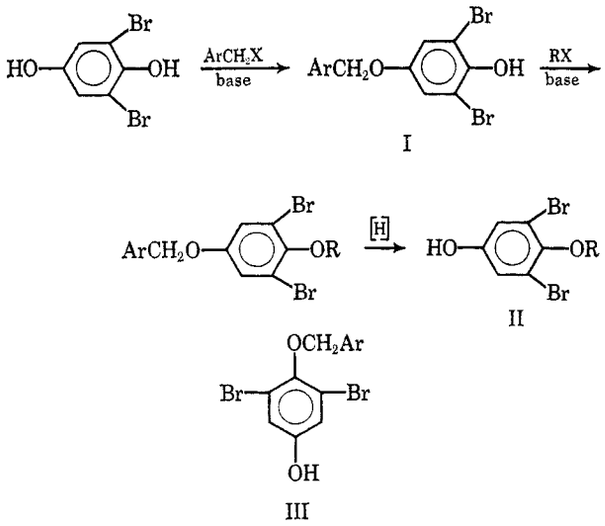
(1) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," Methuen and Co. Ltd., London, 1962, p 96.

(2) Note that intramolecular hydrogen bonding of phenolic OH by two *ortho* bromine atoms as in structure I gives rise to a single, sharp absorption band near 3515 cm^{-1}: I. Brown, G. Eglinton, and M. Martin-Smith, *Spectrochim. Acta*, **18**, 1593 (1962).

(3) During the course of this work, it was learned that A. W. Baker, H. O. Kerlinger, and A. T. Shulgin [*ibid.*, **20**, 1467 (1964)] had found similar results in the methylation of 2,6-dichlorohydroquinone and 2,6-dibromohydroquinone. The author wishes to take this opportunity to express his appreciation to these authors for communicating their results.

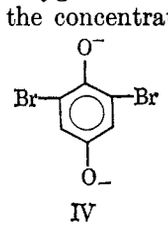
(4) H. E. Ungnade and K. T. Zilch [*J. Org. Chem.*, **16**, 64 (1951); *Chem. Abstr.*, **45**, 6600 (1951)] monomethylated 2,6-dibromohydroquinone in methanol using sodium methoxide and methyl iodide. It remains questionable, however, whether they assigned the correct structure to the major product. The product they reported was "2,6-dibromo-1-methoxyphenol," mp 139.5–140.2°. The correct structure was found to be 3,5-dibromo-4-methoxyphenol (see the Experimental Section).

SCHEME I



Results and Discussion

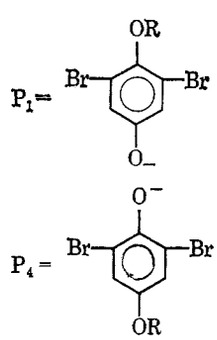
For the sake of clarity and continuity in rationalizing the mono-O-alkylation reactions, the case of 2,6-dibromohydroquinone dianion will be considered first. Rate expressions for mono-O-alkylation of the dianion (IV) at the 1- and 4-oxygen anionic sites are given by eq 1 and 2.[5] Since the concentrations of the anionic



IV

$$\frac{d[P_1]}{dt} = k_1[\text{1-oxygen anion}][RX] \quad (1)$$

$$\frac{d[P_4]}{dt} = k_4[\text{4-oxygen anion}][RX] \quad (2)$$



RX = alkylating agent

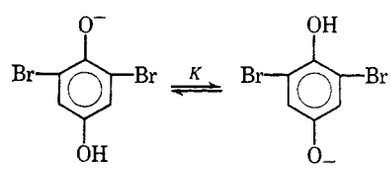
sites of IV are equal,[6] dividing eq 2 by eq 1 gives eq[7] 3 which shows that the distribution of mono-O-alkylated products of the dianion will depend on the relative

$$\frac{d[P_4]}{d[P_1]} = \frac{k_4}{k_1} \quad (3)$$

magnitudes of k_1 and k_4 neglecting dialkyl ether formation.

Sterically, O-alkylation at the 4-oxygen anion is favored over the 1-oxygen anion. The 4-oxygen anion should have the greater charge density or nucleophilicity because of its proximity to the bromine atoms relative to the 1-oxygen anion.[8] The steric and polar effects operate in the direction to make $k_4 > k_1$;[9,10] therefore, eq 3 predicts that O-alkylation at the 4-oxygen anion will be faster than at the 1-oxygen anion. In accordance with this prediction the methylation reaction produces *ca.* a 1.5:1 ratio of 2,6-dibromo-4-methoxyphenol (VI) to 3,5-dibromo-4-methoxyphenol (V) when conducted in water. This ratio is a maximum since a larger proportion of the 3,5-dibromo-4-methoxyphenol anion (P_1) formed initially will be converted to the dimethyl ether (VII); *i.e.*, invoking the same reasoning as above, P_1 is more nucleophilic and less hindered than P_4 toward O alkylation.[11]

The initial rate expressions for the mono-O-alkylation of 2,6-dibromohydroquinone monoanion (VIII) at the 1- and 4-oxygen anions are given by eq 5 and 6.

