

ospheres and a temperature of 50° until absorption of hydrogen stopped. The catalyst was removed by filtration and the solvent distilled from the filtrate in vacuum. The residue was recrystallized twice from benzene. The yield of pure 1,3-dimethyl barbituric acid, m. p. 122–123°, was 39 g. Concentration of the mother liquors gave an additional 8.3 g. of pure material; total yield 47.3 g. (90%). The reduction is exothermic, and will go to completion without heating. It is completed more rapidly (in four to ten hours) if the temperature is maintained at about 50°.

Platinum may also be used as a catalyst for the reduction, but is less convenient because the acetone used as a solvent is also partly reduced, and absorption of hydrogen continues after the dehalogenation is complete.

1,3-Dimethyl barbituric acid was also prepared from ethyl malonate and *sym*-dimethyl urea in the presence of alcoholic sodium ethoxide in 37% yield. The most convenient preparation is the condensation of malonic acid with dimethyl urea described by Biltz and Wittek.<sup>5</sup>

**Pharmacological Data.**—We are indebted to Dr. Paul A. Mattis and Mr. Albert Latven of the Medical Research Division of Sharp and Dohme, Inc., for the pharmacological testing of the 1,3-dimethyl-5-alkyl barbituric acids. The results are summarized in Table II. All of the compounds except the 5-isoamyl, phenyl, and cyclohexyl derivatives produced hypersensitivity in mice, as evidenced by tremors or convulsions which occurred when the animals were touched. The isoamyl and phenyl derivatives induced a lethargic condition in the mice, while the cyclohexyl compound produced no noteworthy symptoms other than typical barbiturate ataxia. Only the 1-methylbutyl and cyclohexyl compounds produced narcosis from which the animals

recovered, and the anesthetic doses of these two compounds closely approximated the lethal doses. It may thus be concluded that barbiturates must be disubstituted in the 5-position in order to possess distinct hypnotic properties, irrespective of substitution on the nitrogen atoms in the 1 and 3-positions.

TABLE II

1,3-DIMETHYL-5-ALKYL BARBITURIC ACIDS. RESULTS OF PHARMACOLOGICAL TESTS IN WHITE MICE<sup>a</sup>

5-Alkyl group	AD 50, mg./kg.	LD 50, mg./kg.
Methyl		3500
Ethyl		1600
Isopropyl		1800
Butyl		1000
<i>s</i> -Butyl		1000
Isoamyl		525
1-Methylbutyl	400	450
Cyclohexyl	425	525
Benzyl		1000
Phenyl		3000

<sup>a</sup> The method of testing and the meaning of symbols are described in THIS JOURNAL, 61, 96 (1939).

### Summary

Methods for preparing 1,3-dimethyl-5-alkyl barbituric acids have been investigated, and ten such compounds have been prepared. Their pharmacological behavior has been studied.

Practical methods have been developed for the sequence of reactions: caffeine → tetramethyl alloxantine → 1,3-dimethyl 5,5-dichlorobarbituric acid → 1,3-dimethyl barbituric acid.

BRYN MAWR, PENNSYLVANIA RECEIVED AUGUST 6, 1940

[CONTRIBUTION FROM THE GEORGE HERBERT JONES LABORATORY, UNIVERSITY OF CHICAGO]

## Hydrogen Exchange Reactions of Aromatic Tertiary Amines

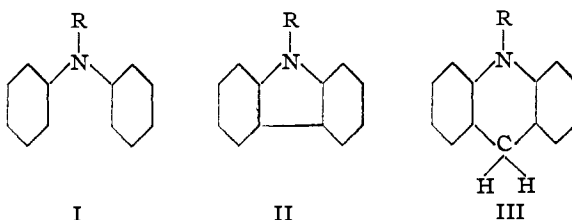
BY WELDON G. BROWN AND NICHOLAS J. LETANG

It was shown previously<sup>1</sup> that the acid catalyzed exchange of the ortho and para hydrogen atoms in aromatic tertiary amines is in general more or less suppressed by a substituent in one of the ortho positions. This was interpreted as primarily a steric effect and it was predicted on the same grounds that the reactivity of 1-dimethylaminonaphthalene in hydrogen exchange would be adversely affected by substituents in the 8 position. Such effects have now been observed for three substances of this type.

