[CONTRIBUTION FROM THE NAVAL STORES RESEARCH STATION[1]]

A Preparation and Some of the Reactions of the Diels-Alder Adducts of Levopimaric Acid and Acrylonitrile

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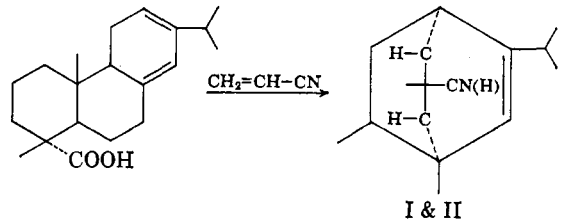
Levopimaric acid and abietic-type acids in rosin were found to form Diels-Alder type condensation products with acrylonitrile. Two *endo* adducts of levopimaric acid were isolated. These are probably structural isomers differing in the position of the nitrile group. Amino alcohols were prepared from these adducts by reduction with lithium aluminum hydride. Amino acids were prepared from one adduct by catalytic hydrogenation.

Levopimaric acid, a constituent of gum oleoresin, forms Diels-Alder addition products under mild conditions with maleic anhydride,[2a] benzoquinone,[3] esters of acetylene dicarboxylic acid,[4] and the naphthoquinones[2b,5] Under more vigorous conditions it has been suggested[2a] that levopimaric acid is in equilibrium with other abietic-type acids. Hence, all the abietic-type diene acids should react with the more active dienophiles under the proper conditions.

This laboratory has reported on the reaction of the abietic-type diene acids with fumaric acid.[6] In continuing a study of the diene reaction we have treated all of these acids in rosin with acrylonitrile, isolated and characterized the major products formed. Although Arbuzov and Khismatullina[7] obtained a noncrystalline adduct melting at 80–90°, $[\alpha]_D$ −12.5°, from the reaction of acrylonitrile with a mixture of resin acids, they assumed that their product consisted of only one isomer.

In this laboratory, a mixed adduct was obtained in 97% yield by refluxing an acrylonitrile solution of pure levopimaric acid for three hours. The neutralization equivalent and elemental analysis of the cyclohexylamine salts of the mixed adduct formed agreed with that calculated for a diene type condensation. The ultraviolet spectrum indicated that no conjugated diene system remained.

The reaction product was separated by partition chromatography into two isomeric adducts; 42% of I, $[\alpha]_D^{25}$ +88.8° and 55% of II, $[\alpha]_D^{25}$ 0°. The finding of two of the four possible *endo* isomeric forms was expected since only two isomers were found in the adduct of abietic acid and fumaric acid.[6] It is reasonable to assume that the condensation is effected from only one side of the levopimaric acid molecule and that the difference in rotation of the two forms depends on the position of the nitrile group. No assignment of structure for the two forms has been made. Only one product has been reported for the maleic anhydride, benzoquinone, and α-naphthoquinone adducts which have symmetrical structures.



I & II

Figure 1

The two adducts of acrylonitrile and levopimaric acid were also separable by fractional crystallization. Adduct I crystallized from alcohol-water (70:30) and would not crystallize from benzene. Adduct II crystallized from benzene. Unchanged resin acids were separated from the reaction mixture as their cyclohexylamine salts. The amine salts of the two isomeric adducts were very soluble in wet acetone, but could be crystallized readily from dry acetone.

Amino alcohols were prepared from I and II by reduction in a dry ether suspension of lithium aluminum hydride. The amino alcohol from I was isolated as the hydrochloride in 87% yield. The corresponding product from II crystallized from the ether solution in 76% yield. Examination of the infrared spectra showed complete elimination of the nitrile and carbonyl bands for each product. When adduct II was catalytically hydrogenated in acetic acid for two hours, two moles of hydrogen per mole of II combined to form the corresponding amino acid. Adduct II was also hydrogenated for eighty hours, absorbing three moles of hydrogen per mole, eliminating ammonia and resulting in the saturated, secondary amine. Presumably the greater length of treatment and a lower concentration of catalyst

(1) One of the laboratories of the Southern Utilization Research and Development Division, Agricultural Research Service, U. S. Department of Agriculture.

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(3) L. Ruzicka and St. Kaufmann, *Helv. Chim. Acta*, **24**, 1425 (1941).

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favored the side reaction leading to the secondary amine.[8]

Gum rosin containing approximately 58% of abietic-type acids[9] was treated with acrylonitrile at atmospheric pressure and a reaction temperature of 225°. Separation of the product by partition chromatography gave fractions of adduct I comprising 18.8%, adduct II comprising 17.6% and unreacted resin acids (principally dehydro- and dihydroabietic and dextro- and isodextropimaric acids) comprising 34% of the acids placed on the column. A fraction obtained by stripping the column with benzene contained 25.6% of the acids placed on the column. The infrared spectrum of this fraction indicated a nitrile content of about half that of adduct I or II.

