The product after recrystallization from ethylene dichloride separated as colorless plates, m. p. 123°; yield 40 g. *Anal.* Calcd. for $C_{10}H_{14}N_4O_2$: N, 25.21. Found: N, 25.29.

XIII. Di-(cyanoethyl) Ether of Benzoin Oxime.—To a stirred solution of 22.7 g. of α-benzoin oxime, 100 g. of dioxane, and 2 g. of "Triton B," there was gradually added 10.6 g. of acrylonitrile at 30–40°. The mixture was stirred for two hours and allowed to stand twenty-four hours at room temperature. It was then made slightly acidic with dilute hydrochloric acid; poured into 400 cc. of water, and the heavy oil taken up in benzene. After evaporation of the benzene, the residual oil (32 g.) was allowed to stand for several months during which time it crystallized. After recrystallization from ethanol to constant melting point the product formed colorless needles, m. p. 72–73°. *Anal.* Calcd. for $C_{20}H_{19}N_3O_2$: N, 12.61. Found: N, 12.42.

XIV. O-(β-Cyanoethyl)-furfuraldoxime.—A mixture of 18 g. of furfuraldoxime (*syn*-form m. p. 88°), 25 cc. of dioxane, and 0.3 g. of sodium methylate was stirred and heated at 50–60° until a clear solution was obtained. This was cooled to 20°, and 8.5 g. of acrylonitrile added gradually to the stirred solution, so that the reaction temperature was 30–40°. The mixture solidified after a short time to a crystalline magma. Dioxane (50 cc.) was added to assist stirring and the mixture filtered after stirring for two hours. The alkalinity was neutralized with dilute hydrochloric acid and the crystalline product filtered off; yield 12 g. After recrystallization from benzene, the pure compound formed water-soluble long colorless needles, m. p. 116°. *Anal.* Calcd. for $C_8H_8N_2O_2$: N, 17.07. Found: N, 16.80.

Summary

1. Acrylonitrile condensed in the presence of strong alkali catalysts with nitroalkanes, malonic esters, cyanoacetic ester, malonamide, benzyl cyanide, and ω-toluenesulfonamide types of compounds having activated methylene or methenyl groups, so as to replace each active hydrogen by a β-cyanoethyl radical.

2. Acrylonitrile also reacted with the hydrogen atoms of water to yield bis-(β-cyanoethyl) ether. This can be obtained in 90% yield by treating acrylonitrile with hydracrylonitrile.

3. Polycyanoethyl ethers were obtained from various glycols and from glycerol by the action of acrylonitrile in the presence of alkali.

4. Oximes reacted with acrylonitrile to yield cyanoethyl oximino ethers.

PHILADELPHIA, PA. RECEIVED SEPTEMBER 14, 1942

[CONTRIBUTION FROM DIVISION OF INSECTICIDE INVESTIGATIONS, AGRICULTURAL RESEARCH ADMINISTRATION, BUREAU OF ENTOMOLOGY AND PLANT QUARANTINE, UNITED STATES DEPARTMENT OF AGRICULTURE]

The Occurrence of Rotenone and Related Substances in the Seeds of the Berebera Tree. A Procedure for the Separation of Deguelin and Tephrosin*

BY E. P. CLARK

During 1932–1933, while making a survey of possible rotenone-bearing plants, we came in possession of some seeds of the African berebera tree (*Millettia ferruginea* Hochst.), which grows along the streets of Addis Ababa. When processed these seeds yielded about 1% of rotenone by direct crystallization, and the mother liquors, when treated with alkali, yielded some dehydrorotenone and about 0.2% of an unknown material. The latter, recrystallized from hot *n*-butanol, was obtained as long, narrow, light lemon-colored rods. While its appearance under the microscope was that of a uniform substance, it was unquestionably a mixture, as it began to sinter at 140° and did not melt clear until 198°.

Because of the low yield obtained, further investigation of this substance was not undertaken at the time, but the recent work by Harper,[1] Meyer and Koolhaas,[2] and Buckley[3] on new con stituents of leguminous fish-poisoning plants stimulated further study of its nature.

Approximately 6 g. of material was available, and as preliminary experiments with various solvents indicated that it could not be resolved by recrystallization, it was subjected to chromatographic analysis. A few trials indicated a satisfactory procedure, which was followed. It resulted in the separation of the mixture into a main fraction of about 3 g. of tephrosin, 0.5 g. of a new substance melting at 189–190°, and 1 g. of a third material melting at 164–165°. There was also evidence of a lower melting substance, but not enough material was available to realize a complete purification.

Neither of the new compounds gave the Durham or ferric chloride test; they would not form dehydro compounds by iodine oxidation in alco-

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[1] Harper, *J. Chem. Soc.*, 812, 1099 (1939); 309, 1178 (1940); 181 (1942).

[2] Meyer and Koolhaas, *Rec. trav. chim.*, **58**, 207 (1939).

