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Ring-butylamination of Toluquinone: Isolation of Products by TLC and an Observation of Their Reaction Course on the Basis of Molecular Reactivity Index

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The ring-butylamination of toluquinone with *n*-butyl-amine was carried out in a chloroform or ethanolic solution at room temperature or at 25.0°C with various molar ratios of the quinone to the amine (designated as Q/A). For the successful separation of each product, TLC was applied, while polarography was used for following the change in the composition of the reacting mixture as well as for measuring the amount of the amino-quinone separated from the reacting mixture by TLC. In the butylamination of toluquinone with excess butylamine (Q/A: 1/5) for 10 hr, the major products were 3,6-bis-(*n*-butylamino)-toluquinone (32%) and 2,5-bis(*n*-butylamino)-*p*-benzoquinone (8%), accompanied by a relatively large amount of unknown by-products: with a Q/A of 2/1 for 2 hr, the major products were 3- and 4-*n*-butylamino-toluquinone (17% and 21%) and 3,6-bis(*n*-butylamino)-toluquinone (3.3%) together with toluhydroquinone (47%). The quantitative formation of 3,6-bis(*n*-butylamino)-toluquinone from 3-*n*-butylamino-toluquinone or the formation of 2,5-bis(*n*-butylamino)-*p*-benzoquinone (34%) and 3,6-bis-(*n*-butylamino)-toluquinone (1%) from 4-*n*-butylamino-toluquinone was also found (Q/A: 1/4, 3 hr or 13 hr), where a faster reaction was found for the 3-isomer than for the 4-isomer under the present conditions. The pathway of the formation of each product was discussed on the basis of the calculated reactivity index of toluquinone or its butylaminated toluquinone isomers toward the amine-attacking.

It is well known that the reactions of *p*-benzoquinone and its derivatives with amines can be classified into three types: (a) the nucleophilic 1,4-addition of an amine to a quinone to give an amino-quinol which, on oxidation, yields the corresponding amino-quinone,[1] (b) the amination of a substituted quinone by replacing the labile substituent (*e.g.*, halogen and alkoxyl) already present[2] and (c) the methylamination of the methylated quinones.[3] Among these reactions, the 1,4-addition reaction of an amine to a quinone was studied by Hofmann *et al.* with aromatic amines.[4] Regarding the reaction mechanism of the 1,4-addition of amines to quinones, however, few papers have been published, though this reaction seems to involve an interesting and attractive redox reaction system, judging from the standpoint of organic chemistry as well as from that of biochemistry. Moreover, the exact mechanism of the reaction of a quinone with an amine still remaines unsolved, since, for example, the amination of *p*-benzoquinone with an amine is so fast that its kinetic treatment is impossible by the usual analytical means.

The aim of this study, which has the ultimate purpose of revealing the quinone-amine reaction mechanism, is to find a quinone-amine reaction which proceeds at a rate measurable by conventional analytical means. Therefore, the system of toluquinone and *n*-butylamine was chosen and examined for the products made in a chloroform or ethanolic solution at room temperature or at 25.0°C, while the molar ratio of toluquinone to the amine was varied. Moreover, the concept of the reactivity index calculated by means of quantum chemistry was applied to the discussion of the product distribution of the amino-quinone formed in the quinone-amine reacting system.

Experimental

Materials. Toluquinone, mp 67.3—67.8°C, was prepared by the oxidation of toluidine by the method described in the literature.[5] The *n*-butylamine, obtained commercially, was of a chemically pure grade and was used without further purification.

TLC Analysis. TLC was carried out to separate each of the reaction products obtained in the reaction of

1) See, *e.g.*, L. Fieser and M. Fieser, "Advanced Organic Chemistry," Reinhold, New York (1961), p. 853.

2) See, *e.g.*, D. Buckley, H. B. Henbst and P. Slade, *J. Chem. Soc.*, **1957**, 4891.

3) D. W. Cameron, P. M. Scott and L. Todd, *ibid.*, **1964**, 42; D. W. Cameron and P. M. Scott, *ibid.*, **1964**, 5569.

