

which was used without further purification in the synthesis of VI.

1,4-Bis-(10-methyl-10,9-borazaro-9-phenanthryl)butane (Vb).—The residue from the final ether extraction in the preparation of Va crystallized from acetone, giving the bisborazarophenanthrylbutane (Vb) as colorless prisms (2.2 g.), m.p. 198–199°.

Anal. Calcd. for C₃₀H₃₀B₂N₂: C, 81.1; H, 6.8; N, 6.4. Found: C, 81.1; H, 6.7; N, 6.3.

9-(4-Morpholino-1-butyl)-10-methyl-10,9-borazarophenanthrene (Vc).—Crude Va (1 g.) was heated with morpholine (2 g.) in ethanol (25 ml.) under reflux for 12 hr. The solution was then evaporated *in vacuo*, water, ether, and sodium hydroxide solution (10 ml. of 20%) were added, and the ethereal layer was washed, dried, (MgSO₄), and evaporated. The residue crystallized from ethanol in colorless needles (0.75 g., 72%) of the morpholino-butylborazarophenanthrene (Vc), m.p. 111–112°.

Anal. Calcd. for C₂₁H₂₇BN₂O: C, 75.5; H, 8.1; N, 8.4. Found: C, 75.3; H, 8.0; N, 8.3.

1,2,3,4-Tetrahydro-14,13-borazarotriphenylene (VI).—A solution of crude Va (67.0 g., 0.2 mole) in dry ether (250 ml.) was added dropwise to magnesium turnings (5 g., 0.21 g.-atom) over 1 hr. and the mixture then boiled overnight under reflux. Carbon dioxide was then bubbled into the solution at such a rate that it continued to boil gently. When the reaction had subsided, the passage of carbon dioxide was continued for a further 15 min. The product was then isolated with ether and chromatographed from petroleum ether (b.p. 60–68°) on alumina (grade IV, 30 × 5 cm.), giving 1,2,3,4-tetrahydro-14,13-borazarotriphenylene which crystallized from petroleum ether (b.p. 60–68°) in colorless prisms (37.3 g., 80%), m.p. 112–114°, raised by sublimation at 90° (0.1 mm.) to 117°.

Anal. Calcd. for C₁₅H₁₅BN: C, 82.5; H, 6.9; N, 6.0. Found: C, 82.5; H, 7.0; N, 5.9.

14,13-Borazarotriphenylene (I).—A mixture of VI (5 g., 0.0215 mole) and sulfur (1.44 g., 0.045 mole) was heated 1 hr. at 250–260°. The residue was extracted with hot benzene and the extract evaporated to 20 ml. An equal volume of petroleum ether (b.p. 60–68°) was added, the solution filtered, and the filtrate chromatographed on alumina (Grade IV, 20 × 3 cm.), eluting with petroleum ether. After a forerun of unchanged VI, the main fraction gave on evaporation 14,13-borazarotriphenylene (I) which crystallized from petroleum ether (b.p. 60–68°) in colorless needles (2.45 g., 48%), m.p. 185–186°; ultraviolet spectrum in ethanol, λ_{max} in mμ (log ε); 258 (4.71), 269 (4.69), 295 (3.62), 316 (3.93), 330 (3.97).

Anal. Calcd. for C₁₅H₁₅BN: C, 83.9; H, 5.3; N, 6.1. Found: C, 84.0; H, 5.3; N, 6.0.

Attempted Reaction of I with Maleic Anhydride.—A mixture of I (0.58 g., 2.5 mmoles) and maleic anhydride (0.25 g., 2.5 mmoles)

in dry benzene (20 ml.) was heated under reflux for 3 hr. and then evaporated until crystallization began. The crystals were collected and found to be pure I (0.42 g.). Further I (0.12 g.) was recovered from the mother liquors; total recovery, 0.54 g. (94%) of material with m.p. and mixture m.p. 184–185°.

Tristetramethyleneborazine (VIII).—4-Amino-1-butene¹² hydrochloride (100 g.) was added slowly and cautiously to a stirred suspension of lithium borohydride (27 g.) in dry ether (200 ml.) contained in the glass liner of a 1-l. autoclave under nitrogen in a drybox. The volume was maintained by periodic addition of ether and the whole operation took 2 hr. Ether (200 ml.) was then added and the mixture left 60 hr. in the drybox. The liner and contents were then transferred to the autoclave (which had been purged overnight with dry nitrogen), heated to 150°, held there for 2 hr., then heated as rapidly as possible to 300° and held 20 min. at 300–310°. The autoclave was then cooled and vented in a hood, and the contents triturated 1 hr. with ether and water. The ether layer was separated and the aqueous layer extracted with ether. The combined ethereal extracts were washed with 10% sodium hydroxide solution, water, 10% hydrochloric acid, and water, dried (MgSO₄), and evaporated. The yellow residue (23 g.) was heated at 50–60° (0.005 mm.) to remove low boiling material and then sublimed at 120° (0.005 mm.). The sublimate crystallized from acetone giving tristetramethyleneborazine (VIII) as colorless plates (18 g., 26%), m.p. 184–186°.

Anal. Calcd. for C₁₂H₂₄B₃N₃: C, 59.4; H, 10.0; B, 13.4; N, 17.3; mol. wt., 243. Found: C, 59.1; H, 9.9; B, 13.6; N, 17.0; mol. wt. (Rast), 266.

14,16,18-Tribora-13,15,17-triazarotriphenylene (II).—A mixture of VIII (1 g.), palladized charcoal (Matheson, 0.5 g. of 10%), and mixed 1-and-2-hexenes (Phillips, 5 ml.) was heated 18 hr. in a Carius tube in an autoclave at 320°. The contents of the tube were then filtered and the solid washed with hot chloroform. The combined filtrates were evaporated and the residue chromatographed on neutral alumina (Woelm activity grade 1), first with petroleum ether (b.p. 60–68°) until all unchanged starting materials had been eluted (130 ml. of eluate), then with petroleum ether-chloroform (9:1) to elute the triboratriazarotriphenylene (II, 100 mg., 10%) which after crystallization from petroleum ether (b.p. 60–68°) and sublimation at 85° (0.005 mm.) had m.p. 193–195°.

Anal. Calcd. for C₁₂H₁₂B₃N₃: C, 62.5; H, 5.2; N, 18.2. Found: C, 62.9; H, 5.4; N, 17.8.

When II was dissolved in cold dilute ethanolic solutions of hydrochloric acid, sodium hydroxide, or sodium ethoxide, the characteristic ultraviolet absorption band rapidly disappeared, indicating hydrolysis.

(12) J. D. Roberts and R. H. Mazur, *J. Am. Chem. Soc.*, **73**, 2509 (1951).

[CONTRIBUTION FROM THE CHEMISTRY RESEARCH DEPARTMENT, AGRICULTURAL DIVISION, AMERICAN CYANAMID CO., PRINCETON, N. J.]

The Mechanism of the Rearrangement of *p*-Quinamines to 4-Aminodiphenyl Ethers¹

BY BERNARD MILLER

RECEIVED SEPTEMBER 18, 1963

The infrared and ultraviolet spectra of the products obtained from reaction of aromatic amines with 4-bromocyclohexadienones confirm the previously proposed quinamine structures (I). Acid-catalyzed rearrangement of a mixture of two quinamines with similar rearrangement rates afforded a mixture of 4-aminodiphenyl ethers containing no cross products from reaction of the two quinamines. The rearrangements are therefore completely intramolecular. The rearrangements are first order in quinamine and first order in hydrogen ion. Electron-withdrawing groups on the cyclohexadienone rings of quinamines increase the rates, while electron-donating groups on the aniline ring increase the rates to a greater extent than can be explained by the expected effects of the substituents on the basicities of quinamines. This suggests that proceeding from the ground state to the transition state increases the positive charge on the anilinium portion of the quinamine and induces a negative charge on the cyclohexadienone portion. The close resemblance between the quinamine and benzidine rearrangement is pointed out, and it is suggested that the two rearrangements proceed through similar mechanisms involving complexes of two roughly parallel aromatic rings.

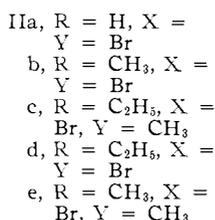
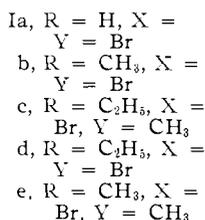
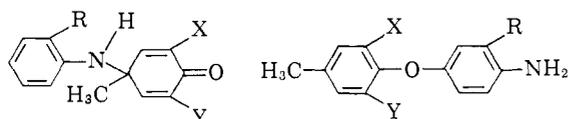
Some 35 years ago, Fries and his co-workers² found that 4-bromocyclohexadienones react with aromatic amines to give yellow, crystalline substitution products, to which they assigned the structures of 4-arylamino-cyclohexadienones (I) and the generic name "quin-

amines." On treatment with hydrochloric acid, quinamines performed a series of remarkable rearrangements which have somehow remained almost unnoticed to this day.

