

centration up to 0.8 *M*, the limit of the present experiments. It is therefore improbable that the reaction is stoichiometric. It is suggested that hydrogen bond formation between salicylate and side chains of the protein molecule may account for a part of the heat of reaction.

The heats of reaction are compared with

changes in the absorption spectra of carboxyhemoglobin and methemoglobin in salicylate and benzoate. It was found that the two effects are unrelated. Colorimetric estimation of the extent of reaction of salicylate with methemoglobin is therefore unreliable.

CAMBRIDGE, MASS.

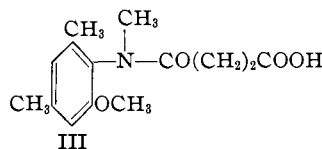
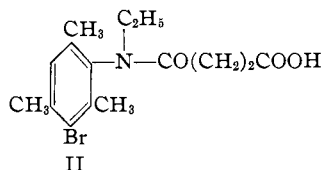
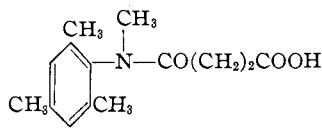
RECEIVED MARCH 10, 1942

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

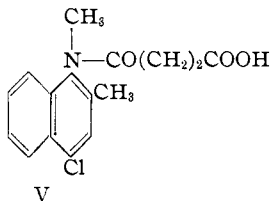
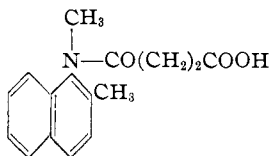
Restricted Rotation in Aryl Amines. III. Preparation and Resolution of *N*-Succinyl-1-methylamino-2-methylnaphthalene and *N*-Succinyl-1-methylamino-4-chloro-2-methylnaphthalene¹

BY ROGER ADAMS AND A. A. ALBERT²

Restricted rotation in simple aromatic amines has been demonstrated by preparation and resolution of three compounds shown in I, II, and III.^{1a,1b}



Two analogs in the naphthalene series have now been prepared and are shown in IV and V.



The half-life periods of these five compounds determined in boiling *n*-butanol are shown in the table.

(1) For previous papers see (a) Adams and Stewart, *THIS JOURNAL*, **63**, 2859 (1941); (b) Adams and Dankert, *ibid.*, **62**, 2191 (1940).

(2) An abstract of a thesis submitted in partial fulfillment of the requirement for the degree of Doctor of Philosophy in Chemistry, Eastman Kodak Fellow, 1941-42.

HALF-LIFE PERIODS OF RESTRICTED ARYL AMINES IN BOILING *n*-BUTANOL

Compound	Half-life in hours
I	9.0
II	28.0
III ^a	2.7
IV	5.7
V	4.1

^a Taken in boiling methyl acetate, b. p. 56°.

A comparison of the values of IV and V with I (compare also with II) indicates that the interference of a —CH= group of the aromatic nucleus is less than that of a CH₃— group. This agrees with the observations in parallel compounds with restricted rotation in the substituted aryl olefin series.³ It is also of interest to note that the 4-chloro substituent in compound V reduces the half-life of the product to 20% less than that of the corresponding unchlorinated derivative (IV).

Compound IV was synthesized by the general procedure used in the benzene series. 1-Amino-2-methylnaphthalene was *N*-methylated and then succinylated. Compound V was formed from 1-nitro-2-methylnaphthalene by reduction with stannous chloride in ethanolic hydrochloric acid to 1-amino-2-methyl-4-chloronaphthalene followed by *N*-methylation and succinylation.

The 1-ethylamino-2-methylnaphthalene was also synthesized and succinylated. The product, however, did not form salts suitable in properties for resolution.