4) See, *e.g.*, A. W. Hofmann, *Jahresber. für Chemie*, **1863**, 415; T. Zincke, *Ber.*, **12**, 1641 (1879).

5) "Handbuch der präparativen Chemie," 2. Band, Ferdinand Enke, Stuttgart (1937), p. 690.

toluquinone with *n*-butylamine, prior to the identification or polarographic analysis of the products, by the ascending chromatographic technique. In this technique Silica Rider, a commercially-available silica-gel purchased from the Daiichi Pure Chemicals Co., Ltd., was used after its activation by heating at 110°C for 2 hr. The chromatography was conducted, in most cases, in a chloroform tank. In the TLC, chromatography was repeated twice in order to obtain sufficiently-separated zones.

Polarographic Study of the Butylamination of Quinone. *Polarographic Potential $E_{(1/2)}$ (vs. SCE).* This was measured at 25.0°C on a pure quinoid compound in a mixed solvent of isopropyl alcohol - aqueous phosphate buffer (pH 6.8) (1 : 1 by volume), using a Yanagimoto Polarograph PA-102. The $E_{(1/2)}$ thus measured can be used for deciding whether an alkylamino-quinoid compound is mono- or di-substituted, since, under the present quinoid system, $E_{(1/2)}$ is *ca.* −0.3 V for the mono-substituted quinone and *ca.* −0.5 V for the di-substituted quinone.

Polarographic Study of the Progress of the Alkylamination of Quinone. In the nucleophilic 1,4-addition of an amine to *p*-benzoquinone, the aminoquinol first formed yields the corresponding amino-quinone upon its oxidation with the parent quinone present in the reacting system; the latter may undergo a second amination in the same way to yield 2,5-bis(*n*-butylamino)-*p*-benzoquinone.[1] When the reaction is carried out in air, however, according to the different redox potentials of the quinone and the related amino-quinones that are participating in the reaction, there is a possibility of hydrogen abstraction with oxygen in air from the amino-hydroquinones formed in the course of the reaction. Therefore, in the polarographic studies of the reaction course of toluquinone and *n*-butylamine, the change in the composition of the reacting mixture *vs.* the reaction time was examined under various conditions for such products detectable by polarography as toluhydroquinone, toluquinone (−0.06 V), and mono- and di-butylaminated toluquinones, as well as hydrogen peroxide (−1.2 V). (None of the three possibly existing isomeric mono-butylaminated toluquinones could be detected in their mixture, nor could the di-butylaminated quinones be distinguished from each other under the present polarographic conditions.)

An example of polarographic analysis of the reacting mixture is as follows: To an ethanolic solution of toluquinone, which had been kept at 25.0°C in a water bath, was instantly added an ethanolic solution of *n*-butylamine, after which the reaction was continued under stirring for a certain time interval. During this reaction 0.1 m*l* portions of the reacting solution were pipetted out at certain time intervals and dissolved into 10.0 m*l* of an isopropyl alcohol solution; then 2.0 m*l* of the resultant solution, mixed with the same volume of the aqueous phosphate buffer (pH 6.0), was submitted to polarographic analysis.

Butylamination of Toluquinone with n-Butylamine. Derivation of 3,6-Bis(n-butylamino)-toluquinone and 2,5-Bis(n-butylamino)-p-benzoquinone by the Reaction of Toluquinone with Excess n-Butylamine. To a mixture of toluquinone (4.88 g, 40 mmol) in ethanol (100 m*l*) in an Erlenmeyer flask, *n*-butylamine (14.6 g, 200 mmol) was added drop by drop, over 30-min period at room temperature; after that the stiaring was continued for 5 hr, and the resultant solution was refrigerated for 2 days and filtered to remove violet crystals (3.4 g). This substance (1.0 g) was submitted to TLC, where the amount of the sample treated per plate (0.14×20×20 cm) was *ca.* 200 mg; a solution of this substance (200 mg) in chloroform (2 m*l*) was applied in line on the silica-gel layer and developed in a chloroform tank. After the solvent had reached the upper edge of the plate, the plate was dried in air for 30 min and then again developed with chloroform. The two separated zones (C′ and D′) were then scrapped from the plate and extracted with 10 m*l* of chloroform and then 10 m*l* of methanol; the extracts thus obtained were collected for C′ or D′, and evaporated to dryness under a reduced pressure of nitrogen to give violet crystals (C, 140 mg) and reddish crystals (D, 45 mg). These substances were recrystallizable from chloroform or ethanol.