Quinamines with unsubstituted *p*-positions in the aniline rings gave as their principal products 4-aminodiphenyl ethers (II), whose structures were clearly demonstrated by reduction to the halogen-free derivatives (II, X = Y = H), which were independently synthesized.^{2b} The aminodiphenyl ethers were usually ob-

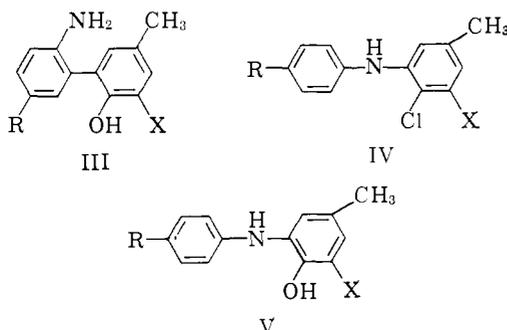
(1) This paper is the fourth in a series on "Reactions of Cyclohexadienones." For preceding papers, see (a) B. Miller, *J. Org. Chem.*, **26**, 4781 (1961); (b) B. Miller, *Tetrahedron Letters*, No. 2, 55 (1962); (c) B. Miller, *J. Org. Chem.*, **28**, 345 (1963).

(2) (a) K. Fries and G. Oehmke, *Ann.*, **462**, 1 (1928); (b) K. Fries, R. Boeker, and F. Wallbaum, *ibid.*, **509**, 73 (1934).



tained in yields of from 90–100%, after a few minutes contact of the quinamine with the hydrochloric acid solution.²

Quinamines which had substituents in the *p*-positions of the aniline rings gave several different types of rearrangements, depending on the position and nature of the substituents. The most general reaction was rearrangement to diphenyls of type III. The positions of the hydroxyl and amino groups in III were shown by reduction of III to carbazoles.^{2b}



Quinamines containing strong electron-withdrawing groups in the aniline rings often rearranged to form diphenylamines (IV) in which, remarkably, the carbonyl oxygen was replaced by a chlorine atom. This type of reaction was observed in both methanol and acetic acid solutions, and in no instance was a phenolic diphenylamine (V) observed.^{2b}

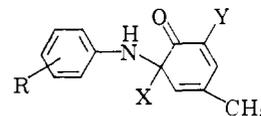
A good many questions about the mechanisms of these rearrangements deserve consideration. In this paper, the kinetics and mechanism of the rearrangements of quinamines to diphenyl ethers of type II will be considered.

Structures of Quinamines.—Before the mechanisms of any quinamine rearrangements can be discussed, it is necessary to demonstrate that quinamines do have the structures assigned to them. The initial assignment was based on their mode of preparation, elemental analyses, and the formation of dibromocresol on reduction of Ia.^{2a} In view of the unusual nature of the products obtained by rearrangement of quinamines, this evidence cannot be considered sufficient.

Of the possible products from reaction of 4-bromocyclohexadienones with aromatic amines, diaryl hydroxylamines, the products of attack by anilines on carbonyl oxygens,³ are readily excluded by the infrared spectra of quinamines, which show strong unsaturated carbonyl peaks at 5.98–6.02 μ . The possibility that the dienones attack the aniline molecules at positions other than nitrogen atoms is eliminated by the presence of single, unsplit N–H stretching peaks at 2.9 μ , and the absence of significant changes in the aromatic hydrogen

bending absorptions of the aniline rings⁴ after formation of the quinamines.

The ultraviolet spectra of quinamines (Fig. 1) show maxima at 247 to 258 $m\mu$, depending on the substituents on the cyclohexadienone rings, with values of ϵ ranging from 11,000 to 18,000. These spectra are consistent with structure I, but not with *o*-quinamine structures (VI) which should absorb some 70 $m\mu$ higher.⁵



VI

The 4-arylamino-cyclohexadienone structures assigned to quinamines by Fries, therefore, are quite in accord with the spectral evidence.

The Intramolecular Nature of the Rearrangements.—After the determination of the structures of quinamines, probably the most important question to be answered in regard to their rearrangement to diphenyl ethers is whether the reactions follow an intermolecular or an intramolecular course. An intermolecular rearrangement would presumably involve cleavage of the N–C bond to give fragments derived from the anilino and the cyclohexadienone portions of the quinamine molecule. The existence of an intermolecular path would be established by identifying the products of combination of fragments which were not combined in the original molecule. Since the reaction of two anilino fragments with one another would be most unlikely to have the same rate as the reaction of an anilino with a cyclohexadienone fragment, the absence of cross products from the rearrangement of a single quinamine would not indicate that the reaction is intramolecular. On the other hand, the absence of cross products from the simultaneous reactions of two different quinamines would be significant, provided that the rearrangement rates of the two quinamines were sufficiently close to assure that both were, in fact, rearranging simultaneously.

Quinamine Ib was found to rearrange only 1.7 times as fast as quinamine Ic (*vide infra*). This pair of quinamines was therefore chosen for mixed rearrangement studies. An equimolar mixture of Ib and Ic in methanol solution was acidified with concentrated hydrochloric acid, and, on completion of the reaction, the solvent was evaporated under vacuum. The residual mixture of amine hydrochlorides was dissolved in methanol containing sufficient sodium methoxide to liberate the amines, and the methanol solution was analyzed by vapor-liquid partition chromatography. It is clear that the isolation and analysis procedure should cause no change in the amounts of 4-aminodiphenyl ethers.

For purposes of comparison, the four possible 4-aminodiphenyl ethers (IIb–IIe) were prepared by rearrangement of the corresponding quinamines (Ib–Ie). All four were readily separated on the column under the conditions employed, and analysis of synthetic mixtures showed that 0.25 mole % of either II d or II e could be readily and reproducibly detected in the chromatogram.

Rearrangement of a mixture of Ib and Ic gave only II b and II c as identifiable products. No trace of II d or II e could be detected. The reactions of quinamines with acid to give 4-aminodiphenyl ethers are, therefore, true intramolecular rearrangements.

(4) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1958.

(5) (a) F. Wessely and F. Sinwell, *Monatsh.*, **81**, 1055 (1950); (b) L. Denivelle and R. Fort, *Compt. rend.*, **238**, 1132 (1959).

(3) See ref. 1c for examples of reactions in which products of displacement on oxygen are obtained from 4-bromocyclohexadienones.

Rates of Rearrangement.—The kinetics of the rearrangement of quinamines formed from anilines with unsubstituted *p*-positions were studied in a mixture of nine parts (by volume) of methanol to one of water at 26.0°. The rates were measured by following the disappearance of the cyclohexadienone bands at 247 to 258 $m\mu$. The acid concentrations employed were normally at least twenty times as large as the quinamine concentrations, so that the reaction rates measured were found to be pseudo-first order in quinamine concentration. Acid concentrations ranged from 10^{-5} to 1 *M*, depending upon the rearrangement rate of the quinamine. The variations of pseudo-first-order rate constants with acid concentration showed that the reactions were also first order in hydrogen ion. This is illustrated in Table I for quinamine Ia.

TABLE I
DEPENDENCE OF RATE OF REARRANGEMENT OF IA ON
QUINAMINE AND ACID CONCENTRATION AT 26.0°

| [quinamine], l./mole $\times 10^6$ | [H ⁺], l./ mole $\times 10^4$ | k_1 , sec. ⁻¹ | k_2 , l. mole ⁻¹ sec. ⁻¹ $\times 10$ |
|---------------------------------------|--|----------------------------|---|
| 1.048 | 1.88 | 4.07×10^{-5} | 2.16 |
| 5.34 | 4.70 | 1.023×10^{-4} | 2.17 |
| 5.28 | 10.45 | 2.28×10^{-4} | 2.18 |
| 2.64 | 10.45 | 2.31×10^{-4} | 2.21 |

The simplest explanation for these rate relationships is that the transition state involves one quinamine molecule and one hydrogen ion. If, however, the quinamine molecule were completely protonated under the conditions employed, reaction of the protonated molecule with a second hydrogen ion (a third-order reaction) would follow the apparent second-order kinetics observed.⁶ To eliminate this possibility, the rates of reaction of quinamines Ia, Ig, and Ij were measured in acid solutions of approximately the same concentration as the quinamines. These rates were first order in quinamine and in hydrogen ion, and the second-order rate constants obtained agreed well with those calculated from the pseudo-first-order rates.

The rearrangement rates measured are listed in Table II. It will be seen that they are, in general, very rapid reactions. The most marked effects on the rates were produced by substituents on the aniline ring. Electron-donating substituents, which would be expected to enhance the basicities of quinamines, increase the rates

TABLE II
RATES OF ACID-CATALYZED REARRANGEMENTS OF QUINAMINES
AT 26.0°

| Quinamine | A | B | X | Y | k_2 , l. mole ⁻¹ sec. ⁻¹ |
|-----------|-------------------------------|-----------------|-----------------|----|--|
| Ia | H | H | Br | Br | 0.218 ± 0.002 |
| Ib | CH ₃ | H | Br | Br | 24.8 ± 0.6 |
| Ic | C ₂ H ₅ | H | CH ₃ | Br | $14.3 \pm .9$ |
| Id | C ₂ H ₅ | H | Br | Br | $28.2 \pm .15$ |
| Ie | CH ₃ | H | CH ₃ | Br | $13.4 \pm .8$ |
| If | H | H | CH ₃ | Br | 0.126 ± 0.011 |
| Ig | H | CH ₃ | Br | Br | 1.82 ± 0.06 |
| Ih | H | CH ₃ | CH ₃ | Br | 0.802 ± 0.017 |
| Ii | CH ₃ | H | Cl | Cl | 40.0 ± 1.5 |
| Ij | Br | H | Br | Br | $(6.43 \pm 0.20) \times 10^{-3}$ |
| Ik | H | O | Br | Br | $(5.31 \pm 0.03) \times 10^{-3}$ |

\parallel
 CCH₃

(6) The author wishes to thank Prof. K. B. Wiberg for very interesting discussions of this point.