Experimental

1-Nitro-2-methylnaphthalene.—This was prepared by the nitration of 2-methylnaphthalene in glacial acetic

(3) Adams and Miller, *THIS JOURNAL*, **62**, 53 (1940); Adams, Anderson and Miller, *ibid.*, **63**, 1589 (1941); Adams and Binder, *ibid.*, **63**, 2773 (1941).

acid by the method of Fierz-David and Mannhart.⁴

1-Amino-2-methylnaphthalene.—A suspension of 25 g. of 1-nitro-2-methylnaphthalene and 5 g. of Raney nickel catalyst in 75 cc. of 95% ethanol was shaken under hydrogen at room temperature and 1–3 atm. pressure until the theoretical amount of hydrogen had been absorbed. The catalyst was filtered off and the filtrate distilled. The product had a b. p. of 111–113° (0.3 mm.); m. p. 31° (cor.); yield, 19.5 g. (93%). Fierz-David and Mannhart⁴ report the same melting point.

1-Methylamino-2-methylnaphthalene.—A mixture of 20 g. of 1-amino-2-methylnaphthalene, 60 cc. of water, and 16 g. of dimethyl sulfate was shaken for thirty minutes at room temperature. The resulting homogeneous solution was made alkaline with aqueous ammonia and extracted with ether. The residue, after distillation of the ether, was shaken for six hours with 13 g. of benzaldehyde-sodium bisulfite compound and 35 cc. of water.⁵ The mixture was then filtered and the residue washed with ether. The ether layer of the filtrate was separated and the aqueous layer extracted again with ether. The ether extracts and washings were treated with saturated sodium bisulfite solution and washed with water. After drying over solid potassium hydroxide, the ether was removed and the product distilled; pale yellow oil, b. p. 106–108° (0.3 mm.); n_{20}^{20} 1.6321; d_{20}^{20} 1.059; yield, 17.6 g. (81%).

Anal. Calcd. for $C_{12}H_{13}N$: C, 84.16; H, 7.66; N, 8.18. Found: C, 83.89; H, 7.74; N, 8.29.

N-Succinyl-1-methylamino-2-methylnaphthalene.—To a solution of 5.9 g. of succinic anhydride in 50 cc. of dry benzene was added 10 g. of 1-methylamino-2-methylnaphthalene and a drop of concentrated sulfuric acid. The solution was refluxed for eight hours, diluted with 50 cc. of ether, and extracted thoroughly with 5% aqueous sodium hydroxide. The alkaline extract was washed with ether and acidified with hydrochloric acid. The product separated as an oil which crystallized on standing. The product was taken up in methanol and treated with Darco. It was then recrystallized from benzene-petroleum ether (b. p. 60–110°) mixture; white crystals, m. p. 109° (cor.); yield, 13.5 g. (80%).

Anal. Calcd. for $C_{16}H_{17}NO_3$: C, 70.82; H, 6.31; N, 5.16. Found: C, 70.59; H, 6.13; N, 5.01.

Resolution of N-Succinyl-1-methylamino-2-methylnaphthalene.—A solution of 5.0 g. of N-succinyl-1-methylamino-2-methylnaphthalene and 6.0 g. of quinine in 50 cc. of boiling ethyl acetate was filtered, cooled to room temperature, and concentrated to 30 cc. by means of a gentle air stream. After standing at room temperature in a loosely stoppered flask for several days, the solution had concentrated to 25 cc. and a small crop of salt had crystallized. The crystals were collected and washed free of the sirupy mother liquor with ethyl acetate. The dry product weighed 1.81 g. The combined mother liquor and washings were concentrated to 20 cc. by air stream. After standing for several days, it yielded a second crop of salt amounting to 0.82 g. A third crop, 2.11 g., was obtained by repetition of this procedure. These three fractions were combined (4.74 g.), dissolved in ethyl acetate, and the

solvent allowed to evaporate slowly. Recrystallization in this manner to constant rotation gave white feathery crystals, m. p. 129.5° (cor.).

Anal. (lBA) Calcd. for $C_{16}H_{17}NO_3 \cdot C_{20}H_{24}N_2O_2 \cdot \frac{1}{2}C_6H_6O_2$: C, 71.32; H, 7.10; N, 6.57. Found: C, 70.91; H, 7.20; N, 6.93.