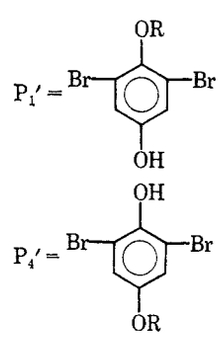


a VIII b

$$K = \frac{[\text{VIIIb}]}{[\text{VIIIa}]} \quad (4)$$

$$\frac{d[P_1']}{dt} = k_1''[\text{VIIIa}][RX] \quad (5)$$

$$\frac{d[P_4']}{dt} = k_4''[\text{VIIIb}][RX] \quad (6)$$



RX = alkylating agent

Dividing eq 6 by eq 5 gives

$$\frac{d[P_4']}{d[P_1']} = \frac{k_4''[\text{VIIIb}]}{k_1''[\text{VIIIa}]} = \frac{k_4''}{k_1''}K \quad (7)$$

Reasoning as in the previous case $k_4'' > k_1''$. The relative concentrations of VIIIa and VIIIb are governed by their equilibrium constant K. Since VIIIa is less basic than VIIIb (proximity of the bromine atoms), at equilibrium [VIIIa] > [VIIIb], therefore $K < 1$. It becomes apparent from eq 7 that the extent of alkyla-

(5) The negative terms, $-k_1'[P_1][RX]$ and $-k_4'[P_4][RX]$, for loss of P_1 and P_4, respectively, in forming the dialkyl ether are omitted from the rate expressions for sake of simplicity.

(6) Hydrolysis of the dianion in water would tend to uneven the concentrations of the anionic sites; however, under the experimental conditions employed, the dianion is only *ca.* 2% hydrolyzed initially and *ca.* 5% hydrolyzed after 90% reacted.

(7) It is fortunate that in this treatment of the rate equations the [RX] term cancels out, since in aqueous reactions one is faced with the difficultly resolvable circumstance of limited solubility of the alkylating agent (see ref 13), in this case dimethyl sulfate.

(8) Conversely, the 1-hydroxyl of the hydroquinone should be the more acidic (the pK values of 2,6- and 3,5-dibromophenols were found to be 6.7 and 8.0, respectively, and of 2,6- and 3,5-dibromo-4-methoxyphenols 7.3 and 8.15, respectively).

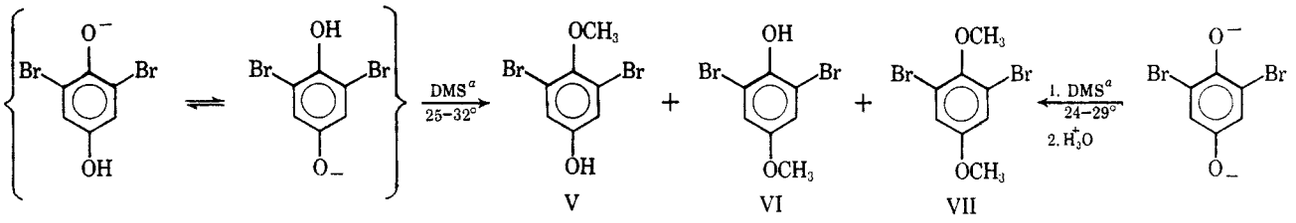
(9) *Cf.* the rate data for O methylation of *o*- and *m*-chlorophenols: G. H. Green and J. Kenyon, *J. Chem. Soc.*, 1589 (1950).

(10) G. D. Leahy, M. Liveris, J. Miller, and A. J. Parker, *Australian J. Chem.*, **9**, 382 (1956).

(11) Note the relative pK values of 2,6- and 3,5-dibromo-4-methoxyphenols in ref 8.

TABLE I

MONOMETHYLATION OF 2,6-DIBROMOHYDROQUINONE MONO- AND DIANIONS. EFFECT OF SOLVENTS



Base (equiv)	Anion	Solvent	Isolable[b,c] total yield (V + VI), %	Relative quantity, %[c] V	VI	Yield (VII), %[d]
NaOH (1)	Mono	H_2O	69	89	11	8
CH_3SOCH_2Na (1)	Mono	DMSO	65	99+	0.5	6
CH_3SOCH_2K (1)	Mono	DMSO	69	99+	0.6	Not isolated
NaOH (2)	Di	H_2O	60	39	61	16
NaOH (3.8)	Di	H_2O	46	42	58	7
CH_3SOCH_2Na (2)	Di	DMSO	73	15	85	4
CH_3SOCH_2K (2)	Di	DMSO	69	11	89	Not isolated

[a] Dimethyl sulfate, equimolar amount used. [b] Crude product mixture, yields in table do not include or take into account unchanged 2,6-dibromohydroquinone present in the mixture. [c] Determined by glpc. [d] Calculated on a mole-to-mole basis with respect to the starting materials.

tion at the 1- and 4-oxygen anionic sites of the monoanion will be determined by the relative magnitudes of k_1'', k_4'', and K.

