[Contribution from the Chemistry Division of the Oak Ridge National Laboratory]

Migration Ratios Observed in the Reaction of Diarylethylamines with Nitrous Acid[1]

By Leon S. Ciereszko[2] and John G. Burr, Jr.

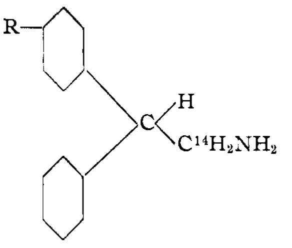
Received June 7, 1952

The migration ratios with reference to phenyl of several substituted aryl groups have been determined by the nitrous acid induced rearrangement of the corresponding 2,2-diarylethyl-1-C^{14}-amine (I). The results obtained are summarized in Table IV. Included in this table, for comparison, are the migratory aptitudes observed in the acid-catalyzed rearrangement of the corresponding C^{14}-labeled diarylethanols[3] (II). These differences in the observed migration ratios are discussed in terms of neighboring group participation theory. There appears to be some possibility that the reaction of the amines with nitrous acid may proceed through a diazo hydrocarbon intermediate rather than a diazonium ion intermediate; and the implications of this are discussed.

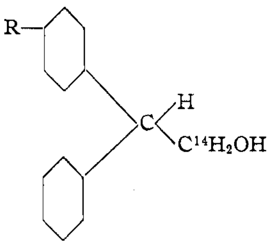
Introduction

This paper reports some preliminary work in the measurement of migration ratios in different types of reactions. The reaction concerned here is that of diarylethylamines (I) with nitrous acid to produce, predominantly, the mixture of carbinols, IVa and IVb. The use of such simple compounds as I, which are free from structural and stereochemical complications, in the study of rearrangements is made possible by the availability of carbon-14. The experimental work necessary for the accurate determination of migration ratios in this reaction is greatly reduced by the easy and precise techniques available for carbon-14 measurement.

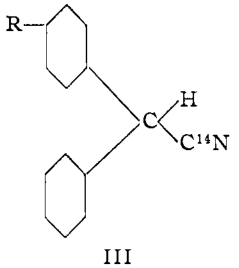
The data discussed here are closely comparable to the data obtained from the rearrangement of diarylethanols[3] since both the amines (I) and the carbinols (II) were obtained, in each case, from the same preparation of the corresponding nitrile III.



I



II



III

The amine was produced by reduction of the nitrile using an alkaline Raney nickel catalyst, and the carbinol *via* acid hydrolysis of the nitrile to the acid followed by lithium aluminum hydride reduction of the acid. The nitriles (III) were the reaction product of the corresponding chlorides with cuprous cyanide-C^{14} at 200–240°.

The amines which have been thus far studied are those where R is *p*-methyl, *m*-methyl, *p*-phenyl and *p*-methoxyl. These were obtained generally in 70–85% yield, and isolated as the hydrochlorides. The reduction of 2-phenyl-2-(*p*-anisyl)-acetonitrile-1-C^{14} was exceptional in that a poor yield of the amine hydrochloride was obtained.

The rearrangements were carried out by mixing a water solution of the amine hydrochloride with an excess of sodium nitrite dissolved in a small amount of water. A clear stable solution resulted. In several cases a crystalline salt precipitated, which dissolved when more water was added or if the solution was warmed. In the case of 2,2-diphenylethylamine, this salt was filtered and washed with water. It then melted at 115–118° with gas evolution. The analysis corresponded to that of the amine nitrite. It contained no ionic halogen, and thus could not be the diazonium chloride which has the same elementary analysis for carbon, hydrogen and nitrogen.

When these clear water solutions of the amine hydrochloride and sodium nitrite were warmed, gas evolution began at about 70–80°, and an oil deposited which in some cases solidified. In the case of 2,2-diphenylethylamine this product has been shown to consist only of benzylphenylcarbinol,[4] and in partial confirmation of this we have observed that 1.70 g. of this amine hydrochloride gave a solid crude product from which a 66% yield of recrystallized benzylphenylcarbinol was isolated.

