[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF UTAH]

The Polymerization of 4-*t*-Butyl-2-cyclohexylaminomethylphenol

BY W. J. BURKE, B. A. BARTON,[1] P. D. GARDNER AND J. D. LEWIS

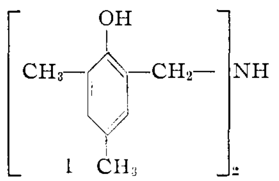
RECEIVED JANUARY 13, 1958

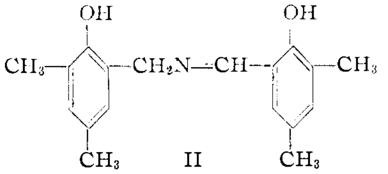
Polymerization of 4-*t*-butyl-2-cyclohexylaminomethylphenol occurred readily upon heating to yield a bright yellow solid polymer, cyclohexylamine, 4-*t*-butylphenol and a high melting crystalline solid tentatively identified as a cyclic tetramer of 4-*t*-butylphenol and formaldehyde. Physical and chemical studies on the yellow polymer indicated the presence of 2-hydroxy-5-*t*-butylbenzyl repeating units and approximately one anil end group per two polymer chains.

The instability of certain phenolic Mannich bases has created problems in the purification and use of these versatile intermediates. For example, Wheatley and Cheney[2] found that attempts to purify 2-benzyl-6-dimethylaminomethylphenol by distillation resulted mainly in the formation of a black residue. Likewise Snyder and Demuth[3] reported *p*-hydroxydibenzylamine to be so heat sensitive that even concentration of an ethanolic solution led to extensive polymerization, and Cromwell and Hoeksema[4] found it expedient to characterize 2-methylaminomethylphenol as the hydrochloride.

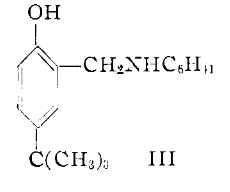
The study of Mannich bases from phenols, formaldehyde and primary amines in this Laboratory[5] has been concerned in part with providing a better understanding of the crosslinking of phenol–formaldehyde condensates with hexamethylenetetramine. In connection with this work it was found that 4-*t*-butyl-2-cyclohexylaminomethylphenol could be converted to a bright yellow solid polymer upon heating. The characterization of this product was of interest in order to obtain additional information concerning the structure of two-stage phenolic polymers and also that of the polymeric products from labile phenolic Mannich bases.

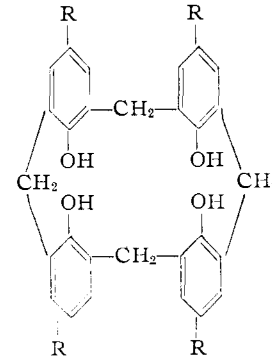
The reaction of hexamethylenetetramine with phenols has been considered in detail.[6] Although it was found[7] early that nitrogen-containing products could be obtained from such systems, it was not generally appreciated until recently that a major portion of the nitrogen in hexamethylenetetramine may be retained in a combined form in cured two-stage phenolics.[6c] In model studies Zinke and co-workers[8] showed that hexamethylenetetramine condensed with 2,4-dimethylphenol to form bis-(3,5-dimethyl-2-hydroxybenzyl)-amine (I), which upon heating yielded the corresponding anil II along with mesitol and 2,4,5,7-tetramethylxanthene.

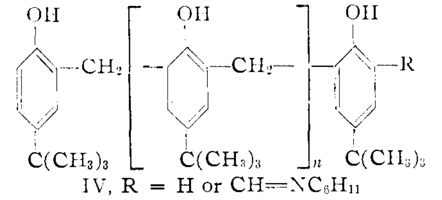

I


II

The 4-*t*-butyl-2-cyclohexylaminomethylphenol (III) used in this work was prepared[5a] by the direct condensation of 4-*t*-butylphenol with formaldehyde and cyclohexylamine. The polymerization was accomplished by heating the monomer III under nitrogen at 200°. Cyclohexylamine started to evolve and the reaction mixture became yellow when the bath temperature reached 165°. In addition to cyclohexylamine (88.5% yield) and the bright yellow polymer IV, 4-*t*-butylphenol (8.5% yield) and a small amount of a very slightly soluble, high melting white crystalline product were recovered. The last was characterized as the acetyl derivative and tentatively identified as the cyclic tetramer V, which was reported earlier to be obtained from 4-*t*-butylphenol and formaldehyde.[9] Physical and chemical studies on the yellow polymer were consistent with a mixture of closely related polymers differing only in end group, as


III


V, R = $C(CH_3)_3$


IV, R = H or $CH{=}NC_6H_{11}$

---

[1] University of Utah Research Committee Fellow, 1954–1956.

[2] W. B. Wheatley and L. C. Cheney, THIS JOURNAL, **74**, 2940 (1952).

[3] H. R. Snyder and J. R. Demuth, *ibid.*, **78**, 1981 (1956).

[4] N. H. Cromwell and H. Hoeksema, *ibid.*, **67**, 1658 (1945).