Compound C; mp 119.7—120.7°C.

Found: C, 67.8; H, 9.3; N, 10.2%. Calcd for $C_{15}H_{24}O_2N_2$: C, 68.1; H, 9.1; N, 10.6%.

$E_{(1/2)}$, −0.53 V. R_f, 0.17.

IR in CCl_4[6]; 3355 and 3297 (m, ν_{N-H}), 1644 (m, $\nu_{C=C}$), 1613 and 1580 (s, $\nu_{C=O}$), 1502 cm^{-1} (s, amido II type).

NMR in $CDCl_3$ (see (1)): 9.05 and 8.95 τ (6 H_h), 8.50 τ (8 H_g), 7.93 τ (3 H_f), 6.87 τ (2 H_e, quartet coupled with H_g and H_a), 6.46 τ (2 H_d, quartet coupled with H_g and H_b), 4.80 τ (1 H_c) and 3.32 τ (1 H_a and 1 H_b, broadened).

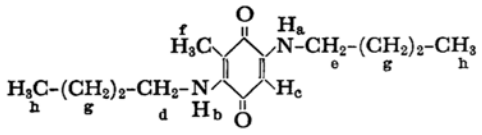
Compound D; mp 163.5—164.5°C.

Found: N, 11.2%. Calcd for $C_{14}H_{22}O_2N_2$: N, 11.2%.

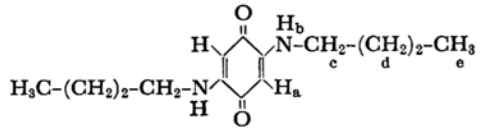
$E_{(1/2)}$, −0.57 V. R_f, 0.08.

IR in CCl_4[6]: 3355 (m, ν_{N-H}), 1650 (m, $\nu_{C=C}$), 1589 (s, $\nu_{C=O}$), 1503 cm^{-1} (s, amido II type).

NMR in $CDCl_3$ (see (2)): 9.07 and 8.96 τ (6 H_e), 8.44 τ (8 H_d), 6.84 τ (4 H_c, quartet coupled with H_d and H_b), 4.73 τ (2 H_a) and 3.36 τ (2 H_b, broadened).



(1)



(2)

From the above results, it was concluded that Compound C is 3,6-bis(*n*-butylamino)-toluquinone and that Compound D is 2,5-bis(*n*-butylamino)-*p*-benzoquinone.

The change in the composition of the reacting mixture *vs.* the reaction time was followed polarographically for a reaction carried out at a moderate reagent concentration in an ethanolic solution; it is shown in Fig. 1.

To determine the amount of each of the di-butylaminated quinones, 1.0 m*l* of the reacting solution obtained 10 hr after the beginning of the reaction was

6) Unpublished data; a paper on the spectral data of the amino-quinoid compound will be shortly submitted for publication.

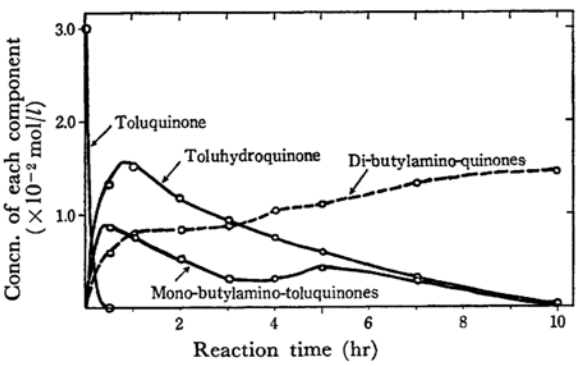


Fig. 1. Change of composition *vs.* reaction time in the reaction of toluquinone with excess *n*-butylamine (Q/A: 1/5); ethanolic solutions of toluquinone (36.6 mg, 0.3 mmol in 10 m*l*) and *n*-butylamine (1.0 m*l* of 15 vol%).