In order to determine whether appreciable amounts of unrearranged primary carbinol (IVc) were present in the crude carbinol mixture so obtained, a portion of it was oxidized (as shown in the scheme below for the *p*-tolyl series) and another portion was dehydrated with phosphorus pentoxide in boiling xylene. The stilbene so obtained was isolated, purified and oxidized. The purpose of this acid treatment was to rearrange any primary carbinol that might be present in the carbinol mixture from the amine rearrangement. Since the migration ratios observed in the acid rearrangement were known from previous work, since there was small possibility of appreciable amounts of the unsymmetrical diarylethylene being formed, and since any primary carbinol present in the carbinol

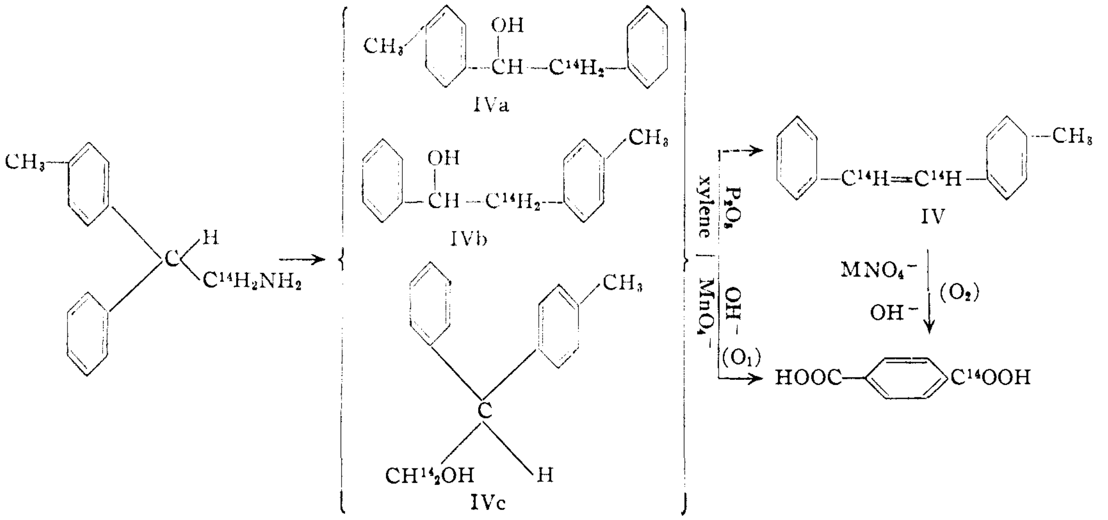
---

[1] This document is based upon work performed under Contract Number W-7405-eng-26 for the Atomic Energy Commission at the Oak Ridge National Laboratory. Presented in part at the Milwaukee Meeting of the American Chemical Society, March 30–April 3, 1952.

[2] Member of the Research Participation Program sponsored jointly by the Oak Ridge Institute of Nuclear Studies and the Oak Ridge National Laboratory; permanent address, University of Oklahoma, Norman, Oklahoma.

[3] J. G. Burr, Jr., and L. S. Ciereszko, This Journal, **74**, 5426 (1952).

[4] L. Hellerman, M. L. Cohn and R. E. Hoen, *ibid.*, **50**, 1724 (1928).



mixture would probably oxidize to unlabeled phthalic acid, the effect upon the observed migration ratios of the presence of primary diarylethanol in the carbinol mixture could be easily calculated from the carbon-14 content of the acids obtained in the oxidations O_1 and O_2. In the cases of the *p*-tolyl series, the *m*-tolyl series and the *p*-xenyl series, these calculations showed that insufficient primary carbinol(IVc) was present to affect appreciably the migration ratios observed.

The data thus obtained by these processes are shown in Table I. The C^{14}-values are shown for the acids, since they were generally more easily handled than the nitriles and in addition were needed for the study of the carbinol rearrangement.[3] The yields, derivatives and physical constants of the amines,

$R—C_6H_4\underset{\textstyle C^{14}H_2NH_2}{\underset{|}{CH}}—C_6H_5$ are shown in Table II.