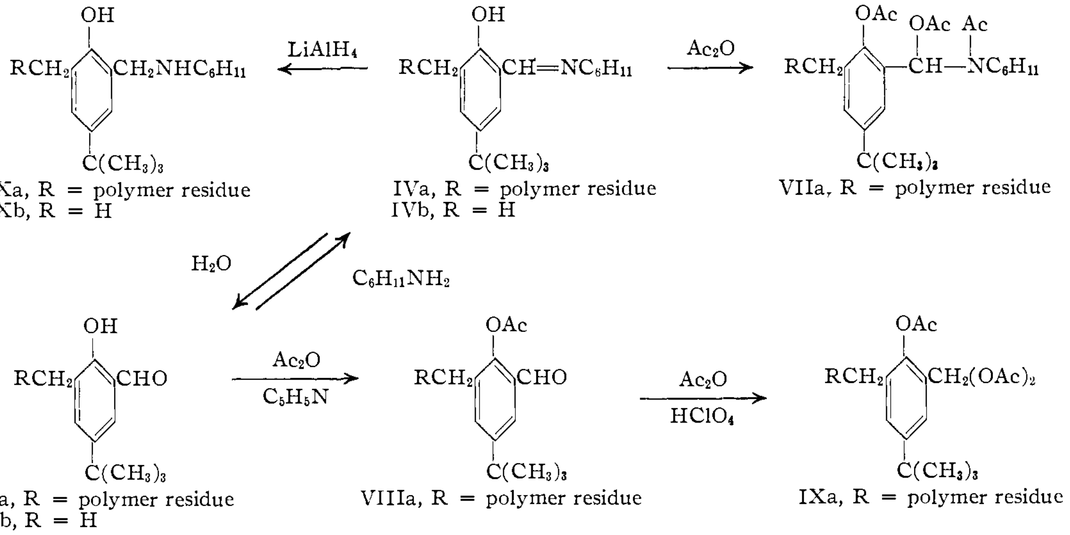
[5] (a) W. J. Burke, *ibid.*, **71**, 609 (1949); (b) W. J. Burke, R. P. Smith and C. Weatherbee, *ibid.*, **74**, 602 (1952); (c) W. J. Burke and C. W. Stephens, *ibid.*, **74**, 1518 (1952).

[6] (a) K. Hultzsch, "Chemie der Phenolharze," Springer-Verlag, Berlin, Ger., 1950; (b) A. Zinke, *J. Appl. Chem.* (*London*), **1**, 257 (1951); (c) R. W. Martin, "The Chemistry of Phenolic Resins," John Wiley and Sons, Inc., New York, N. Y., 1956.

[7] L. V. Redman, A. J. Weith and F. P. Brock, *Ind. Eng. Chem.*, **6**, 3 (1914).

[8] A. Zinke and St. Pucker, *Monatsh. Chem.*, **79**, 26 (1948); A. Zinke, G. Zigeuner and G. Weiss, *ibid.*, **80**, 148 (1949).

[9] A. Zinke, R. Kretz, E. Leggewie and H. Hossinger, *ibid.*, **83**, 1213 (1952).



shown in IV. Cryoscopic molecular weight determinations indicated an average value of about seven for *n* in this formula.

The bright yellow color of a dioxane solution of the polymer disappeared rapidly upon heating in the presence of aqueous hydrochloric acid. An essentially white polymer (VI) and cyclohexylamine were isolated from the reaction mixture. This behavior is characteristic of an anil type linkage. An infrared spectrum (Fig. 1) of the original yellow polymer showed a definite band at 6.10 μ, which is characteristic of an anil group. While the spectrum (Fig. 1) of the hydrolyzed polymer VI did not have this band, this product did absorb in the region of 6.03, an absorption characteristic of hydroxyaromatic aldehydes.

Since these bands were relatively close, 5-*t*-butyl-3-methylsalicylaldehyde (VIb) and the previously undescribed N-(5-*t*-butyl-2-hydroxy-3-methylbenzylidene)-cyclohexylamine (IVb) were prepared as model compounds for infrared studies. The anil IVb showed an absorption maximum at 6.11 μ and the aldehyde VIb absorbed strongly at 6.03 μ (Fig. 1). Both the models and the original and hydrolyzed polymers showed strong bands characteristic of a phenolic hydroxyl group in the region of 2.8 to 3.1 μ. Treatment of the white hydrolyzed polymer with cyclohexylamine yielded a yellow polymer. The infrared spectrum of this product and that of the original yellow polymer were essentially identical. These studies, accordingly, were consistent with the presence of an anil end group in the yellow polymer IVa[10] and of an aldehyde end group in the hydrolyzed polymer VIa.

Condensation of the hydrolyzed polymer VI with aniline gave a bright orange product which showed a definite absorption band at 6.17 μ, typical of conjugated anils. Reaction of aniline with 5-*t*-butyl-3-methylsalicylaldehyde provided a convenient synthesis for the previously unknown N-(5-*t*-butyl-2-hydroxy-3-methylbenzylidene)-aniline, which served as a model in spectral studies. This product showed a strong band at 6.16 μ.

