in ethylene glycol (160 ml.) was added in the course of 10 minutes and the resulting solution refluxed for 24 hours. After cooling, the solution was neutralized with diluted hydrochloric acid and the excess ethylene glycol removed under reduced pressure.

Acetylation of the oil was accomplished by stirring at 0° with acetic anhydride (200 ml.) and concentrated sulfuric acid (4 ml.) for two hours, then overnight at room temperature and finally at 100° for 2.5 hours. Removal of the excess acetic anhydride under reduced pressure was followed by the addition of ice and neutralization with sodium bicarbonate. Extraction with ether gave an oil which was fractionated through a 15-cm. vacuum-jacketed Vigreux column; b.p. 184–187° (2 mm.), yield 27 g. (76%), $n^{28.5}_{D}$ 1.4454, $d^{28.5}_{4}$ 1.165.

Anal. Calcd. for $C_{15}H_{24}O_9$: C, 51.72; H, 6.94; sapn. equiv., 87. Found: C, 51.51; H, 6.89; sapn. equiv., 87.

Pentaerythritol β-Hydroxyethyl Ether.—Pentaerythritol tetraacetate β-hydroxyethyl ether (28 g.) was saponified by heating with sodium ethoxide (0.2 g. of sodium) in absolute ethanol (500 ml.) for one hour. Partial removal of the solvent (540 ml.) was followed by neutralization with dilute hydrochloric acid and evaporation to dryness under reduced pressure. The oil upon distillation and then recrystallization twice from acetone melted at 77.5–78.5°, yield 6.5 g. (45%). A mixture with a sample prepared from the Tollens condensation melted at the same point.

Pentaerythrityl Dichloride.—To a well-stirred solution of monobenzalpentaerythritol[6] (156.8 g.) in dry pyridine (110.7 g.) at 0° was added slowly pure thionyl chloride (176 g.) in chloroform (175 ml.). The resulting mixture was stirred for 12 hours at room temperature and then refluxed for 4 hours. Removal of the chloroform under reduced pressure followed by the addition of water and extraction with ether gave a solid melting at 74–76°. The solid was not purified but refluxed with 0.5 *N* hydrochloric acid (1200 ml.) and dioxane (600 ml.) for four hours. Removal of the benzaldehyde by steam distillation was followed by concentration of the solution to 200 ml. and extraction with seven 150-ml. portions of ether. The solid obtained in this manner was recrystallized from a mixture of chloroform and carbon tetrachloride; m.p. 79–80°, yield 93 g. (77%). Two further recrystallizations from carbon tetrachloride gave a white solid melting at 80.5–81.5°.

Anal. Calcd. for $C_5H_{10}O_2Cl_2$: C, 34.70; H, 5.82. Found: C, 35.05; H, 5.94.

The following melting points have been recorded in the literature for pentaerythrityl dichloride: 65°,[7] 70–80°,[8] 83°[9] and 95°.[10]

Monobenzalpentaerythrityl Dichloride.—A mixture of pentaerythrityl dichloride (8.6 g.), benzaldehyde (5.3 g.) and concentrated hydrochloric acid (1 ml.) in water (100 ml.) was shaken mechanically at room temperature for 60 hours. The solid formed when recrystallized from an ethanol–water mixture melted at 77.5–78.5°, yield 7.7 g. (75%).

Anal. Calcd. for $C_{12}H_{14}O_2Cl_2$: C, 55.19; H, 5.40. Found: C, 55.37; H, 5.39.

This solid when mixed with the sample isolated in the reaction of monobenzalpentaerythritol and thionyl chloride melted at the same point.

2,6-Dioxaspiro[3,3]heptane (VII).—This compound was prepared according to the method of Backer and Keuning[11] using pentaerythrityl dichloride in place of the pentaerythrityl bromide. Pentaerythrityl dichloride (40 g.) gave 2,6-dioxaspiro[3,3]heptane (4 g.) (17%) melting at 89–90° (b.p. 168–173° (750 mm.)).

Pentaerythritol Tetraacetate Di-β-hydroxyethyl Ether.—To a solution of sodium (1.84 g.) in ethylene glycol (120 ml.) at 140–150° was added in the course of 10 minutes 2,6-dioxaspiro[3,3]heptane (4 g.) in ethylene glycol (80 ml.). The resulting solution was heated at 145–155° for 11 hours, at 160° for 11 hours and finally at reflux for 1.5 hours. Neutralization with hydrochloric acid was followed by removal of the ethylene glycol under reduced pressure and acetylation with acetic anhydride (80 ml.) and sulfuric acid (1.2 ml.) in a manner similar to that used for the monoethylene glycol ether of pentaerythritol. Distillation of the residual oil gave di-β-hydroxyethylpentaerythrityl ether tetraacetate (8.7 g.) (55%) boiling at 195–197° (2 mm.), n^{25}_{D} 1.4487.