When the monoanion is O-alkylated in water, methanol,[4] or dimethyl sulfoxide, the hindered 1-oxygen anionic form is alkylated very selectively. Accepting that $k_4'' > k_1''$, this preponderance of alkylation at the 1-oxygen anion indicates that the equilibrium concentration of the 1-oxygen anionic form is large enough to offset substantially the greater nucleophilicity and lower steric requirements of the 4-oxygen anionic form in determining product distribution. A satisfactory experimental method for determining K has not been found. The ultraviolet spectra of 2,6-dibromohydroquinone, its monoanion, and dianion show only single symmetrical peaks for each specie absorbing at 295, 320, and 337 mμ, respectively; pK_1 and pK_2 were determined to be 7.7 and 10.4, respectively.

Dimethyl sulfoxide increases the selectivity of mono-O-alkylation of both the monoanion and dianion of 2,6-dibromohydroquinone. Consider first the mono-O-methylation product distribution of the dianion (Table I); whereas the ratio of 2,6-dibromo-4-methoxyphenol (VI) to 3,5-dibromo-4-methoxyphenol (V) is 1.5:1 in the aqueous methylation, it is *ca.* 5:1 when the methylation is conducted in DMSO. These results indicate that the difference in the relative nucleophilicities of the 1- and 4-oxygen anions increases in changing from water to DMSO. This difference is best explained by consideration of solvation effects. Water has a large capacity to solvate "selectively"[12] phenoxide anions[13] thereby lowering the charge density at the oxygen by spreading the charge over the solvation sphere. Thus, the net effect of solvation at each oxygen anion of 2,6-dibromohydroquinone dianion would be to minimize the difference in their relative nucleophilicities, *viz.*, to level them out. Conversely, DMSO has a small capacity to solvate anions[14,15] and, in the absence of solvation in this solvent, the difference in the relative nucleophilicities of the oxygen anions would tend to be maximized.

It should follow from the solvation argument that the lower yield of the dimethyl ether (VII) of the reaction run in DMSO is attributable to a larger difference in the relative nucleophilicities between IV and either P_1 or P_4 in DMSO than in water.

The data in Table I shows that monomethylation of 2,6-dibromohydroquinone monoanion is also more selective in DMSO than in water. On the basis of the dianion data, it can be expected that $(k_4''/k_1'')_{DMSO} > (k_4''/k_1'')_{H_2O}$, hence, the greater selectivity of this reaction in DMSO is best accounted for on the grounds that the equilibrium (eq 4) is even more favorable to the 1-oxygen anionic form in DMSO than in water, *i.e.*, $K_{DMSO} << K_{H_2O}$. In this connection Steiner and Gilbert[17] in their study of the acidities of weak acids in DMSO suggest that the inherent acidity of alcohols is very low and that materials capable of reducing the activities of their alkoxides (*e.g.*, by hydrogen bonding or coordination with cations) increase their apparent acidities. The same general trend might be anticipated for phenols. As a consequence the difference in the relative acidities of hydroxyls of dihydric phenols such as 2,6-dibromohydroquinone would be minimal in strongly phenoxide solvating solvents such as water because of a leveling out effect, and maximal in weakly phenoxide solvating solvents such as DMSO. Hence, the assumption that $K_{DMSO} << K_{H_2O}$ is congruent with this supposition as is $(k_4''/k_1'')_{DMSO} > (k_4''/k_1'')_{H_2O}$.[10]

2,6- and 3,5-dibromophenols were employed as model compounds in this study because of their formal resemblance to 2,6-dibromohydroquinone. Relative rates of methylation of their sodium salts were determined in water and DMSO (Table II). The results corroborate the interpretations of the 2,6-dibromohydroquinone O-alkylation reactions. In summary, these

(12) See footnote 20 of ref 13 for a definition of "selective solvation."

(13) N. Kornblum, P. J. Berrigan, and W. J. le Noble, *J. Am. Chem. Soc.*, **85**, 1141 (1963).

(14) J. Miller and A. J. Parker, *ibid.*, **83**, 117 (1961); E. Tommila and Murto, *Acta Chem. Scand.*, **17**, 1947 (1963).

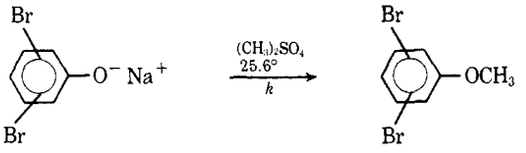
(15) N. Kornblum, R. Seltzer, and P. Haberfield, *J. Am. Chem. Soc.*, **85**, 1148 (1963); see ref 16 and references cited therein.

(16) M. S. Masri, D. J. Robbins, O. H. Emerson, and F. Needs, *Nature*, **202**, 878 (1964).

(17) E. C. Steiner and J. M. Gilbert, *J. Am. Chem. Soc.*, **85**, 3054 (1963).