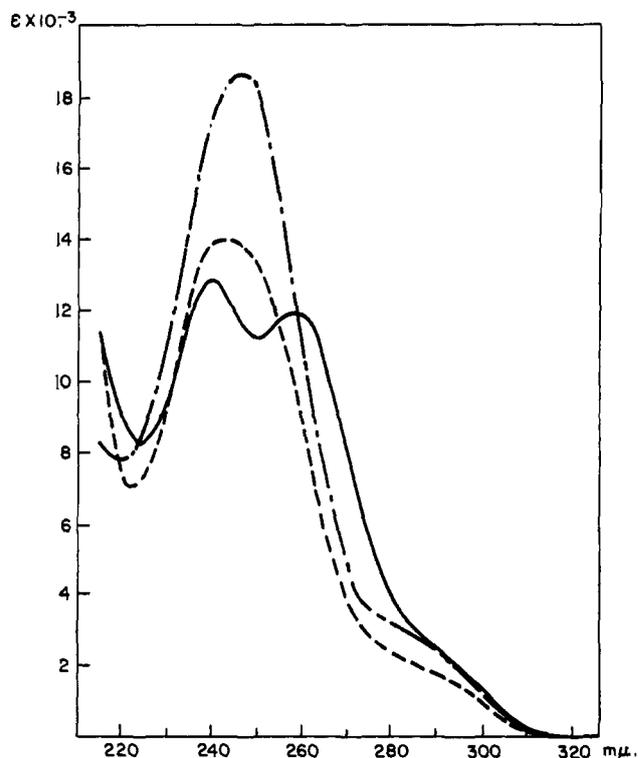


Fig. 1.—Ultraviolet spectra of quinamines: —, Ib; - · -, Ie; - - - -, II.

of rearrangement, while electron-withdrawing substituents decrease the rates.

These effects confirm the assumption that quinamines are protonated on nitrogen atoms rather than on carbonyl groups, as would be expected from the normally far greater basicities of amines—even such hindered amines as quinamines⁷—and the complete absence of the normal dienone-phenol rearrangements which should result from protonation of the carbonyl group.⁸

Since proton transfer reactions of amines are normally fast and reversible,⁹ the measured rearrangement rates (k_2) must be products of the form $K_b k'$, where K_b is the basicity constant of the quinamine and k' the rearrangement rate of the protonated quinamine. It is of interest to try to separate these two quantities, in order to determine the effects of substituents on k' alone.

The basicities of quinamines are unknown. Since the basicities of substituted anilines are readily available,¹⁰ these were chosen as convenient models for the effects of substituents on the basicities of quinamines. Table III compares the effects of substituents on the basicities of anilines with their effects on the rearrangement rates of quinamines of the 2,6-dibromocyclohexadienone series.

It would be desirable to study the rearrangement rates of quinamines with substituents in the *m*- and *p*-positions of the aniline ring.¹¹ Unfortunately, *p*-substituents could not be used since they led to types

(7) G. Vexlarschi (*Compt. rend.*, **228**, 1655 (1949)) showed that *N*-*t*-butylaniline is actually much more basic than aniline itself, owing to steric inhibition of conjugation between the amine group and the phenyl ring. Although quinamines also bear a tertiary alkyl group on the nitrogen atom, examination of models shows that the two double bonds in the cyclohexadienone ring reduce steric effects enough to allow coplanarity of the amine and phenyl functions.

(8) See S. M. Bloom, *Tetrahedron Letters*, No. 21, 7 (1959), for leading references.

(9) J. Hine, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1956, p. 195.

(10) J. M. Vandenbelt, C. Henrich, and S. G. Vanden Berg, *Anal. Chem.*, **26**, 726 (1954).

(11) L. P. Hammett, "Physical Organic Chemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1940, Chapter VII.

TABLE III

| EFFECTS OF AMINE BASICITIES ON REARRANGEMENT RATES | | | | |
|--|----------|-----------------------|-----------------------|-------------|
| Subst. ^a | pK_a^b | K_H/K_a^c | k/k_H^d | k'/k'_H^e |
| H | 4.67 | 1 | 1 | 1 |
| <i>o</i> -Br | 2.55 | 7.60×10^{-3} | 2.95×10^{-2} | 3.9 |
| <i>o</i> -CH ₃ | 4.53 | 7.25×10^{-1} | 114 | 160 |
| <i>m</i> -CH ₃ | 4.81 | 1.37 | 8.35 | 6.1 |
| <i>m</i> -O | 3.59 | 8.34×10^{-2} | 2.43×10^{-2} | 0.29 |
| CCH ₃ | | | | |

^a Substituent on the aniline ring of a 4-anilino-2,6-dibromo-4-methyl-2,5-cyclohexadien-1-one. ^b pK_a of substituted aniline (ref. 10). ^c $K_H = K_a$ for aniline. ^d Measured rearrangement rates relative to rearrangement rate of quinamine Ia. ^e Rearrangement rates of protonated quinamines relative to quinamine Ia.

of quinamine rearrangements^{2b} different from the rearrangement to diphenyl ethers which is considered in this paper. Quinamines with halogens in the *m*-positions of the aniline rings gave colored reaction mixtures whose rates could not readily be measured by the spectroscopic techniques we employed. Only the methyl and acetyl groups (fortunately having appreciably different polar characteristics) could be studied as substituents in the *m*-position.

Polar Effects of Substituents.—As may be seen in Table III, the rearrangement rate of a protonated quinamine with a *m*-methyl substituent is more than six times that of its unsubstituted analog, while substitution of a *m*-acetyl group for hydrogen decreases the rate more than threefold. These effects, while small, suggest that in the transition state for the rearrangement the aniline ring bears a greater positive charge than in the ground state of a protonated quinamine. Similarly, the value of k' for the quinamine prepared from *o*-toluidine is forty times that of the quinamine prepared from *o*-bromoaniline. The steric effects of methyl and bromine substituents in the *o*-position in aromatic rings have been observed to be essentially identical,¹² so it seems reasonable to ascribe the difference in rates to the polar effects of the substituents. While this conclusion must be tempered by the reservations which always accompany discussions of the effects of *o*-substituents, it is consistent with the observed effects of *m*-substituents.

The effects of substituents on the cyclohexadienone ring are smaller than those on the aniline ring. Rates of rearrangement increase by a factor of only two when a bromine atom is substituted for a methyl group, and by a factor of three when a chlorine atom replaces a methyl group. It should be noted, however, that electron-withdrawing substituents on the cyclohexadienone ring will decrease the observed rates of rearrangement somewhat by decreasing the basicity of the amine. The observed rates of rearrangement therefore minimize the role of polar influences of substituents on the cyclohexadienone ring. Corrections for this error, however, would probably be small.¹³

The most obvious explanation for the rate enhancing effect of electron-withdrawing substituents on the cyclohexadienone ring is that a negative charge is developed on the ring in the transition state. This interpretation is consistent with the previously noted polar effects of

(12) R. W. Taft, Jr., *J. Am. Chem. Soc.*, **74**, 3120 (1952); see also L. Pauling, "The Nature of the Chemical Bond," 2nd Ed., Cornell University Press, Ithaca, N. Y., 1940, pp. 189-190.

(13) γ,γ -Dichloroallylamine [A. N. Nesmeyanov, L. I. Zakharin, and R. K. Freidlina, *Izvest. Akad. Nauk S.S.S.R., Otdel. Khim. Nauk*, 841 (1958)] is only about one half as basic as allylamine [G. Vexlarschi and P. Rumf, *Compt. rend.*, **236**, 939 (1953); L. Majs, *Zh. Obshch. Khim.*, **29**, 561 (1959)]. If we use allylamines as models for 4-aminocyclohexadienones, therefore, we must conclude that 2-methyl and 2-chloro-4-aminocyclohexadienones should differ in basicity by less than a factor of two.

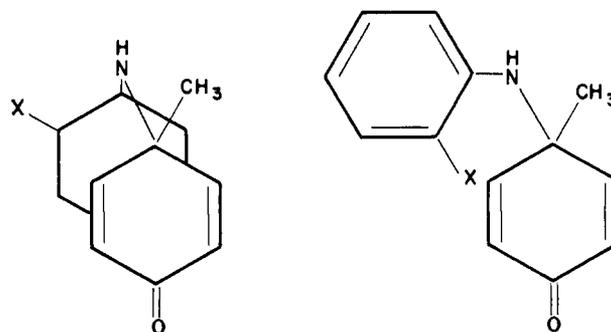
substituents on the aniline ring which suggest that the positive charge on that ring is greater in the transition state than in the ground state.

Alternatively, the possibility must be considered that the carbon-nitrogen bond in the ground state of the quinamine is weakened by repulsion between the anilinium ion and the positive end of a carbon-halogen dipole. Such repulsion should lower the energy needed for formation of a transition state in which the distance between the two positive charges is increased.

It is, of course, quite possible that both factors play a part in determining the substituent effect. There is no way of deciding their relative importance at present.

Steric Effects of Substituents.—As we noted above, rearrangement of a quinamine derived from *o*-toluidine is much faster than that of a quinamine derived from *o*-bromoaniline. Both *o*-substituted quinamines, however, react faster than their unsubstituted analog. In view of the opposing nature of the polar effects of methyl and bromine substituents, this "ortho effect" must be steric in nature.

