The Preparation of Alkylhydroquinones by the Reductive Alkylation of Quinones with Trialkylboranes

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The reaction of trialkylboranes with 1,4-benzoquinone produces the corresponding alkylhydroquinones in nearly quantitative yields, and alkylboronic acids may be obtained as by-products. This method of preparing alkylhydroquinones appears to be widely applicable and limited solely by the availability of the required trialkylboranes. The scope, limitations, and a probable mechanism of the reaction are discussed.

In the past, alkylhydroquinones have been prepared through routes which involved the reaction of quinones with diacyl peroxides,[2] electrophilic alkylation of hydroquinones,[3] or acylation by the Friedel–Crafts and Fries reactions[4,5] followed by the reduction of the resulting ketones to yield monoalkylhydroquinones or the corresponding ethers.[6-9] Most of these syntheses involve several steps, give only moderate yields, and are often restricted to a particular compound or group of compounds. Direct alkylation of hydroquinone results in mixtures of isomers and polyalkylated products which differ in the structure of the side chain. Acylation suffers from the disadvantages that only primary carbon atoms may be attached to the aromatic nucleus and the synthesis involves a two-step process.

In this paper we wish to expand our discussion of the synthesis of alkylhydroquinones from the direct reaction of 1,4-benzoquinone and the corresponding trialkylboranes.[10] The reaction is strongly exothermic, extremely rapid, and gives nearly pure products in almost quantitative yields. Potentially, any alkyl- or aralkylhydroquinone may be prepared by this method if the corresponding trialkyl- or triaralkylborane is available.

Results and Discussion

Syntheses. The trialkylboranes were prepared by the hydroboration of alkenes.[11,12] It was not convenient to employ the hydroboration procedure in which diborane is generated *in situ*, since the trialkylboranes prepared in this manner must be distilled from the reaction mixture and partial disproportionation to olefin and dialkylborane results. The resulting product is undesirable for the subsequent reaction with quinone since 1,4-benzoquinone is readily reduced by dialkylboranes.

The most satisfactory procedure for the preparation of trialkylboranes employed externally generated diborane[12] and diethyl ether as the hydroboration solvent. A 25–50% excess of olefin was employed to ensure complete conversion to the trialkylborane. The solvent and excess olefin are removed from the product under reduced pressure at low temperature, and the resulting trialkylborane is employed without further purification.

The reaction of trialkylboranes with quinone is essentially instantaneous at ambient temperature and strongly exothermic. In large-scale preparations carried out in diethyl ether solvent the reaction was allowed to proceed at the reflux temperature. The 1,4-benzoquinone, dissolved in diethyl ether, was added to a solution of the trialkylborane in the same solvent instead of the inverse addition to minimize the possible oxidation of reaction product by 1,4-benzoquinone.

The initial product of the reductive alkylation reaction, when carried out in anhydrous solvents and with the exclusion of air, is the dialkylborinic ester of the alkylated hydroquinone. This ester is hydrolyzed during steam distillation and the released borinic acid degraded to the corresponding boronic acid. The resulting steam distillate contains boronic acid, unreacted starting materials, and volatile degradation products. The steam distillation residue is relatively pure alkylhydroquinone. Table I presents yield and characterization data for a series of alkylhydroquinones and the corresponding benzoates and alkyl-1,4-benzoquinones.

Scope and Mechanism. The reductive alkylation reaction apparently has no limitations when trialkyl- or triaralkylboranes are employed. Triphenylborane did not react with 1,4-benzoquinone under the conditions employed in this study, and quinones other than 1,4-benzoquinone appear to react very sluggishly, if at all. These include 1,2-benzoquinone, 1,4-naphthoquinone, 1,2-naphthoquinone, and phenanthroquinone. No useful products were obtained from these reactions after 5 days in benzene at the reflux temperature. The reaction of bis(3-methyl-2-butyl)hex-1-enylborane with 1,4-benzoquinone gave only (3-methyl-2-butyl)hydroquinone. Oxidation of the alkylhydroquinone to the alkyl-1,4-benzoquinone, followed by further reaction with trialkylborane, appeared to produce slowly a mixture of the three possible isomeric dialkylhydroquinones which was not examined in detail.