Anal. Calcd. for $C_{17}H_{28}O_{10}$: C, 52.03; H, 7.19; sapn. equiv., 98. Found: C, 51.56; H, 7.20; sapn. equiv., 102.

A sample of the tetraacetate (4.0 g.) after transesterification and tritylation in a manner similar to that used with the sample from the tetrapropionate gave the tetratrityl ether (4.1 g.) melting at 148–150°. A mixture with the trityl ether prepared from the tetrapropionate melted at the same point.

Acknowledgment.—The authors are indebted to the Research Corporation for financial support.

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[6] E. Bograchov, THIS JOURNAL, **72**, 2268 (1950).

[7] J. Bougault, *Compt. rend.*, **123**, 187 (1896).

[8] H. Rapoport, THIS JOURNAL, **68**, 341 (1946).

[9] A. Mooradian and J. B. Cloke, *ibid.*, **67**, 942 (1945).

[10] H. Fecht, *Ber.*, **40**, 3883 (1907).

[11] H. J. Backer and K. J. Keuning, *Rec. trav. chim.*, **53**, 812 (1934).

IOWA CITY, IOWA

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

Restricted Rotation in Aryl Amines. XV. Stereoisomeric Diglutarimidomesitylenes

BY ROGER ADAMS AND DALE C. BLOMSTROM[1]

RECEIVED DECEMBER 29, 1952

Bis-(α,α-dimethylglutarimido)-mesitylene (IV) has been prepared and separated into two forms which are shown to be *cis–trans* isomers by infrared spectra and by nitration to give an analogous pair of stereoisomeric nitro compounds. The previously reported explanation of the absence of isomerism in homologous five-membered ring compounds is thus confirmed.

Previous papers in this series[2] have reported the separation of numerous N,N′-dialkyl-N,N′-diarylsulfonyldiaminomesitylenes into *cis* and *trans* isomers. The stereoisomerism is caused by restricted rotation about two carbon–nitrogen bonds. *cis* and *trans* forms were also isolated in analogous derivatives of diaminodurene[3] and triaminomesitylene.[4]

Adams and Campbell[5] prepared several compounds such as I and II, in which the nitrogen atoms of diaminomesitylene were incorporated into five-membered rings, but were able to find only one product in each case. However in compound III, which is closely related to II, *cis* and *trans* forms were isolated. This difference in behavior between II and III was attributed to a decrease

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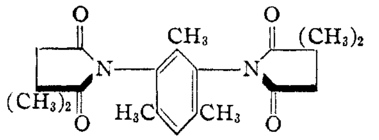
[1] An abstract of a thesis submitted by Dale C. Blomstrom to the Graduate College of the University of Illinois, 1953, in partial fulfillment of the requirements for the Degree of Doctor of Philosophy; Cincinnati Chemical Company Fellow, 1950–1951; Standard Oil Company of Indiana Fellow, 1951–1952; University of Illinois Fellow, 1952–1953.

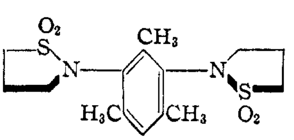
[2] R. Adams and J. J. Tjepkema, THIS JOURNAL, **70**, 4204 (1948); R. Adams and M. Rothstein, *ibid.*, **71**, 1620 (1949).

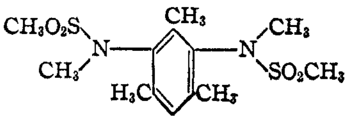
[3] R. Adams and N. K. Nelson, *ibid.*, **72**, 132 (1950).

[4] R. Adams and B. Englund, *ibid.*, **72**, 135 (1950).

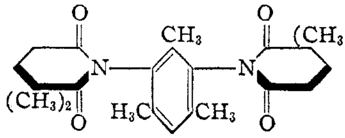
[5] R. Adams and J. B. Campbell, *ibid.*, **72**, 128 (1950).