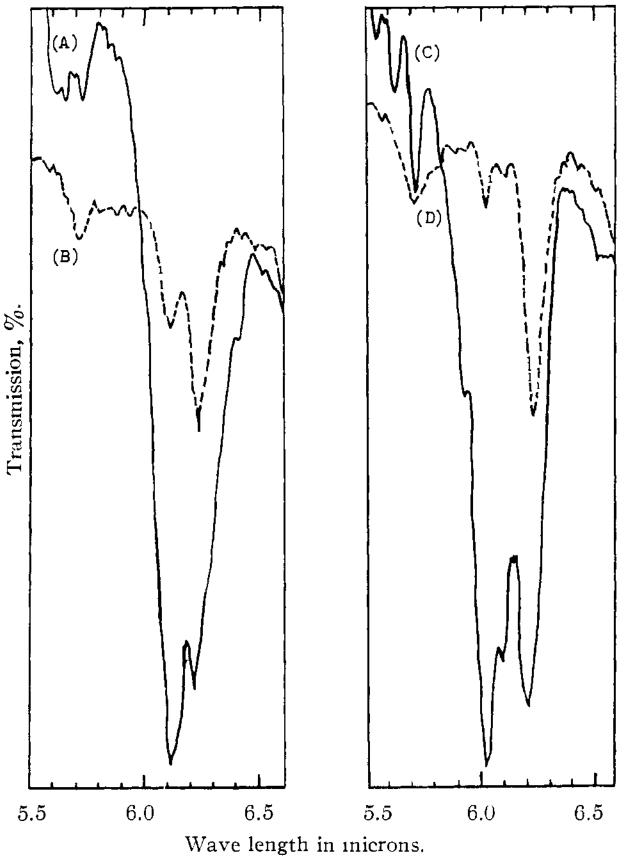


Fig. 1.—Infrared spectra: (A) N-(5-*t*-butyl-2-hydroxy-3-methylbenzylidene)-cyclohexylamine (IVb); (B) polymer IV from 4-*t*-butyl-2-cyclohexylaminomethylphenol; (C) 5-*t*-butyl-3-methylsalicylaldehyde (VIb); (D) hydrolyzed polymer (VI). All samples were observed as solutions in cyclohexane.

Molecular weight determinations on the original polymer IV from 4-*t*-butyl-2-cyclohexylaminomethylphenol, the hydrolyzed polymer VI and the polymers formed from the condensation of the

---

(10) Throughout the paper IV is used to designate the polymer mixture and IVa to indicate polymer chains having an anil end group. The derivatives obtained from IV are treated in the same manner. Thus VI indicates the complete hydrolysis mixture, while VIa is used to designate the polymer chains from IVa, *i.e.*, those having aldehyde end groups.

hydrolyzed polymer with cyclohexylamine and with aniline were all in the same range (1490 to 1530). This indicated that no significant changes took place in the polymer residue during the hydrolysis or condensation reactions. All of these polymers softened in the range of 165–185° and were soluble in most of the common organic solvents.

In the hydrolysis of the polymer IV from 4-*t*-butyl-2-cyclohexylaminomethylphenol the amount of cyclohexylamine isolated was equivalent to about one mole per 18 repeating polymer units when care was taken to make the extraction quantitative. With an average molecular weight of about 1500 this is equivalent to about one anil type end group per two polymer chains. Elemental nitrogen analyses on the polymer were rather inconsistent and less reproducible than the amount of cyclohexylamine directly recoverable from the hydrolysis reaction. Considering the polymeric nature of the material and a probable nitrogen content of the order of 0.5% or less, this is perhaps understandable.

The original yellow polymer IV reacted readily at room temperature with acetic anhydride in pyridine. The infrared spectrum of the resulting white polymer (VII) had the expected ester carbonyl band at 5.78 μ and did not show bands in the region of 2.8 to 3.1 or at 6.10 μ, characteristic of phenolic hydroxyl and anil groups, respectively. Since acetic anhydride has been shown[11] to add across the double bond of an anil with the formation of O-acetyl and N-acetyl linkages, the absence of an anil bond in the acetylated polymer would be anticipated. Further indication of this type of reaction was obtained from the determination of both O-acetyl and total acetyl. The analytical results indicated the presence of one N-acetyl group per two polymer chains.

The hydrolyzed polymer VI also was subjected to acetylation studies. Reaction with acetic anhydride in pyridine yielded a product (VIII), the analysis of which corresponded very closely to one acetyl group per 2-hydroxy-5-*t*-butylbenzyl repeating unit. However, further acetylation with acetic anhydride in acetic acid solution occurred in the presence of perchloric acid as catalyst. In this instance the acetyl analysis agreed very well with that calculated for a product (IX) having a salicylidene triacetate end group for each eighteen 2-acetoxy-5-*t*-butylbenzyl repeating units. This would be equivalent to about one end group of this type for each two polymer chains.

The hydrolyzed polymer VI was treated with lithium aluminum hydride. The infrared spectrum of the resulting product did not have the characteristic hydroxyaromatic aldehyde band at 6.03 μ. The reduced product yielded a light tan polymer of higher molecular weight when heated at 150° for 36 hours in bis-(2-ethoxyethyl) ether as solvent and *p*-toluenesulfonic acid as catalyst. This behavior can be accounted for on the basis of a hydroxymethyl end group in the reduced polymer.

The original yellow polymer IV also was treated with lithium aluminum hydride. The absence of the band at 6.10 μ in the infrared spectrum of the resulting white polymer X indicated the reduction of the anil end groups. Caldwell and Thompson[12] found that the dialkylaminomethyl group of related monomeric phenolic Mannich bases was replaced with methyl by high temperature catalytic hydrogenation. In order to determine whether this type of reaction was important under the mild conditions used to reduce the polymer IV, the model compound N-(5-*t*-butyl-2-hydroxy-3-methylbenzylidene)-cyclohexylamine (IVb) was treated with lithium aluminum hydride. The isolation of 4-*t*-butyl-2-cyclohexylaminomethyl-6-methylphenol (Xb) in 97% yield showed that little if any replacement of an anil radical with a methyl group occurred. Since the polymer IV contained a much larger number of phenolic hydroxy groups, which liberate hydrogen upon reaction with lithium aluminum hydride, than the model compound IVb, the reduction of the latter (IVb) with lithium aluminum hydride also was performed in the presence of 2,6-bis-(2-hydroxy-5-methylbenzyl)-4-methylphenol. The presence of the added phenolic model compound did not appear to alter the reduction, as again 4-*t*-butyl-2-cyclohexylaminomethyl-6-methylphenol was obtained in high yield. Direct condensation of 4-*t*-butyl-2-methylphenol with formaldehyde and cyclohexylamine provided an independent synthesis of this previously undescribed Mannich base (Xb).

The reduced polymer X was acetylated readily with acetic anhydride in pyridine. Acetyl determinations indicated the presence of about one N-acetyl group for each two polymer chains. The characteristic odor of cyclohexylamine was observed when the reduced polymer was heated at 200°. The resulting polymer had a higher molecular weight and showed a weak band at 6.10 μ, indicating the presence of an anil end group.

