

0.25 g. of water was burned with oxygen in an ordinary combustion apparatus consisting of a 1.8-cm. Vycor tube, containing cupric oxide and a plug of silver wool, and a macro combustion furnace. Cylinder oxygen was dried by bubbling it through two washing bottles filled with concentrated sulfuric acid. The gas was then passed through a 3-ft. 1.5-in. i.d. tube packed with potassium hydroxide pellets, a plug of glass wool and anhydrous calcium sulfate. The water was collected in a U-tube that was cooled in a Dry Ice-acetone bath. The apparatus was prepared for combustion by passing oxygen through the combustion tube while the latter was heated to dull redness. Solids were introduced in a porcelain boat and liquids were stored in glass ampules. Just before introduction into the furnace the top of the ampule was cut off and the ampule was pushed, tip first, into the tube until it touched the copper oxide packing. Heat transferred to the ampule from the packing was sufficient to produce slow volatilization of the liquid samples allowing burning of liquids with no "flash backs."

Water samples were purified by the method of Keston, Rittenberg and Schoenheimer,<sup>21</sup> which involves refluxing

(21) A. S. Keston, D. Rittenberg and R. Schoenheimer, *J. Biol. Chem.*, **122**, 227 (1937).

with and distillation from potassium permanganate. The purified water was transferred to a clean, dry serum vial equipped with a self-sealing serum stopper.

The falling drop method<sup>22</sup> was used to analyze the water. The falling drop tube was filled with a mixture of bromobenzene and kerosene having a density of 0.9988 at 26.2°, the temperature of the thermostat. A micro pipet constructed by drawing out 0.5-mm. capillary tubing, was used to deliver water samples. Very reproducible rates of fall were obtained, showing that the drop size was uniform. The rate of fall through a marked 20-cm. length was observed with a cathetometer. An empirical calibration curve was established using water samples of known deuterium content.

**Acknowledgments.**—Financial support of this work by Office of Basic Ordnance Research is gratefully acknowledged. Helpful discussions with Professors O. Chapman, C. H. DePuy, G. A. Russell and E. Wenkert are much appreciated.

(22) U. Kirshenbaum, "Physical Properties and Analysis of Heavy Water," McGraw-Hill Book Co., Inc., New York, N. Y., 1951, pp. 324-343.

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## Restricted Rotation in Aryl Amines. XXII. Effect of *meta* Substitution on the Optical Stability of Some N-Benzenesulfonyl-N-carboxymethylmesidines

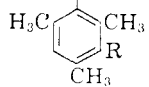
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The half-life of optically active N-benzenesulfonyl-N-carboxymethyl-*t*-butylmesidine was shown to be very short (1.5 hr.) in comparison with the half-lives of the corresponding methyl, ethyl, *n*-propyl and isopropyl derivatives (7.3-11.4 hr.).

The possible inductive and steric influences on the optical stability of 3-substituted N-benzenesulfonyl-N-carboxymethylmesidines have been reported.<sup>1</sup> The influence of field effect alone on the half-lives of such systems has also been studied.<sup>2</sup> More recently, research on 3-substituted mesidine derivatives was extended to a comparison of the stability of N-benzenesulfonyl-N-carboxymethyl-*t*-butylmesidine with the corresponding methylmesidine in order to determine whether the bulky *t*-butyl group<sup>3</sup> might have a buttressing effect in the molecule. It was found, however, that the *t*-butyl derivative exhibits a marked decrease in optical stability (half-life 1.49 hr.) as compared to that of the isoduridine homologs (half-life 7.3 hr.).

The purpose of the present investigation was to determine the optical stability of the 3-ethyl-, 3-isopropyl- and 3-*n*-propylmesidines and to correlate their stabilities with those of the methyl and *t*-butyl homologs. The values of the half-lives of the compounds studied in this investigation as well as of the methyl and *t*-butyl homologs are shown in Table I.

$C_6H_5O_2SNCH_2CO_2H$	R	Half-life, hr.
	CH <sub>3</sub>	7.3 <sup>3</sup>
	C <sub>2</sub> H <sub>5</sub>	9.6
	<i>i</i> -C <sub>3</sub> H <sub>7</sub>	10.6
	<i>n</i> -C <sub>3</sub> H <sub>7</sub>	11.4
	<i>t</i> -C <sub>4</sub> H <sub>9</sub>	1.5 <sup>3</sup>

(1) R. Adams and M. J. Gortatowski, *J. Am. Chem. Soc.*, **79**, 5525 (1957).

(2) R. Adams and K. R. Brower, *ibid.*, **78**, 663 (1956).

(3) R. Adams and J. S. Dix, *ibid.*, **80**, 4579 (1958).

The regular increase of the optical stability in the sequence methyl, ethyl, isopropyl might be due merely to inductive effect but the unexpected value for the *t*-butyl homolog is inexplicable on this basis. In fact, to make certain that no experimental error was involved the *t*-butyl derivative was re-synthesized and the racemization experiment repeated. The value of the half-life found in this investigation (1.6 hr.) agrees closely with the value previously reported (1.5 hr.).<sup>4</sup>

A possible explanation is that the bulky *t*-butyl group pushes the adjacent methyl groups out of the plane of the benzene ring causing reduction of the interference to rotation around the ring-carbon to nitrogen bond and thus shortening the half-life. A Stuart-Briegleb model of the molecule indicates such an interference. Non-bonded interaction may also cause considerable angle distortion.<sup>5</sup> The possibility that a decomposition was being measured in the case of the *t*-butyl derivative rather than a racemization was eliminated by isolation of unchanged racemic product after racemization. Moreover, the racemic *t*-butyl derivative was subjected to very long heating under the conditions of the racemization experiments with no sign of decomposition, even though the corresponding ester by refluxing with dilute sulfuric and acetic acid is

(4) In previous studies on optically active compounds with restricted rotation, activation energies of a series of 2-nitro-6-carboxy-2'-alkoxy biphenyls were measured (C. C. Li and Roger Adams, *J. Am. Chem. Soc.*, **57**, 1565 (1935)). The results indicated that the heat of activation of each member of the series was the same, about 20,000 calories, within experimental error. The racemization half-lives thus appear to have more significance.