Further studies of the exchange reactions of

(1) Brown, Widiger and Letang, THIS JOURNAL, 61, 2597 (1939).

heterocyclic tertiary amines have furnished results in which the role of the steric factor is not clear. Whereas previously the activating effect of an amino nitrogen on the ortho and para hydrogen atoms was found to be greatly increased



R = methyl, phenyl

when the nitrogen atom forms part of a fused five or six membered ring (N-methylindoline, N-methyltetrahydroquinoline), a comparison of I with types II and III has shown an opposite result of ring closure.

### Experimental

**Procedure.**—The essential features of the procedure for the preparation and analysis of reaction mixtures with deuterio-alcohol have been described previously.<sup>2,3</sup> To guard against errors due to isotopic fractionation,<sup>4</sup> all distillations of alcohol and of the water of combustion were carried out at atmospheric pressure. For each substance control determinations (no catalyst added) were carried through. These showed a small and constant decrease in deuterium concentration due to isotopic fractionation and the results obtained subsequently were corrected for this effect.

The materials used were prepared by methods described in the literature, except as noted below.

**8-Nitro-1-dimethylaminonaphthalene.**—8-Nitro-1-naphthylamine was prepared in 16% yield by the nitration of 1-naphthylphthalimide.<sup>5</sup> Methylation with methyl sulfate produced a highly impure product which was first purified by the acetic anhydride method, then by recrystallization from alcohol, and finally by fractional sublimation in high vacuum. The pure product formed canary yellow crystals of m. p. 75°.

*Anal.* Calcd. for C<sub>12</sub>H<sub>12</sub>N<sub>2</sub>O<sub>2</sub>: N, 12.96. Found: N, 13.11.

**8-Chloro-1-dimethylaminonaphthalene.**—8-Chloro-1-nitronaphthalene was prepared by the chlorination of 1-nitronaphthalene,<sup>6</sup> and was reduced with stannous chloride and hydrochloric acid to 8-chloro-1-naphthylamine, m. p. 88–89°. Methylation with methyl sulfate, and purification of the product by treatment with acetic anhydride, yielded 8-chloro-1-dimethylaminonaphthalene, b. p. 111–112° (4 mm.); *n*<sub>D</sub><sup>20</sup> 1.6420.

*Anal.* Calcd. for C<sub>12</sub>H<sub>12</sub>NCl: Cl, 17.27. Found: Cl, 17.43.

**1,8-Bis-dimethylaminonaphthalene.**—The reduction of 1,8-dinitronaphthalene with stannous chloride and hydrochloric acid yielded 1,8-diaminonaphthalene which was methylated using 5 moles of methyl sulfate and the product was purified by treatment with acetic anhydride, b. p. 144–145° (4 mm.).

*Anal.* Calcd. for C<sub>14</sub>H<sub>18</sub>N<sub>2</sub>: N, 13.08. Found: N, 12.92.

**1,5-Bis-dimethylaminonaphthalene.**—1,5-Dinitronaphthalene was reduced quantitatively with hydrogen using the Adams platinum catalyst. Methylation with methyl sulfate yielded a product which was refluxed with acetic anhydride for two hours, and then recrystallized from alcohol; light brown crystals, m. p. 90.5°.

*Anal.* Calcd. for C<sub>14</sub>H<sub>18</sub>N<sub>2</sub>: N, 13.08. Found: N, 12.98.

(2) Kharasch, Brown and McNab, *J. Org. Chem.*, **2**, 36 (1937).

(3) Brown, Kharasch and Sprowls, *ibid.*, **4**, 442 (1939).

(4) Widiger and Brown, *THIS JOURNAL*, **61**, 2453 (1939).

(5) Hodgson and Cook, *J. Chem. Soc.*, 1844 (1936).