TABLE I

The numerals indicate C^{14}-content in μc./mmole

Compound	Series *p*-Tolyl	*m*-Tolyl	*p*-Phenyl	*p*-Methoxyl
Nitrile	. .	. .	. .	4.16
Acid	4.42	4.08	4.32	. .
Amine hydrochloride	4.45	4.06	4.23	. .
Average	4.43	4.07	4.28	4.16
Oxidation product				
O_1	1.96	1.97	2.04	. .
O_2	2.14	1.96	2.14	2.44
% migration of substituted phenyl	47	48	50	59

The conditions of oxidation of the carbinol mixtures and stilbenes, and the isolated oxidation product are shown in Table III.

TABLE II

R	Amine Yield, %	°C.	Hydrochloride °C.	Picrate °C.
p-Methyl	68	Oil	236[a]	203[b]
m-Methyl	86	Oil	245[c]	196[d]
p-Phenyl	70	90[e]	252[f]	220[g]
p-Methoxyl	23	Oil	195[h]	172[i]

[a] Calcd. for $C_{15}H_{18}ClN$: Cl, 14.3; N, 5.66. Found: Cl, 14.2; N, 5.64. [b] Calcd. for $C_{21}H_{20}N_4O_7$: N, 12.7. Found: N, 12.7. [c] Calcd. for $C_{15}H_{18}ClN$: Cl, 14.3; N, 5.66. Found: Cl, 14.5; N, 5.66. [d] Calcd. for $C_{21}H_{20}N_4O_7$: N, 12.6. Found: N, 12.6. [e] Calcd. for $C_{20}H_{19}N$: N, 5.12. Found: N, 5.07. [f] Calcd. for $C_{20}H_{20}NCl$: Cl, 11.3; N, 4.47. Found: C, 11.3; N, 4.60. [g] Calcd. for $C_{26}H_{22}N_4O_7$: N, 11.2. Found: N, 11.0. [h] Calcd. for $C_{15}H_{18}ONCl$: Cl, 13.4; N, 5.31. Found: Cl, 13.6; N, 5.34. [i] Calcd. for $C_{21}H_{20}O_8N_4$: N, 12.3. Found: N, 12.1.

TABLE III

Series	Stilbene, m.p., °C.	Oxidation conditions	Oxidation product isolated, and m.p., °C.
p-Tolyl	120[a]	Boiling aqueous alkaline permanganate	Terephthalic acid > 300
m-Tolyl	Oil[e]	Boiling aqueous alkaline permanganate	Isophthalic acid > 300
p-Xenyl	222[b]	Permanganate in anhydrous acetone, boiling	*p*-Phenylbenzoic acid 225
p-Anisyl	135[c]	Permanganate in boiling aqueous acetone	*p*-Hydroxybenzoic acid[d] 204

[a] Lit. 120°, Auschütz, *Ber.*, 18, 1946 (1885). [b] Lit. 221°, Bergmann and Weymann, *J. Org. Chem.*, 9, 415 (1944). [c] Lit. 135–136°, Van Duin, *Rec. trav. chim.*, **45**, 347 (1926). [d] The oxidation products were benzoic and *p*-anisic acids. The anisic acid was cleaved by refluxing the mixture with aluminum bromide in benzene and the *p*-hydroxybenzoic acid isolated from the cleavage mixture by carbon disulfide extraction in which it is insoluble. [e] Lit. 49–50°, Bergmann and Shapiro, *J. Org. Chem.*, 12, 57 (1947).

Experimental[5]

Each of these series of compounds was carried through the same series of reactions under essentially the same conditions, and the pertinent experimental data are summarized in Tables II and III. Thus below are given only the experimental details for the 2-phenyl-2-(*p*-xenyl)-ethylamine-1-C^{14} series which is typical of all except the series where R was *p*-methoxyl, and here conditions were similar but yields were lower

2-Phenyl-2-(*p*-xenyl)-ethylamine-1-C^{14}.—Reduction of the nitrile (3.0 g., 11.5 mmoles) in alcohol solution with an alkaline (briefly washed) W-7 Raney nickel catalyst was complete in 18 hours, with a hydrogen uptake of 15 mmoles (65%). The nitrile was difficultly soluble in alcohol and some remained at the end. The catalyst was filtered off and the filtrate evaporated. The residue partly crystallized. It was stirred with 50 ml. of 20% hydrochloric acid. The resulting solid was filtered, dissolved in alcohol and precipitated by addition of ether to give 1.90 g. of white crystalline