pipetted out, submitted to the TLC (thickness of the silica-gel layer: 0.6 mm), and chromatographed in a chloroform tank such as has already been described. The product (C or D) thus separated was dissolved in 5.0 m*l* or 10.0 m*l* of isopropyl alcohol to prepare a solution with a suitable concentration for the polarographic analysis; 2.0 m*l* of the resultant solution was mixed with the same volume of the aqueous phosphate buffer (pH 6.0) and submitted to the polarographic analysis. The product ratio of C to D was found to be 4/1.

Derivation of 3- and 4-n-Butylamino-toluquinone with a Q/A of 2:1. A solution of toluquinone (2.44 g, 20 mmol) in chloroform (10 m*l*) was instantly mixed with achloroform solution of *n*-butylamine (5 m*l* of 19.3 vol %) at room temperature in an Erlenmeyer flask and stirred magnetically for 1 hr, refrigerated for a day, and filtered to remove the precipitated crystals of toluhydroquinone. The resultant chloroform solution was submitted to the TLC in the same manner as has already been described, thus affording the crystals in yields of 450 mg (A′) and 290 mg (B′); 30 m*l* of dried ether were used for the extraction (200 mg of the sample were treated per plate).

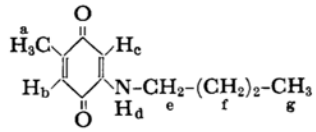
The A′ (20—30 mg), shown by its polarogram to consist of two components, A and C, was dissolved in a small amount of chloroform, applied on the silica-gel layer (thickness, 0.6 mm) and chromatographed with a mixed solvent of ethyl acetate - carbon tetrachloride (1: 15 by volume). The chromatogram thus obtained was again developed in the same solvent tank to give pure A and C. The purity of the substance, A or C, was confirmed by a.c. polarography. A was isolated as a sublimate from its mixture with Compound C by heating the mixture under reduced pressure. B gave only one peak in its polarogram. The chemical and physical constants of the compounds, A and B, are shown below.

Compound A recrystallizable from *n*-hexane: mp 63.6—65.6°C.

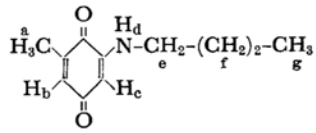
Found: N, 7.2%; mol wt (v.p.o.), 207. Calcd for $C_{11}H_{15}O_2N$: N, 7.3%; mol wt 193.

$E_{(1/2)}$, −0.30 V. R_f, 0.15.

UV: λ_{max}^{EtOH} 214 (ε 28200), 275 (ε 12200), 485 mμ (ε 2740).



(3)



(4)

NMR in $CDCl_3$ (see (3)); 9.05 and 8.95 τ(3 H_g), 8.42 τ(4 H_f), 7.95 τ(3 H_a, doublet coupled with H_b[7]), 6.90 τ(2 H_e, quartet coupled with H_d and H_f), 4.60 τ(H_c), 4.46 τ(H_d), broadened), 3.60 τ(H_b, quartet coupled with H_a).

Compound B recrystallizable from *n*-hexane: mp 72.2—73.3°C.

Found: C, 67.6; H, 7.8; N, 7.2%; mol wt (v.p.o.), 189. Calcd for $C_{11}H_{15}O_2N$: C, 68.4; H, 7.8; N, 7.3%; mol wt, 193.

$E_{(1/2)}$, −0.28 V. R_f, 0.07.

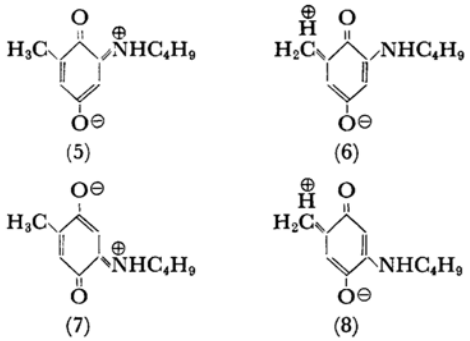
UV: λ_{max}^{EtOH} 218 (ε 22800), 278 (ε 9150), 485 mμ (ε 2940).