Rotation. (lBA) 0.050 g. made up to 25 cc. with absolute ethanol at 27° gave $\alpha_D -0.51^\circ$; *l*, 2; $[\alpha]^{27}_D -128^\circ$.

By continuing to allow the original solution to stand for several days at a volume of about 20 cc., two more successive crops of salt were obtained weighing 1.36 g. and 1.08 g., respectively. These were discarded. The mother liquor was concentrated to 15 cc. in an air stream and placed in a refrigerator; 0.73 g. of salt was obtained. Concentration of the mother liquor to 10 cc. and refrigeration yielded an additional 0.81 g. of salt. These two fractions were combined (1.54 g.), and dissolved in ethyl acetate. An equal volume of petroleum ether (b. p. 60–110°) was added and the solvent allowed to evaporate. Recrystallization thrice in this manner gave white crystals, m. p. 99–100° (cor.).

Rotation. (lBdA salt) 0.057 g. made up to 25 cc. with absolute ethanol at 27° gave $\alpha_D -0.26^\circ$; *l*, 2; $[\alpha]^{27}_D -57^\circ$.

No additional crystalline material could be obtained from the original solution. The dry residue amounted to 2.10 g.; $[\alpha]^{27}_D -69^\circ$.

d- and l-N-Succinyl-1-methylamino-2-methylnaphthalene.—The salts were decomposed by stirring with 20% hydrochloric acid at 0° for several hours until the product, which at first was a gum, appeared crystalline. The material was filtered and the digestion with hydrochloric acid repeated as many times as was necessary to give a filtrate free of alkaloid as shown by Polin's reagent. The acids were recrystallized from benzene-petroleum ether (b. p. 60–110°) mixture. The rotations were unchanged by the recrystallization.

The *l*-acid was obtained from the less-soluble salt in white crystals, m. p. 108° (cor.).

Anal. (*l*-acid) Calcd. for $C_{16}H_{17}NO_3$: C, 70.82; H, 6.31. Found: C, 70.78; H, 6.30. *Rotation.* (*l*-acid) 0.050 g. made up to 25 cc. with absolute ethanol at 27° gave $\alpha_D -0.30^\circ$; *l*, 2; $[\alpha]^{27}_D -75^\circ$.

Decomposition of the more-soluble salt gave white crystals, m. p. 107–108° (cor.).

Rotation. (*d*-acid) 0.023 g. made up to 10 cc. with absolute ethanol at 27° gave $\alpha_D +0.17^\circ$; *l*, 1; $[\alpha]^{27}_D +74^\circ$.

Racemization of l-N-Succinyl-1-methylamino-2-methylnaphthalene.—In boiling ethanol, no change in rotation occurred in twelve hours.

Racemization occurred in boiling *n*-butanol. The experiment was carried out in a polarimeter constructed from Pyrex tubing (25 mm. outside diameter, 100 mm. internal length) and fitted at the center to a reflux condenser by means of a ground-glass joint.⁶ A solution of 0.110 g. of the *l*-acid was made up to 25 cc. with *n*-butanol, transferred to the polarimeter tube, and the rotation observed. Several small carborundum boiling chips were added and the polarimeter tube with its contents was weighed. The polarimeter tube was then placed on a hot-plate and the

(4) Fierz-David and Mannhart, *Helv. Chim. Acta*, **20**, 1024 (1937).

(5) Ferry and Buck, *This Journal*, **58**, 2444 (1936).

(6) This apparatus was designed and constructed by Dr. L. O. Binder, Jr.

solution concentrated to 15 cc. by boiling without reflux. The reflux condenser was attached and the solution boiled for one and one-half hours. The solution was cooled rapidly, made up to the previously determined weight with *n*-butanol, and the rotation observed. By repetition of this process, the following α_D values were obtained: at the start, -0.33° ; after one and one-half hours, -0.27° ; after four hours, -0.20° ; after seven and one-half hours, -0.13° ; after thirteen hours, -0.07° ; after twenty-three hours, -0.02° . Calculated for a reversible unimolecular reaction, the half-life was five and seven-tenths hours. Experiments carried out in *n*-butanol with the usual technique^{1a} gave an average half-life of five and one-half hours.