(6) Ferrero and Cañisch, *Helv. Chim. Acta*, **11**, 806 (1928).

**N-Methylacridane.**—This was prepared from methylacridinium iodide by the Decker reaction,<sup>7</sup> and also by the reduction of N-methylacridone, which is a product of the Decker reaction, with sodium and amyl alcohol.<sup>8</sup> The yields by the two methods are almost quantitative but the latter furnishes a better product. The substance was obtained, after crystallization from alcohol and fractional sublimation in high vacuum, as colorless crystals, m. p. 95°, which rapidly become colored on standing.

**Experimental Results.**—The experimental results for the acid catalyzed exchange reactions are summarized in Tables I, II and III. The analytical data reproduced in these tables refer to the concentration of deuterium in the water obtained by the combustion of the original and the recovered deuterioalcohol. The "exchange number" has been defined previously.<sup>3</sup>

TABLE I  
EXCHANGE REACTIONS OF NAPHTHALENE DERIVATIVES<sup>a</sup>

Compound, -naphthalene	% D <sub>2</sub> O from alcohol		Exchange number
	Initial	Final	
1-Dimethylamino-	2.60	2.06	1.73
8-Nitro-1-dimethylamino-	2.60	2.60	0
8-Chloro-1-dimethylamino-	2.60	2.60	0
1,8-Bis-dimethylamino-	2.60	2.02	1.99
1,5-Bis-dimethylamino-	2.80	1.82	3.52

<sup>a</sup> In these experiments, 5 cc. (0.085 mole) of deuterio-alcohol, 0.0130 mole of compound and 0.020 cc. of sulfuric acid were allowed to react at 115° for 65 hours.

TABLE II  
EXCHANGE REACTIONS OF POLYNUCLEAR AROMATIC AMINES<sup>a</sup>

Compound	Final % D <sub>2</sub> O <sup>b</sup>		Exchange number
N-Methyldiphenylamine, at 80°	2.22		1.76
	1.67		4.48
	1.57		5.18
N-Methylcarbazole, at 80°	2.77		0.10
	2.70		.27
	2.61		.50
N-Methylacridane, at 80°	2.76		.13
	2.64		.44
	2.47		.91
Triphenylamine, at 125°	2.74		.17
	2.64		.43
	2.48		.89
N-Phenylcarbazole, at 125°	2.78		.08
	2.74		.16
	2.69		.29

<sup>a</sup> The reaction mixtures consisted of 5 cc. (0.085 mole) of deuterio-alcohol, 0.0130 mole of compound, and 0.00010 mole of hydrogen chloride. For each compound three results are given; these are for reaction times of one-half, two and six hours. It was established for each compound, by experiments conducted at 115° for fifty hours, that no exchange occurred in the absence of acid.

<sup>b</sup> Initial % D<sub>2</sub>O for all experiments, 2.81.

(7) Pictet and Patry, *Ber.*, **35**, 2534 (1902).

(8) Bergmann, *Ann.*, **483**, 87 (1930).

TABLE III  
LIMITING VALUES OF EXCHANGE NUMBERS<sup>a</sup>

Compound	Exchange number	Active H atoms, theor.
N-Methyldiphenylamine	5.22	6
N-Methylcarbazole	3.38	4
N-Methylacridane	3.41	4
Triphenylamine	7.71	9
N-Phenylcarbazole	5.93	7

<sup>a</sup> These were determined by experiments in which mixtures of 5 cc. of deuterioalcohol, 0.0130 mole of compound, and 0.068 g. of sulfuric acid were allowed to react at 115° for fifty hours. Under these conditions the exchange reactions in each case reached virtual equilibrium. The theoretical number of active hydrogen atoms is based on the assumption that only hydrogen atoms ortho or para to a nitrogen atom are active.