NMR in $CDCl_3$ (see (4)); 9.05 and 8.93 τ(3 H_g), 8.48 τ(4 H_f), 7.98 τ(3 H_a, doublet coupled with H_b), 6.88 τ(2 H_e, quartet coupled with H_d and H_f), 4.59 τ(H_c, doublet (J=2.5 cps) coupled with H_b[8]), 4.38 τ(H_d, broadened), 3.58 τ(H_b, quartet or quintet coupled with H_a and H_c).

Compound C: $E_{(1/2)}$, −0.53 V. Its infrared spectrum was in agreement with that of the authentic sample given in the preceding section.

According to the study made by Yates *et al.*[9] of the out-of-plane bending of the C–H of *p*-benzoquinone and its derivatives by infrared spectroscopy, it became evident that neither A nor B, each having a characteristic absorption band at 880 cm^{-1} or 894 cm^{-1} in CS_2 respectively, was identical with the 2,3-disubstituted *p*-benzoquinone isomer. Upon determining which compound, A or B was identical with one of the two possible isomers, 3- and 4-*n*-butylamino-toluquinone, we attempted to acertain the difference between the wave numbers of the two carbonyl groups within a molecule of each 3- and 4-*n*-butylaminotoluquinone. The results thus obtained were correlated with the expected $\Delta\nu_{C=O}$, originating from the different "aufrichtung" effect of the carbonyl group, which was given by the different hyperconjugation and the electron-donating effects of the existing methyl group or the different inductomeric effect of the *n*-butylamino group already present; (5) and (6) show 3-*n*-butylamino-toluquinone, and (7) and (8), 4-*n*-butylamino-toluquinone.

7) E. R. Wagner, R. D. Moss and R. M. Brooker, *Tetrahedron Letters*, **47**, 4236 (1965).
8) J. H. Day and A. Jaochim, *J. Org. Chem.*, **30**, 4108 (1965).
9) P. Yates, M. I. Ardao and L. F. Fieser, *J. Am. Chem. Soc.*, **78**, 652 (1956).



(5) (6) (7) (8)

Thus, on the basis of a comparison between the observed facts that $\Delta\nu_{C=O}$ is 36 cm^{-1} for A and 47 cm^{-1} for B, it is concluded that Compound A is 4-*n*-butylamino-toluquinone and Compound B is 3-*n*-butylamino-toluquinone.

This is in agreement with the NMR spectra.

The change in the composition of the reacting mixture *vs.* the reaction time was followed polarographically (see Fig. 2).

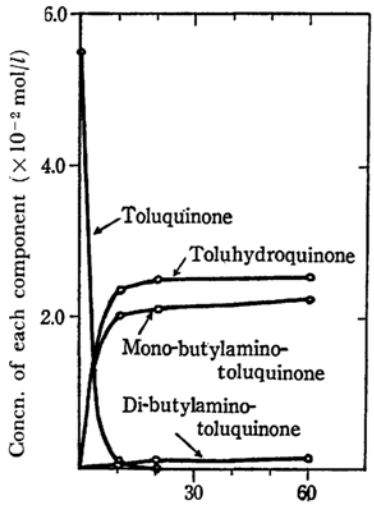


Fig. 2. Change of composition *vs.* reaction time in the reaction of toluquinone with *n*-butylamine-(Q/A: 2/1); a solution of toluquinone (36.6 mg, 0.3 mmol in ethanol (5.0 m*l*) was reacted with an ethanolic *n*-butylamine solution (0.5 m*l* of 3.0 vol%)

To determine the amount of each of the butylamino-toluquinones, 1.0 m*l* of the reacting solution obtained was, 2 hr after the beginning of the reaction, pipetted out and submitted to the TLC (thickness, 0.6 mm). Each of the substances, A′ and B′ extracted with 30 m*l* of ether, was submitted to polarographic analysis in the same way as has been described before; the A: B: C ratio was found to be 51: 41: 8.