1-Amino-4-chloro-2-methylnaphthalene.—A mixture of 56.1 g. of 1-nitro-2-methylnaphthalene, 200 cc. of 95% ethanol, and 300 cc. of concentrated hydrochloric acid was refluxed and stirred while a solution of 203 g. of stannous chloride dihydrate in 400 cc. of concentrated hydrochloric acid was added over a period of five hours.^{4,7} Refluxing and stirring was continued for one hour longer. The mixture was cooled and the precipitated tin-amine complex collected and washed with ethanol. The complex was suspended in water and treated with 800 cc. of 50% aqueous sodium hydroxide. The amine was extracted with benzene. The extract was washed with 10% aqueous sodium hydroxide and then with water. The extract was distilled and the fraction, b. p. 138–145° (0.5 mm.), which solidified in the receiver, was collected. Recrystallization from petroleum ether (b. p. 60–110°) gave grayish needles, m. p. 65° (cor.); yield, 41 g. (72%). Lesser^{7a} reports the same melting point.

1-Methylamino-4-chloro-2-methylnaphthalene.—Following the procedure used for the preparation of 1-methylamino-2-methylnaphthalene, 20 g. of 1-amino-4-chloro-2-methylnaphthalene gave 14.6 g. (70%) of 1-methylamino-4-chloro-2-methylnaphthalene; b. p. 136–137° (0.5 mm.); m. p. 30° (cor.).

Anal. Calcd. for $C_{12}H_{12}ClN$: C, 70.07; H, 5.87. Found: C, 69.91; H, 5.17.

N-Succinyl-1-methylamino-4-chloro-2-methylnaphthalene.—Succinylation of 10.3 g. of 1-methylamino-4-chloro-2-methylnaphthalene by the previously described procedure gave 13.4 g. of N-succinyl-1-methylamino-4-chloro-2-methylnaphthalene; white crystals from benzene-petroleum ether (b. p. 60–110°) mixture, m. p. 167.5–168.5° (cor.).

Anal. Calcd. for $C_{16}H_{16}ClNO_2$: C, 62.83; H, 5.28. Found: C, 63.09; H, 5.17.

Resolution of N-Succinyl-1-methylamino-4-chloro-2-methylnaphthalene.—A solution of 6.1 g. of N-succinyl-1-methylamino-4-chloro-2-methylnaphthalene and 6.7 g. of quinine in 100 cc. of boiling ethyl acetate was filtered, cooled to room temperature, and concentrated to 35 cc. by means of a gentle air stream. The salts in this resolution showed the same crystallization characteristics as did those of N-succinyl-1-methylamino-2-methylnaphthalene and the same procedure was followed. At 35 cc., 0.59 g. of salt crystallized out; at 30 cc., 0.90 g.; at 25 cc., 1.15 g.; at 20 cc., two successive crops of 0.33 g. and 1.14 g. These

five fractions were combined (4.11 g.) and recrystallized from ethyl acetate to constant rotation. White feathery crystals were obtained; m. p. 117–119° (cor.).

Anal. (lBdA) Calcd. for $C_{16}H_{16}ClNO_2 \cdot C_{20}H_{24}N_2O_2 \cdot \frac{1}{2} C_4H_8O_2$: C, 67.68; H, 6.58; N, 6.23. Found: C, 67.66; H, 6.59; N, 6.45. *Rotation.* (lBdA) 0.047 g. made up to 25 cc. with absolute ethanol at 30° gave $\alpha_D -0.21^\circ$; *l*, 2; $[\alpha]^{30D} -56^\circ$.

Upon concentration of the original solution to 15 cc., 3.67 g. of crystalline salt was obtained and at 12 cc., another crop of 1.39 g. crystallized. These two fractions were discarded. At 10 cc., 0.75 g. of salt crystallized and by allowing the mother liquor to remain in a refrigerator for several days, another 0.53 g. of salt was obtained. These two crops were combined (1.28 g.). Recrystallization failed to change the rotation of this fraction; white crystals; m. p. 111–113° (cor.).