TABLE II

RELATIVE RATES OF METHYLATION OF 2,6- AND 3,5-DIBROMOPHENOLS



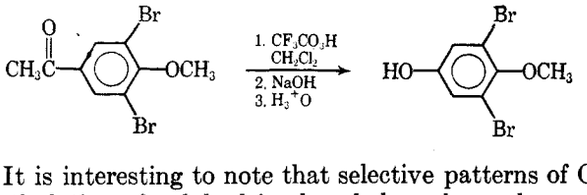
$r^a = k_{3,5}/k_{2,6}$

Solvent	r
Water	1.8
DMSO	3.6

[a] See the Experimental Section.

data demonstrate (a) the more basic and unhindered phenoxide anion is alkylated at a faster rate than the less basic and hindered phenoxide anion; (b) the relative rates of O methylation are influenced by the solvent medium; (c) the difference in the relative nucleophilicities of the 3,5- and 2,6-dibromophenoxide anions is increased in changing from a solvent of high anion-solvating power to one of low anion-solvating power.

Infrared analysis was the primary diagnostic tool in differentiating the structures of isomeric 2,6- and 3,5-dibromo-4-alkoxyphenols. The structure of 3,5-dibromo-4-methoxyphenol (V) was confirmed by an unequivocal synthesis from known 3,5-dibromo-4-methoxyacetophenone[18] by a per acid oxidation reaction.



It is interesting to note that selective patterns of O-methylation of polyhydric phenols have been observed in animal and plant systems with the enzyme O-methyltransferase.[16]

Experimental Section

Melting and boiling points are uncorrected.

Alkyl halides and dimethyl sulfate were either reagent grades or were purified by distillation before use. Unless otherwise stated, purified dimethyl sulfoxide was used. The commerical product was stored over sodium hydroxide pellets for 1 day, decanted, and distilled, bp 98° (32 mm).[19] 2,6-Dibromohydroquinone was prepared according to the procedure of Ungnade and Zilch,[4] mp 161–162°. 3,5-Dibromophenol was prepared according to the method of Kohn and Zink,[20] mp 80–81°. Eastman Kodak Co. White Label 2,6-dibromophenol was used without further purification, mp 54–56°. 3,5- and 2,6-dibromoanisoles were prepared from their respective phenols with dimethyl sulfate in aqueous alkaline solution and purified by distillation through a Vigreux column, the former, bp 124° (10 mm), mp 38.5–39.5° (lit.[21] mp 36–37°), the latter, bp 112–113° (10 mm) [lit.[22] bp 143–145° (34 mm)]; each anisole had a glpc purity of better than 99.5%. Dimethyl sulfoxide solutions of sodium methylsulfinyl carbanion ("dimsylsodium")[23] were prepared from reaction of sodium amide and excess dimethyl sulfoxide.[24] In a typical run, 100 ml of stirred DMSO was evacuated to *ca.* 0.5 mm and restored to atmospheric pressure with nitrogen, and this cycle was repeated several times. Sodium amide (0.6–1.4 g) was added in one portion under nitrogen, the ammonia liberated was removed *in vacuo*, atmospheric pressure was restored with nitrogen. These solutions were used within 2 hr after preparation and protected at all times under an atmosphere of nitrogen. The normality was determined by removing several aliquots, dissolving in water, and titrating with standard hydrochloric acid.

The p*K* values of 2,6- and 3,5-dibromophenols, 2,6-dibromohydroquinone, and 2,6- and 3,5-dibromo-4-methoxyphenols were determined using the ultraviolet spectrophotometric method by Mr. J. Simek of the Special Services Laboratory.[25] Infrared spectra were determined and interpreted by Dr. R. A. Nyquist of the Chemical Physics Research Laboratory.[25] Gas–liquid partition chromatographic (glpc) analyses were carried out with an F & M instrument Model 300. Columns employed were a 1/4 in. × 2 ft diethylene glycol succinate (LAC-728, 1% on Gas-Chrom Z, 60–80 mesh), 1/4 in. × 10 ft 410 gum rubber (20% on Gas-Chrom Z, 60–80 mesh), and a 1/4 in. × 2 ft diethylene glycol adipate (LAC-446; 20% on Chromosorb WAW). Internal standards used in glpc analyses were Eastman Kodak White Label iodobenzene and analytical 2,3,4-trichloroanisole, mp 68.8°.

3,5-Dibromo-4-benzyloxyphenol (III).—To a stirred suspension of 71.0 g (0.288 mole) of 2,6-dibromohydroquinone, 41.6 g (0.298 mole) of potassium carbonate, and 200 ml of commercial dimethyl sulfoxide was added 51 g (0.298 mole) of benzyl bromide. After the resulting exothermic reaction began to subside, the reaction mixture was heated slowly from 47 to 75° and maintained between 65 and 88° for *ca.* 1 hr, then allowed to cool and stand at room temperature overnight. The reaction mixture was diluted with one and one-half times its volume of water and extracted with 1 l. of methylene chloride. The methylene chloride portion was extracted with strong caustic (200 ml of 5 *N* + 50 ml of 50%). The aqueous caustic layer was acidified with acetic acid and extracted with methylene chloride and chloroform. The combined and dried (Drierite) organic extracts were freed of solvents *in vacuo* leaving a dark, viscous residue that could not be made to crystallize. It was taken up in warm, excess, strong caustic, treated with Darco, and filtered (suction) through Filter-Cel. The filtrate was slowly acidified with acetic acid while stirring. The resulting precipitate was filtered, washed (water), and dried yielding 57.8 g of light tan crystals, mp 113–114°. Additional product (6.0 g, mp 108–112°) was obtained from the mother liquor on further standing and treatment with excess acetic acid. The total yield was 63.8 g (62%). The analytical sample was obtained by recrystallization from chloroform–cyclohexane, mp 114.5–115.5°. Infrared (0.5% CCl_4) showed ν 3430 (broad, OH intermolecularly hydrogen bonded) and 3610 (sharp, monomeric OH) cm^{-1}.