Derivation of 3,6-Bis(n-butylamine)-toluquinone by the Reaction of 3-n-Butylamino-toluquinone and n-Butylamine with a Q/A of 1/4. A solution of 3-*n*-butylamino-toluquinone (63.7 mg, 0.33 mmol) in ethanol (10 m*l*) was instantly mixed with an ethanolic *n*-butylamine solution (1.0 m*l* of 12 vol%) at 25.0°C, stirred for 3 hr, and then submitted to the TLC on a silica-gel layer such as has been described for the mono-butylamination of toluquinone. The major separated zone was extracted with 5.0 m*l* of chloroform and then 5.0 m*l* of methanol; the extracts thus obtained were combined, and the solution was submitted to evaporation to dryness under reduced nitrogen pressure to give crystals as the residue; recrystallization from chloroform or ethanol gave violet crystals; mp 119.7—120.7°C; $E_{(1/2)}$, −0.53 V; R_f, 0.17; (Found: C, 68.2; H, 9.2; N, 10.3%). The identity of this compound with 3,6-bis(*n*-butylamino)-toluquinone was also established by its infrared spectral agreement with an authentic sample already prepared in the reaction of toluquinone with excess amine.

The relation obtained polarographically regarding the change in the reacting mixture *vs.* the reaction time is shown in Fig. 3.

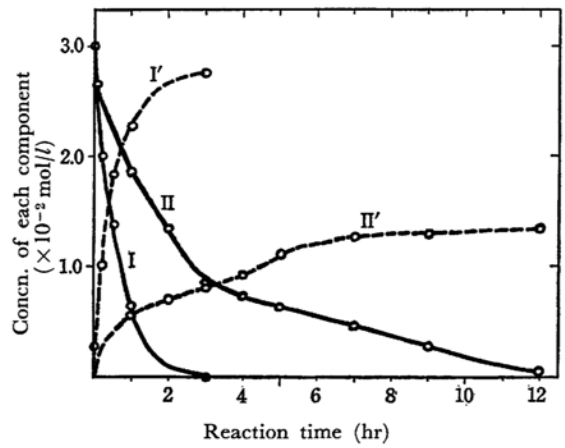


Fig. 3. Reaction of 3-*n*-butylamino-toluquinone (I) and 4-*n*-butylamino-toluquinone (II) with *n*-butylamine; (I) ethanolic solutions of 3-aminoquinone (63.7 mg, 0.33 mmol in 10 m*l*) and *n*-butylamine (1 m*l* of 12 vol%), (II) ethanolic solutions of 4-aminoquinone (28.9 mg, 0.15 mmol in 5 m*l*) and *n*-butylamine (0.5 m*l* of 12 vol%).

Upon the measurement of the yield, a 1.0 m*l* portion of the reacting solution pipetted out was submitted to TLC similar as that used in the preceding section; the yield of this substance was 95%.

Derivation of 2,5-Bis(n-butylamino)-p-benzoquinone and 3,6-Bis(n-butylamino)-toluquinone by the Reaction of 4-n-Butylamino-toluquinone with Excess n-Butylamine. A solution of 4-*n*-butylamino-toluquinone (28.9 mg, 0.15 mmol) in ethanol (5.0 m*l*) was reacted with an ethanolic *n*-butylamine solution (0.5 m*l* of 12 vol%) for 13 hr such as has already been described in connection with other reactions, and a half volume of the reacting solution was applied in line on the silica-gel layer (thickness: 0.6 mm) and chromatographed in the chloroform tank in the manner already described. Then, each of the violet- and pink-colored zones obtained was extracted with 5 m*l* of chloroform and then 5 m*l* of methanol. The extracts thus obtained gave violet- and pink-colored crystals after the removal of the solvent; the infrared spectra were identical with those of 3,6-bis-(*n*-butylamino)-toluquinone and 2,5-bis(*n*-butylamino)-*p*-benzoquinone respectively. The yield of each of these

products was measured by submitting a 1.0 m*l* portion of the remaining half volume of the reacting solution to an analysis combining TLC and polarography, as had already been used for the other cases; the yields of 3,6-bis-(*n*-butylamino)-toluquinone and 2,5-bis (*n*-butylamino)-*p*-benzoquinone were 1.0% and 34% respectively.