(5) R. F. Bryan and J. D. Dimitz, *Helv. Chim. Acta*, **43**, 3 (1960).

converted in essentially quantitative yield to the acid with the *t*-butyl group replaced by hydrogen.

Racemization in presence of two equivalents of pyridine, using the usual solvent and temperature took place at the same rate within the limit of the experimental error.

It seems unlikely that solvation, which might lead to a higher activation energy, would occur in all the alkyl derivatives except the *t*-butyl.

*N*-Benzenesulfonyl-*N*-carboxymethyl-ethyl-, *n*-propyl-, isopropyl- and *t*-butyl-mesidine were synthesized by benzenesulfonation of the corresponding 3-alkylmesidines followed by introduction of the carboxymethyl group by action of ethyl bromoacetate on the sodium salts of the *N*-benzenesulfonyl derivatives in dimethylformamide, and then saponification.

3-Ethyl- and 3-*n*-propyl-mesitylene were prepared by a Clemmensen reduction of 3-acetyl- and 3-propionyl-mesitylene, respectively. They were converted to the 3-ethyl- and *n*-propyl-mesidines by nitration and then reduction of the nitro group. 3-Ethylmesidine was formed in another way involving more steps; nitration of acetylmesitylene, reduction of the nitro group, catalytic hydrogenation of the ketonic function, dehydration of the secondary carbinol, and catalytic hydrogenation of the vinylmesidine. Clemmensen reduction of both 3-acetyl- and 3-propionyl-mesidine yielded mixtures of products from which pure entities were not separated.

3-Isopropylmesidine was synthesized in two ways: (1) by nitration of 3-isopropylmesitylene (prepared by catalytic reduction of isopropenylmesitylene) followed by reduction; (2) by nitration of isopropenylmesitylene followed by reduction in two steps, first of the nitro group and second of the double bond. Isopropenylmesitylene was obtained by condensation of mesitylmagnesium bromide with acetone and then dehydration of the tertiary carbinol with formic acid.

3-*t*-Butylmesidine was synthesized in the manner previously described, by the coupling reaction of mesitylmagnesium bromide with *t*-butyl chloride, followed by nitration and reduction.

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### Experimental

All melting points are uncorrected.

**Acylmesitylenes** were prepared by the procedure of Noller and Adams.<sup>6</sup>

**Acetylmesitylene**, 86% yield, b.p. 86.5–87° at 3 mm. (lit.<sup>6</sup> b.p. 90° at 3 mm.).

**Propionylmesitylene**, 90% yield, b.p. 95–96° at 2.8 mm. (lit.<sup>7</sup> b.p. 120–124° at 11 mm.).

**Alkylmesitylenes** were prepared by the procedure of Smith and Kiess.<sup>8</sup>

**Ethylmesitylene**, 80% yield, b.p. 62–63° at 3.2 mm. (lit.<sup>8</sup> b.p. 97–98° at 22 mm.).

(6) C. R. Noller and R. Adams, *J. Am. Chem. Soc.*, **46**, 1889 (1924).

(7) P. L. Julian, W. Cole, A. Magnani and E. W. Meyer, *ibid.*, **67**, 1728 (1945).

(8) L. I. Smith and M. A. Kiess, *ibid.*, **61**, 284 (1939).

***n*-Propylmesitylene**, 49% yield, b.p. 74–75° at 3.2 mm. (lit.<sup>9</sup> b.p. 221°).

**Alkylnitromesitylenes.**—The procedure used by Adams and Dix<sup>3</sup> was followed. After addition of the fuming nitric acid, the reaction mixture was allowed to stand at room temperature for 10 minutes, taking care not to allow the temperature to rise above 30°. The ethereal solution of the alkylnitromesitylene was thoroughly washed with 10% aqueous sodium hydroxide, then with water. After drying and evaporation of the solvent, the product was distilled *in vacuo*. The first fraction was essentially unchanged alkylmesitylene; the second fraction contained the desired nitro compound; the third fraction partially solidified on cooling.

**Ethylnitromesitylene:** first fraction, b.p. 46–50° at 0.8 mm.; second fraction, b.p. 100–105° at 0.8 mm.; third fraction, b.p. from 105° at 0.7 mm. to 123° at 2.2 mm. By redistillation of the second fraction the pure product was obtained in 48% yield, b.p. 88–90° at 0.3 mm.,  $n_D^{24}$  1.5260.

*Anal.* Calcd. for C<sub>11</sub>H<sub>15</sub>NO<sub>2</sub>: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.59; H, 7.75; N, 6.95.

The fibrous white crystals in the third fraction were collected by filtration and purified by recrystallization from petroleum ether (b.p. 60–100°); m.p. 70–70.5°. The yield was about 10%. This compound is isomeric with the ring substituted compound, and probably has the nitro substituent in the ethyl group though substitution in one of the methyl groups is not excluded.

*Anal.* Calcd. for C<sub>11</sub>H<sub>15</sub>NO<sub>2</sub>: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.57; H, 8.03; N, 7.25.

This latter nitro compound (1.8 g.) was reduced with hydrazine hydrate and Raney nickel.<sup>10</sup> The solution was filtered from the catalyst, and on cooling a small amount (0.2 g.) of product separated; yellow crystals, m.p. 187–188°. This appears to be a binuclear compound, either an azo or isomer of an azo compound.

*Anal.* Calcd. for C<sub>22</sub>H<sub>30</sub>N<sub>2</sub>: C, 81.93; H, 9.37; N, 8.69. Found: C, 82.18; H, 8.98; N, 8.54.

The filtrate from the crystals was concentrated to about 5 ml., and 3 ml. of concentrated hydrochloric acid added. Further concentration yielded a total of 0.9 g. of product, contaminated with orange colored material. Crystallization from water gave white crystals, m.p. 236–239° dec. This hydrochloride was dissolved in a little pyridine and treated with benzenesulfonyl chloride. The benzenesulfonyl derivative was purified by crystallization from ethanol; m.p. 111.5–112°.