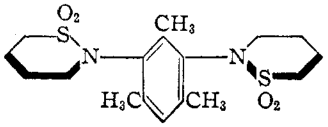

I


II

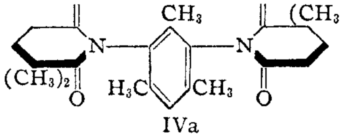

III

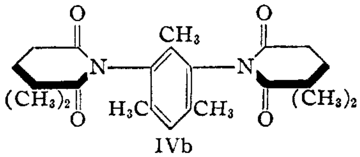
in the nitrogen bond angles in the slightly-strained five-membered rings. The groups attached to nitrogen are thus pulled away from the ring methyls enough to permit free rotation. If this explanation is correct, expansion of the rings from five to six members should allow the bond angles of the nitrogen atoms to assume more nearly the normal size, with the result that sufficient hindrance to rotation should exist to cause *cis–trans* isomerism. The purpose of this investigation was to synthesize compounds IV and V.


IV


V

The feasibility of forming a six-membered cyclic imide by the method of Adams and Campbell was first determined. N-Glutarylaniline could not be converted to N-phenylglutarimide by dehydration with acetic anhydride and sodium acetate, but N,N′-diglutaryldiaminomesitylene yielded diglutarimidomesitylene upon treatment with this reagent. N,N′-Di-(α,α-dimethylgutaryl)-diaminomesitylene was obtained from α,α-dimethylglutaric anhydride and diaminomesitylene; this compound cyclized under dehydrating conditions to bis-(α,α-dimethylglutarimido)-mesitylene (IV) in 87% yield. The product was a mixture of two isomers which were separated by means of their different solubilities in methanol. The higher-melting, less-soluble isomer was assigned the *trans* configuration (IVa); the lower-melting, more-soluble isomer, the *cis* configuration (IVb). Infrared spectra in solution of the two forms proved that they are actually isomers and not merely different crystalline modifications. Differences in the spectra are small but significant. Confirmatory evidence of *cis–trans* isomerism was obtained by separately nitrating the isomers. The *trans* form gave a nitro compound melting at 256.5–257.5°, while the *cis* form yielded one melting at 234–236°. The two were shown to be *cis–trans* isomers by their infrared spectra in solution.


IVa


IVb

The glutarimide derivatives represent the first pairs of stereoisomers described in which the restriction is caused by the equivalent of two different acyl groups on the nitrogens.

The synthesis of V failed. The methods used for the corresponding five-membered ring compound (II) could not be applied because 4-bromobutanesulfonyl chloride could not be prepared.

Acknowledgment.—The authors are indebted to Miss Emily Davis, Mrs. Esther Fett, Mrs. Jean Fortney, Mrs. Katherine Pih and Mr. J. Nemeth for the microanalyses and to Miss Helen Miklas for the infrared spectra.

Experimental[6]

Attempts to Prepare N-Phenylglutarimide.—Attempts to cyclize N-glutarylaniline to N-phenylglutarimide by heating in acetic anhydride with anhydrous sodium acetate from 3 to 7 hours were unsuccessful. Only unreacted starting material could be isolated.

N,N′-Diglutaryldiaminomesitylene.—To a refluxing solution of 3 g. of glutaric anhydride in 50 ml. of dry benzene was added over a period of one hour 2 g. of diaminomesitylene in 40 ml. of dry benzene. The solution was cooled and the product filtered and washed with benzene. The yield was 4.5 g. (90%). Recrystallization from ethanol gave white crystals, m.p. 243.5–244.5°.

Anal. Calcd. for $C_{19}H_{26}N_2O_6$: C, 60.30; H, 6.93. Found: C, 60.51; H, 6.93.

Diglutarimidomesitylene.—A mixture of 2 g. of N,N′-diglutaryldiaminomesitylene, 2 g. of anhydrous sodium acetate and 20 ml. of acetic anhydride was refluxed for 6 hours. The excess acetic anhydride was then cautiously hydrolyzed with 10 ml. of water. The solution was evaporated to about 15 ml. and 30 ml. of water added to the hot solution. The tan crystals which separated upon cooling were filtered and dried. The yield was 1 g. (55%). The compound crystallized from ethanol as large white prisms, m.p. 280.5–282.5°.

Anal. Calcd. for $C_{19}H_{22}N_2O_4$: C, 66.65; H, 6.48. Found: C, 66.76; H, 6.52.

N,N′-Di-(α,α-dimethylglutaryl)-diaminomesitylene.—To a stirred refluxing solution of 7.7 g. of α,α-dimethylglutaric anhydride[7,8] in 80 ml. of dry benzene was added 4.07 g. of diaminomesitylene in 80 ml. of dry benzene. The addition required one hour and refluxing was continued 30 minutes longer. The solution was cooled and the product filtered, washed with benzene and dried. The yield was 11.1 g. (94%). Recrystallization from glacial acetic acid gave fine white needles, m.p. 258–259.5°.