The change in the composition of the ethanolic reacting mixture *vs.* the reaction time was followed polarographically; it is plotted in Fig. 3.

Results and Discussion

Correlation of Each of the Butylaminated Quinones. In the reaction of toluquinone with an ethanolic solution of excess *n*-butylamine, the major butylaminated quinone derivatives were 3,6-bis(*n*-butylamino)-toluquinone (32% for the toluquinone used) and 2,5-bis(*n*-butylamino)-*p*-benzoquinone (8%), together with a relatively large amount of by-products. Upon the determination of the reaction course producing each of the butylaminated toluquinones, the reaction of toluquinone with the amine was carried out with a Q/A molar ratio of 2/1; as expected, this led to the formation of mono-butylaminated toluquinones, the products being toluhydroquinone (47%), 3- and 4-*n*-butylamino-toluquinone (17% and 21%), and 3,6-bis-(*n*-butylamino)-toluquinone (3.3%).

Among these products, 3,6-bis(*n*-butylamino)-toluquinone can be considered to be made through either 3- or 6-*n*-butylamino-toluquinone. It will be clearly explained below.

Further in the reaction of 3-*n*-butylamino-toluquinone with an ethanolic solution of *n*-butylamine (Q/A: 1/4), 3,6-bis(*n*-butylamino)-toluquinone was prepared approximately quantitatively, while, with 4-*n*-butylamino-toluquinone (Q/A: 1/4), 2,5-bis(*n*-butylamino)-*p*-benzoquinone (34%) and a trace of 3,6-bis(*n*-butylamino)-toluquinone were obtained, with a complete consumption of the amino-toluquinone. The former was, presumably, a result of the methylamination mechanism already proposed by Cameron *et al.*[8] for the methylamination of toluquinone with methylamine; the latter found by the TLC technique, was readily assumed to be produced by such a complex reaction as is illustrated by the formation of larger amounts of by-products, *e.g.*, through the redistribution of the butylamino-residue of the amino-quinones between the products existing in the reaction course.

Concerning the alkylamination of toluquinone or its derivation with alkylamine, the formation of 3,6-bis(methylamino)-toluquinone[3,10,11] from toluquinone and that of 2,5-bis(methylamino)-*p*-benzoquinone from 4-methoxyl-toluquinone[8,10] by reaction with methylamine have been reported. However, in the former case the pathway leading to the amino-quinone has not yet been established, and in the latter case 4-methylamino-toluquinone has been proposed as an intermediate on the basis of no evidence. The results obtained by the present authors for the reactions of *n*-butylamine and toluquinone or its amino-derivatives give exact evidence for the pathway of the alkylamination of toluquinone with an amine.

Polarographic Study of the Progress of the Reaction of Toluquinone with *n*-Butylamine. In the reaction of *n*-butylamine with toluquinone (Q/A: 2/1) it was revealed that the reaction was saturated within 20 min (see Fig. 2). The major products were mono-butylaminated toluquinones plus a minor quantity of dibutylaminated quinones; no detectable amount of hydrogen peroxide was found, indicating that the hydrogen-abstraction from the alkylamino-hydroquinone was made first with the parent quinone, not with oxygen in air.

With a Q/A of 3/2, due to the decrease in the amount of the mono-butylaminated toluquinone once formed through its further reaction, the reaction product obtained 2 hr after the beginning of the reaction was found to be contaminated with relatively large amounts of mono- and dibutylaminated quinones; this procedure is, then, unsuitable for the selective preparation of either mono- or di-butylaminated toluquinone in an excellent yield. Under the present conditions, the formation of hydrogen peroxide was detected by observing a polarographic wave corresponding to that of hydrogen peroxide at -1.2 V.