*Anal.* Calcd. for C<sub>17</sub>H<sub>21</sub>NO<sub>2</sub>S: C, 67.29; H, 6.98; N, 4.62. Found: C, 67.47; H, 6.90; N, 4.77.

***n*-Propylnitromesitylene:** first fraction, b.p. up to 58° at 0.7 mm.; second fraction, b.p. 113–115° at 0.7 mm.; third fraction, b.p. from 115° at 0.7 mm. to 125° at 1.2 mm. By redistillation of the second fraction, the pure product was obtained in 38% yield, b.p. 97–99° at 0.3 mm.,  $n_D^{24}$  1.5198.

*Anal.* Calcd. for C<sub>12</sub>H<sub>17</sub>NO<sub>2</sub>: C, 69.53; H, 8.27; N, 6.76. Found: C, 69.96; H, 8.28; N, 6.87.

The solid material in the third fraction was purified by recrystallization from petroleum ether (b.p. 60–100°), and then sublimed *in vacuo*, m.p. 80.5–81°. The yield was 8%.

*Anal.* Calcd. for C<sub>12</sub>H<sub>17</sub>NO<sub>2</sub>: C, 69.53; H, 8.27; N, 6.76. Found: C, 69.63; H, 8.26; N, 6.92.

**3-Alkylmesidines (from Alkylnitromesitylenes).**—The reduction method of Balcom and Furst,<sup>10</sup> employing hydrazine hydrate and Raney nickel, was used.

**3-Ethylmesidine**, 90% yield, b.p. 76–78° at 0.25 mm. *Anal.* Calcd. for C<sub>11</sub>H<sub>17</sub>N: C, 80.92; H, 10.50; N, 8.58. Found: C, 80.68; H, 10.34; N, 8.41.

**3-*n*-Propylmesidine**, 92% yield, b.p. 86–87° at 0.25 mm. *Anal.* Calcd. for C<sub>12</sub>H<sub>19</sub>N: C, 81.29; H, 10.80; N, 7.91. Found: C, 80.72; H, 10.79; N, 7.54.

Both mesidines, after diazotization, gave with an alkaline solution of β-naphthol bulky red precipitates.

**Acylnitromesitylenes (from Acylmesitylenes).**—The procedure for nitrating the alkylmesitylenes was used, but dur-

(9) A. Klages and C. Stamm, *Ber.*, **37**, 1719 (1904).

(10) D. Balcom and A. Furst, *J. Am. Chem. Soc.*, **75**, 4334 (1953).

ing the addition of fuming nitric acid the temperature was maintained at  $-10^{\circ}$ .

**Acetylnitromesitylene**, 71% yield, b.p.  $112-113^{\circ}$  at 0.3 mm. *Anal.* Calcd. for  $C_{11}H_{13}NO_3$ : C, 63.75; H, 6.32; N, 6.76. Found: C, 64.05; H, 6.35; N, 6.58.

**Propionynitromesitylene**, 80% yield, m.p.  $60-61^{\circ}$ , after crystallization from petroleum ether (b.p.  $60-100^{\circ}$ ) and sublimation *in vacuo*. *Anal.* Calcd. for  $C_{12}H_{15}NO_3$ : C, 65.14; H, 6.83; N, 6.33. Found: C, 65.26; H, 6.83; N, 6.26.

**3-Acylmesidines**.—The acylnitromesitylenes were reduced by use of hydrazine and Raney nickel.<sup>8</sup>

**3-Acetylmessidine**, 92% yield, b.p.  $113-114^{\circ}$  at 0.2 mm., m.p.  $45-46^{\circ}$ . *Anal.* Calcd. for  $C_{11}H_{13}NO$ : C, 74.54; H, 8.53; N, 7.90. Found: C, 74.78; H, 8.57; N, 8.12.

Hydrochloride, after sublimation, m.p.  $243^{\circ}$  dec. *Anal.* Calcd. for  $C_{11}H_{13}NO \cdot HCl$ : C, 61.82; H, 7.55; N, 6.56. Found: C, 61.52; H, 7.50; N, 6.38.

**3-Propionylmessidine**, 95% yield, m.p.  $58.5-59.5^{\circ}$  after sublimation. *Anal.* Calcd. for  $C_{12}H_{17}NO$ : C, 75.35; H, 8.96; N, 7.32. Found: C, 75.58; H, 9.28; N, 7.27.

**Methylmesidylcarbinol**.—A solution of 7 g. of 3-acetylmessidine in 40 ml. of ethanol was reduced with hydrogen at 120 atm. and  $120-130^{\circ}$ , using copper chromite as a catalyst. After filtration and removal of the solvent, the carbinol solidified on cooling. It was recrystallized from benzene; white crystals, m.p.  $107-108^{\circ}$ , yield 6 g. (85%).

*Anal.* Calcd. for  $C_{11}H_{17}NO$ : C, 73.70; H, 9.56; N, 7.82. Found: C, 73.91; H, 9.41; N, 8.08.

**3-Vinylmessidine**.—A mixture of 7 g. of methylmesidylcarbinol, 7 g. of powdered fused potassium hydrogen sulfate and 0.1 g. of *p*-*t*-butylcatechol was heated in an oil-bath at  $200^{\circ}$  for 15 minutes while the pressure was reduced to 100 mm. in order to distill off the water of reaction. After cooling, the solid mass was dissolved in warm water, the solution was alkalized and extracted with ether. The ethereal solution was washed with water, dried and then evaporated. The product boiled at  $84-86^{\circ}$  at 0.6 mm.,  $n_D^{25}$  1.5698, yield 4.2 g. (66%).

*Anal.* Calcd. for  $C_{11}H_{16}N$ : C, 81.93; H, 9.38; N, 8.69. Found: C, 81.67; H, 9.18; N, 8.49.