[3] Buckley, *J. Soc. Chem. Ind.*, **55**, 285 (1936).

holic acetate solution or by dehydration with acetic anhydride, and no crystalline acetates or oximes could be obtained. The compound melting at 189–190° has the composition $C_{23}H_{20}O_6$ and has one methoxyl group. The compound with the melting point of 164–165° has the composition $C_{21}H_{20}O_6$ and has two methoxyl groups. While these two materials have formulas similar to the rotenone group of fish poisons, they have, in so far as they have been studied, only one characteristic in common, namely, that they separate from alcoholic extracts of plant material upon treatment with alkali.

The limited quantity of material with which to work precluded an extensive investigation of the new compounds, but the experience gained with them has made it possible to demonstrate that the melting points recorded for tephrosin and isotephrosin must be revised upward. The most highly purified tephrosin recrystallized to constant melting point of 198° has been shown to contain some isotephrosin. When this is removed, tephrosin melts at 201–202°. Likewise isotephrosin recrystallized to constant melting point of 252° contains some tephrosin, and when the latter is completely removed isotephrosin melts at 260°.

This study also led to a simple method of separating deguelin and tephrosin. This is usually a difficult procedure when pure materials are desired.

Experimental

Rotenone.—The ground berebera seeds (3500 g.) were extracted with petroleum ether to remove fat and oil, the dried marc was exhaustively percolated with ether, and the extract freed from solvent and dissolved in 3500 cc. of methanol. This liquid was passed through a thin layer of norit, evaporated to 300 cc., and allowed to crystallize. Thirty-six grams of fairly pure rotenone was obtained. Upon crystallization from ethanol it melted at 163° and did not depress the melting point of an authentic sample of rotenone.

Treatment of the Rotenone Mother Liquors with Alkali.—The rotenone mother liquors were diluted to 600 cc., and 5 cc. of 50% aqueous potassium hydroxide was added. After standing overnight a little over 6 g. of crystals separated. Upon standing another day a second crop of crystals, 2.5 g., was obtained. The latter were essentially dehydrorotenone, for when they were recrystallized from a mixture of chloroform and methanol they melted at 218° and did not depress the melting point of an authentic sample of dehydrorotenone.

Tephrosin.—Two gram lots of the mixture, melting point 140–198°, were dissolved in 20 cc. of chloroform, and passed through 150 by 12 mm. columns of aluminum oxide. The percolates were collected in small fractions, and each evaporated to a sirupy consistency, dissolved in methanol, and further boiled to remove all chloroform. The resulting solutions were then allowed to crystallize. The first fractions contained the lower melting compounds, while the last fractions contained largely material melting above 190°. All the material was thus roughly divided into four fractions with increasing melting point ranges. The process was repeated many times with each fraction until three materials having sharp melting points were obtained. One fraction, melting at 198–200°, was dissolved in benzene, adsorbed upon aluminum oxide, thoroughly washed with benzene, and eluted with chloroform. The material, *ca.* 3 g., consisted of dense, colorless prisms which melted at 201° and cleared at 202°. Further chromatographic treatment and recrystallization from a mixture of chloroform and methanol did not change its melting point. When treated with acetic anhydride and sodium acetate it gave dehydrodeguelin, its optical crystallographic properties were those of tephrosin; and when mixed with the purest tephrosin available (m. p. 198°) the mixed melting point was 199–200°. These properties conclusively prove the material to be tephrosin.

The melting point of the material thus obtained led to the suspicion that all samples of tephrosin previously at hand contained some impurity. A sample of so-called pure tephrosin was therefore subjected to the process outlined above. The first fraction obtained, a few milligrams from 1 g., had a melting point of 259°. Several subsequent fractions had melting points between 201° and 230°, while the remaining fractions, consisting of the greater part of the material taken, melted at 201°. Isotephrosin was suspected as being the impurity, and to verify this a sample of isotephrosin, recrystallized to constant melting point of 252°, was subjected to chromatographic treatment. The first fractions obtained, consisting of most of the material, melted at 259–260°, while the last fractions melted unsharply between 200° and 250°. The 259–260° melting material was passed through a new column and recrystallized from chloroform and methanol. It then melted sharply at 260°. When mixed with the substance melting at 259° from tephrosin, the melting point was not depressed. Thus, the melting points for tephrosin and isotephrosin are 201° and 260°, respectively.

The Compound Melting at 164–165°.—The second pure product obtained from the mixture was recrystallized by the procedure indicated above and melted at 164–165°. As it passed through the column more quickly than the others, the first fractions from a new column frequently gave this material in pure condition.

Anal. Calcd. for $C_{21}H_{20}O_6$: mol. wt., 368.4; C, 68.47; H, 5.47; $OCH_3(2)$, 16.85. Found: mol. wt., 350; C, 68.45; H, 5.26; OCH_3, 16.7.

The Compound Melting at 189–190°.—The third pure compound obtained melted at 189–190°. It usually crystallized as a mat of long, narrow, colorless rods or needles, but when left in the mother liquors for any length of time it changed to dense, colorless prisms. There was no difference in the melting point of the two forms.