Inspection of molecular models shows that quinamines may exist in two essentially strain-free conformations: an "eclipsed" conformation (VII) and a "skew" conformation (VIII).



Placing a substituent ("X") in the *o*-position of the aniline ring does not result in any visible increase of strain in the "eclipsed" conformation, but does result in marked interference between "X" and the adjacent carbons and vinylic hydrogens of the cyclohexadienone ring in the "skew" arrangement.

An *o*-substituent should therefore tend to freeze a quinamine into the "eclipsed" conformation. It is quite reasonable to assume that rearrangements of quinamines proceed *via* the "eclipsed" conformation, and the rate-enhancing effect of *o*-substituents is thus quite explicable.

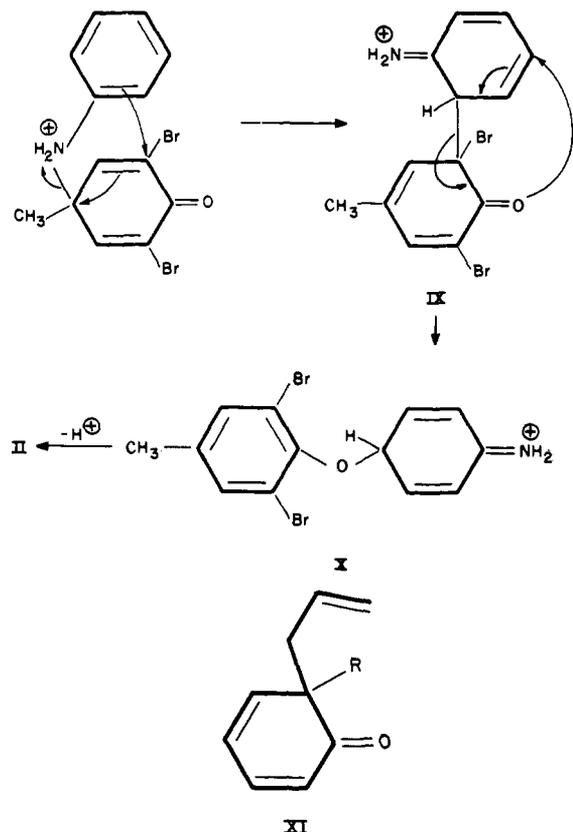
An *o*-ethyl group can exist in a conformation in which the terminal methyl group is directed away from the cyclohexadienone ring. In this conformation there is little more interference between neighboring atoms and the ethyl group than between these atoms and a methyl group. An ethyl group, therefore, is only slightly more effective than a methyl group in accelerating quinamine rearrangements, in spite of its appreciably greater size.

Mechanism of the Reaction.—Two possible intramolecular reaction paths may be written for the quinamine-diphenyl ether rearrangement. In the first the reaction proceeds through an intermediate allylic 1-6 shift, similar in principle to the Cope¹⁴ and Claisen¹⁵ rearrangements, to give the conjugated cyclohexadienone IX, which undergoes a further Cope rearrangement to X, which tautomerizes to II. This mechanism thus bears a formal resemblance to the *para*-Claisen rear-

(14) A. C. Cope and E. M. Hardy, *J. Am. Chem. Soc.*, **62**, 441 (1940), and succeeding papers.

(15) D. S. Tarbell, *Org. Reactions*, **2**, 1 (1944).

rearrangement, which also proceeds through two successive allylic rearrangements.¹⁶

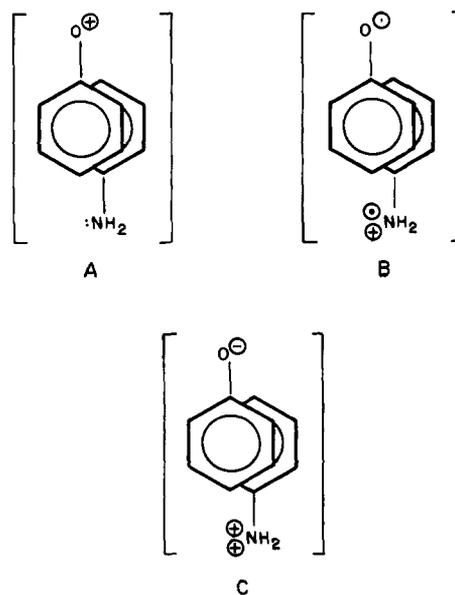


The very analogy with the Claisen rearrangement, however, emphasizes the difficulties faced by this mechanism. Allyl-1-naphthylamine requires 3 hr. at 280° to rearrange to 2-allyl-1-naphthylamine, while allylanilines cannot be made to rearrange at all.¹⁷ It is difficult to see any structural features in a quinamine that would cause it to undergo a Claisen rearrangement in a few minutes at room temperature. Furthermore, *para*-Claisen rearrangements normally proceed only when the intermediate cyclohexadienones (XI) cannot tautomerize to phenols. When R = H, only products of *ortho*-Claisen rearrangements are obtained.¹⁸ The cyclohexadienoneimine IX should tautomerize to the aromatic form even more readily, since the reaction proceeds in a highly polar medium and the intermediate, IX is already protonated—both factors which should greatly accelerate the loss of a proton. Yet it must be argued that in the quinamine rearrangement, if it proceeds by this mechanism, a second Cope rearrangement proceeds quantitatively in preference to aromatization of the aniline ring. This argument seems quite implausible.

Since the quinamine rearrangement, therefore, cannot proceed by way of a series of Claisen and Cope rearrangements, the only reasonable path remaining for consideration is one in which the transition state re-

sembles a "sandwich" of the two rings in a more or less parallel orientation, depending on how far the process of breaking the carbon-nitrogen bond has proceeded at the transition state.

The electronic distribution in the transition state sandwich may be represented by one of the three structures A, B, or C.



In drawing these three transition states, it was assumed that the carbon-nitrogen bond is completely broken, and that no interaction occurs between the two rings. These are, of course, unlikely assumptions, and these structures simply represent extreme resonance forms, which will be useful for purposes of discussion. Similarly, the use of single electrons in structure B is not meant to imply that a change in multiplicity occurs and that the transition state resembles a diradical, but simply that the electrons of the carbon-nitrogen bond are divided evenly between the two rings, so that the transition state is no more polar than the starting state.

As was discussed in the preceding section, the effects of substituents on both the aniline and cyclohexadienone rings are consistent with the hypothesis that the positive charge on the anilinium ion is increased on going to the transition state, and that a negative charge is induced on the cyclohexadienone ring. These effects eliminate the possibility that resonance structure A contributes significantly to the over-all structure of the transition state, and show that the charge distribution resembles that of structure C. This does not exclude the possibility of significant contributions from structure B, since B and C are not mutually exclusive. Indeed, a preponderant contribution from structure B is consistent with the rather small over-all effects of polar substituents on rearrangement rates, although the small size of these effects may also be explained by assuming that the transition state occurs before the "ions" have separated enough to develop appreciable charge on the two fragments. While the amount of charge separation incurred on going to the transition state may not be large, however, it is quite significant, since it determines the nature of substituent effects on the reaction.¹⁹

(19) A quite different picture of the transition state is obtained by assuming that the rate-determining step is the collapse of an intermediate π -complex. Since the rate of such a process would be increased by substituents which tend to destabilize the intermediate, a transition state resembling structure "A" would best explain the observed substituent effects. We have rejected this mechanism, however, on the grounds that collapse of a π -complex should be a much more rapid process than its formation, since formation of the complex involves a reduction in the number of "classical" chemical bonds, while collapse of the complex increases the number of such bonds.

(16) H. C. Conroy and R. A. Firestone, *J. Am. Chem. Soc.*, **75**, 2530 (1953); D. Y. Curtin and H. W. Johnson, Jr., *ibid.*, **76**, 2276 (1954); K. Schmid, W. Haegle, and H. Schmid, *Helv. Chim. Acta*, **37**, 1080 (1954).

(17) S. Macinkiewicz, J. Green, and P. Mamalis, *Chem. Ind. (London)*, 438 (1961); *Tetrahedron*, **14**, 208 (1961).

(18) Allyl ethers of catechol derivatives have been reported to yield *para*-Claisen rearrangement products together with the products of the normal *ortho*-Claisen rearrangement [cf. W. H. Perkin, Jr., and W. M. Trikojus, *J. Chem. Soc.*, 1663 (1927); W. A. Baker, A. R. Pernfeld, and J. L. Simonsen, *ibid.*, 439 (1939); and H. Staudinger, W. Kress, and W. Silit, *Helv. Chim. Acta*, **5**, 743 (1922)]. These rearrangements, however, presumably proceed through the nonenolizable ketone XI (R = OR') and do not, therefore, bear on the question of whether an enolizable intermediate could rearrange faster than it tautomerizes.