It was possible to isolate the monodialkylborinic acid ester of the alkylhydroquinone as a viscous oil or glass from reactions carried out in the complete absence of
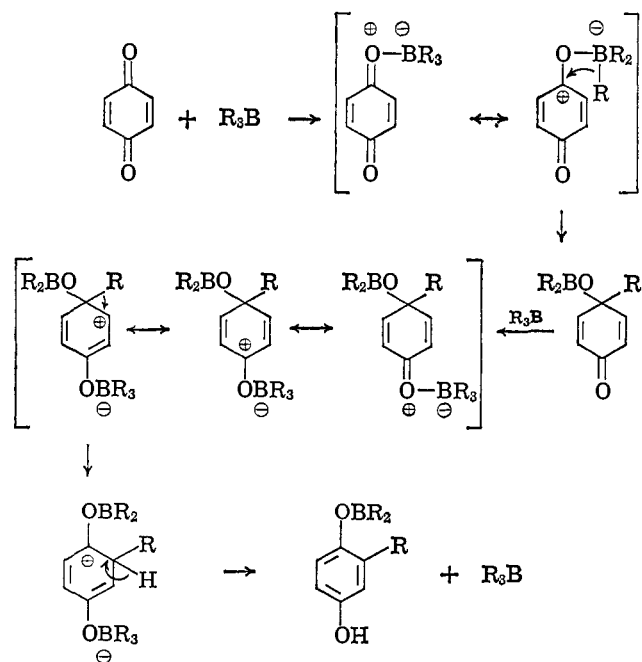
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Table I. Alkylhydroquinones and Characterization Data

Compound	Crude yield, %	M.p., °C.	Analysis, % Calculated C	Calculated H	Found C	Found H
(1-Butyl)hydroquinone	86	87–87.5ᵃ	72.29	8.43	71.85	8.19
quinone		34–35	73.17	7.32	73.37	7.46
dibenzoate		97–98	77.01	5.88	77.14	6.00
(1-Hexyl)hydroquinone	99	84–84.5ᵃ	74.23	9.28	73.93	8.95
quinone		48–49	75.00	8.33	74.78	8.40
dibenzoate		53–54	77.61	6.47	77.45	6.49
Cyclohexylhydroquinone	99	163–165 (0.4)ᵇ				
quinone		53–54ᶜ	75.79	7.37	75.78	7.34
dibenzoate		106–108	78.00	6.00	77.93	5.82
(2-Methylpropyl)hydroquinone	91	111.5–112	72.29	8.43	72.40	8.55
quinone		35–36	73.17	7.32	72.92	7.54
dibenzoate		120.5–121	77.01	5.88	76.84	5.84
(2-Butyl)hydroquinone	94	100–101	72.29	8.43	72.22	8.45
quinone		66 (1.0)ᵇ	73.17	7.32	72.89	7.56
dibenzoate		92–93	77.01	5.88	77.02	5.86
Cyclooctylhydroquinone	91	160–160.5	76.36	9.09	76.19	9.03
quinone		43.5–44.5	77.06	8.26	76.94	8.17
dibenzoate		123–126	78.50	6.54	78.47	6.48
Benzylhydroquinone	90	101–103ᵈ	78.00	6.00	77.95	6.31
dibenzoate		151–153	79.41	4.90	79.66	5.09
(3-Methyl-2-butyl)hydroquinoneᵉ	95	…ᶠ				
quinone		78 (1.2)ᵇ	74.16	7.87	73.89	8.09
dibenzoate		101–102	77.32	6.19	77.41	6.35