EXPERIMENTAL[10]

Acrylonitrile adduct of levopimaric acid. Levopimaric acid, $[\alpha]_D^{25}$ −266°, was prepared according to the procedure of Harris and Sanderson.[11] A mixture of 10 g. (0.03 mole) of the levopimaric acid and 20 ml. (0.31 mole) of acrylonitrile was heated at 110° in an oil bath with stirring under nitrogen for 3 hr. The mixture became homogeneous after 1 hr. and after 3 hr. was poured into 200 ml. of water. The water was heated to boiling and decanted leaving a white gum which was dissolved in 100 ml. of benzene. The benzene solution was washed with water. Evaporation of the benzene and drying under vacuum 3 hr. at 100° gave 11.5 g. (98%) of the crude product, $[\alpha]_D^{25}$ +37.6°, neut. equiv. 358, m.p. 115–118°. The product gave a cyclohexylamine salt from acetone solution which could not be recrystallized to constant melting point and rotation. The yield of salt was 80%.

Anal. Calcd. for $C_{29}H_{46}N_2O_2$: C, 76.60; H, 10.20; N, 6.16; neut. equiv. 454.7. Found: C, 76.64; H, 10.31; N, 6.17; neut. equiv. 454.5.

Chromatographic separation of the products from the levopimaric acid–acrylonitrile reaction. The adduct was subjected to a partition chromatographic technique similar to that described by Ramsey and Patterson[12] with the exception that furfuryl alcohol was replaced with monoacetin as a component of the stationary phase and a mixture of isooctane-benzene (85:15) was used for the mobile phase. The chromatographic tube was 27 mm. O. D. × 200 cm. long. The eluting solvent was prepared by saturating 1 l. of the isooctane-benzene with 48 g. of the 2-aminopyridine-monoacetin mixture (25:75). The column was packed with 45 g. of silicic acid which had previously been mixed with 34 g. of the 2-aminopyridine-monoacetin phase separated from the isooctane-benzene wash. A 550 mg. sample was placed on the column and developed with the isooctane-benzene. The effluent was collected in 10 ml. fractions and the milliequivalents of acid in each fraction determined by titration with alkali. The first peak, eluted at 100 ml., contained 3% of the product and was not investigated. The second peak, eluted at 450 ml. contained 42% of the acids placed on the column. A third peak eluted at 640 ml. contained 55% of the resin acids placed on the column. The fractions forming each peak were combined, acidified with acetic acid and washed with water. The solution was concentrated to 15–20 ml., cyclohexylamine added and the amine salt allowed to form overnight. The white crystals were collected, washed with pentane and dried in a vacuum desiccator over calcium sulfate.

Separation of adduct I. The solution from peak 2 gave a 90% yield of the acid as the cyclohexylamine salt; $[\alpha]_D^{25}$ +68.5°; neut. equiv. 455.0; m.p. 207–208.5°. The free acid was obtained by dissolving 158 mg. of the amine salts in 3 ml. of alcohol, adding an excess of 3*N* acetic acid, diluting with water to 30% by volume and storing in the refrigerator overnight for crystallization; yield 89%. The sample was recrystallized from alcohol-water and the crystals dried at 100° under vacuum; neut. equiv., 355.2; m.p. 191.0–192.0°; $[\alpha]_D^{25}$ +88.2°.

Separation of adduct II. Peak 3 was worked up in a similar manner to give an 89% yield of cyclohexylamine salt; $[\alpha]_D^{25}$ 0°; m.p. 188.5–189.5°; neut. equiv., 454.3. The free acid was obtained by suspending 200 mg. of the amine salt in 10 ml. of benzene, washing with 3*N* acetic acid, and washing with water until neutral. The solution was evaporated to 2 ml. and 2 ml. of isooctane added. The crystals which separated were dried at 140°, under vacuum, yield 78%; neut. equiv., 355.8; m.p. 181.5–182.5°; $[\alpha]_D^{25}$ 0°.

Separation of products by crystallization. The reaction product of 34 g. (0.11 mole) of levopimaric acid, $[\alpha]_D^{25}$ −270° and 26.5 g. (0.5 mole) of acrylonitrile was recrystallized twice from a 50:50 benzene-isooctane mixture and once from benzene to give 9.3 g. of adduct II. Drying in vacuum at 140° for 4 hr. gave the analytical sample; m.p. 181.5–182.5°; $[\alpha]_D^{25}$ 0°. Admixture with adduct II obtained by partition chromatography gave no depression in melting point.