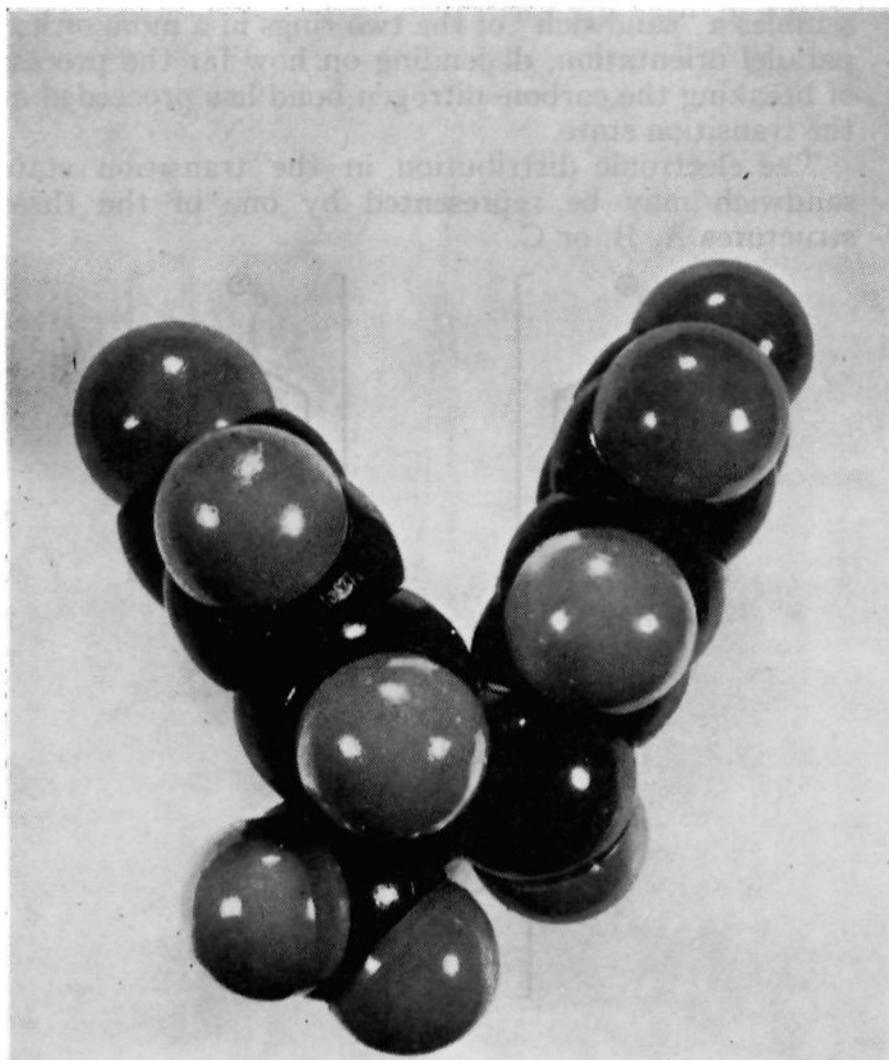
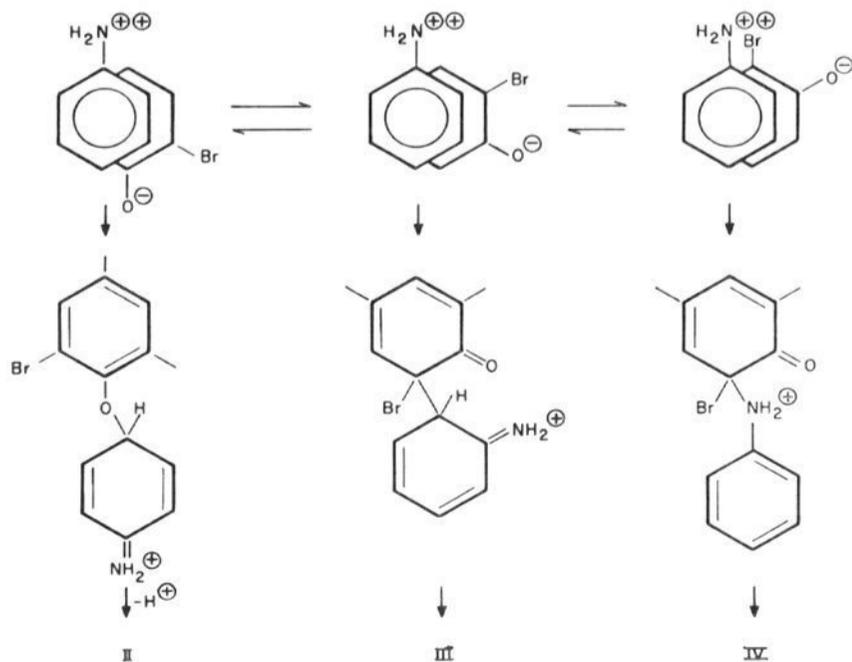


Fig. 2a.—4-Anilino-4-methyl-2,5-cyclohexadien-1-one, both rings planar.

The apparently high energy required to separate the charges in the process leading to transition state C may be supplied by the very strong charge-transfer complexing which would be expected to occur between a phenolate anion and an anilinium dication. The energy supplied by formation of such a complex should be appreciably greater than the energy supplied by complex formation in transition state B, and could well be enough to overcome the otherwise unfavorable distribution of charges.

The π -Complex as an Intermediate.—The rearrangement of quinamines to diphenyl ethers may occur in a single step (other than that required to lose a proton) or through one or more metastable intermediates. These studies provide no evidence about this point. The assumption that a π -complex exists as an intermediate, however, provides a simple rationalization for the formation of all three types of rearrangement products of quinamines.



As shown in the diagram, collapse of the initially formed complex would give II. When this path is blocked by substituents on the aniline ring, a minimal rotation around the axis of the two rings would allow collapse to III. Finally, further rotation would allow IV to be formed. The probability of production of the three types of products is therefore in the order $II > III > IV$, as is experimentally observed.²

While the mechanism proposed above rationalizes the preparation of all the rearrangement products by a single path, it is, of course, possible that three different paths may be involved; II may be formed through a π -complex, III by a Cope rearrangement, and IV by an allylic rearrangement. However, as was pointed out above, Claisen rearrangements of allylamines do not occur at rates great enough to account for the rearrangements of quinamines. Similarly, we are unaware of any example of allylic rearrangement of amines under such mild conditions. The mechanism presented above, therefore, seems to be uniquely capable of explaining the observed reactions.

Comparison with the Benzidine Rearrangement.—

There are many striking similarities between the rearrangements of quinamines and the complex of rearrangements which may conveniently be labeled "benzidine" rearrangements, including those in which the products are semidines and diphenyls.²⁰

Rearrangements of hydrazobenzenes to benzidines, like those of quinamines to 4-aminodiphenyl ethers, are completely intramolecular.²¹ Both types of rearrangement proceed readily in dilute acid, under conditions far milder than are necessary, for instance, for dienone-phenol rearrangements.⁸ The marked similarity in

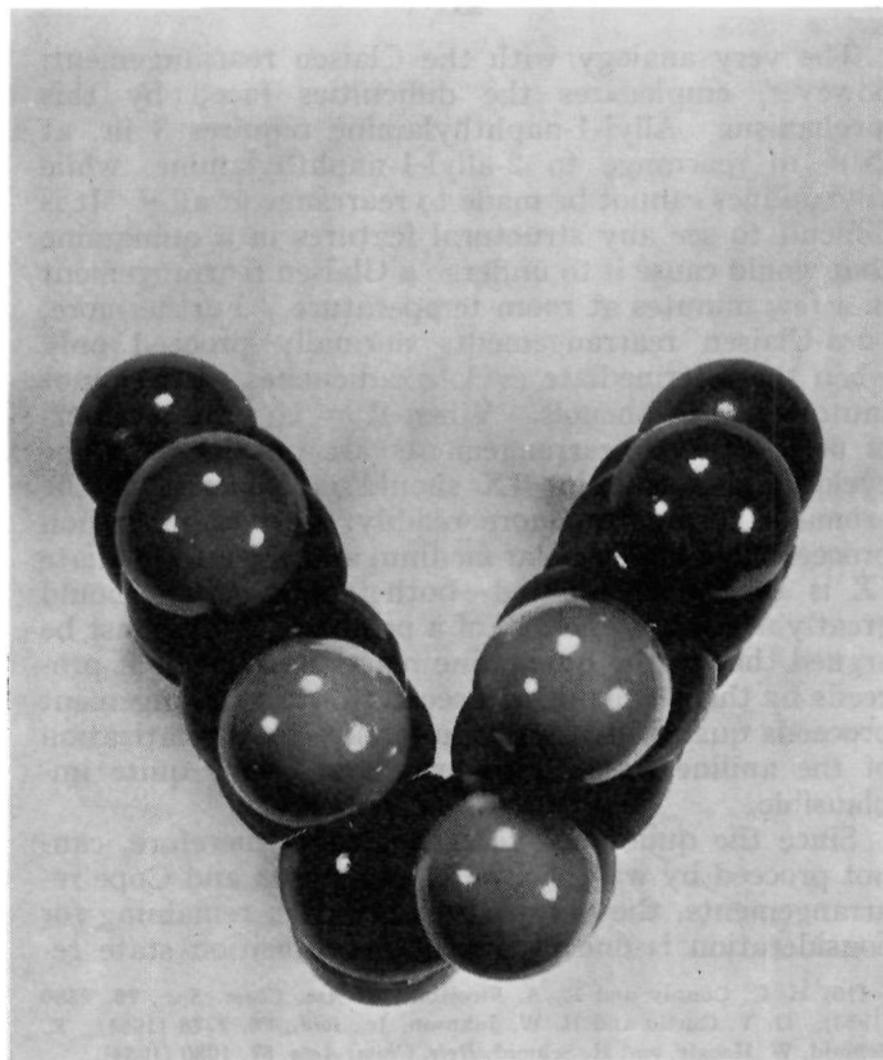


Fig. 2b.—Hydrazobenzene.

geometry of quinamines and hydrazobenzenes is clearly demonstrated in Fig. 2a and 2b, in which the two molecules are pictured in the "eclipsed" conformation. In

(20) For a summary of the products obtained from rearrangement of hydrazobenzenes, see P. Jacobson, *Ann.*, **428**, 76 (1922).