Anal. Calcd for $C_{13}H_{10}Br_2O_2$: C, 43.61; H, 2.81; Br, 44.65. Found: C, 43.67; H, 2.97; Br, 44.91.

Evaporation of the initial caustic-extracted methylene chloride layer and recrystallization of the residue from a mixture of ethanol and petroleum ether (bp 60–70°) afforded 8.4 g (12.7%) of the bisbenzyloxy ether, [2,5-bis(benzyloxy)-1,3-dibromobenzene], mp 73–74°, and 79–80° after recrystallization from methanol–chloroform.

Anal. Calcd for $C_{20}H_{16}Br_2O_2$: C, 53.59; H, 3.59; Br, 35.59. Found: C, 53.63; H, 3.63; Br, 35.95.

Monomethylation Reactions of 2,6-Dibromohydroquinone. A. Water.—The reactions were conducted in a rubber-stoppered, single-necked, 50-ml, round-bottomed flask which had two side arms, one supporting a thermometer and the other sealed with a serum cap. The weighed amount (each run, 2.68 g, 0.010 mole) of 2,6-dibromohydroquinone and a magnetic stirring bar were placed in the flask (preswept with nitrogen). The requisite volume of 3.80 *N* sodium hydroxide (2.64 ml = 0.010 equiv), diluted to 10 ml with water, to form either the mono- or dianion was added and the mixture was stirred (and warmed if necessary) to dissolve the hydroquinone completely, the solution being protected by a nitrogen atmosphere. When solution was complete, the flask was stoppered and to the stirred solution (cooled to room temperature if necessary) was added dimethyl sulfate (1.26 g, 0.010 mole) in small droplets through the side arm with a syringe during 12–15 min. Stirring was continued for *ca.* 7 hr; the reaction temperature ranged from 25 to 32° during the reaction.

(18) H. M. Priestley and E. Moness, *J. Org. Chem.*, **5**, 355 (1940).
(19) B. T. Gillist and P. E. Beck, *ibid.*, **28**, 1388 (1963).
(20) M. Kohn and A. Zink, *Monatsh.*, **44**, 188 (1924).
(21) F. G. Pope and A. S. Wood, *J. Chem. Soc.*, **101**, 1823 (1912).
(22) L. Ellion and C. Janssen, *Rec. Trav. Chim.*, **44**, 192 (1925).
(23) E. J. Corey and M. Chayakowski, *J. Am. Chem. Soc.*, **84**, 866 (1962).
(24) Dimsylpotassium solution (*N* = 0.147) was generously supplied by Miss J. Gilbert of this laboratory. The author wishes to express his appreciation.
(25) The Dow Chemical Co.

The reaction mixture was diluted with 15 ml of 5 *N* sodium hydroxide, stirred to dissolve any precipitated phenolic products, and extracted twice with 25-ml portions of chloroform. The aqueous layer was stirred with 0.3 g of Darco, filtered (suction) through a Filter-Cel mat, and acidified with an excess of acetic acid. This mixture was seeded with crystals of each monomethylated product, allowed to stand for 1 day, chilled in ice–water for *ca.* 1 hr, and filtered. The crude product mixture was washed with water and dried, its weight was recorded, and its composition was determined by glpc as described below.

The combined chloroform extracts (above) were washed twice with water and dried over anhydrous magnesium sulfate. This mixture was filtered (suction), the filter cake was rinsed with chloroform, and the filtrate was carefully concentrated *in vacuo*. The residue was analyzed for 2,6-dibromohydroquinone dimethyl ether by glpc as described below.

B. Dimethyl Sulfoxide.—The apparatus was similar to that used in part A except that a 125-ml flask was used. In the potassium series, to 1.29 g (4.82 mmoles) of 2,6-dibromohydroquinone contained in the reaction flask was added 80 ml (10.0 mequiv, dianion preparation) of 0.125 *N* dimsylpotassium in DMSO under a nitrogen atmosphere. The flask was stoppered and the contents were stirred to dissolve the hydroquinone, some warming resulting. When the system had cooled to room temperature, 0.616 g (4.88 mmoles) of dimethyl sulfate was added as previously during 7 min, the temperature changing from 26 to 29°. Stirring was continued for *ca.* 1.5 hr at 29–25° and the reaction was acidified with excess acetic acid. The reaction mixture was concentrated to *ca.* 20 ml *in vacuo* [60–70° (4 mm)] on a rotary evaporator. Neutral and acidic products were separated for analysis as in part A. Monomethylation of the monoanion was conducted in a similar manner. The same quantity of 2,6-dibromohydroquinone was used and 32 ml (4.72 mequiv) of 0.147 *N* dimsylpotassium solution was required to prepare the monoanion solution and this was diluted with 48 ml of DMSO before adding dimethyl sulfate. In the sodium series, the same basic procedure was used as in the potassium series. The quantitity of 2,6-dibromohydroquinone used was 1.32 g (4.91 mmoles); 70 ml (10.3 mequiv) and 33 ml (4.85 mequiv) of 0.147 *N* dimsylsodium in DMSO were required to prepare solutions of the dianion and monoanion, respectively, the former being diluted with 30 ml of additional DMSO and the latter with 67 ml. The sodium dianion being less soluble than the potassium dianion required more DMSO for solution. At the concentration used the sodium dianion was practically completely solubilized.