**3-Ethylmessidine (from 3-Vinylmessidine)**.—A solution of 3.2 g. of 3-vinylmessidine in 25 ml. of glacial acetic acid was hydrogenated at room temperature and atmospheric pressure in the presence of 245 mg. of platinum oxide. The absorption was very fast and ceased after 10% more than the theoretical amount of hydrogen was taken up. The solvent was evaporated under reduced pressure, the residue was dissolved in ether and the ether solution was washed with aqueous sodium bicarbonate. After drying and evaporation of the ether, 2.9 g. (91%) of 3-ethylmessidine resulted, b.p.  $74-75^{\circ}$  at 0.2 mm.

*Anal.* Calcd. for  $C_{11}H_{17}N$ : C, 80.92; H, 10.50; N, 8.58. Found: C, 80.68; H, 10.34; N, 8.41.

**Mesityldimethylcarbinol**.—A modification of a previously described method<sup>11</sup> was employed. A solution of 169 g. of bromomesitylene<sup>12</sup> in 590 ml. of absolute ether was introduced during 2 hours into a three-necked flask containing 21 g. of magnesium turnings. The reaction was started with a few drops of methyl iodide. After the addition of bromomesitylene was completed, the solution spontaneously continued refluxing for 2 hours more, after which time it was heated for 30 minutes. To the solution of mesitylmagnesium bromide, cooled with ice and water, was added 50.7 g. of Merck pure acetone dissolved in 50 ml. of ether. Heat developed and a very viscous precipitate formed which made the stirring difficult. The use of a Hershberg stirrer and a high speed of rotation made it possible to stir until completion of the reaction. The reaction mixture was poured into ice-water, neutralized with tartaric acid and the ethereal layer isolated. The aqueous layer was extracted five times with ether, the extracts were combined and dried. After elimination of the ether under reduced pressure, the residue was kept for 24 hours in a refrigerator. The first crop of crystals weighed 20 g., m.p.  $107-111^{\circ}$ . After 2 days a second crop of 2 g. was isolated; total yield 22 g. (14.6%). After four recrystallizations from petroleum

ether (b.p.  $60-100^{\circ}$ ), prisms, m.p.  $112-113^{\circ}$ , were obtained (lit.<sup>9</sup> m.p.  $111-112^{\circ}$ ).

*Anal.* Calcd. for  $C_{12}H_{18}O$ : C, 80.85; H, 10.18. Found: C, 80.78; H, 10.15.

Attempts to hydrogenolyze this carbinol to the hydrocarbon either by hydrogen in presence of Raney nickel at  $125-150^{\circ}$  and 130–160 atm. pressure or by sodium and ethanol in liquid ammonia failed.

**Isopropenylmessitylene**.—A solution of 46.0 g. of mesityldimethylcarbinol in 930 ml. of 98–100% formic acid, in which was dissolved 16 g. of anhydrous sodium carbonate, was refluxed for 2 hours, cooled, and the two layers separated.<sup>13</sup> The formic acid layer (lower) was diluted with 5 l. of water and extracted three times with ether. The ether extracts were combined with the upper layer, washed thoroughly with aqueous sodium bicarbonate, water, and dried. After elimination of the solvent, 38.5 g. (93.5%) of isopropenylmessitylene resulted, b.p.  $65^{\circ}$  at 2.7 mm.,  $n_D^{25}$  1.5115.

*Anal.* Calcd. for  $C_{12}H_{16}$ : C, 89.93; H, 10.06. Found: C, 89.88; H, 9.90.

**Isopropylmessitylene**.—A solution of 8 g. of isopropenylmessitylene in 50 ml. of glacial acetic acid was hydrogenated at room temperature and atmospheric pressure in the presence of 90 mg. of platinum oxide. After 1 hour, 10% more than the theoretical amount of hydrogen was taken up and the absorption ceased. After filtration, most of the acetic acid was evaporated under reduced pressure and the residue was poured into water. The water was extracted three times with ether. After washing the ether solution with aqueous sodium bicarbonate, water and drying, the solvent was removed. The residue was distilled to yield 7.5 g. (93%) of isopropylmessitylene, b.p.  $70-71^{\circ}$  at 2.2 mm.,  $n_D^{25}$  1.5080.

*Anal.* Calcd. for  $C_{12}H_{18}$ : C, 88.82; H, 11.18. Found: C, 89.13; H, 11.30.

**Isopropynitromesitylene**.—The isopropylmessitylene was nitrated in a manner similar to the other alkylmessitylenes. Two distillations afforded pure isopropynitromesitylene in 55% yield, b.p.  $88-90^{\circ}$  at 0.25 mm.,  $n_D^{25}$  1.5242.

*Anal.* Calcd. for  $C_{12}H_{17}NO_2$ : C, 69.53; H, 8.27; N, 6.76. Found: C, 69.71; H, 8.19; N, 6.84.

**Isopropylmessidine (from Isopropynitromesitylene)**.—Reduction to the amine was effected by hydrazine hydrate and Raney nickel.<sup>8</sup> The amine was obtained in 85% yield, b.p.  $81-83^{\circ}$  at 0.25 mm.,  $n_D^{25}$  1.5438.

*Anal.* Calcd. for  $C_{12}H_{19}N$ : C, 81.29; H, 10.80; N, 7.91. Found: C, 81.50; H, 10.73; N, 8.15.

**Isopropenylnitromesitylene**.—Nitration of isopropenylmessitylene was effected as previously described for the isopropylmessitylene. The nitro olefin was obtained in 77% yield, b.p.  $92-93^{\circ}$  at 0.6 mm.,  $n_D^{25}$  1.5308.

*Anal.* Calcd. for  $C_{12}H_{15}NO_2$ : C, 70.22; H, 7.37; N, 6.83. Found: C, 70.06; H, 7.39; N, 6.75.

**Isopropylmessidine**.—The reduction procedure of the nitro compound was similar to that for the isopropyl analog. The amino olefin was obtained in 95% yield, b.p.  $84-85^{\circ}$  at 0.4 mm.,  $n_D^{25}$  1.5476.