Anal. Calcd. for $C_{23}H_{20}O_6$: mol. wt., 392.4; C, 70.40; H, 5.14; $OCH_3(1)$, 7.91. Found: mol. wt., 390; C, 70.20; H, 5.03; OCH_3, 7.8.

Separation of Deguelin and Tephrosin.—Deguelin and tephrosin may be separated by the chromatographic method because tephrosin is eluted with chloroform from aluminum oxide more slowly than is deguelin. When chloroform solution of the two substances is passed through a column of the adsorbent, deguelin practically free from tephrosin is obtained in the first fractions while pure tephrosin is obtained in the subsequent fractions. An example follows:

A mixture of 1 g. of deguelin and 0.5 g. of tephrosin dissolved in 20 cc. of chloroform was passed through a 150 by 12 mm. column of aluminum oxide and eluted with chloroform. The first 50 cc. of percolate gave 0.7 g. of deguelin, melting at 170–171°. The second 50-cc. fraction gave 85 mg. of a mixture melting at 165–172°. The third fraction gave 180 mg. of tephrosin (m. p. 198–200°); the fourth 50-cc. fraction gave 40 mg. of tephrosin (m. p. 199–201°). The mother liquors were not reworked. There appeared to be some decomposition of the deguelin as it and its solution were somewhat yellow. However, passing the recovered deguelin dissolved in chloroform through a bed of norit removes all color and gives a sharp melting product, melting at 171°. Repetition of the process upon the tephrosin fraction is necessary for complete purification.

Summary

1. Rotenone, dehydrorotenone, tephrosin, and two new compounds, one, $C_{21}H_{20}O_6$, m. p. 164–165°, and the second, $C_{23}H_{20}O_6$, m. p. 189–190°, have been isolated from the seeds of the African berebera tree.

2. A revision of the melting point of tephrosin from 198° to 201° and of isotephrosin from 252° to 260° has been made.

3. A procedure is suggested for the separation and purification of deguelin and tephrosin when the two substances occur together.

BELTSVILLE, MD. RECEIVED OCTOBER 7, 1942

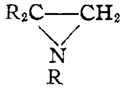
[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF THE JOHNS HOPKINS UNIVERSITY]

The Configuration of Tervalent Nitrogen. A Bicyclic Hydrazine Derivative[1]

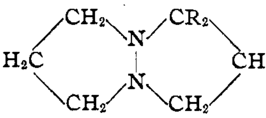
BY EMMETT L. BUHLE, ALEXANDER M. MOORE AND F. Y. WISELOGLE

The problem of the configuration of tervalent nitrogen has held a peculiar fascination for chemists ever since the first indication that the bonds did not all lie in a common plane. Although the configuration of the ammonia molecule has now been determined to within narrow limits,[2] the organic chemists doubtless will consider the problem "solved" only when a structure of the type $R_1R_2R_3N$ has been separated into optical isomers. Despite many ingenious attempts at such resolutions not one has been successful.[3] The consistent failure to isolate such optical isomers has now been rationalized by postulating a rapid inversion of configuration resulting from the vibration of the nitrogen through the plane of the three attached groups.

Accordingly, the more recent studies of the problem have centered around compounds in which the activation energy for the inversion of configuration would be increased through structural idiosyncrasies of the molecule. Thus several researchers have been studying substituted ethyleneimines, (I), in which one of the nitrogen valency angles has been reduced to 63° through its incorporation in a three-membered ring.[3b,4] Although theoretical calculations have indicated a stable configuration for such derivatives[5] no optically active compounds have yet been obtained, largely owing to difficulties in the synthesis of requisite intermediates.



(I)



(II)

We have begun what we believe is a new approach to the problem since all of the valence angles remain normal and there is no structural strain within the molecule. In our projected structure the inversion restriction is achieved by locking two nitrogen atoms together in a bicyclic molecule in which the nitrogens are common to both rings. A representative member of such a class of compounds is a 3,3-disubstituted-1,2-trimethylenepyrazolidine (II). In this model

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[1] Most of the material reported herein was taken from the dissertation submitted by A. M. Moore in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Johns Hopkins University. Preliminary work was carried out by F. Y. Wiselogle in the University of Illinois during the summer of 1940. He is grateful for the facilities which were made available and for many stimulating discussions with various members of the Chemistry Staff. We are indebted to the Hynson, Westcott and Dunning Research Fund for a grant-in-aid covering a part of the cost of this research.

(2) Migeotte and Barker, *Phys. Rev.*, **50**, 418 (1936).

(3) (a) Gilman, "Organic Chemistry, An Advanced Treatise," John Wiley and Sons, Inc., New York, N. Y., 1938, pp. 328–338; (b) "Annual Reports on the Progress of Chemistry," The Chemical Society, London, **36**, 239–246 (1939).

(4) Cairns, THIS JOURNAL, **63**, 871 (1941).

(5) Kincaid and Henriques, *ibid.*, **62**, 1474 (1940).