C. Analysis of Products.—Ethanolic solutions of the crude phenolic product mixtures of the monomethylation reactions were analyzed by glpc using the LAC-728 column which was programmed from 175 at 9°/min to 200°. The order of emergence of the components from the column was 2,6-dibromo-4-methoxyphenol (VI), 3,5-dibromo-4-methoxyphenol (V), and unchanged 2,6-dibromohydroquinone. Peak area per cent was converted to weight per cent using appropriate factors based on a chromatograph of a reference mixture of these components. The combined yields of V and VI were calculated from the glpc data. The quantity and yield of the 2,6-dibromohydroquinone dimethyl ether (VII) was determined by glpc (410 gum rubber column, 250°) by the internal standard method[26] with 2,3,4-trichloroanisole as the internal standard.

D. Product Identification.—3,5-Dibromo-4-methoxyphenol was readily obtained from the monomethylation product mixtures of the monoanion by recrystallization from benzene: mp 139.5–141°; infrared (1% CCl_4) at ν_{OH} 3600 cm^{-1} (monomeric OH). This product was identical (mixture melting point and infrared spectra) with that prepared by the procedure of Ungnade and Zilch[4] and with authentic 3,5-dibromo-4-methoxyphenol prepared from 3,5-dibromo-4-methoxyacetophenone. 2,6-Dibromo-4-methoxyphenol was best separated from 3,5-dibromo-4-methoxyphenol on an anion-exchange column (Dowex 2X8, acetate form), eluting with 0.25% acetic acid (methanol).[27] The analytical sample was prepared by recrystallization from heptane: mp 88–89°; infared (CS_2) of ν_{OH} 3517 cm^{-1} (sharp, intramolecularly bonded OH).

Anal. Calcd for $C_7H_6Br_2O_2$: C, 29.81; H, 2.15; Br, 56.67. Found: 30.21; H, 2.29; Br, 56.60.

(26) R. L. Pecsok, "Principles and Practice of Gas Chromatography," R. L. Pecsok, Ed., John Wiley and Sons, Inc., New York, N. Y., 1961, p 144.

(27) The author is indebted to Mr. N. Skelly of the Special Service Laboratory for carrying out the separation.

Crude 2,6-dibromohydroquinone dimethyl ether was recrystallized from dilute methanol, mp 51.5–52.5° (lit.[28] mp 53°).

Authentic 3,5-Dibromo-4-methoxyphenol.—A cold methylene chloride solution of trifluoroperacetic acid was prepared according to the procedure of Emmons and Lucas[29] from 5.1 ml (0.036 mole) of trifluoroacetic anhydride, 0.82 ml (0.03 mole) of 90% hydrogen peroxide, and 5 ml of methylene chloride. This was added dropwise to a stirred suspension of 6.2 g (0.02 mole) of 3,5-dibromo-4-methoxyacetophenone,[18] 13 g (0.092 mole) of anhydrous sodium dihydrogen phosphate, and 35 ml of methylene chloride during 40 min. The reaction was exothermic but not sufficient to cause reflux. After the addition the reaction mixture was refluxed, stirring was continued, for 1.5 hr, and the mixture was filtered. The filter residue was washed well with methylene chloride. The combined filtrate and washings were washed with 10% sodium carbonate solution and dried over anhydrous magnesium sulfate. Evaporation of the solvent left a pale yellow solid of 6.1 g. This material was stirred in 50 ml of 2 *N* sodium hydroxide with intermittent warming (to 70°) for several hours. When cooled, the mixture was filtered. The filter cake was washed with water and dried to afford a recovery of 5.0 g (mp 74–77°) of the starting ketone (mp 76–77°). The filtrate and washings were acidified with acetic acid precipitating the product. After filtering, washing, and drying, there was obtained 0.68 g (64% yield) of cream-colored crystals, mp 140.5–141.5°.

Anal. Calcd for $C_7H_6Br_2O_2$: C, 29.81; H, 2.15; Br, 56.67. Found: C, 29.75; H, 2.07; Br, 56.52.