(21) C. K. Ingold and H. V. Kidd, *J. Chem. Soc.*, 984 (1933); D. H. Smith, J. R. Schwartz, and G. W. Wheland, *J. Am. Chem. Soc.*, **74**, 2282 (1952).

Fig. 2a, it is assumed that the cyclohexadienone ring is planar, to provide a maximum of orbital overlap between the carbonyl group and the double bonds. The angle between the two rings of the quinamine is 40° ; of hydrazobenzene, 40° . The distance between the carbonyl oxygen and the aniline ring of the quinamine is 4.31 Å.; between the two *p*-positions in hydrazobenzene, 4.31 Å.²² Molecular models indicate that the cyclohexadienone ring should exist in a boat form, in which the two rings (when the nitrogen and carbonyl oxygen atoms are *cis*) are closer than in hydrazobenzenes (Fig. 2c).

The products of the quinamine and benzidine rearrangements show close resemblances, both in types and in variety. Both rearrangements result, whenever possible, in joining those atoms which are most widely separated in the starting compounds, giving benzidines from hydrazobenzenes and diphenyl ethers from quinamines. Other products of both rearrangements are diphenylamines (III or semidines) and aminobiphenyls (II or diphenylines).^{2,20}

The very close resemblances between the quinamine and benzidine rearrangements suggest that the mechanisms of these two types of reactions are closely related. Although many mechanisms have been proposed for the benzidine rearrangement,²³ logical difficulties have gradually eliminated almost all of the competitors, and left the Dewar " π -complex"²⁴ in relatively undisputed possession of the field. In its essential details, Dewar's mechanism is identical with the mechanism we have proposed for the quinamine rearrangement.

The symmetry of the hydrazobenzene molecule makes the analysis of substituent effects in the benzidine rearrangement unusually difficult. This is especially true of those hydrazoaromatic compounds which are doubly protonated in the transition state,^{25,26} since it is extremely difficult to estimate the effects of substituents on the basicity constant of an already protonated hydrazobenzene. Nonetheless, several authors have considered the question of charge distribution in the transition state for the benzidine rearrangement. In a recent discussion of the subject, Ingold stated "...one of the half-structures (of the transition state for the benzidine rearrangement), that have now become differentiated, will have gained more charge, so resembling a doubly charged cation, whilst the other will have lost charge, so approaching the condition of an aniline molecule."²⁷ Clearly this picture is very similar to that which we have drawn for the transition state for the quinamine rearrangement, although Ingold avoids describing his concept as a " π -complex." Similarly, Dewar has offered the rather curious structure XII to describe the benzidine rearrangement transition state.^{24a} If the monoprotonated transition state favored by Dewar^{24a} is converted to the more commonly accepted

(22) These angles and bond lengths were calculated on the assumption that bond lengths and angles in the cyclohexadienone ring are the same as those in *p*-benzoquinone. Values for bond lengths and angles were obtained from "Tables of Interatomic Distances and Configuration in Molecules and Ions," Special Publication No. 11, The Chemical Society, London, 1958.

(23) C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, pp. 631-642.

(24) (a) M. J. S. Dewar, "Aromatic Rearrangements," in "Theoretical Organic Chemistry," Butterworths Scientific Publications, London, 1959, and papers cited therein; also (b) G. S. Hammond and J. S. Clovis, *Tetrahedron Letters*, No. 21, 945 (1962); (c) L. C. Snyder, *J. Am. Chem. Soc.*, **84**, 340 (1962).

(25) G. S. Hammond and H. J. Shine, *ibid.*, **72**, 220 (1950); R. B. Carlin, R. G. Nelb, and R. C. Odioso, *ibid.*, **73**, 1002 (1951).

(26) D. V. Banthorpe, E. D. Hughes, and C. K. Ingold, *J. Chem. Soc.*, 2386 (1962), and succeeding papers.

(27) C. K. Ingold in "The Transition State," Special Publication No. 16, The Chemical Society, London, 1962, p. 135.

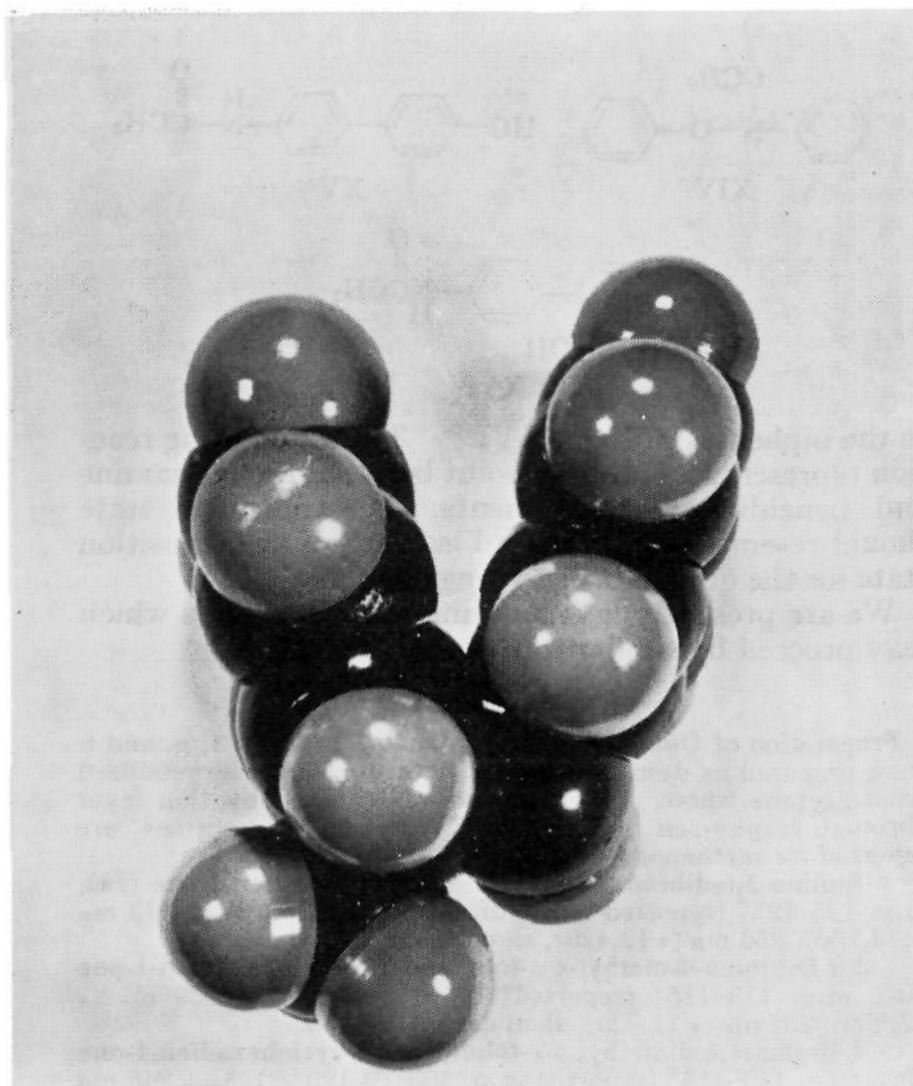
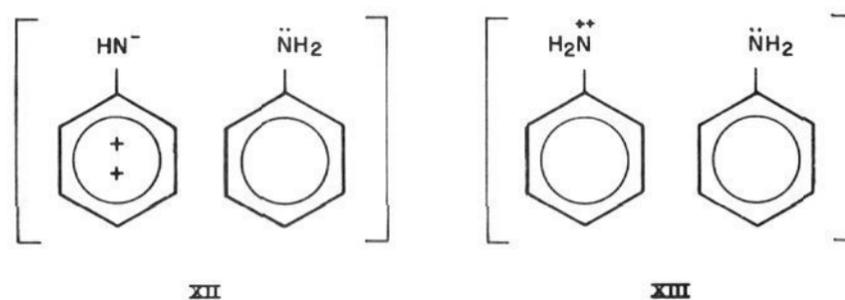


Fig. 2c.—4-Anilino-4-methyl-2,5-cyclohexadien-1-one, cyclohexadienone ring in boat form.

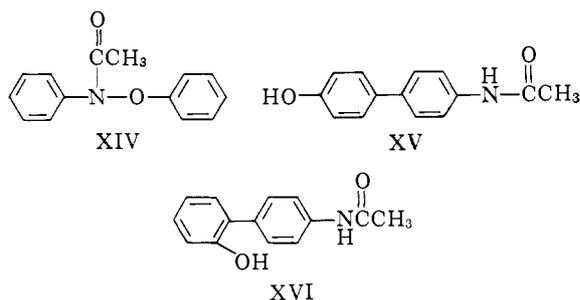
diprotonated form,^{25,26} structure XIII is obtained. Except for the rather small difference in electron availability between a phenoxide anion and an aniline molecule, XIII closely resembles our resonance form C for the quinamine transition state.



It should be emphasized, however, that Ingold and (apparently) Dewar based their ideas of charge distribution in transition states for the benzidine rearrangement on consideration of probable bonding energies of such transition states rather than empirical studies of substituent effects, since the symmetrical nature of the hydrazobenzene molecule makes such effects exceedingly difficult to interpret. As was discussed above, a reasonable interpretation of substituent effects in the quinamine rearrangement is possible without *a priori* judgments about the nature of the transition state.