Anal. Calcd. for $C_{22}H_{33}NO_2$: C, 77.70; H, 9.36; N, 3.94; neut. equiv. 355.5. Found: C, 77.59; H, 9.34; N, 3.92; neut. equiv. 355.5.

The cyclohexylamine salt was prepared by neutralizing an acetone solution of the acid with the amine. The crystals which formed were collected, washed with a little acetone and dried in an evacuated desiccator over calcium sulfate, $[\alpha]_D^{25}$ 0°; m.p. 190.5–191.5°.

Anal. Calcd. for $C_{29}H_{46}N_2O_2$: C, 76.60; H, 10.20; N, 6.16; neut. equiv. 454.7. Found: C, 76.41; H, 10.12; N, 6.17; neut. equiv. 455.1.

The isooctane-benzene filtrate from the first crystallization was evaporated and the residual resin, 22.0 g., was dissolved in 200 ml. of acetone containing about 1% water, and neutralized with cyclohexylamine. The salt which crystallized overnight consisted mostly of unchanged resin acids. Another recrystallization of this salt, from 150 ml. of acetone, was done to gain further separation of the adduct from the unchanged acids. The liquors from the first and second crystallizations were then evaporated to one-fourth volume and 16.2 g. of crystals collected. Recrystallization from alcohol-water and drying in a vacuum desiccator over calcium sulfate gave the analytical sample. Yield 11.2 g.; $[\alpha]_D^{25}$ +68.5°; m.p. 207–208.5°.

Anal. Calcd. for $C_{29}H_{46}N_2O_2$: C, 76.60; H, 10.20; N, 6.16; neut. equiv., 454.7. Found: C, 76.45; H, 10.18; N, 6.15; neut. equiv., 455.0.

The salts were dissolved in alcohol-water (70:30) and the acid freed by addition of 3*N* hydrochloric acid. The acid was recrystallized from alcohol water (70:30) to yield 8.6 g. (52% of the calculated quantity by chromatographic analysis) of adduct I, $[\alpha]_D^{25}$ +88.8°; $[\alpha]_D^{25}$ (1.1% chloroform) +93.7°; m.p. 191.5–192.0°. Admixture with I obtained by partition chromatography gave no depression in melting point.

(8) A discussion of the preparation of primary and secondary amines by catalytic hydrogenation is given in R. B. Wagner and H. D. Zook, *Synthetic Organic Chemistry*, Wiley, New York, 1953, p. 658, and in references cited therein.

(9) D. E. Baldwin, V. M. Loeblich and R. V. Lawrence, *Chem. & Eng. Data Ser.*, **3**, 342 (1958).

(10) All reported melting points are uncorrected. Optical rotations were determined on 2% solutions in 95% ethanol, except where indicated.

(11) G. C. Harris and T. F. Sanderson, *J. Am. Chem. Soc.*, **70**, 334 (1948).

(12) (a) L. L. Ramsey and W. I. Patterson, *J. Assoc. Offic. Agr. Chemists*, **31**, 441 (1948). (b) V. M. Loeblich, D. E. Baldwin and R. V. Lawrence, *J. Am. Chem. Soc.*, **77**, 2823 (1955).

Anal. Calcd. for $C_{23}H_{33}NO_2$: C, 77.70; H, 9.36; N, 3.94; neut. equiv. 355.5. Found: C, 77.82; H, 9.34; N, 3.90; neut. equiv., 355.0.

Reduction of I *and* II *by lithium aluminum hydride to the corresponding amino alcohols.* A solution of 3.00 g. (0.008 mole) of I in 60 ml. of dry ether was added slowly to a suspension of 4.80 g. (0.126 mole) of lithium aluminum hydride in 100 ml. of dry ether under nitrogen. The solution was stirred and heated at reflux under nitrogen 4 hr. and cooled. Excess hydride was decomposed with water, 5 ml. of 20% sodium hydroxide added, and stirring continued 15 min. Separation was effected by filtration and leaching the granular mass with 200 ml. of ether. The ether was washed until neutral and evaporated to dryness giving a 93% yield. A partially crystalline product having $[\alpha]_D^{25}$ +88.7° was obtained from an alcohol-water solution. This material showed complete absence of nitrile and carbonyl absorption in the infrared. The hydrochloride was prepared by adding 10 ml. of 6*N* hydrochloric acid to 10 ml. of alcohol containing 0.3 g. of the reduction product heating at reflux for 5 min. and cooling. The crystalline hydrochloride was obtained in 87% yield, m.p. 317.0–318.0° dec.

Anal. Calcd. for $C_{23}H_{40}ClNO$: C, 72.31; H, 10.55; Cl, 9.28; N, 3.67. Found: C, 72.13; H, 10.40; Cl, 9.18; N, 3.57.