N-Methylacridane was also investigated with regard to a base catalyzed hydrogen exchange reaction. The following experiment is typical. A mixture of 1.95 g. of N-methylacridane, 5 cc. (0.085 mole) of deuterioalcohol, and 0.0020 g. of sodium hydroxide was heated in an evacuated sealed tube at 110° for ninety-five hours. The original deuterioalcohol on combustion yielded 2.80% D<sub>2</sub>O, the recovered alcohol yielded 2.56% D<sub>2</sub>O. The decrease corresponds to an exchange of 0.79 hydrogen atom. In the absence of acid and base no exchange was observed.

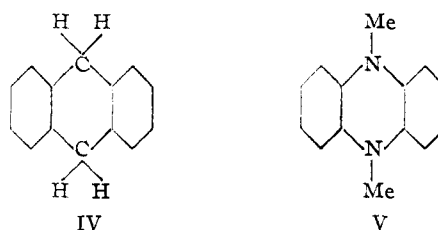
### Discussion

The results for 1-dimethylaminonaphthalene and peri substituted derivatives (Table I) show decisively the loss of reactivity accompanying this type of substitution. Bearing in mind that the limiting value for the exchange number, according to our previous results (*cf.* also Table III), is about 15% less than the actual number of hydrogen atoms reacting, it will be noted that the reaction of 1-dimethylaminonaphthalene is practically at equilibrium while there has been no measurable reaction of the peri nitro and chloro derivatives. The mutual hindrance of two dimethylamino groups is seen in the lower rate of reaction of the 1,8 compound (60% complete for the exchange of four hydrogen atoms for the conditions given) as compared with the 1,5 compound (complete exchange for four hydrogens). These results lie within the framework of the theory of steric effects previously outlined.<sup>1,3</sup> Supporting evidence based on reactivity in other types of substitution reactions appears to be not yet available, but doubtless the "peri" effect will prove to be as characteristic as is the "ortho" effect.

For the variations in exchange reactivity in the series of diphenylamine and carbazole derivatives, the steric factor is evidently subordinate. The lower reactivity of carbazole derivatives<sup>9</sup> notwithstanding the favorable planar structure, is probably a consequence of the additional resonance stabilization of the pyrrole ring which would have to be overcome in the formation of a quinonoid intermediate.

The hydrogen exchange of N-methylacridine is subject to catalysis by both acids and bases. The active hydrogens in the base catalyzed reaction are doubtless the methylene hydrogen atoms, and the rate of the reaction is of the same order of magnitude (actually three times greater for identical experimental conditions) as that previously observed for xanthene<sup>10</sup> which is structurally analogous. The acid-catalyzed reaction involves the four hydrogen atoms which are ortho or para to the nitrogen atom as is shown by the observed limiting value for the exchange number (Table III).

The rate of the acid catalyzed reaction is very much smaller than the rate for N-methyldiphenylamine. In the absence of any conceivable electronic effects which could account for it, this result points to the conclusion that N-methylacridane does not have a planar structure. N-Methylacridane (III, R = Me) resembles dihydroanthracene (IV) and N,N'-dimethyldihydrophenazine (V), for both of which a structure folded



about a central axis is considered probable by Campbell and co-workers<sup>11</sup> who have summarized the experimental evidence. A similarly folded structure for N-methylacridane might account for our results.<sup>12</sup>

(9) Similar differences are to be seen in the condensation reactions of N-diphenylamine and N-methylcarbazole with aldehydes (Sen and Sen, *J. Indian Chem. Soc.*, **7**, 965 (1930)), as well as in ordinary substitution reactions, the former substance being much more reactive.

(10) Heuse, Master's Dissertation, University of Chicago, 1937.

(11) Campbell, LeFèvre, LeFèvre and Turner, *J. Chem. Soc.*, 404 (1938).

(12) Strictly speaking, the question in our case revolves about the configuration of the quinonoid amine salt (or cation) and this, whether folded or planar, would be a strained structure.

### Summary

1. The acid catalyzed hydrogen exchange reaction of 1-dimethylaminonaphthalene is greatly retarded by a chloro or nitro group in the 8 position. 1,8-Bis-dimethylaminonaphthalene exchanges hydrogen more slowly than the 1,5 isomer. These observations support a mechanism previously advanced.