Rotation. (lBlA) 0.052 g. made up to 25 cc. with absolute ethanol at 30° gave $\alpha_D -0.38^\circ$; *l*, 2; $[\alpha]^{30D} -91^\circ$.

No additional crystalline material could be obtained from the original solution; weight of dry residue, 1.96 g.

***d*- and *l*-N-Succinyl-1-methylamino-4-chloro-2-methylnaphthalene.**—The salts were decomposed by digestion with 20% hydrochloric acid as in the previous case. The *d*-acid was recrystallized from benzene-petroleum ether (b. p. 60–110°) mixture without effecting any change in rotation; white crystals; m. p., 115.5–116° (cor.).

Anal. (*d*-acid) Calcd. for $C_{16}H_{16}ClNO_2$: C, 62.83; H, 5.28. Found: C, 63.09; H, 5.40. *Rotation.* (*d*-acid) 0.067 g. made up to 25 cc. with absolute ethanol at 30° gave $\alpha_D +0.30^\circ$; *l*, 2; $[\alpha]^{30D} +56^\circ$.

The *l*-acid obtained from the more-soluble salt was apparently not entirely pure; white crystals, softening at 116° (cor.) but not melting completely until a temperature of 163–167° was reached.

Rotation. (*l*-acid) 0.045 g. made up to 25 cc. with absolute ethanol at 30° gave $\alpha_D -0.13^\circ$; *l*, 2; $[\alpha]^{30D} -36^\circ$.

Racemization of *d*-N-Succinyl-1-methylamino-4-chloro-2-methylnaphthalene.—Racemization was carried out in boiling *n*-butanol in the apparatus described under the racemization of N-succinyl-1-methylamino-2-methylnaphthalene. A solution of 0.149 g. of the *d*-acid made up to 25 cc. with *n*-butanol gave the following α_D values: at the start, $+0.33^\circ$; after one and one-half hours, $+0.26^\circ$; after three hours, $+0.20^\circ$; after five and one-half hours, $+0.13^\circ$; after eight and one-half hours, $+0.08^\circ$; after twelve and one-half hours, $+0.04^\circ$. Calculated for a reversible unimolecular reaction, the half-life was four and one-tenth hours. An experiment carried out by the usual technique^{1a} gave a half-life of four and three-tenth hours.

1-Ethylamino-2-methylnaphthalene.—A mixture of 18.5 g. of 1-amino-2-methylnaphthalene, 15.4 g. of diethyl sulfate, and 60 cc. of water was shaken until a homogeneous solution was obtained (about twenty hours). The reaction mixture was worked up as for the methylamino compound. The product was a yellow oil, b. p. 108–109° (0.3 mm.); n_D^{20} 1.6148; d_4^{20} 1.032; yield 16.5 g. (75.6%).

Anal. Calcd. for $C_{13}H_{13}N$: C, 84.27; H, 8.17. Found: C, 84.56; H, 7.95.

N-Succinyl-1-ethylamino-2-methylnaphthalene.—From 10 g. of 1-ethylamino-2-methylnaphthalene and 5.4 g. of

(7) (a) Lesser, *Ann.*, **402**, 34 (1914); (b) Blanksma, *Rec. trav. chim.*, **25**, 365 (1906).

succinic anhydride was obtained 12 g. (80%) of N-succinyl-1-ethylamino-2-methylnaphthalene. It was purified from benzene-petroleum ether (b. p. 60–110°) mixture; white crystals, m. p. 123° (cor.).

Anal. Calcd. for $C_{17}H_{19}NO_3$: C, 71.54; H, 6.72. Found: C, 71.67; H, 6.83.

A salt of the racemic acid suitable for resolution could not be found.

Summary

1. N-Succinyl-1-methylamino-2-methylnaphthalene and N-succinyl-1-methylamino-4-chloro-

2-methylnaphthalene have been synthesized and resolved. N-Succinyl-1-ethylamino-2-methylnaphthalene was synthesized but no salts suitable for resolution were found.