*Anal.* Calcd. for  $C_{12}H_{17}N$ : C, 82.23; H, 9.78; N, 8.00. Found: C, 82.50; H, 9.68; N, 7.89.

**Isopropylmessidine (from Isopropenylmessidine)**.—Isopropenylmessidine was hydrogenated following the procedure employed for the preparation of isopropylmessitylene from isopropenylmessitylene. For hydrogenating 15.5 g. of amino olefin, 3 g. of platinum oxide was necessary, probably because of the poisoning effect of the amino group. The isopropylmessidine was obtained in 86% yield, b.p.  $90-93^{\circ}$  at 0.7 mm.,  $n_D^{25}$  1.5445. After diazotization the product coupled with  $\beta$ -naphthol.

*Anal.* Calcd. for  $C_{12}H_{19}N$ : C, 81.29; H, 10.80; N, 7.91. Found: C, 81.22; H, 10.58; N, 7.87.

**N-Benzenesulfonylalkylmessidines**.—To a pyridine solution of the free amine was added 1.05 molar equivalents of benzenesulfonyl chloride dissolved in an equal volume of pyridine. After heating at  $70^{\circ}$  for 1 hour the mixture

(11) H. C. Brown and M. Grayson, *J. Am. Chem. Soc.*, **75**, 20 (1953).

(12) L. I. Smith, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 95.

(13) P. A. Plattner and H. Roniger, *Helv. Chim. Acta*, **26**, 905 (1943); J. Heer and K. Miescher, *ibid.*, **28**, 1506 (1946).

was cooled and then poured into ice-water. The product was collected and recrystallized from ethanol.

**N-Benzenesulfonylethylmesidine**, 88% yield, m.p. 155–156°. *Anal.* Calcd. for  $C_{17}H_{21}NO_2S$ : C, 67.29; H, 6.98; N, 4.62. Found: C, 67.43; H, 6.94; N, 4.90.

**N-Benzenesulfonyl-*n*-propylmesidine**, 81% yield, m.p. 172–172.5°. *Anal.* Calcd. for  $C_{18}H_{23}NO_2S$ : C, 68.10; H, 7.30; N, 4.41. Found: C, 68.31; H, 7.51; N, 4.65.

**N-Benzenesulfonylisopropylmesidine**, 87% yield, m.p. 175–176°. *Anal.* Calcd. for  $C_{18}H_{23}NO_2S$ : C, 68.10; H, 7.30; N, 4.41. Found: C, 67.90; H, 7.25; N, 4.37.

**Preparation of Sodium Salts of N-Benzenesulfonylalkylmesidines.**—To a solution of 0.05 mole of an N-benzenesulfonylalkylmesidine in 400–500 ml. of boiling absolute ethanol was added an ethanol solution of sodium ethoxide prepared from 0.05 mole of sodium and 50 ml. of absolute ethanol. Upon evaporation of the ethanol *in vacuo* (the precaution was taken to protect from carbon dioxide) the sodium salts of the N-benzenesulfonylalkylmesidines were collected (quantitative). They were dried in a vacuum desiccator. The products melted 310–325° dec.

**Preparation of N-Benzenesulfonyl-N-carboxymethylalkylmesidines.**—A solution of 0.05 mole of the sodium salt of an N-benzenesulfonylalkylmesidine, 0.15 mole of ethyl bromoacetate and 120–140 ml. of dimethylformamide was heated on a steam-bath for 20 hours. The solvent was evaporated under reduced pressure, and the remaining oil and solid were shaken in a separatory funnel with 120 ml. of chloroform and 50 ml. of water. The chloroform solution was then washed twice with water and the chloroform evaporated. The N-benzenesulfonyl-N-carboxymethylalkylmesidines did not crystallize. They were therefore saponified.

The ester obtained in the condensation reaction, 250–300 ml. of acetic acid and 100 ml. of 1:10 sulfuric acid, were heated under reflux for 6 hr., during which time 50 ml. more of 1:10 sulfuric acid was added. After 2 hr. about 15 ml. of solvent was allowed to distil off and after each successive 1.5 hr. of heating this was repeated until a total of 45 ml. of solvent had been collected. The reaction mixture, after cooling, was poured with vigorous stirring into 2 l. of ice-water. The stirring was continued for 30 min. and the suspension permitted to stand overnight. The product was collected by filtration, ground in a mortar, and dried in a vacuum desiccator. The crude N-benzenesulfonyl-N-carboxymethylisopropylmesidine after standing overnight in water was still gummy; it solidified completely on standing for 3 days in the air.

The three acids were purified by recrystallization from benzene. The yields given below refer to the crude products and are calculated on the basis of the benzenesulfonylalkylmesidines.

**N-Benzenesulfonyl-N-carboxymethylethylmesidine**, 64% yield, m.p. 159–160°. *Anal.* Calcd. for  $C_{19}H_{23}NO_4S$ : C, 63.13; H, 6.41; N, 3.88. Found: C, 63.21; H, 6.49; N, 4.09.

**N-Benzenesulfonyl-N-carboxymethyl-*n*-propylmesidine**, 72% yield, m.p. 167–168.5°. *Anal.* Calcd. for  $C_{20}H_{25}NO_4S$ : C, 63.97; H, 6.71; N, 3.73. Found: C, 64.05; H, 6.43; N, 3.94.

**N-Benzenesulfonyl-N-carboxymethylisopropylmesidine**, 67% yield, m.p. 173–175°. *Anal.* Calcd. for  $C_{20}H_{25}NO_4S$ : C, 63.97; H, 6.71; N, 3.73. Found: C, 64.35; H, 6.93; N, 3.90.

**N-Benzenesulfonyl-N-carboxymethyl-*t*-butylmesidine** was prepared from N-benzenesulfonyl-*t*-butylmesidine<sup>3</sup> by the procedure used for the other analogs. It was recrystallized from ethanol, m.p. 114–115°.

*Anal.* Calcd. for  $C_{23}H_{31}NO_4S$ : C, 66.15; H, 7.48; N, 3.35. Found: C, 66.18; H, 7.28; N, 3.56.