Methylenequinones have been proposed[13] as intermediates in reactions involving the elimination of ammonia or an amine from a phenolic Mannich base. A mechanism utilizing such an intermediate in the polymerization of 4-*t*-butyl-2-cyclohexylaminomethylphenol offers a plausible route to the products formed. The attack of a 5-*t*-butyl-2-hydroxybenzyl carbonium ion (XI) on the free *o*-position of the monomer III would yield a dimeric product (XII), which upon elimination of cyclohexylamine would yield a substituted benzylcarbonium ion. Repetition of this process would result in chain growth. Introduction of a terminal anil group ($R = C_6H_{11}N{=}CH{-}$ in IV) by the dehydrogenation of a cyclohexylaminomethyl substituent would provide a means of stopping the polymerization. Reaction of a substituted benzylcarbonium ion (XI) with 4-*t*-butylphenol, shown to be present in the reaction mixture, could also stop the chain growth with the formation of an end group where R = H in IV.

An alternative route involving the condensation of two molecules of the monomer III to form N,N-bis-(2-hydroxy-5-*t*-butylbenzyl)-cyclohexylamine (XIII) might also be considered in view of

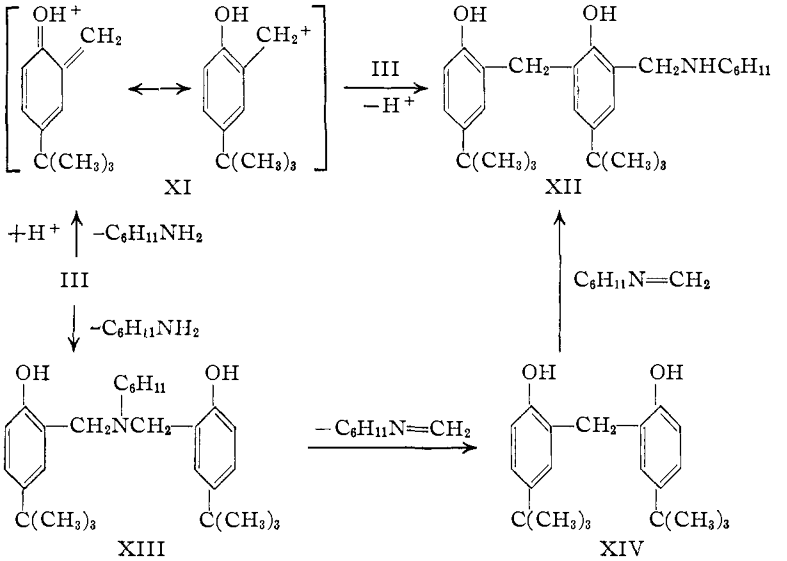
---

[11] H. R. Snyder, R. H. Levin and P. F. Wiley, This Journal, **60**, 2025 (1938).

[12] W. T. Caldwell and T. R. Thompson, *ibid.*, **61**, 2354 (1939).

[13] H. R. Snyder and J. H. Brewster, *ibid.*, **70**, 4230 (1948) ref. 6a, p. 99.

the results of Zinke[8] and Hultzsch.[14] Elimination of N-methylenecyclohexylamine from the tertiary base XIII would yield bis-(2-hydroxy-5-*t*-butylphenyl)-methane (XIV). Condensation of the latter with N-methylenecyclohexylamine would serve as a route to the dimeric amine XII, which is also proposed as an intermediate in the above mechanism. It is of course possible that the elimination of cyclohexylamine may take place by both intramolecular and intermolecular routes.



Experimental

Polymerization of 4-*t*-Butyl-2-cyclohexylaminomethylphenol (III). Procedure A.—4-*t*-Butyl-2-cyclohexylaminomethylphenol (190.0 g.) was heated under nitrogen in a flask connected to a distilling condenser and traps cooled in ice and in methanol–Dry Ice. Amine elimination was initially observed when the bath temperature reached 165° The bath was heated to 200°. After three hours the pressure was reduced slowly to 0.3 mm. and maintained there as long as amine distilled (45 minutes). The product in the reaction flask was digested with 600 ml. of acetone and the white insoluble solid (1.28 g., fraction A) was removed by filtration. Fraction A melted[15] above 300°. The residue obtained by removal of the acetone was taken up in 500 ml. of absolute ethanol and the small amount (0.9 g., fraction B) of insoluble material removed by filtration was not investigated further. Water was added to the alcohol solution of the polymer until a 70–30 alcohol water mixture resulted. The yellow product (fraction C) which separated was removed by filtration, washed thoroughly with water and air-dried. The polymer (110.2 g.) melted in the range of 165–170° and had an inherent viscosity of 0.048.[16] The infrared spectrum showed a peak at 6.10 μ.

Anal. Fraction A, Calcd. for $(C_{11}H_{14}O)_4$: C, 81.44; H, 8.70. Found: C, 81.17; H, 8.84. Fraction C, Calcd. for $H(C_{11}H_{14}O)_8(C_{10}H_{12.5}O)(CH=NC_6H_{11})_{0.5}$: C, 81.1; H, 8.8; mol. wt., 1503. Found: C, 81.1; H, 9.0; mol. wt., 1500 (cryoscopic in benzene).