2. The half-life periods of the active forms were smaller than those of the corresponding bromomesitylene derivative when determined in boiling *n*-butanol, thus indicating the interference of a $-\text{CH}=\text{}$ group to be less than that of a CH_3- .

URBANA, ILLINOIS

RECEIVED MARCH 14, 1942

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF TEXAS]

The Molal Electrode Potential of the Silver-Silver Chloride Electrode in Ethyl Alcohol-Water Mixtures¹

BY ANDREW PATTERSON² WITH W. A. FELSING

Harned and his co-workers have demonstrated in a number of papers^{3,4} the feasibility of determining the ionization constants of weak acids in water-alcohol solutions. In this Laboratory it was desired to study the effect of the lengthening of the aliphatic chain of the alcohol used in the solvent medium (and of the acid) upon this method of determining the ionization constants of weak acids. In such determinations, the value of the molal electrode potential of the silver-silver chloride electrode in the solvent used is necessary for the calculation of the ionization constant.

These molal electrode potential values are available for ten and twenty per cent. methyl alcohol-water mixtures.⁵ The purpose of this investigation was the determination of the molal electrode potential of the silver-silver chloride electrode in 10 and 20% ethyl alcohol-water mixtures. The method used was essentially that of Harned and Thomas.⁵

Materials Used

Hydrochloric Acid.—Reagent grade stock was purified by repeated distillation in an all-glass still; the final fractions resulting from several distillations were combined and distilled at a constant pressure of 750 mm. corresponding to a concentration of 20.245% hydrogen chloride.⁶ **Ethyl**

Alcohol.—Commercial ethyl alcohol was agitated with silver oxide to remove aldehydes and was dried by refluxing with calcium oxide for about one week. The dried alcohol was distilled through a packed tower one meter long, the middle portions being collected and protected against moisture; immediately before use, the alcohol was further dried by passing in vapor form over heated anhydrous calcium sulfate. **Hydrogen.**—Cylinder hydrogen was passed over heated copper wire to remove the oxygen it might contain. **Solutions.**—Concentrated stock solutions of hydrochloric acid in the desired alcohol-water mixtures were made gravimetrically from the necessary amounts of the purified acid, alcohol, and water, using proportions such as to make the resultant solution approximately one molal in hydrochloric acid. Five hundred gram portions of such stock solutions were prepared; the weight of each constituent was known to within one milligram.

Five-liter quantities of stock alcohol-water mixtures, containing either 10 or 20% ethyl alcohol, were prepared by weight on a balance sensitive to 0.1 g. The alcohol was weighed on a more sensitive balance in order that the weights of alcohol and water would be known to the same comparable degree of accuracy (*i. e.*, to at least one part in 10,000).

Experimental Procedure

The Silver-Silver Chloride Electrodes.—These electrodes were prepared by a method similar to that employed by Keston⁷ in preparing silver-silver bromide electrodes. Platinum spirals were coated with a paste of 10% silver chlorate and 90% silver oxide, both highly purified. The spirals and their coating were then heated in a quartz furnace at 650° for seven minutes. After undergoing an initial aging period, these electrodes proved highly satisfactory. **Hydrogen Electrodes.**—These electrodes consisted of platinized platinum strips one centimeter wide and two and one-half centimeters long. **The Cells.**—The cells were constructed of Pyrex glass in U-shape, equipped

(1) Constructed from a portion of a dissertation presented to the Graduate Faculty of The University of Texas by Andrew Patterson in partial fulfillment of the requirements for the degree of Doctor of Philosophy, June, 1942.

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(3) Harned and Owen, *THIS JOURNAL*, **52**, 5079 (1930).

(4) Harned and Embree, *ibid.*, **57**, 1669 (1935).

(5) Harned and Thomas, *ibid.*, **57**, 1666 (1935).

(6) Fouk and Hollingsworth, *ibid.*, **45**, 1220 (1923).

(7) Keston, *ibid.*, **57**, 1671 (1935).