Relative Rates of Methylation of 2,6- and 3,5-Dibromophenols. A. Water.—Water solutions of the sodium salts of 2,6- and 3,5-dibromophenols (0.1000 *M* each) were prepared from the corresponding phenols, standardized, carbonate-free sodium hydroxide, and carbon dioxide free water. The concentration of hydroxide ion was 0.0680 *M* in excess of the amount required to make the phenoxides. Through the side arm of a 125-ml, single-necked flask (equipped with a stirring assembly, propeller made of Teflon) suspended in a constant-temperature bath at 25.6 ± 0.3° was pipetted an aliquot of 45 or 50 ml of the phenoxides solution. The side arm was sealed with a serum cap giving a closed system. After 15 min of temperature equilibration, dimethyl sulfate was added in small droplets to the stirred solution through the side arm with a syringe. The amount of dimethyl sulfate used was insufficient to methylate completely either of the phenoxides. After about 5 hr of stirring, the contents of the flask were carefully transferred to a separatory funnel. The flask was washed well, alternately, with several portions (totaling 50 ml each) of water and benzene. Layers were separated, the aqueous layer was washed with 25 ml of benzene, and this washing was added to the initial benzene layer. The benzene layer was washed with 25 ml of 2 *N* sodium hydroxide and twice with 25-ml portions of dilute salt solution, and dried over a minimal amount of anhydrous magnesium sulfate. The dried benzene extract was filtered carefully through a sintered-glass funnel and the filter cake was rinsed thoroughly with benzene. The filtrate was gently concentrated *in vacuo* on a rotary evaporator. Internal standard iodobenzene was weighed into the concentrate and the resulting solution was gas chromatographed on the 410 gum rubber column operated at 190°. At least three chromatographs for each run were recorded.

Peak areas of iodobenzene and the anisole products were determined (planimeter and an automatic disk integrator were equally satisfactory) and converted to moles based on the quantity of iodobenzene added to the mixture and on appropriate correction factors as determined from several chromatographs of a reference mixture of all the components. The ratio of the methylation rate constants, *r*, was calculated by eq 8 following

$$r = \frac{k_{3,5}}{k_{2,5}} = \frac{\log\left(\frac{a-x}{a}\right)}{\log\left(\frac{b-y}{b}\right)} \qquad (8)$$

where *a* and *b* are the initial concentrations of 3,5- and 2,6-dibromophenoxides, respectively, and *x* and *y* are the concentrations of 3,5- and 2,6-dibromoanisoles, respectively. Values of *r* for two runs made in this manner were 1.79 and 1.75. Two additional runs were made in the same manner except that the glpc product concentrations were determined by conversion of peak areas to weight per cents in accordance with correction

(28) F. M. Irvine and J. C. Smith, *J. Chem. Soc.*, **130**, 74 (1927).

(29) W. D. Emmons and G. B. Lucas, *J. Am. Chem. Soc.*, **77**, 2287 (1955).

factors based on a reference mixture; these values of r were 1.84 and 1.80.

B. Dimethyl Sulfoxide.—In a typical run, a 25-ml solution, 0.1052 and 0.2052 M in 2,6- and 3,5-dibromophenoxides, respectively, prepared from the phenols and dimethylsodium solution under nitrogen, and contained in a 100-ml volumetric flask (containing a magnetic stirring bar) sealed with a serum cap, was placed in the constant-temperature bath at 25.6 ± 0.3°. After temperature equilibration a solution of dimethyl sulfate (an insufficient amount to methylate completely either of the phenoxides) in *ca.* 1 ml of DMSO was added slowly to the stirred solution as before during *ca.* 7 min. After stirring for 1 hr the reaction was quenched with 1 ml of acetic acid. Internal standard 2,3,4-trichloroanisole was added, and the concentrations of the anisole products were determined as before by glpc (2-ft LAC-446 column at 165°, then at 220° to remove the unchanged phenols). The glpc reference solution was made up to approximate the reaction solutions. The values of r for two runs in DMSO were 3.57 and 3.60.

Acknowledgment.—Sincere appreciation is extended to Dr. J. W. Crump of Albion College for valuable discussions of the work and for suggesting some of the experiments. Appreciation is also extended to Mr. D. V. Wysong for technical assistance.

Some New Sulfonyl- and Trifluoromethylthio-*p*-benzoquinones. Their Reactions, Polarographic Reduction Potentials, and π Acid Strengths

RICHARD M. SCRIBNER

Contribution No. 1191 from the Central Research Department, Experimental Station, E. I. du Pont de Nemours and Company, Wilmington, Delaware 19898

Received March 29, 1966

Several new *p*-benzoquinones substituted with one to four electron-withdrawing groups were prepared, including 2,3-dicyano-5-phenylsulfonyl-*p*-benzoquinone (**3**), 2,3-dicyano-5-chloro-6-phenylsulfonyl-*p*-benzoquinone (**6**), trifluoromethylsulfonyl-*p*-benzoquinone (**8**), 2,6-bis(trifluoromethylthio)-*p*-benzoquinone (**10**), and tetrakis(trifluoromethylthio)-*p*-benzoquinone (**15**). Polarographic reduction potentials of the new quinones were measured in anhydrous acetonitrile, and quinones **3** and **15** were found to have half-wave reduction potentials ($E_{1/2}$) close to those of the well-known oxidizing reagents, 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) and chloranil, respectively. Addition and substitution reactions of several of the new quinones were examined, and dehydrogenations of steroid 4-en-3-ones by quinones **3** and **15** were compared to dehydrogenations by DDQ and chloranil. From quinone polarographic reduction data, substituent constants ($\Delta E_{1/2}$) were calculated which correspond to the additive effects of each of the substituents Cl, CF_3S, $C_6H_5SO_2$, C≡N, and CF_3SO_2 on polarographic (first wave) reduction potentials. The constants $\Delta E_{1/2}$ were shown to correlate approximately with the corresponding Hammett substituent parameters, σ_{meta}. The absorption spectra of π complexes formed between these quinones and pyrene in methylene chloride were also analyzed and the wave numbers of the absorption peaks associated with these π complexes were found to fall in the same order as the polarographic $E_{1/2}$ values observed for the corresponding quinones. The novel 1,4-dimethoxytetrakis(trifluoromethylsulfonyl)benzene (**17**) was prepared and found to have a marked affinity for electrons; it undergoes polarographic reduction more readily than chloranil, it is reduced by iodide ion in benzene to form a paramagnetic species formulated as an anion free radical (**26**), and, though it can be crystallized unchanged from boiling concentrated nitric acid, it undergoes rapid nucleophilic substitution by water in acetone at room temperature.