**N-Benzenesulfonyl-N-carboxymethylmesidine.**—By acid hydrolysis of the *t*-butyl ester carried out as previously described, the *t*-butyl group is almost quantitatively replaced by hydrogen, and N-benzenesulfonyl-N-carboxymethylmesidine is obtained; purified from ethanol, it has a m.p. 180–180.5°.

*Anal.* Calcd. for  $C_{17}H_{19}NO_4S$ : C, 61.24; H, 5.74; N, 4.20. Found: C, 61.46; H, 5.49; N, 3.59.

**N-Benzenesulfonyl-N-carboxymethyl-*t*-butylmesidine** was obtained by alkaline hydrolysis of the corresponding ester. It was recrystallized from benzene, m.p. 184–185°.

*Anal.* Calcd. for  $C_{21}H_{27}NO_4S$ : C, 64.75; H, 6.99; N, 3.60. Found: C, 64.62; H, 6.71; N, 3.36.

**Resolution of N-Benzenesulfonyl-N-carboxymethylethylmesidine.**—A hot solution of 4.870 g. of N-benzenesulfonyl-N-carboxymethylethylmesidine and 3.966 g. of cinchonidine in 300 ml. of ethyl acetate was filtered, then placed in a refrigerator. The solution was allowed to evaporate slowly to dryness over a period of 6 days. Four crops were collected: 1.04 g.,  $[\alpha]^{25}_D = 66.7^\circ$ ; 1.13 g.,  $[\alpha]^{25}_D = 66.4^\circ$ ; 3.93 g.,  $[\alpha]^{25}_D = 58.9^\circ$ ; 2.13 g.,  $[\alpha]^{25}_D = 45.6^\circ$ . The rotations were determined in absolute ethanol.

The first three crops (69%) were put together and recrystallized from 350 ml. of ethyl acetate. Upon evaporation of the solvent the following crops were collected: 1.53 g.,  $[\alpha]^{27}_D = 68.0^\circ$ ; 1.24 g.,  $[\alpha]^{27}_D = 67.1^\circ$ ; 1.18 g.,  $[\alpha]^{27}_D = 64.6^\circ$ ; 0.76 g.,  $[\alpha]^{27}_D = 52.7^\circ$ ; 1.20 g. (rotation not determined). The rotations were determined in absolute ethanol.

The first three crops of this series were combined and recrystallized. The specific rotation remained unchanged, and the pure less-soluble salt crystallized, m.p. 188–189°; rotation, 0.0742 g. made up to 5 ml. with absolute ethanol at 26° gave  $\alpha_D = -1.01^\circ$  (l 1),  $[\alpha]^{25}_D = 68.0^\circ$ .

(–)–N-Benzenesulfonyl-N-carboxymethylethylmesidine. —The optically active acid was regenerated from the less-soluble salt in a manner previously described.<sup>14</sup> The product after crystallization from benzene melted at 155–157°; rotation, 0.0164 g. made up to 2 ml. with absolute ethanol at 27° gave  $\alpha_D = 0.10^\circ$  (l 1),  $[\alpha]^{27}_D = 12.4^\circ$ . The yield was 96%.

*Anal.* Calcd. for  $C_{19}H_{23}NO_4S$ : C, 63.13; H, 6.41; N, 3.88. Found: C, 62.85; H, 6.32; N, 3.91.

**Resolution of N-Benzenesulfonyl-N-carboxymethyl-*n*-propylmesidine.**—A solution of 4.0 g. of N-benzenesulfonyl-N-carboxymethyl-*n*-propylmesidine and 3.136 g. of cinchonidine in 65 ml. of absolute ethanol was kept at 15° for 2 days. The first crop of salt weighed 3.486 g., m.p. 206–208°; rotation, 0.0729 g. made up to 5 ml. with absolute ethanol at 23° gave  $\alpha_D = -1.00^\circ$  (l 1),  $[\alpha]^{25}_D = 68.6^\circ$ . The mother liquors yielded 3.427 g. of crystalline salt, m.p. 105–110°; rotation, 0.0710 g. made up to 5 ml. with absolute ethanol at 23° gave  $\alpha_D = -0.73^\circ$  (l 1),  $[\alpha]^{25}_D = 51.4^\circ$ . The first crop was dissolved in 40 ml. of absolute ethanol, and after standing for 24 hours at 15° yielded 2.924 g. of crystals; rotation, 0.0797 g. made up to 5 ml. with absolute ethanol at 22° gave  $\alpha_D = -1.13^\circ$  (l 1),  $[\alpha]^{25}_D = 70.9^\circ$ . Upon recrystallization the specific rotation of this crop did not change; it was considered to be pure less-soluble salt; m.p. 212–213°.

(–)–N-Benzenesulfonyl-N-carboxymethyl-*n*-propylmesidine. —The optically active acid was regenerated from the less-soluble salt by the procedure used for the ethyl analog. The product from benzene had a m.p. 148–149°; rotation, 0.0418 g. made up to 2 ml. with absolute ethanol at 28° gave  $\alpha_D = -0.48^\circ$  (l 1),  $[\alpha]^{25}_D = 22.9^\circ$ . The yield was 97%.

*Anal.* Calcd. for  $C_{20}H_{25}NO_4S$ : C, 63.97; H, 6.71; N, 3.73. Found: C, 63.88; H, 6.91; N, 3.69.

**Resolution of N-Benzenesulfonyl-N-carboxymethylisopropylmesidine.**—A solution of 3.452 g. of N-benzenesulfonyl-N-carboxymethylisopropylmesidine and 2.707 g. of cinchonidine in 65 ml. of absolute ethanol was filtered, then placed in a refrigerator. The solution was allowed to evaporate slowly to dryness over a period of 20 days. Six crops were collected: 0.298 g.,  $[\alpha]^{25}_D = 47.7^\circ$ ; 0.077 g.,  $[\alpha]^{25}_D = 47.4^\circ$ ; 1.415 g.,  $[\alpha]^{25}_D = 52.9^\circ$ ; 0.162 g.,  $[\alpha]^{27}_D = 52.1^\circ$ ; 0.710 g.,  $[\alpha]^{27}_D = 62.8^\circ$ ; 3.015 g. (rotation not determined). The rotations were determined in absolute ethanol.