Adduct II was reduced as described above for the reduction of adduct I. Evaporation of the ether yielded 2.38 g. (76%) of the amino alcohol. Recrystallization from ether and drying at 100° in vacuum for 3 hr. gave the analytical sample, $[\alpha]_D^{25}$ 0°; m.p. 117–117.5°.

Anal. Calcd. for $C_{23}H_{39}NO$: C, 79.94; H, 11.37; N, 4.05; neut. equiv., 345.6. Found: C, 79.92; H, 11.29; N, 4.02; neut. equiv., 344.8.

Catalytic reduction of II *to the amino acid.* A solution of 0.710 g. (0.002 mole) of II in 15 ml. of prereacted glacial acetic acid was hydrogenated at atmospheric pressure and room temperature over 0.71 g. of 5% palladium carbon catalyst. After 2.25 hr. 2.04 moles of hydrogen per mole of adduct had been absorbed. The catalyst was removed by filtration and the hydrogenated product evaporated to a viscous liquid under vacuum at 60°. The amino acid was heated to boiling in 10 ml. of hydrochloric acid–alcohol (30:70) solution, filtered, and allowed to crystallize. Two recrystallizations and drying in a vacuum desiccator gave the analytical sample. The yield was 0.444 g. (56%), m.p. 318–319° dec., $[\alpha]_D^{25}$ 0°.

Anal. Calcd. for $C_{23}H_{38}ClNO_2$: C, 69.76; H, 9.67; Cl, 8.95; N, 3.54. Found: C, 69.65; H, 9.76; Cl, 8.88; N, 3.24.

Catalytic reduction of II *on the secondary amine.* In another experiment, 1.22 g. (0.0034 mole) of II and 0.61 g. of the catalyst were used. The hydrogenation was allowed to continue for 80 hr. During this time 3.06 moles of hydrogen per mole adduct was absorbed. The product after removal of the acetic acid was crystallized from 12 ml. of alcohol-6*N* hydrochloric acid (75:25) by heating to reflux and allowing to cool, yield 85%. Recrystallization and drying in vacuum over calcium sulfate gave the analytical sample, m.p. 316–318° dec.; $[\alpha]_D^{25}$ −5.10°.

Anal. Calcd. for $C_{46}H_{76}ClNO_4$: C, 74.40; H, 10.30; Cl, 4.77; N, 1.88. Found: C, 74.10; H, 9.91; Cl, 4.77; N, 1.82.

Acrylonitrile adduct of rosin. An adduct was prepared using 500 g. of WW gum rosin containing approximately 290 g. (0.96 mole) of abietic-type acids. The rosin was heated to 200° with slow stirring and practical grade acrylonitrile was added at such a rate that the reaction mixture refluxed at 225°. Heating at 200–225° was continued for 7 hr. The mixture was then steam sparged to remove excess acrylonitrile. The increase in weight was 70 g. The product was dark brown, and had a neut. equiv. of 130; m.p., 96–104°.

Chromatographic separation of components in the rosin acrylonitrile adducts. The partition chromatographic technique for separation of the isomers was used to separate the reaction product into 3 peaks. A fourth fraction was eluted from the column by stripping with benzene. The first fraction contained the unchanged resin acids amounting to 34.2% of the acids placed on the column. The infrared spectra of the unchanged acids indicated the presence of dextro- and isodextropimaric acids. Chromatographic separation of the acids of this peak according to the method of Ramsey and Patterson as modified by Loeblich, *et al.*[12] showed the presence of isodextropimaric and some abietic, neoabietic, and dehydroabietic acid.

The second peak contained 18.8% of the acids placed on the column. Recovery from the eluting solvent as the cyclohexylamine salt gave an 83.4% yield of the acids in the peak. The acid was freed from the amine and recrystallized from alcohol-water to give the analytical sample; m.p., 191–192°; $[\alpha]_D^{25}$ +88.0°. Admixture with I gave no depression in melting point.

The third peak contained 17.6% of the acids placed on the column. The acids were precipitated from the eluting solvent as their cyclohexylamine salt (98.5% recovery). The acid was freed from the amine and crystallized from benzene to give the analytical sample; m.p. 178–179°; $[\alpha]_D^{25}$ 0°. Admixture with II gave no depression in melting point.

The fourth fraction obtained by stripping the column with benzene contained 25.6% of the acids placed on the column. The acid was extracted from the eluting solvent with 2*N* sodium hydroxide. The aqueous solution was acidified and extracted with ether, the ether washed with water dried, and evaporated to dryness; neut. equiv., 234. The infrared analysis indicated about half as much nitrile as was present in the adduct.

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