The colorless liquid (60.1 g.) which collected in the receiver was distilled, b.p. 129° (654 mm.). Reaction of a portion of this liquid with *p*-toluenesulfonyl chloride resulted in a product which melted at 88–89° and did not depress the m.p. of N-cyclohexyl-*p*-toluenesulfonamide (lit.[17] m.p. 86°). The cyclohexylamine recovered corresponded to 0.825 mole of amine per mole of monomer used. Recrystallization of the residue left after distillation of the cyclohexylamine, from petroleum ether (b.p. 30–60°), gave 8.2 g. of material which melted at 99–100° and was undepressed on admixture of *p*-*t*-butylphenol. The benzoate melted at 81.5–82° (lit.[18] m.p. 83°). The material (3.92 g.) soluble in 70% alcohol solution (fraction D) was not characterized.

Procedure B.—The polymerization was carried out as in procedure A above except that a trap containing 130 ml. of 6 *N* sulfuric acid followed the receiving flask cooled in ice. The yellow polymer (110.8 g.) melted in the range of 178–185° and had an inherent viscosity of 0.051. The infrared spectrum was essentially identical to that of the polymer from procedure A.

Anal. Calcd. for $H(C_{11}H_{14}O)_8(C_{10}H_{12.5}O)(CH=NC_6H_{11})_{0.5}$: C, 81.1; H, 8.8; mol. wt., 1503. Found: C, 81.5; H, 8.9; mol. wt., 1530 (cryoscopic in benzene).

As in procedure A there was obtained from the reaction flask small amounts of acetone-insoluble (2.7 g.) and absolute alcohol-insoluble (1.1 g.) solids. The cyclohexylamine recovered by distillation of the material in the receiving flask weighed 60.3 g. and an additional 3.07 g. was recovered from the acid trap. This corresponded to 0.885 mole of cyclohexylamine per mole of monomer. There was 9.3 g. of *p*-*t*-butylphenol recovered (8.5%). The cyclohexylamine and *p*-*t*-butylphenol were identified as described in procedure A.

Acetylation of the Cyclic Tetramer V.—To 0.5 g. of fraction A, procedure A, suspended in 10 ml. of dry pyridine was added 2 ml. of acetic anhydride. After ten days at 25° the suspension was poured into 250 ml. of ice and water, the solid removed by filtration, washed free of pyridine, and air-dried. The product did not melt below 310°.

Anal. Calcd. for $(C_{11}H_{13}O\cdot CH_3CO)_4$: CH_3CO, 21.07. Found: CH_3CO, 21.00, 21.18.

Hydrolysis of the Polymer from 4-*t*-Butyl-2-cyclohexylaminomethylphenol (IV).—Concentrated hydrochloric acid (3 ml. in 25 ml. of absolute ethanol) was added to a cold solution of 15.5 g. of the polymer from 4-*t*-butyl-2-cyclohexylaminomethylphenol (procedure A) in 150 ml. of dioxane. The resulting mixture was heated for two hours on a steam-bath, cooled and added to water agitated in a Waring Blendor. The almost white polymer was removed by filtration, washed with water and dried. The filtrate was extracted three times with 200-ml. portions of ether, neutralized with sodium bicarbonate and then extracted with 200-ml. portions of ether four times. After drying over anhydrous sodium sulfate and then over calcium sulfate the ether solution was saturated with dry hydrogen chloride. The resulting product (0.53 g.) was removed by filtration. Reaction of a portion of this material with acetic anhydride in pyridine gave a product which melted at 104° and did not depress the m.p. of N-cyclohexylacetamide (lit.[19] m.p. 104°). The infrared spectrum of the polymer showed a medium peak at 6.03 μ. The inherent viscosity was 0.044.

Anal. Calcd. for $H(C_{11}H_{14}O)_8(C_{10}H_{12.5}O)(CHO)_{0.5}$: C, 80.9; H, 8.7; mol. wt., 1463. Found: C, 80.8; H, 9.1; mol. wt., 1490 (cryoscopic in benzene).

The hydrolysis was repeated in order to obtain a quantitative estimate of the amount of cyclohexylamine liberated. The almost white polymer was removed by filtration, washed with water and dried. The filtrate was acidified with 50 ml. of dilute hydrochloric acid and the distillation was continued until most of the *p*-dioxane was removed. The solution was then neutralized with sodium hydroxide and the cyclohexylamine distilled into 1.2 *N* hydrochloric acid. Evaporation of the acid solution resulted in the

---

(14) Reference 6a, p. 94.

(15) Zinke (ref. 9) reported that the cyclic tetramer of *p*-*t*-butylphenol and formaldehyde (V) gradually decomposed above 300°.

(16) All inherent viscosities reported in this paper were measured in N,N-dimethylformamide at 25° at a concentration of 0.5 g. of polymer per 100 ml. of solution.

(17) A. Skita and H. Rolfes, *Ber.*, **53**, 1254 (1920).

(18) R. L. Shriner, R. C. Fuson and D. Y. Curtin, "The Systematic Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1956, p. 326.

(19) Ref. 18, p. 288.

recovery of 0.70 g. of cyclohexylamine hydrochloride. This is equivalent to about one molecule of cyclohexylamine for every two polymer chains.

Anal. Calcd. for $H(C_{11}H_{14}O)_8(C_{10}H_{12.5}O)(CHO)_{0.5}$: C, 80.9; H, 8.7; mol. wt., 1463. Found: C, 80.4; H, 8.8; mol. wt., 1500 (cryoscopic in benzene).

Reaction of Hydrolyzed Polymer VI with Cyclohexylamine.—A solution of 1.5 g. of the hydrolyzed polymer in 15 ml. of cyclohexylamine was heated for 45 minutes on a steam-bath. The reaction mixture was dissolved in 200 ml. of ether. The solution was washed successively with saturated aqueous citric acid solution, water, aqueous sodium bicarbonate and water and then dried over sodium sulfate. The residue obtained by removal of ether was dissolved in absolute alcohol. The alcohol solution was added to water agitated in a Waring Blendor. The yellow precipitate was washed thoroughly with water. The infrared spectrum showed a medium peak at 6.10 μ and was essentially identical with that for the polymer from 4-*t*-butyl-2-cyclohexylaminomethylphenol.