The first four crops were combined and recrystallized from 60 ml. of absolute ethanol. The specific rotation remained substantially unchanged, and the pure less-soluble salt crystallized; m.p. 194° dec.; rotation, 0.0125 g. made up to 2 ml. with absolute ethanol at 28° gave  $\alpha_D = -0.30^\circ$  (l 1),  $[\alpha]^{25}_D = 48.0^\circ$ .

(+)–N-Benzenesulfonyl-N-carboxymethylisopropylmesidine. —The optically active acid was regenerated from the less-soluble salt by the usual procedure. The product purified from benzene had an m.p. 149–150°; rotation, 0.0648 g. made up to 2 ml. with dimethylformamide at

(14) R. Adams and K. V. Y. Sundstrom, *J. Am. Chem. Soc.*, **76**, 5477 (1954).

24° gave  $\alpha_D + 0.42^\circ$  (*l* 1),  $[\alpha]^{24}_D + 12.9^\circ$ . The yield was 94%.

*Anal.* Calcd. for  $C_{20}H_{23}NO_4$ : C, 63.97; H, 6.71; N, 3.73. Found: C, 63.64; H, 6.70; N, 3.74.

**Resolution of N-Benzenesulfonyl-N-carboxymethyl-*t*-butylmesidine.**—This resolution was carried out as previously described.<sup>3</sup> The less-soluble salt melted at 195–196° (lit.<sup>3</sup> m.p. 195–196°); rotation, 0.0176 g. made up to 2 ml. with absolute ethanol at 27° gave  $\alpha_D - 0.25^\circ$  (*l* 1),  $[\alpha]^{27}_D - 29^\circ$  (lit.<sup>3</sup>  $[\alpha]^{28}_D - 36.0^\circ$ ).

(+)-N-Benzenesulfonyl-N-carboxymethyl-*t*-butylmesidine.—The optically active acid was regenerated from the less-soluble salt by the usual procedure. The product, purified from benzene, had m.p. 170–171° (resolidified and melted again at 182.5–183.5°); rotation, 0.0644 g. made up to 2 ml. with dimethylformamide at 28° gave  $\alpha_D + 1.23^\circ$  (*l* 1),  $[\alpha]^{28}_D + 38.2^\circ$ . The yield was 90%.

*Anal.* Calcd. for  $C_{21}H_{27}NO_4$ : C, 64.75; H, 6.99; N, 3.60. Found: C, 64.71; H, 7.01; N, 3.55.

**Racemization of N-Benzenesulfonyl-N-carboxymethyl-alkylmesidines.**—The optically active acid was dissolved in purified dimethylformamide, and the solution was transferred to glass tubes (55 mm. long, 9 mm. internal diameter) in 6 to 10 equal portions. The tubes were sealed and immersed all at the same time (within 20 seconds) in boiling 1-butanol (118°). The first tube was withdrawn after 8–15 minutes, after which time the thermal equilibrium was assumed to be reached; this was considered as zero time. The remaining tubes were removed at successive time intervals, quenched in ice-water, then allowed to come to room temperature, and the rotation determined.

The following results were obtained.

N-Benzenesulfonyl-N-carboxymethylethylmesidine: 0.0 hr.,  $\alpha^{26}_D - 0.88^\circ$ ; 1.0 hr.,  $\alpha^{26}_D - 0.83^\circ$ ; 2.25 hr.,  $\alpha^{26}_D - 0.74^\circ$ ; 3.5 hr.,  $\alpha^{27}_D - 0.67^\circ$ ; 4.9 hr.,  $\alpha^{27}_D - 0.62^\circ$ ; 6.0 hr.,  $\alpha^{27}_D - 0.56^\circ$ ; 7.25 hr.,  $\alpha^{27}_D - 0.53^\circ$ ; 8.5 hr.,  $\alpha^{28}_D - 0.47^\circ$ ; 9.8 hr.,  $\alpha^{28}_D - 0.43^\circ$ ; 11.0 hr.,  $\alpha^{28}_D - 0.39^\circ$ .

A plot of  $\ln \alpha$  vs. time afforded a straight line from whose slope was derived the rate constant,  $K = 7.26 \times 10^{-2}$  hr.<sup>-1</sup> and the half-life,  $t_{1/2} = 9.6$  hr.

Two check racemizations were carried out in the same manner. The values of the rate constant and half-life were:

$K 7.10 \times 10^{-2}$  hr.<sup>-1</sup>,  $t_{1/2}$  9.8 hr. and  $K = 7.22 \times 10^{-2}$  hr.<sup>-1</sup>,  $t_{1/2} = 9.6$  hr.

N-Benzenesulfonyl-N-carboxymethyl-*n*-propylmesidine: 0.0 hr.,  $\alpha^{27}_D - 1.02^\circ$ ; 1.5 hr.,  $\alpha^{27}_D - 0.90^\circ$ ; 3.0 hr.,  $\alpha^{27}_D - 0.87^\circ$ ; 5.0 hr.,  $\alpha^{27}_D - 0.75^\circ$ ; 7.0 hr.,  $\alpha^{27}_D - 0.64^\circ$ ; 9.0 hr.,  $\alpha^{27}_D - 0.58^\circ$ ; 11.0 hr.,  $\alpha^{27}_D - 0.50^\circ$ ; 13.0 hr.,  $\alpha^{27}_D - 0.48^\circ$ .

Rate constant derived is  $K = 6.14 \times 10^{-2}$  hr.<sup>-1</sup>, and half-life  $t_{1/2} = 11.3$  hr. Two check racemizations gave:  $K = 5.68 \times 10^{-2}$  hr.<sup>-1</sup>,  $t_{1/2} = 12.2$  hr., and  $K = 6.34 \times 10^{-2}$  hr.<sup>-1</sup>,  $t_{1/2} = 10.9$  hr.