Substitution of *p*-benzoquinone with electron-withdrawing groups enhances its oxidation potential,[1] its strength as a π acid,[2] and its reactivity in reactions involving the transfer of hydride ions[3] or addition of free radicals.[4] For example, 2,3-dichloro-5,6-dicyano-*p*-benzoquinone has a relatively high oxidation–reduction potential and finds widespread use as a dehydrogenating agent in organic synthesis.[5] Tetracyano-*p*-benzoquinone is a strong oxidizing agent and an exceptionally strong π acid.[6]

Hammett σ parameters indicate that sulfonyl groups (*e.g.*, CH_3SO_2) are more strongly electron withdrawing than cyano groups.[7a] In fact, among the uncharged groups, the trifluoromethylsulfonyl group (CF_3SO_2)[7b] is exceeded in strength as an electron-withdrawing substituent only by the tricyanomethyl group.[7c] Since very few sulfonyl quinones[8] and no trifluoromethylsulfonyl quinones have been reported, the following study of their synthesis and chemical properties was undertaken.

Synthesis and Reactions

Sulfonyl Quinones.—The first synthetic route to new sulfonyl quinones studied was based on the reaction of sulfinic acids with *p*-benzoquinones. Addition of 2,3-dicyanobenzoquinone to excess benzenesulfinic acid in acetonitrile gave 2,3-dicyano-5-phenylsulfonylhydroquinone (**1**) conveniently and in good yield (62%). A second product, 2,3-dicyano-5,6-bis(phenylsulfonyl)-

(1) See, for example, D. J. Cram and G. S. Hammond, "Organic Chemistry," 2nd ed, McGraw-Hill Book Co., Inc., New York, 1964, p 551.

(2) (a) P. R. Hammond, *J. Chem. Soc.*, 471 (1964); (b) R. E. Merrifield and W. D. Phillips, *J. Am. Chem. Soc.*, **80**, 2778 (1958).

(3) See, for example, D. H. Reid, M. Fraser, B. B. Molloy, H. A. S. Payne, and R. G. Sutherland, *Tetrahedron Letters*, 530 (1961).

(4) F. J. Lopez Aparicio and W. A. Waters, *J. Chem. Soc.*, 4666 (1952).

(5) (a) D. Walker and T. D. Waugh, *J. Org. Chem.*, **30**, 3240 (1965); (b) P. J. Neustaedter, "Steroid Reactions," C. Djerassi, Ed., Holden-Day, Inc., San Francisco, Calif., 1963, p 129.

(6) (a) K. Wallenfels and G. Bachmann, *Angew. Chem.*, **73**, 142 (1961); (b) K. Wallenfels, D. Hofmann, and R. Kern, *Tetrahedron*, **21**, 2231 (1965); (c) K. Wallenfels, G. Bachman, D. Hoffman, and R. Kern, *ibid.*, **21**, 2239 (1965).

(7) (a) D. H. McDaniel and H. C. Brown, *J. Org. Chem.*, **23**, 420 (1958); L. M. Yagupolskii and L. M. Yagupolskaya, *Proc. Acad. Sci. USSR* (Eng. Transl.), **134**, 1207 (1960); (b) W. A. Sheppard, *J. Am. Chem. Soc.*, **85**, 1314 (1963); (c) J. K. Williams, E. L. Martin, and W. A. Sheppard, *J. Org. Chem.*, **31**, 919 (1966).

(8) O. Hinsberg, *Ber.*, **27**, 3259 (1894); *ibid.*, **28**, 1315 (1895); W. H. Hunter and D. E. Kvalnes, *J. Am. Chem. Soc.*, **54**, 2869 (1932); D. Libermann and A. Rouaix, French Patent 1,022,812 (1953). N. Dost [*Rec. Trav. Chim.*, **71**, 856 (1952)] claimed to have prepared 2,5-bis(ethylsulfonyl)-3,6-bis(ethylsulfinyl)-*p*-benzoquinone (mp 221–222°) by oxidation of tetrakis(ethylthio)-*p*-benzoquinone. The product (mp 218–219°) that we obtained from this reaction is instead the corresponding *hydroquinone*. See the Experimental Section for details.