We believe the preceding discussion indicates that the quinamine rearrangement, by virtue of the inherent asymmetry of the molecule, provides a somewhat simpler framework for experiment and discussion than does the benzidine rearrangement.

It seems probable that other types of rearrangement can be obtained which, like the quinamine and benzidine rearrangements, proceed *via* a π -complex of two aromatic rings. A recent example is the probable rearrangement of *N*-acetyl-*O,N*-diphenylhydroxylamine (XIV)



to the biphenyls XV and XVI.²⁸ This fascinating reaction represents a half-way point between the quinamine and benzidine rearrangements. Its transition state should resemble a "rotational isomer" of the transition state for the quinamine rearrangement.

We are presently investigating other reactions which may proceed by similar routes.

Experimental²⁹

Preparation of Quinamines.—Quinamines Ia, b, e, f, g, and h were prepared as described in the literature,² and recrystallized from acetone-water. Their purity was checked by thin layer chromatography on silica gel. Ultraviolet absorptions are reported for methanol solutions.

4-Anilino-2,6-dibromo-4-methyl-2,5-cyclohexadien-1-one (Ia), m.p. 125–127° (reported m.p. 107–125°,^{2a} 136°^{2b}); λ_{\max} 242 μ (ϵ 13,950), 256 μ (ϵ 12,420), shoulder *ca.* 290 μ .

2,6-Dibromo-4-methyl-4-*o*-toluidino-2,5-cyclohexadien-1-one (Ib), m.p. 113–115° (reported^{2a} m.p. 112°); λ_{\max} 239 μ (ϵ 12,850), 257 μ (ϵ 11,900), shoulder *ca.* 290 μ .

2-Bromo-4,6-dimethyl-4-*o*-toluidino-2,5-cyclohexadien-1-one (Ie), m.p. 115–116° (reported m.p. 103°,^{2a} 120°^{2b}); λ_{\max} 245 μ (ϵ 18,700), shoulder *ca.* 290 μ .

4-Anilino-2-bromo-4,6-dimethyl-2,5-cyclohexadien-1-one (If), m.p. 105–106° (reported^{2a} m.p. 107°); λ_{\max} 250 μ (ϵ 18,140), shoulder *ca.* 280 μ . *Anal.* Calcd. for C₁₄H₁₄OBrN: C, 57.54; H, 4.83; N, 4.79; Br, 27.34. Found: C, 57.93; H, 5.02; N, 4.89; Br, 27.28.

2,6-Dibromo-4-methyl-4-*m*-toluidino-2,5-cyclohexadien-1-one (Ig), m.p. 116–118° (reported^{2b} m.p. 121°); λ_{\max} 242 μ (ϵ 12,970), 258 μ (ϵ 12,200), shoulder *ca.* 290 μ . *Anal.* Calcd. for C₁₄H₁₃NOBr₂: C, 45.42; H, 3.54; N, 3.78; Br, 43.18. Found: C, 44.99, 45.17; H, 3.99, 3.91; N, 3.65, 3.89; Br, 42.92, 42.81.

2-Bromo-4,6-dimethyl-4-*m*-toluidino-2,5-cyclohexadien-1-one (Ih), m.p. 109–110° (reported^{2b} m.p. 110°); λ_{\max} 250 μ (ϵ 18,280), shoulder *ca.* 284 μ .

2-Bromo-4,6-dimethyl-4-(*o*-ethyl)-phenylamino-2,5-cyclohexadien-1-one (Ic).—A mixture of 2,4-dibromo-4,6-dimethylcyclohexadien-1-one (9.5 g., 0.034 mole) and 9.5 ml. of ethanol was stirred to form a thin paste, and cooled to –10°. A solution of 6.1 ml. of *o*-ethylaniline in an equal volume of ethanol was added slowly with continuous stirring, while the temperature of the reaction mixture was kept below 0°. After stirring for 10 min., the product was filtered and washed with a little cold ethanol. Four recrystallizations from acetone-water gave 1.1 g. (0.00344 mole, 10%) of bright yellow crystals, m.p. 101–102°, λ_{\max} 247 μ (ϵ 17,970). *Anal.* Calcd. for C₁₆H₁₈NOBr: C, 59.99; H, 5.67; Br, 24.95; N, 4.37. Found: C, 60.28; H, 5.16; Br, 24.97; N, 4.72.

2,6-Dibromo-4-methyl-4-(*o*-ethyl)-phenylamino-2,5-cyclohexadien-1-one (Id).—2,4,6-Tribromo-4-methylcyclohexadien-1-one (14.0 g., 0.041 mole) and 14 ml. of ethanol were stirred and cooled to –17° in a Dry Ice bath. A solution of 9 ml. of *o*-ethylaniline in 9 ml. of ethanol was added slowly. Appreciable heat was evolved, and the mixture was kept below 10° by occasional immersion in the Dry Ice bath. After stirring for 10 min., the mixture was filtered and the product washed with 60 ml. of cold ethanol to give 6.6 g. (0.0172 mole, 42%) of bright yellow powder. This was recrystallized from acetone-water, washed with methanol, and dried to give 3.9 g., m.p. 104–105°; λ_{\max} 240 μ (ϵ 12,550), 258 μ (ϵ 11,100), shoulder *ca.* 290 μ .

Anal. Calcd. for C₁₅H₁₅NOBr₂: C, 46.77; H, 3.93; Br, 41.50; N, 3.64. Found: C, 46.74; H, 3.92; Br, 41.52; N, 3.87.

2,6-Dichloro-4-methyl-4-*o*-toluidino-2,5-cyclohexadien-1-one (Ii).—A slurry of 4-bromo-2,6-dichloro-4-methyl-2,5-cyclohexadien-1-one (25.0 g., 0.097 mole) in 25 ml. of ethanol was cooled

in a Dry Ice-acetone bath and a solution of 25 ml. of *o*-toluidine in 25 ml. of ethanol was added very slowly. The mixture was allowed to stand in the Dry Ice bath for 10 min., and filtered to give a brown, slimy product. This was dissolved in acetone and precipitated by the addition of water to give a brown solid, which on washing with ethanol became bright yellow. The yield was 5.0 g. (0.0177 mole, 18%), m.p. 98–100°. Three recrystallizations from acetone-water gave 3.0 g., m.p. 110.5–111.5°, λ_{\max} 243 μ (ϵ 13,950), shoulder *ca.* 275 μ . *Anal.* Calcd. for C₁₄H₁₃NOCl₂: C, 59.58; H, 4.63; Cl, 25.13; N, 4.96. Found: C, 59.72; H, 4.90; Cl, 24.88; N, 5.00.

2,6-Dibromo-4-methyl-4-(*o*-bromo)-anilino-2,5-cyclohexadien-1-one (Ij).—The procedure used to prepare Id was followed to give a 23% yield of Ij, m.p. 131–132°, λ_{\max} 240 μ (ϵ 11,920), 256 μ (ϵ 12,200), shoulder *ca.* 290 μ . *Anal.* Calcd. for C₁₃H₁₀NOBr₃: C, 35.81; H, 2.31; N, 3.21; Br, 54.98. Found: C, 35.76; H, 2.21; N, 3.26; Br, 55.23.

2,6-Dibromo-4-methyl-4-(3-acetylanilino)-2,5-cyclohexadien-1-one (Ik).—The procedure used to prepare Id was followed to give a 38% yield of Ik, m.p. 151–153°; λ_{\max} 233 μ (ϵ 22,200), 257 μ (ϵ 17,000), 338 μ (ϵ 1,980). *Anal.* Calcd. for C₁₅H₁₃NO₂Br₂: C, 45.13; H, 3.28; N, 3.51; Br, 40.04. Found: C, 45.05; H, 3.74; N, 3.49; Br, 40.10.

Products of Rearrangement of Quinamines.—4-(2,6-Dibromo-4-toluoxy)-*o*-toluidine (Iib), m.p. 121–122° (reported m.p. 122.5°), and 4-(6-bromo-2,4-xylyloxy)-*o*-toluidine (Iie), m.p. 130–131° (reported m.p. 131°), were obtained from Ib and Ie, respectively, as described by Fries, Boeker, and Wallbaum.^{2b}

4-(2,6-Dibromo-4-toluoxy)-*o*-ethylaniline (Iid).—2,6-Dibromo-4-methyl-4-(*o*-ethyl)-phenylamino-2,5-cyclohexadien-1-one (Id) (1.0 g., 0.0026 mole) was suspended in 50 ml. of methanol and 5 ml. of concentrated HCl added. The solid dissolved immediately, and the solution was evaporated under vacuum to give 1.20 g. of the crude hydrochloride, which was suspended in 20 ml. of ethanol. The solid dissolved immediately on addition of 20 ml. of 10% NaOH, and after 2 min. a white precipitate appeared. The mixture was extracted with methylene chloride and the extract was washed with water, dried, and evaporated to give 1.0 g. (100%) of white crystals, m.p. 105–107°. Recrystallization from hexane raised the m.p. to 109–111°. *Anal.* Calcd. for C₁₅H₁₅NOBr₂: C, 46.77; H, 3.93; N, 3.64; Br, 41.50. Found: C, 45.44; H, 3.66; N, 3.76; Br, 42.77.