Anal. Calcd. for $H(C_{11}H_{14}O)_8(C_{10}H_{12.5}O)(CH{=}NC_6H_{11})_{0.5}$: C, 81.1; H, 8.8; mol. wt., 1503. Found: C, 81.8; H, 9.5; mol. wt., 1500 (cryoscopic in benzene).

Reaction of Hydrolyzed Polymer VI with Aniline.—A solution of 1.0 g. of the hydrolyzed polymer from 4-*t*-butyl-2-cyclohexylaminomethylphenol in 15 ml. of aniline was heated on a steam-bath for 45 minutes. The resulting orange polymer was isolated by a procedure similar to that described above. The product showed a medium absorption band at 6.16 μ.

Anal. Calcd. for $H(C_{11}H_{14}O)_8(C_{10}H_{12.5}O)(CH{=}NC_6H_5)_{0.5}$: C, 81.3; H, 8.6; mol. wt., 1500. Found: C, 80.6; H, 8.9; mol. wt. 1550 (cryoscopic in benzene).

Acetylation of the Polymer IV from 4-*t*-Butyl-2-cyclohexylaminomethylphenol.—To 5.0 g. of polymer from 4-*t*-butyl-2-cyclohexylaminomethylphenol (procedure B) in 50 ml. of dry pyridine was added 15 ml. of acetic anhydride. After 15 hours at room temperature the light yellow solution was added with stirring to 1500 ml. of ice and water and the nearly white material removed by filtration, washed free of pyridine and air-dried. The method of Kunz[20] was used for O-acetyl analysis and total acetyl analysis was determined by the method of Freudenberg as modified by Matchett and Levine.[21]

Anal. Calcd. for $H(C_{11}H_{13}O\cdot COCH_3)_8(C_{10}H_{11.5}OCOCH_3)(CH\cdot OCOCH_3\cdot C_6H_{11}NCOCH_3)_{0.5}$: O-acetyl, 21.2; total acetyl, 22.3. Found: O-acetyl, 21.0, 21.2; total acetyl, 22.8, 22.9, 22.8.

Acetylation of the Hydrolyzed Polymer VI.—To 5.0 g. of hydrolyzed polymer from 4-*t*-butyl-2-cyclohexylaminomethylphenol in 50 ml. of dry pyridine was added 15 ml. of acetic anhydride. After 18 hours at room temperature the light red solution was added with stirring to 1500 ml. of ice and water. The pink polymer was removed by filtration, washed with water and air-dried.

Anal. Calcd. for $H(C_{11}H_{13}O\cdot COCH_3)_8(C_{10}H_{11.5}O\cdot COCH_3)(CHO)_{0.5}$: acetyl, 21.0. Found: O-acetyl,[20] 20.8, 20.9; total acetyl,[21] 20.9.

Acetylation of the Acetate of the Hydrolyzed Polymer VIII under Acid Conditions.—To 1.70 g. of the acetate of the hydrolyzed polymer, prepared as described above, in 8 ml. of glacial acetic acid, was added 10 ml. of acetic anhydride. Four drops of 72% perchloric acid[22] were added with shaking and the resulting mixture kept at room temperature for five days. The solution was added with stirring to one liter of a mixture of ice and water. The tan colored solid product which precipitated was removed by filtration, washed thoroughly with water and air-dried.

Anal. Calcd. for $H(C_{11}H_{13}O\cdot COCH_3)_8(C_{10}H_{11.5}O\cdot COCH_3)(CH\cdot(OCOCH_3)_2)_{0.5}$: CH_3CO, 22.7. Found: CH_3CO,[20] 22.6, 22.4, 22.6.

Reduction of Hydrolyzed Polymer VI with Lithium Aluminum Hydride.—A solution of 7 g. of the hydrolyzed polymer from 4-*t*-butyl-2-cyclohexylaminomethylphenol in 100 ml. of purified tetrahydrofuran was added dropwise with stirring to 1.0 g. of lithium aluminum hydride dissolved in 100 ml. of dry ether. After the reaction mixture was stirred for two hours and kept overnight at room temperature, the excess hydride was destroyed with water. The reaction mixture was poured into 600 ml. of 10% hydrochloric acid at 2°. The aqueous phase was adjusted to *p*H 6 by addition of sodium bicarbonate. The ether layer was separated, washed with water, and dried over anhydrous sodium sulfate. The residue obtained by removal of ether was dissolved in absolute alcohol. The white polymer obtained by pouring the alcohol solution into water agitated in a Waring Blendor was thoroughly washed with water. The product had an inherent viscosity of 0.045.

Anal. Calcd. for $H(C_{11}H_{14}O)_8(C_{10}H_{12.5}O)(CH_2OH)_{0.5}$: C, 80.9; H, 8.7; mol. wt., 1464. Found: C, 81.1; H, 8.9; mol. wt., 1490 (cryoscopic in benzene).

Thermal Treatment of the Reduced Hydrolyzed Polymer.—The above reduced hydrolyzed polymer (4.0 g.), 0.1 g. of *p*-toluenesulfonic acid and 6 ml. of bis-(2-ethoxyethyl) ether were heated in a sealed tube at 150° for 36 hours. The solution was added dropwise to 700 ml. of a mixture of ice and water agitated in a Waring Blendor. The precipitate was removed by filtration and washed thoroughly with water and dried. The inherent viscosity was 0.070.

Anal. Calcd. for $H(C_{11}H_{14}O)_{11}\cdot C_{10}H_{13}O$: C, 81.4; H, 8.7; mol. wt., 1947. Found: C, 80.2; H, 8.7; mol. wt., 1960 (cryoscopic in benzene).