N-Benzenesulfonyl-N-carboxymethylisopropylmesidine: 0.0 hr.,  $\alpha^{28}_D + 0.30^\circ$ ; 3.25 hr.,  $\alpha^{28}_D + 0.23^\circ$ ; 6.0 hr.,  $\alpha^{28}_D + 0.20^\circ$ ; 9.0 hr.,  $\alpha^{28}_D + 0.17^\circ$ ; 11.5 hr.,  $\alpha^{28}_D + 0.15^\circ$ ; 15.0 hr.,  $\alpha^{28}_D + 0.12^\circ$ . Rate constant derived is  $K = 6.10 \times 10^{-2}$  hr.<sup>-1</sup>, and half-life  $t_{1/2} = 11.3$  hr. Two check racemizations gave:  $K = 6.70 \times 10^{-2}$  hr.<sup>-1</sup>,  $t_{1/2} = 10.3$  hr., and  $K = 6.74 \times 10^{-2}$  hr.<sup>-1</sup>,  $t_{1/2} = 10.3$  hr.

N-Benzenesulfonyl-N-carboxymethyl-*t*-butylmesidine: 0.0 hr.,  $\alpha^{28}_D + 1.35^\circ$ ; 0.5 hr.,  $\alpha^{28}_D + 1.10^\circ$ ; 1.25 hr.,  $\alpha^{28}_D + 0.76^\circ$ ; 2.25 hr.,  $\alpha^{28}_D + 0.52^\circ$ ; 3.5 hr.,  $\alpha^{28}_D + 0.29^\circ$ ; 5.0 hr.,  $\alpha^{28}_D + 0.17^\circ$ . Rate constant derived is  $K = 42.2 \times 10^{-2}$  hr.<sup>-1</sup>,  $t_{1/2} = 1.6$  hr.

The average rate constants, half-lives, melting points and specific rotations of the optically active acids are summarized in Table II.

TABLE II  
RACEMIZATION OF N-BENZENESULFONYL-N-CARBOXYMETHYL-3-SUBSTITUTED MESIDINES

Substituent	Opt. active acid, m.p., °C.	Wt., g.	Vol., ml.	Rotation in dimethylformamide, $[\alpha]_D(l)$	$t_{1/2}$ , °C.	$K^b$ av. $\times 10^2$ hr. <sup>-1</sup>	$t_{1/2}$
CH <sub>3</sub> <sup>a</sup>	184–186	0.7670	10.0	+ 2.9	30	9.4	7.3
C <sub>2</sub> H <sub>5</sub>	155–157	1.2021	10.5	-12.5	26	7.18	9.6
<i>n</i> -C <sub>4</sub> H <sub>9</sub>	148–149	0.9713	15.0	-15.8	27	6.06	11.4
<i>t</i> -C <sub>4</sub> H <sub>9</sub>	149–150	.0648	2.0	+12.9	24	6.52	10.6
<i>t</i> -C <sub>6</sub> H <sub>5</sub>	170–171	.0644	2.0	+38.2	28	46.22	1.6 <sup>a</sup>

<sup>a</sup> Lit.<sup>3</sup> m.p. 171.5–172.5° (cor.);  $K = 23.2 \times 10^{-2}$  hr.<sup>-1</sup>,  $t_{1/2} = 1.49$  hr. <sup>b</sup> In some of the previous papers, ref. 1 and 3, the rate constants have been given as  $k$  (invers. instead of  $k$  (rac.))

[CONTRIBUTION FROM THE NAVAL STORES RESEARCH STATION, OLUSTEE, FLA.]

### Air Oxidation of Resin Acids. III. The Photosensitized Oxidation of Neoabietic Acid and the Configurations of the Pine Gum Resin Acids

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The photosensitized oxidation of the exo, endo transoid diene, neoabietic acid, was found to yield a crystalline diperoxide; analytical and chemical evidence indicate the structure to be 18-hydroperoxy-6,14-peroxy- $\Delta^7(8)$ -dihydroabietic acid. Pimaric, isopimaric and dehydroabietic acids were found to be unreactive. A transition state is proposed which appears to accommodate many of the known facts regarding the photosensitized oxidation of olefins. Data are cited to suggest the configurations for all asymmetric centers in palustric acid and for the C-13-hydrogen atom in levopimaric acid. The conclusion is drawn that all seven of the major pine gum resin acids contain the same absolute configurations in the "asymmetric backbone chain" (positions 1, 11, 12 and 13) with the exception of the C-13-hydrogen atom in isopimaric acid.

The photosensitized oxidation of levopimaric and palustric acids, two of the seven major resin acids of known structure found in pine gum, has been investigated and the structure of the transannular peroxide obtained in each case has been established.<sup>2–4</sup> At about the same time, it was noted that neoabietic acid (I), a third major resin acid of pine gum, was oxidizable under the same

(1) One of the laboratories of the Southern Utilization Research and Development Division, Agricultural Research Service, U. S. Department of Agriculture. Article not copyrighted.

(2) R. N. Moore and Ray V. Lawrence, *J. Am. Chem. Soc.*, **80**, 1438 (1958).

(3) R. N. Moore and Ray V. Lawrence, *ibid.*, **81**, 458 (1959).

(4) W. H. Schuller, R. N. Moore and Ray V. Lawrence, *ibid.*, **82**, 1734 (1960).

conditions.<sup>5</sup> This reaction has now been investigated in some detail.

The absorption of oxygen on photosensitized oxidation was followed quantitatively and found to be linear with respect to time up to about 1.3 moles of oxygen/mole of neoabietic acid after which the rate progressively decreased to a final value of 1.78 moles of oxygen/mole of resin acid. The reaction was also followed by the change in optical rotation and ultraviolet absorption spectrum (Fig. 1). Suitable blank experiments were carried out which demonstrated that all three elements of air, light and dye were necessary for reac-

(5) Unpublished observation by Mr. R. N. Moore.