2. Carbazole and acridane derivatives are less reactive in hydrogen exchange than the corresponding diphenylamine derivatives. The role of steric factors is discussed.

3. N-Methylacridane also exhibits a base catalyzed exchange reaction which is thought to involve the methylene hydrogen atoms.

CHICAGO, ILLINOIS

RECEIVED NOVEMBER 25, 1940

[CONTRIBUTION FROM THE PHYSICAL RESEARCH LABORATORY, B. F. GOODRICH COMPANY]

## Dielectric Properties of Plasticized Polyvinyl Chloride

BY J. M. DAVIES, R. F. MILLER AND W. F. BUSSE

### I. Introduction

Plasticized  $\gamma$ -polyvinyl chloride<sup>1</sup> (Koroseal) has physical properties such as toughness, flexibility, oil-resistance, non-inflammability, as well as high electrical resistance, which make it very valuable as an insulator and a protecting sheath for electrical conductors.<sup>2,3,4</sup> It is also important from the scientific standpoint because changes in each of three variables—frequency of the current, temperature and ratio of  $\gamma$ -polyvinyl chloride to plasticizer in the sample—can be made to produce roughly equivalent changes in dielectric properties. This offers the possibility of using this system to gain more information about the general theories of energy loss in dielectrics, and, perhaps, also of using the available theories of dielectric loss to get information about the molecular structure of the  $\gamma$ -polyvinyl chloride-plasticizer systems.

In general, the dielectric constant of these systems is about 3 at sufficiently low temperatures, or low plasticizer contents, or high frequencies. If the temperature or the plasticizer content is raised, or the frequency lowered enough, the dielectric constant increases to a high value of 8 to 12, depending on the kind and amount of plasticizer. In the region where the dielectric constant changes most rapidly, the loss factor reaches a maximum, as required by all theories of dielectric loss.

Previous work<sup>5</sup> on the dielectric properties of

(1) Semon, U. S. Patent 1,929,453, October 10 (1933).

(2) Brous and Semon, *Ind. Eng. Chem.*, **27**, 667 (1935).

(3) Schoenfeld, *Trans. Am. Inst. Chem. Eng.*, **35**, 447 (1939).

(4) Schoenfeld, Browne and Brous, *Ind. Eng. Chem.*, **31**, 964 (1939).

(5) Davies and Busse, "Conference on Electrical Insulation," National Research Council, Cambridge, Mass., meeting, 1939 Annual Report, p. 30.

samples having a wide range of plasticizer (tricresyl phosphate) content at a wide range of temperatures, suggested that there might be a relation between the dielectric properties and the mechanical flexibility of the samples having various amounts of any one plasticizer. By varying the plasticizer content at any one temperature, or varying the temperature at any one plasticizer content, the hardness can be varied over a very wide range—from a hard, tough, horny product to one that is soft, flexible and elastic. However, when the samples of different plasticizer contents were compared at the respective temperatures at which each showed its dielectric loss maximum, the hardness of the samples, as measured by a durometer, was found to be roughly the same.

Because the dielectric measurements were made on unstabilized samples, and because the durometer is not an ideal hardness measuring instrument, this work was repeated and extended using stabilized samples, and measuring the hardness in absolute units by a method developed in this Laboratory.<sup>6</sup> In addition, data are presented on the direct current resistance of these systems, and on the dielectric properties of some samples with plasticizers other than tricresyl phosphate. Some more fundamental interpretations of the data are suggested.

II. Preparation of Samples.—Three series of samples were prepared by adding commercial  $\gamma$ -polyvinyl chloride to dimethylthianthrene, tricresyl phosphate, and, in a few cases, dioctyl phthalate, as plasticizers. Samples containing 46%, by volume, dimethylthianthrene were prepared with and without the addition of 0.8%, by volume, of lead silicate as stabilizer. Seven concentrations of tri-

(6) Larrick, Meeting of the Rheology Society, Akron, Ohio, 1937; *Phys. Rev.*, **57**, 358 (1940). In this reference the equation is misprinted.