Reduction of the Polymer IV from 4-*t*-Butyl-2-cyclohexylaminomethylphenol.—A solution of 7.0 g. of the polymer from 4-*t*-butyl-2-cyclohexylaminomethylphenol (procedure A) in 100 ml. of purified tetrahydrofuran was added with stirring to 1.0 g. of lithium aluminum hydride dissolved in 100 ml. of dry ether. After the reaction mixture was stirred for two hours and kept overnight at room temperature, the excess hydride was destroyed with water. The reaction mixture was poured into 300 ml. of 15% hydrochloric acid at 2°. The aqueous phase was adjusted to *p*H 6 by the addition of sodium bicarbonate. The ether layer was separated, washed with water and dried over sodium sulfate. The residue resulting from the removal of the ether was dissolved in absolute ethanol. The white polymer obtained by pouring the alcohol solution into water agitated in a Waring Blendor was thoroughly washed with water and dried. The infrared spectrum did not have an absorption maximum at 6.10 μ. The inherent viscosity was 0.049.

Anal. Calcd. for $H(C_{11}H_{14}O)_8(C_{10}H_{12.5}O)(CH_2NHC_6H_{11})_{0.5}$: C, 81.1; H, 8.9; mol. wt., 1504. Found: C, 80.3; H, 8.9; mol. wt., 1510 (cryoscopic in benzene).

Acetylation of the Reduced Polymer X from 4-*t*-Butyl-2-cyclohexylaminomethylphenol.—To 5.0 g. of the polymer in 50 ml. of dry pyridine was added 15 ml. of acetic anhydride. After 18 hours at room temperature the solution was added with stirring to 1500 ml. of ice and water. The light yellow polymer was removed by filtration, washed free of pyridine and air-dried.

Anal. Calcd. for $H(C_{11}H_{13}O\cdot COCH_3)_8(C_{10}H_{11.5}O\cdot COCH_3)(CH_2NC_6H_{11}\cdot COCH_3)_{0.5}$: O-acetyl, 20.4; total acetyl, 21.5. Found: O-acetyl, 20.2; total acetyl, 21.4.

Thermal Treatment of the Reduced Polymer X from 4-*t*-Butyl-2-cyclohexylaminomethylphenol.—The reduced polymer (1.25 g.) and 1.5 g. of methoxypolyethylene glycol (Carbowax 750) were dissolved in 10 ml. of ether and the ether slowly removed. The mixture was heated under nitrogen for three hours at atmospheric pressure and for 15 minutes at 0.3 mm. A solution of the mixture in 10 ml. of bis-(2-ethoxyethyl) ether was added to 750 ml. of ice and water agitated in a Waring Blendor. The light yellow product was removed by filtration, washed with water and dried. The polymer melted in the range of 195–199° and had an inherent viscosity of 0.080. The molecular weight was 2180 (cryoscopic in benzene). The infrared spectrum showed a weak band at 6.10 μ.

Preparation of 4-*t*-Butyl-2-cyclohexylaminomethyl-6-methylphenol (Xb).—To 60 ml. of isobutyl alcohol containing 15.0 ml. of 37% aqueous formaldehyde (0.2 mole) was added, with cooling, 21 g. of cyclohexylamine (0.212 mole). 4-*t*-Butyl-2-methylphenol (30.0 g., 0.2 mole) in 90 ml. of isobutyl alcohol was added and the solution heated at reflux for 7 hours. After removal of the solvents under reduced pressure the colorless oil was dissolved in 100 ml. of acetone and the solution saturated with dry hydrogen

---

[20] A. Kunz and C. S. Hudson, THIS JOURNAL, **48**, 1982 (1926).

[21] J. R. Matchett and J. Levine, *Ind. Eng. Chem., Anal. Ed.*, **13**, 98 (1941).

[22] H. Burton and P. F. G. Praill, *J. Chem. Soc.*, 522 (1951).

chloride. The white crystalline solid was removed by filtration, washed with cold 70% acetone and dried, 53.2 g. (86% yield), m.p. 230°.

Anal. Calcd. for $C_{18}H_{30}ClNO$: Cl, 11.37. Found: Cl, 11.47, 11.30.

The free base was prepared by dissolving 42.0 g. of the hydrochloride in methanol and adding sodium bicarbonate. The white crystals which separated were recrystallized three times with 80% methanol and once from 80% ethanol, m.p. 69–70°.

Anal. Calcd. for $C_{18}H_{29}NO$: C, 78.49; H, 10.61. Found: C, 77.71; H, 10.63.

Reduction of N-(5-*t*-Butyl-2-hydroxy-3-methylbenzylidene)-cyclohexylamine (IVb).—Three grams of N-(5-*t*-butyl-2-hydroxy-3-methylbenzylidene)-cyclohexylamine (0.011 mole) in 75 ml. of dry ether was added dropwise with stirring to 0.41 g. of lithium aluminum hydride (0.044 equiv.) dissolved in 100 ml. of dry ether. After the reaction mixture was stirred for three hours and kept overnight at room temperature, the excess hydride was destroyed with water. The reaction mixture was poured into 15% hydrochloric acid at 2°. After adjusting the acidity of the aqueous layer to *p*H 6 with sodium bicarbonate, the ether layer was separated, washed with water and dried over sodium sulfate. The oil left after removing the ether was dissolved in 100 ml. of acetone. Addition of dry hydrogen chloride and cooling resulted in the precipitation of a hydrochloride (3.31 g., 97.4%).

Anal. Calcd. for $C_{18}H_{30}ClNO$: Cl, 11.37. Found: Cl, 11.33, 11.28.