ᵃ J. Renz [*Helv. Chim. Acta*, **30**, 124 (1947)] reports m.p. 84–85° (1-butyl) and m.p. 79–80° (1-hexyl). ᵇ B.p. (mm.), °C. The product was not directly characterized. ᶜ L. F. Fieser [*J. Am. Chem. Soc.*, **70**, 3165 (1948)] reports m.p. 53.5–54.5°. ᵈ R. Stolle and W. Moring [*Ber.*, **37**, 3486 (1940)] report m.p. 105°. ᵉ From bis(3-methyl-2-butyl)hex-1-enylborane. ᶠ The product was obtained as a glass which was not directly characterized.

air and water. Alkaline hydrolysis of these crude esters produced the corresponding borinic anhydrides. The infrared spectra of the crude esters contained OH and BO stretching bands at 3280 and 1340 cm.⁻¹, respectively, and ¹H n.m.r. spectra proved the presence of aromatic protons at δ 6.60–6.75, relative to tetramethylsilane.

Scheme I

These data point to the fact that the initial product of the reductive alkylation reaction is the borinic ester of the alkylated hydroquinone. The most plausible mechanism for the reductive alkylation reaction appears to involve the initial formation of a quinol ester, which

rearranges in the presence of a Lewis acid (trialkylborane) to the corresponding hydroquinone. Goodwin and Witkop[13] have reported the reactions of p-quinols and their O-acetates. The rearrangement of p-toluquinol to methylhydroquinone is catalyzed by aqueous acids, bases, and boron trifluoride, while p-toluquinol acetate rearranges to cresorcinol 2-acetate (1,2-shift of the acetoxy group) in the presence of boron trifluoride.

Scheme I is consistent with Lewis acid catalysis and the experimental data presently available.

Experimental Section

Materials. Diglyme (diethylene glycol dimethyl ether) was obtained from the Ansul Chemical Co. and purified as described below. Boron trifluoride ethyl etherate was distilled in an all-glass apparatus under reduced pressure and stored at 0°.

1-Butene, 2-butene (mixed isomers), cis-2-butene, and isobutylene were Matheson C.P. grade. The gases were passed through a silica gel drying column prior to use. 2-Methylbutene-2 was Phillips Pure Grade (99%). 1-Hexene (97.8%) was obtained as a gift from the Gulf Oil Corp. Cyclooctene (95%) was obtained as a gift from the Cities Service Research and Development Co. 1-Hexyne was obtained from Farchan Research Laboratories.

Tribenzylborane was prepared by the method of Krause and Noble.[14] The procedure of Brown and Zweifel[15] was employed to prepare bis(3-methyl-2-butyl)hex-1-enylborane. Infrared spectra were determined with a Perkin-Elmer Model 137 spectrophotometer with sodium chloride optics, and ¹H n.m.r. spectra were obtained with a Varian Model A-60

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spectrometer. Reported melting points are uncorrected.

Purification of Diglyme. Initially, diglyme was purified as described by Brown[12] by treatment with calcium hydride and subsequent distillation from lithium aluminum hydride. However, in one case a violent explosion occurred in the distillation flask following distillation, and a modified procedure was then developed. Diglyme was first heated to the reflux temperature under nitrogen with vigorous stirring in the presence of sufficient sodium to maintain shiny globules of the molten metal. After heating for 4 hr., the diglyme was distilled at atmospheric pressure. Sufficient lithium aluminum hydride was then added to the distillate to ensure an excess of active hydride. The solvent was then distilled at 0.1 mm. while the receiver was cooled in an ice bath. An explosion of diglyme–lithium aluminum hydride has also been described elsewhere.[16]

Hydroboration of Olefins (Trialkylboranes). The apparatus and procedure were essentially those described by Zweifel and Brown,[12] and diethyl ether was employed as the hydroboration solvent. The following quantities of reagents were employed: 750 ml. of 1 M sodium borohydride in diglyme, 234 g. (1.65 moles, 65% excess) of boron trifluoride etherate, and 4.5 moles (50% excess) of olefin. After completion of the diborane addition, the trialkylborane solution was allowed to stand overnight at room temperature. The solvent was removed at 20–25° using a water aspirator and a nitrogen bubbler (capillary), and the crude boranes were used without further purification. Yields were virtually quantitative.