With a Q/A of 1/5, as may be seen from Fig. 1, the step-by-step butylamination of toluquinone to 3,6-bis(*n*-butylamino)-toluquinone through the well-known reaction course, the participation of toluquinone in the further reaction made through the air-oxidation of toluhydroquinone accumulated at the early stage of the reaction, and the saturation of the product distribution 10 hr after the beginning of the reaction can clearly be seen; the fact that the conversion curve observed on the rate of mono-butylaminated toluquinone shows two upward peaks indicates the complexity of the reaction. Of course, in this system the formation of hydrogen peroxide was also found polarographically.

An Observation of the Reactivity of Toluquinone toward *n*-Butylamine in Terms of the Reactivity Index Calculated. In the methylamination of *p*-benzoquinone leading to the formation of 2,5-bis(methylamino)-*p*-benzoquinone, it was proposed by Cameron *et al.*[8] that the first step is the nucleophilic 1,4-addition of the amine to the quinone, thus giving monomethylamino-hydroquinone. Then, as a parameter of the reactivity of toluquinone toward the attack by *n*-butylamine, the reactivity index was calculated for toluquinone and its mono-butylamino derivatives by utilizing the ω-technique in a simple linear combination of

10) F. Fichter, *Ann.*, **361**, 400 (1908).
11) W. K. Anslow and H. Raistrick, *J. Chem. Soc.*, **1939**, 1447.

TABLE 1. REACTIVITY INDEX FOR THE NUCLEOPHILIC SUBSTITUTION

Compound	Superdelocalizability $S_r^{(N)}$ (Formal charge Q_r) Position			
	1	3	4	6
Toluquinone	0.9724 (+0.087)	0.9614 (+0.064)	1.0202 (+0.070)	0.8825 (+0.043)
3-Alkylaminotoluquinone	0.9796 (+0.078)	0.9924 (+0.084)	0.8627 (+0.018)	1.0107 (+0.044)
6-Alkylaminotoluquinone	0.8848 (+0.041)	1.1817 (+0.067)	1.0910 (+0.059)	0.9790 (+0.064)
4-Alkylaminotoluquinone	1.1125 (+0.090)	0.8017 (+0.013)	1.0551 (+0.090)	0.8772 (+0.033)

the atomic orbital theory, using the Streitwieser heteroatom parameter.[12] (The calculations were performed on the HITAC 5020 Computer, in the Computer Center, The University of Tokyo; see Table 1.)

Ring Butylamination. The preferential attack at the 3 or 4 position of toluquinone with *n*-butylamine, and the subsequent amine-attack at the para-position of the first substituted amino group on the quinoid ring, can be readily predicted from their reactivity index, presented in Table 1. (The ring carbon to which the methyl or alkylamino group is linked is not considered, because of its steric effect toward the amine-attack.)

Moreover, it is obviously shown that a greater contribution by 3-*n*-butylamino-toluquinone than by the 6-isomer to the formation of 3,6-bis(*n*-butylamino)-toluquinone can be considered. The participation of 6-*n*-butylamino-toluquinone, of course, can not always be obviated, since, if this amino-quinoid compound were an intermediate in the present reaction course, the reactivity index of this compound toward butylamination would be relatively large.

Side-chain Butylamination. In order to elucidate the reactivity of the substituted methyl group on the quinoid ring toward the methyl-butylamination, the reactivity indices of the three possible monobutylaminated toluquinone isomers were compared; the formal charge or superdelocalizability calculated for the three isomers (at 1 position) shows that the carbon atom of the quinoid ring to which the methyl group is linked is most positive, causing the hydrogens of the methyl group to be more positive and then to undergo the formation of quinone methide readily, followed by methyl-butylamination.

In comparison with those reactivty indices (see Table 1) calculated for the three mono-alkylaminated toluquinone isomers, a larger reactivity for the methyl-butylamination can be predicted for the 4-alkylamino-toluquinone; this is in agreement with the experimental result of the preferential methyl-butylamination of 4-*n*-butylamino-toluquinone, whereas 3-*n*-butylamino-toluquinone could not be methyl-butylaminated and was converted quantitatively into 3,6-bis(*n*-butylamino)-toluquinone.

12) A. Streitwieser, Jr., *J. Am. Chem. Soc.*, **82**, 4123 (1960), A. Streitwieser, Jr. and P. M. Nair, *Tetrahedron*, **1959** 149.