After two recrystallizations from dilute ethanol the free base melted at 68.5–69° and did not depress the m.p. of 4-*t*-butyl-2-cyclohexylaminomethyl-6-methylphenol, prepared as described above.

Reduction of N-(5-*t*-Butyl-2-hydroxy-3-methylbenzylidene)-cyclohexylamine (IVb) in the Presence of *p*-Cresol Trimer.—N-(5-*t*-Butyl-2-hydroxy-3-methylbenzylidene)-cyclohexylamine (2.50 g.) and 10.5 g. of 2,6-bis-(2-hydroxy-5-methylbenzyl)-4-methylphenol in 650 ml. of absolute ether was added with stirring to 2.50 g. of lithium aluminum hydride in 500 ml. of dry ether. After stirring six hours the reaction mixture was allowed to stand at room temperature overnight. The excess hydride was destroyed by the cautious addition of water and the resulting slurry was poured into 15% hydrochloric acid at 2°. After adjusting the *p*H to 6 with sodium bicarbonate the ether layer was removed, washed with water and dried over anhydrous sodium sulfate and then over anhydrous calcium sulfate. Dry hydrogen chloride was added and the solid removed by filtration, washed with ether and air-dried, 2.50 g., 88.5%.

Anal. Calcd. for $C_{18}H_{30}ClNO$: Cl, 11.37. Found: Cl, 11.32, 11.42.

The free base melted at 69–70°. The m.p. was not depressed by admixture with 4-*t*-butyl-2-cyclohexylaminomethyl-6-methylphenol.

Preparation of N-(5-*t*-Butyl-2-hydroxy-3-methylbenzylidene)-cyclohexylamine (IVb).—To 5.8 g. of 5-*t*-butyl-3-methylsalicylaldehyde (0.03 mole) in 35 ml. of dry benzene was added 3.0 g. of cyclohexylamine (0.03 mole) in 20 ml. of dry benzene. The solution was kept at room temperature for 15 hours. After removal of the benzene under reduced pressure the product was distilled. A yellow liquid (8.2 g.) boiling at 151–153° at 0.3 mm. was recovered. The infrared spectrum showed a prominent band at 6.10 μ.

Anal. Calcd. for $C_{18}H_{27}NO$: C, 79.07; H, 9.96. Found: C, 78.95; H, 9.88.

Preparation of N-(5-*t*-Butyl-2-hydroxy-3-methylbenzylidene)-aniline.—To 5.8 g. of 5-*t*-butyl-3-methylsalicylaldehyde (0.03 mole) in 40 ml. of dry benzene was added 3.1 g. of aniline (0.033 mole) in 40 ml. of dry benzene. The solution was heated at reflux for 30 minutes. After removal of the benzene under reduced pressure the bright orange oil was dissolved in 150 ml. of ether and the solution extracted three times with 75 ml. of saturated citric acid solution to remove the excess amine. After drying over sodium sulfate the ether was removed under reduced pressure and the material distilled at 140–143° at 0.45 mm. The resulting dark orange crystals (8.0 g.) melted at 60–61°. The product absorbed strongly at 6.17 μ.

Anal. Calcd. for $C_{18}H_{21}NO$: C, 80.86; H, 7.92. Found: C, 80.55; H, 7.82.

Infrared Absorption Spectra.—A Perkin-Elmer model 21 spectrophotometer equipped with a sodium chloride prism was used.

Acknowledgment.—This work was sponsored by the Office of Ordnance Research, U. S. Army.

SALT LAKE CITY, UTAH

[CONTRIBUTION FROM THE MOORE LABORATORY OF CHEMISTRY, AMHERST COLLEGE]

The Rearrangement of Isoquinoline-N-Oxides. II. Observations with N-Hydroxyisocarbostyrils and Other Substituted Derivatives[1]

BY MICHAEL M. ROBISON AND BONNIE L. ROBISON

RECEIVED JANUARY 15, 1958

Rearrangement of 3-chloroisoquinoline-N-oxide with acetic anhydride produces mainly 3-chloro-4-acetoxyisoquinoline and very little 3-chloroisocarbostyril. Other oxides studied included derivatives of N-hydroxyisocarbostyril, which was synthesized by cyclization of *o*-carboxyphenylacetaldoxime. N-Tosyloxyisocarbostyril rearranges readily under various conditions at about 90° to yield mainly 4-substituted isocarbostyrils, though in one reaction in an aqueous medium substitution at the 3-position also was observed. The products and conditions of these transformations, together with observations on other substituted N-oxides, are considered in connection with possible mechanisms for the rearrangements.

Treatment of isoquinoline-N-oxide with refluxing acetic anhydride and hydrolysis of the resulting acetates produces isocarbostyril, the expected rearrangement product, in approximately 60% yield, along with 4-hydroxyisoquinoline in yields averaging 9%.[2] Similar results have been observed with 3-methylisoquinoline-N-oxide, and no products of substitution at the 3-position have been isolated from either reaction.[2] On treatment of isoquinoline-N-oxide with *p*-toluenesulfonyl chloride, however, substitution at the 4-position is predominant, only relatively small quantities of isocarbostyril being formed.[3] Several possible mechanisms have been considered for the rearrangement to the 4-position[2,3] but little evidence has been offered for any of them. In an effort to learn more about the detailed course of the transformation, the rearrangements of various substituted isoquinoline-N-oxides were investigated to determine the effects of substituent groups on the course of the reaction. Although the investigations have not provided any

---

[1] This investigation was supported in part by a research grant, number C-2574, from the National Cancer Institute of the National Institutes of Health, Public Health Service.

[2] M. M. Robison and B. L. Robison, *J. Org. Chem.*, **21**, 1337 (1956).

[3] E. Ochiai and M. Ikehara, *Pharm. Bull. Japan*, **3**, 454 (1955).