General Procedure for the Preparation of Alkylhydroquinones. The apparatus consisted of a three-neck, round-bottom flask, equipped with a reflux condenser, a pressure-equalizing dropping funnel, and an inlet for dry nitrogen. The apparatus was flushed with nitrogen and maintained under a slight static pressure. In all cases 0.10 mole of 1,4-benzoquinone dissolved in diethyl ether was added to a solution of 0.11 mole of trialkylborane in the same solvent at the reflux temperature. Following the addition (30–60 min.) the reaction mixture was maintained at the reflux temperature for 30 min. The reaction mixture was then steam distilled to remove solvent, boronic and borinic acids, and unused reagents. On cooling, the alkylhydroquinone separated as a crystalline mass in the steam distillation flask. The product was separated by filtration and air-dried. Yields are based on the crude products, which were exceptionally clean. For elemental analyses and melting point determination, the products were recrystallized from ethyl ether–pentane. These results are shown in Table I.

Preparation of Alkyl-1,4-benzoquinones. The corresponding alkylhydroquinones were oxidized according to the method of Underwood and Walsh[17] using

sodium chlorate and a catalytic amount of vanadium pentoxide in a mixture of equal volumes of glacial acetic acid and acetone with sufficient water to dissolve the sodium chlorate. The quinones were recovered from this solvent mixture in almost quantitative yield. Elemental analyses and melting point determinations were obtained with freshly sublimed products. Characterization data are given in Table I.

Alkylhydroquinone Dibenzoates. The dibenzoates were prepared by dissolving 0.2 g. of the hydroquinone in 10 ml. of pyridine and adding 1.0 g. of benzoyl chloride. After the initial reaction subsided, the mixture was heated on the steam bath for 15 min. and then poured into 200 ml. of ice–water. After thorough stirring to decompose excess benzoyl chloride, the product was extracted with ether. The ether extract was washed three times with dilute aqueous sodium bicarbonate solution and twice with water. After drying over sodium sulfate the solvent was evaporated and the product dissolved in hot 95% ethanol. The benzoates crystallized in long white needles from this solvent. Characterization data are given in Table I.

Isolation of Diisobutylborinic Acid. The reaction was carried out in the usual manner with triisobutylborane except that the solvent was removed with rigorous exclusion of air. A fivefold excess of 20% aqueous sodium hydroxide solution was then added, and the mixture was heated to the reflux temperature for 2 hr. The alkali-insoluble fraction was separated and distilled under reduced pressure. Two fractions were obtained. The first fraction corresponded to diisobutylborinic acid and had b.p. 38–39° (0.1 mm.), n^{20}D 1.4152. The second fraction was the diisobutylborinic anhydride and had b.p. 65–67° (0.1 mm.), n^{20}D 1.4224 (lit.[18] 111–112° (9 mm.), n^{20}D 1.4230). The ethanolamine derivative prepared from both fractions had m.p. 85–85.5°.

The ethanolamine derivative was prepared by heating 1 mole of anhydride and 2 moles of ethanolamine dissolved in benzene to the reflux temperature in a Soxhlet extractor. Calcium hydride was placed in the thimble to remove water from the azeotrope. The product was recrystallized from ether–pentane at room temperature. *Anal.* Calcd. for $C_{10}H_{22}BNO$: C, 64.86; H, 12.97. Found: C, 64.76; H, 13.27. The infrared spectra of the anhydride and ethanolamine derivative are in agreement with similar characterization data obtained for diisobutylborinic anhydride prepared from diisobutylboronium acetylacetonate.[19]

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