Anal. Calcd. for $C_{23}H_{34}N_2O_6$: C, 63.57; H, 7.89; N, 6.45. Found: C, 63.68; H, 7.95; N, 6.39.

Bis-(α,α-dimethylglutarimido)-mesitylene.—A mixture of 3.5 g. of N,N′-di-(α,α-dimethylglutaryl)-diaminomesitylene, 4.2 g. of anhydrous sodium acetate and 70 ml. of acetic anhydride was refluxed one hour, then hydrolyzed cautiously with 25 ml. of water. The solution was slowly

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[6] All melting points are corrected.

[7] B. Shive, J. T. Horeczy and H. L. Lochte, THIS JOURNAL, **62** 2744 (1940).

[8] W. H. Perkin, Jr., *J. Chem. Soc.*, **81**, 251 (1902).

neutralized with concentrated sodium hydroxide while cooling under running tap water. The precipitated solid was filtered and dried. It was thoroughy extracted with chloroform; the insoluble sodium acetate was removed by filtration. Evaporation of the chloroform extract yielded 2.79 g. of crude product (87%). It was dissolved in methanol, treated with Darco and evaporated with an air jet until about one-third of the solid crystallized. The crystals were removed and redissolved in methanol and the solution again partially evaporated. The operation was performed three times. The resulting solid was recrystallized twice from toluene. The yield of the *trans* isomer was 0.35 g. It melted at 225–226°.

Anal. Calcd. for $C_{23}H_{30}N_2O_4$: C, 69.32; H, 7.59; N, 7.03. Found: C, 69.25; H, 7.43; N, 7.07.

The combined methanol filtrates were concentrated to about one-third of their original volume and the precipitated solid removed. The filtrate was evaporated to dryness. This residue was recrystallized to constant melting point from toluene. The yield of the *cis* isomer was 0.28 g. It melted at 204–205°.

Anal. Calcd. for $C_{23}H_{30}N_2O_4$: C, 69.32; H, 7.59; N, 7.03. Found: C, 69.48; H, 7.65; N, 7.13.

An attempt was made to brominate the *trans* isomer with bromine in chloroform using powdered iron as catalyst. After 6 hours of refluxing, most of the compound was recovered unchanged.

The infrared spectra of the isomers in chloroform solution are very similar but not identical. Small differences were observed in the intensities of peaks and bands in the regions 840 to 1010 cm.$^{-1}$ and 1325 to 1350 cm.$^{-1}$. A shift of 3 to 4 cm.$^{-1}$ toward the higher frequencies was found for the *cis* isomer in the region 925 to 1010 cm.$^{-1}$. Spectra were also run in nitromethane solution in the region of intense absorption by chloroform. The spectrum of the *cis* isomer in nitromethane shows a band and peak at 1227 and 1210 cm.$^{-1}$ which appears only as a slight shoulder in the spectrum of the *trans* isomer.

Bis-(α,α-dimethylglutarimido)-nitromesitylene. A.—*trans*-Isomer.—To 5 ml. of 90% fuming nitric acid (sp. g. 1.5) at 0° was added 0.14 g. of *trans*-bis-(α,α-dimethylglutarimido)-mesitylene. The solution was maintained at 0° for 45 minutes, then poured onto 50 g. of cracked ice. The precipitated solid was filtered, washed with water and dried. The yield was 0.16 g. (quant.). Recrystallization from ethanol gave white shiny leaflets, m.p. 256.5–257.5°.

Anal. Calcd. for $C_{23}H_{29}N_3O_6$: C, 62.29; H, 6.59; N, 9.47. Found: C, 62.19; H, 6.41; N, 9.58.

B. *cis*-Isomer.—Treatment of 0.14 g. of *cis*-bis-(α,α-dimethylglutarimido)-mesitylene in the same manner yielded 0.14 g. (90%) of the lower-melting nitro compound, which crystallized from aqueous ethanol as colorless prisms, m.p. 234–236°.

Anal. Calcd. for $C_{23}H_{29}N_3O_6$: C, 62.29; H, 6.59; N, 9.47. Found: C, 62.58; H, 6.62; N, 9.68.