---

(5) Melting points were taken either upon a calibrated Fisher-Johns block or upon a Kofler Heizbank. C-14 assays were accomplished by a wet combustion of the compounds, and ionization chamber counting of the evolved carbon dioxide on a vibrating reed electrometer. Microanalyses for carbon, hydrogen, nitrogen and halogen were done by Dr. H. W. Galbraith, Knoxville, Tennessee.

solid melting at 252°. Rework of the solvents gave an additional 0.50 g. making a total of 2.40 g. (70%). The hydrochloride was difficultly soluble in water. Recrystallization from that solvent did not change the melting point. The picrate formed yellow needles melting at 220°.

Rearrangement of 2-Phenyl-2-(*p*-xenyl)-ethylamine-1-C^{14}.—A solution of 1.60 g. of the hydrochloride in 176 ml. of water was prepared by heating (on cooling, the salt crystallized), and to this was added a solution of 2.0 g. of sodium nitrite in a few ml. of water. A thick mush of colorless crystals resulted. At 70–80° this suspension evolved a gas, and after about a half hour of heating the formation of a yellow oil was complete. On cooling this oil crystallized.

Oxidation—O$_1$.—A portion (0.65 g.) of this crude carbinol mixture was refluxed three hours with a solution of 3 g. of potassium permanganate in 50 ml. of acetone. The acetone was filtered, and the manganese dioxide cake washed thoroughly with dilute sodium hydroxide and water. Acidification of the aqueous filtrate gave a white precipitate. The crude *p*-phenylbenzoic acid was filtered, washed repeatedly with hot water and recrystallized from benzene. It formed white needles (70–80 mg.) melting at 225°.

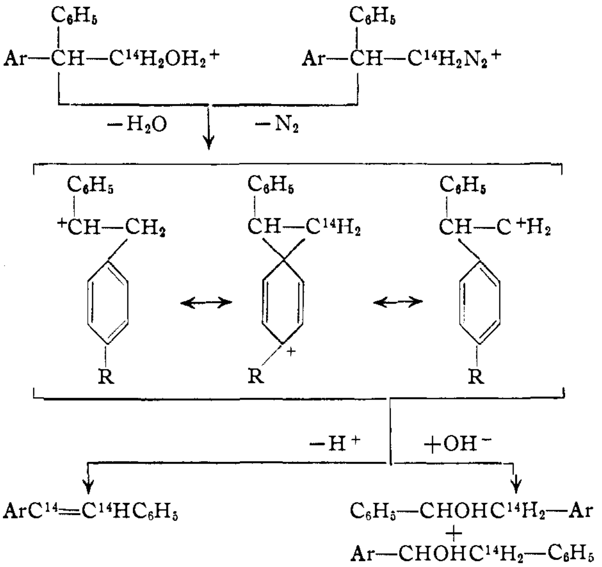
Oxidation—O$_2$.—The remaining crude carbinol mixture (0.61 g.) was refluxed for 30 minutes with phosphorus pentoxide in benzene (30 ml.). The solvent was then decanted, chased with benzene, and evaporated. The residual pale yellow crystalline solid (m.p. 217°) was recrystallized from benzene–hexane to give 0.35 g. of white lustrous plates, m.p. 222°. This crystalline product was oxidized as above. The yield of recrystallized *p*-phenylbenzoic acid, m.p. 225°, was 70–80 mg.