4-(6-Bromo-2,4-xylyloxy)-*o*-ethylaniline (Iic).—2-Bromo-4-(*o*-ethyl)-phenylamino-2,4-dimethyl-2,5-cyclohexadien-1-one (Ic) (1.0 g., 0.0031 mole) was rearranged as described above for Id to give 0.89 g. (89%) of pink solid, m.p. 94–98°. Recrystallization from hexane raised the melting point to 98–100°. *Anal.* Calcd. for C₁₆H₁₈NOBr: C, 59.99; H, 5.67; N, 4.37; Br, 24.96. Found: C, 59.82; H, 5.89; N, 4.23; Br, 24.87.

Rearrangements of Mixtures of Quinamines. Analytical Methods.—Methanol solutions of the diphenyl ethers Iib–Iie were analyzed on an F and M No. 500 gas chromatograph, using a 10-ft. HiVac silicone grease column at 250°. A helium pressure of 30 lb. and a flow rate of 100 ml./min. were employed. The retention times were Iib, 24.7 min.; Iic, 17.3 min.; Iid, 28.9 min.; Iie, 12.9 min. Retention times were unchanged when solutions of the amine hydrochlorides in sodium methoxide solutions were analyzed. Mixtures containing Iib–Iie were prepared and analyzed. No change in retention times was noted, and the presence of 0.25 mole % of Iid or Iie was clearly detected (Iie gave a sharper peak and was somewhat preferable for analytical purposes.)

In a typical analysis, the hydrochlorides of Iib (37.8 mg.), Iid (1.4 mg.), Iie (1.0 mg.), and Iic (34.0 mg.) were dissolved in 1 ml. of 0.196 *N* sodium methoxide solution. The results of g.l.p.c. analysis are

| Retention time, min. | Area, % | Compd. |
|----------------------|---------|--------|
| 13.2 | 3.4 | Iie |
| 17.1 | 58.8 | Iic |
| 24.6 | 34.8 | Iib |
| 29.0 | 3.0 | Iid |

Rearrangement of Ib and Ic.—A mixture of 177.6 mg. of Ib (0.00479 mole) and 164.3 mg. of Ic (0.00508 mole) was dissolved in 150 ml. of methanol; 15 ml. of 4 *N* HCl were added slowly, with stirring, to the solution, which turned pale blue. After being allowed to stand at room temperature for 30 min., the solution was evaporated under vacuum to give 391.7 mg. of a mixture of amine hydrochlorides. This was dissolved in 5 ml. of 0.196 *N* sodium methoxide solution, which was analyzed as described above. Two peaks were observed in the g.l.p.c. record, corresponding to Iic (retention time 17.3 min.) and Iib (retention time 24.6 min.). No change in the base line could be seen at retention times corresponding to those observed for Iid and Iie. Repeated analyses gave identical results.

Rate Measurements.—Spectroscopic grade absolute methanol and distilled water were kept overnight in a thermostat at 26.0°, and solvent for rate studies was then prepared by adding

(28) J. R. Cox, Jr., and M. F. Dunn, *Tetrahedron Letters*, No. 15 985 (1963).

(29) Microanalyses by G. Galbraith, Knoxville, Tenn. Melting points are corrected; those reported for quinamines are all decomposition temperatures.

25 ml. of water to 225 ml. of methanol and storing the resulting solvent in the thermostat. Commercial 12 *N* hydrochloric acid was diluted to *ca.* 0.1 *N*, and mixed with methanol as described above to give a stock acid solution, which was standardized by titration with sodium hydroxide solution, and diluted as necessary for kinetic runs. More concentrated acid solutions were prepared as needed. Solutions of quinamines were prepared on the day they were to be used. For each run, the acid solution was

added to a measured volume of the quinamine solution from a rapid flow pipet, the mixture quickly shaken in a volumetric flask, and the solution transferred to a jacketed ultraviolet absorption cell kept at 26.0°. The rate of disappearance of the cyclohexadienone peak at 247–258 $m\mu$ was followed on a Cary Model 11 spectrophotometer. The concentration of acid was usually at least twenty times as great as that of quinamine, to allow pseudo-first-order rates to be calculated.

[CONTRIBUTION FROM THE CHEMISTRY RESEARCH DEPARTMENT, AGRICULTURAL CENTER, AMERICAN CYANAMID CO., PRINCETON, N. J.]

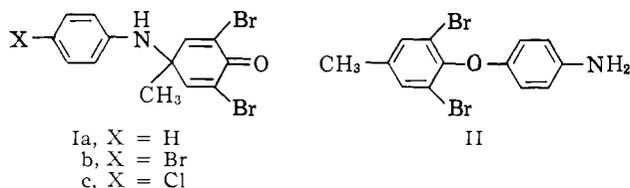
A Re-examination of Some Reported Rearrangements of Quinamines¹

By BERNARD MILLER

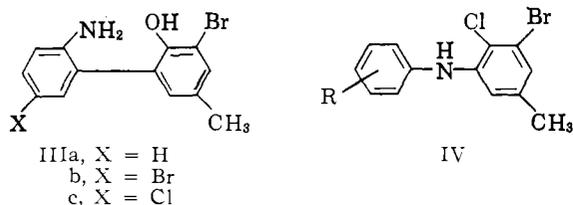
RECEIVED SEPTEMBER 18, 1963

The rearrangement of Ia in acid has been shown to give a mixture of IIIa and IIIb rather than IIIc as previously reported. Yields of IIIa and IIIb were increased by increasing acid concentrations. A by-product of the rearrangement of Ib, which had been assigned structure V, has been shown to have structure VI. Quinamine VIIa gives largely 2,6-dibromo-4-methylaniline and X on reaction with acid, while VIIb gives the same amine and 2,6-dibromo-4-methylphenol. No evidence has been found for occurrence of a dienone-phenol rearrangement. These results are interpreted in terms of the formation of a " π -complex" as an intermediate.

In the preceding paper² it was shown that the acid-catalyzed rearrangement of *p*-quinamines (I) to 4-aminodiphenyl ethers (II) proceeds by an intramolecular path, and a mechanism was proposed involving a transition state resembling a π -complex of two aromatic rings.



The conversion of I to II proceeds in excellent yield when the *p*-position of the aniline ring of I is unsubstituted. When the *p*-position is substituted, *p*-quinamines react with mineral acids to give phenols of type III or oxygen-free diphenylamines of type IV.³



While there is no direct evidence concerning the mechanism by which I is converted to III and IV, it is tempting to regard these reactions as being intramolecular rearrangements analogous to the rearrangement of I to II. A particularly satisfying mechanism would involve the production of II, III, and IV from a common intermediate π -complex, as is outlined in the preceding paper.²

Although all the major products of quinamine rearrangements can be explained by the " π -complex" mechanism, several minor products isolated by Fries and his co-workers were assigned structures which cannot be easily rationalized by this mechanism.

These minor products have now been re-examined, and new structures have been assigned to them. As a result, the structures assigned to all the known products of quinamine rearrangements are consistent with those which might be expected to result from collapse or rearrangement of a single intermediate complex.

Minor Products from the Rearrangement of Ia.—Rearrangement of Ia in glacial acetic acid containing high concentrations of hydrochloric acid was reported to give, in addition to II, a side product, m.p. 168°, whose analysis corresponded to the formula $C_{13}H_{11}NOBrCl$ and which was assigned structure IIIc. This unusual reaction was explained by assuming that Ia was first cleaved to give aniline hydrochloride and a 4-chlorocyclohexadienone. The 4-chlorocyclohexadienone was believed to act as a chlorinating agent, converting quinamine Ia to Ic; Ic could then rearrange to IIIc.³

Although mechanisms proposed 30 years ago often seem strange to us today, it is indeed difficult to explain the production of IIIc without assuming the occurrence of a 4-chlorocyclohexadienone as an intermediate. Once the existence of such cleavage products are assumed, however, it becomes possible to rationalize the production of products such as III and IV by intermolecular paths, rather than the intramolecular path which was shown to be exclusively followed in the formation of II.² A reinvestigation of the structure of the 168° product was therefore of more than usual interest. We initially attempted to confirm Fries' assignment of structure IIIc to his 168° product by forming IIIc by rearrangement of Ic. When Ic was treated with acid, however, the diphenyl derivative IIIc which was obtained had a melting point of 198–199°, and did not seem likely to be identical with Fries' product.

Fries' procedure for the preparation of his 168° material was therefore repeated, and a 9% yield of a side product, m.p. 153–173°, was obtained. This proved, after a rather tedious separation, to be composed of approximately equal amounts of two compounds: A, m.p. 202–203°, whose analysis fit the formula $C_{13}H_{11}ONBr_2$, and B, m.p. 147–148°, with the formula $C_{13}H_{12}OBrN$. No chlorine-containing product corresponding to that reported by Fries could be obtained. It seems probable that Fries' "compound" was, in fact, a mixture of A and B, which would give a total halogen content agreeing reasonably well with that required for the formula $C_{13}H_{11}NOBrCl$.

Both A and B showed split N-H stretching peaks at 2.92 and 3.02 μ , as would be expected for primary amines, and in addition showed broad phenolic hydroxyl peaks at 3.8–3.9 μ , indicating that the hydroxyl group forms strong hydrogen bonds. Compound IIIc showed similar absorption in its infrared spectrum, as would be expected of a compound in which strong interaction can occur between the hydroxyl and amino groups. Other

(1) Reactions of Cyclohexadienones. V. For paper IV, see ref. 2.

(2) B. Miller, *J. Am. Chem. Soc.*, **86**, 1127 (1964).

(3) K. Fries, R. Boeker, and F. Wallbaum, *Ann.*, **509**, 73 (1934).