The spectra of the isomers in chloroform show much the same differences found for the unsubstituted glutarimides—small intensity variations in the regions 860 to 1010 cm.$^{-1}$ and 1300 to 1400 cm.$^{-1}$, and a 1 to 2 cm.$^{-1}$ shift toward the higher frequencies between 900 and 1000 cm.$^{-1}$ in the spectrum of the *cis* isomer.

4-Bromobutyl Thiocyanate.—To a stirred refluxing solution of 333 g. of tetramethylene bromide in 600 ml. of absolute ethanol was added over a period of 1.5 hours a solution of 82.5 g. of potassium thiocyanate in 60 ml. of water. Refluxing was continued for one additional hour, then the reaction mixture was poured into 1.5 l. of water and the oily layer decanted. The aqueous layer was extracted with ether, and the combined oil and ether extract was dried first over sodium sulfate, then over magnesium sulfate. Distillation yielded 150 g. of recovered tetramethylene bromide. The product was a colorless liquid, b.p. 97–99° (1 mm.). The yield was 81 g. (50%). A portion was redistilled for analysis, n^{20}_{D} 1.5288.

Anal. Calcd. for C_5H_8BrNS: C, 30.94; H, 4.15; N, 7.22. Found: C, 31.42; H, 4.34; N, 6.90.

4-Chlorobutyl Thiocyanate.—To a stirred refluxing solution of 282 g. of tetramethylene chloride in 500 ml. of absolute ethanol was added over a period of 3 hours 108 g. of potassium thiocyanate in 50 ml. of water. Refluxing was continued for 30 minutes longer. The isolation procedure described for 4-bromobutyl thiocyanate was used. Distillation at the water-pump yielded 142 g. of tetramethylene chloride. The product was obtained as a colorless liquid, b.p. 88.5–90.5° (1.5 mm.). The yield was 72 g. (44%). A portion was redistilled for analysis, n^{20}_{D} 1.5023.

Anal. Calcd. for C_5H_8ClNS: C, 40.13; H, 5.39. Found: C, 40.43; H, 5.48.

Attempts to prepare 4-bromobutanesulfonyl chloride and 4-chlorobutanesulfonyl chloride were unsuccessful. No distillable product was obtained by oxidation of the thiocyanates with chlorine in water at 5–10° or with chlorine in acetic acid solution containing the theoretical amount of water at 25–35°. In some cases no attempt was made to distil the product, but a dried chloroform extract of the oxidation mixture was allowed to react with diaminomesitylene. Only intractable orange oils and tars were isolated which failed to yield a solid product when subjected to ring closure conditions (refluxing aqueous sodium hydroxide).

URBANA, ILLINOIS

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

Dicrotaline. The Structure and Synthesis of Dicrotalic Acid

BY ROGER ADAMS AND BENJAMIN L. VAN DUUREN

RECEIVED JANUARY 23, 1953

Dicrotalic acid, obtained by the hydrolysis of the alkaloid dicrotaline, from *Crotalaria dura* (Wood and Evans) and *Crotalaria globifera* (E. Mey) has been shown by degradation studies to be β-methyl-β-hydroxyglutaric acid. The latter acid was synthesized and proved to be identical with the natural acid. The structure of dicrotaline is therefore completely elucidated.

Dicrotaline, $C_{14}H_{19}O_5N$, first isolated by Marais[1] yielded on hydrolysis a base, retronecine, which constitutes the basic portion of many Senecio alkaloids,[2] and a new dibasic acid, $C_6H_{10}O_5$, for which the name dicrotalic acid was suggested. A sample of this acid was kindly supplied us by Dr. J. S. C. Marais of the Department of Agriculture of the Union of South Africa which permitted the determination of its structure in this Laboratory.

The infrared absorption spectrum of dicrotalic acid showed an alcoholic hydroxyl band at 3215 cm.$^{-1}$, a bonded OH band at 2660 cm.$^{-1}$, and a carbonyl band at 1710 cm.$^{-1}$ (shoulder at 1695 cm.$^{-1}$). The acid could not be oxidized with lead dioxide in phosphoric acid and did not give a coloration with ferric chloride[3] from which it seemed improbable that the hydroxyl was in an α-position

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[1] J. S. C. Marais, *Onderstepoort J. Vet. Sci. Animal Ind.*, **20**, 61 (1944).

[2] N. J. Leonard, "The Alkaloids" (Editors R. H. F. Manske and H. L. Holmes), Vol. I, Academic Press, Inc., New York, N. Y., 1950, p. 108.

[3] A. Berg, *Bull. soc. chim.*, **11**, 882 (1894).