Discussion

A comparison of the data reported here with the results of the diarylethanol rearrangement (see Table IV) reveals the striking contrast in the migration ratios observed under these different conditions. It seems possible that the selectivity in migrations such as these is closely related to the selective participation of the aryl groups in the formation of the carbonium ion transition state (in the first paper[3] on this subject will be found literature citations and discussion supporting this concept). If this is the case, then the difference in selectivity observed in these two reactions is probably related to the relative ease with which the functional group ($-OH_2^+$ or $-N_2^+$)[6] is displaced from the molecule. The $-N_2^-$ group apparently departs with great facility (in which the stability of molecular nitrogen is the driving force) and without participation by the adjacent aryl groups. Since it is expelled without serious energy drain on the rest of the molecule, it leaves a relatively high energy carbonium ion, which then attacks the migrating groups on a nearly statistical basis, except when the point of attack is extremely rich in electrons as is apparently the case with the *p*-anisyl group. Even here, however, the selectivity between this and phenyl is greatly reduced from that observed in the carbinol rearrangement.

TABLE IV

Series (R)	% of substituted phenyl group migrating: Carbinol (II) rearran.	Amine (I) rearran.
p-Methyl	66	47
m-Methyl	61	48
p-Phenyl	57	50
p-Methoxy	96	59



These considerations, however, depend upon the assumption that these amines react with nitrous acid *via* a mechanism similar to that found in other aliphatic amines[5]—*i.e.*, through a carbonium ion intermediate. If, however, they react with nitrous acid by an entirely different mechanism, then some other explanation must be advanced for the lack of selectivity observed.[7]

In the hope of casting additional light upon the mechanism of the amine rearrangements discussed in this paper, work is in progress in this Laboratory to compare the rearrangements of carbon-14 labeled diaryldiazoethanes with the rearrangements, under similar conditions, of the corresponding diarylethylamines.

Acknowledgment.—The authors wish to express their gratitude to Professors John D. Roberts, Nathan Kornblum and Walter M. Lauer for their friendly interest in this problem, and for the many valuable discussions by which they helped us. Thanks are also owing to Dr. Clair J. Collins for his interest in and support of this work.

OAK RIDGE, TENN.

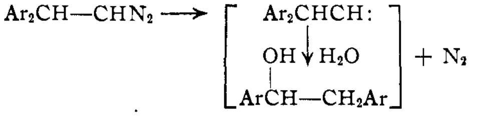
---

[6] The grouping, $-N_2^+$ is the probable intermediate in the reaction of aliphatic amines with nitrous acid. *Cf.* (a) E. R. Alexander, "Principles of Ionic Organic Reactions," John Wiley and Sons, Inc., New York, N. Y., 1950, p. 49; and also (b) M. J. S. Dewar, "The Electronic Theory of Organic Chemistry," Clarendon Press, Oxford, England, 1949, p. 210.

[7] Such an alternate mechanism has indeed been suggested by Hellerman, *et al.*,[3] (*cf.* also later papers: THIS JOURNAL, **57**, 139 (1935); **68**, 819 (1946)) who proposed that the reaction of diphenylethylamine proceeded through a diazohydrocarbon intermediate

$$Ar_2CH-CH_2-NH_2 + HNO_2 \longrightarrow Ar_2CH-CH_2-N_2^+OH^-$$

$$Ar_2CH-CH_2-N_2^+OH^- \longrightarrow Ar_2CH-CHN_2 + H_2O$$



$$Ar_2CH-CHN_2 \longrightarrow \left[\begin{array}{c} Ar_2CHCH: \\ OH \downarrow H_2O \\ ArCH-CH_2Ar \end{array}\right] + N_2$$

Hellerman supported this theory by the observations that diphenyldiazoethane underwent rearrangement at the same temperature when heated with dilute acid to give stilbene; and that triphenyldiazoethane rearranged to triphenylethylene in the presence of warm water, dilute acids, copper powder or iodine. Dewar says that substituted methylamines with powerful $+E$ or $+I$ substituents can give stable diazohydrocarbons when treated with nitrous acid (Dewar, ref. 5b, p. 182). Examples of such amines are ω-aminoacetophenone, and trifluoroethylamine. The substituted benzhydryl group, involved in the subject of the present study, would probably not be sufficiently electronegative to promote the formation of a stable diazohydrocarbon; but it might possibly be sufficiently electronegative to promote the existence of such a diazo compound as a transient intermediate in preference to a transient diazonium ion as intermediate. The data in the literature are insufficient for a reasonable prediction.