[CONTRIBUTION FROM THE NAVAL STORES STATION, U. S. DEPARTMENT OF AGRICULTURE[1]]

The Occurrence of Dextropimarinal and Isodextropimarinal in Commercial Gum Rosin

BY EDWARD MCC. ROBERTS AND RAY V. LAWRENCE

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It is shown here that dextropimarinal, an aldehyde present in *P. silvestris*, but not previously reported to be in *P. palustris* or *P. elliotti*, is present in commercial gum rosin derived from the latter sources. Previous reports on the aldehyde components of various rosins and resinous extracts leave the reported occurrence of isodextropimarinal in doubt. However, it is demonstrated here that isodextropimarinal is present in gum rosin, as previous authors have indicated.

Harris and Sanderson[2] isolated an aldehyde from *P. palustris* and *P. elliotti* (*P. caribaea*) which was thought to be identical with cryptopinone, a carbonyl compound isolated from *P. silvestris* by Sörensen and Bruun.[3] The former authors isolated isodextropimaric acid from the oxidation product of the aldehyde, concluded that the aldehyde was isodextropimarinal,[2] and confirmed the previous supposition that this aldehyde and cryptopinone were identical by a comparison of their 2,4-dinitrophenylhydrazones.[4]

Later, in collaboration with Barton,[4] Sörensen and Bruun proved cryptopinone to be dextropimarinal on the basis of a comparison of the 2,4-dinitrophenylhydrazone of the isolated aldehyde with authentic samples of the derivatives of both isodextropimarinal and dextropimarinal, synthesized from the corresponding acids. Inasmuch as the two acids are well characterized, the aldehyde syntheses were straightforward, and the comparisons clear-cut, there can be little doubt that cryptopinone is indeed dextropimarinal.

Considering the fact that the occurrence of isodextropimarinal is thrown into some doubt and that dextropimarinal has not been reported in American naval-stores pine, the present investigation was undertaken.

The presence of both dextropimarinal and isodextropimarinal in commercial samples of gum rosin (*ca.* 90% *P. elliotti* and 10% *P. palustris*) has been demonstrated by the isolation of the corresponding acids from mixtures of resinates obtained by the oxidation of the carbonyl fraction of gum rosin, using chromium trioxide under conditions sufficiently mild that only aldehydes would be expected to yield acids. In both cases the fractions in question were isolated using carbonyl reagents. That aldehydes were present in the carbonyl fractions was demonstrated by positive Tollens tests, chromium trioxide oxidation, and the fact that the infrared absorption spectrum showed two maxima characteristic of aldehydes (2695, 1733 cm.$^{-1}$).[5]

Dextropimarinal was shown to be present in the carbonyls isolated from rosin using Girard P reagent. Isodextropimarinal was isolated by a modified version of the Harris procedure. In both cases the regeneration of the carbonyls from the derivatives led to a mixture of carbonyls (main ultraviolet absorption peak, 234 mμ, indicating the presence of carbonyls with isolated conjugated diene systems) rather than to pure dextropimarinal or isodextropimarinal, which should show no ultraviolet absorption in the 220–280 mμ region due to the lack of diene conjugation.

The chromium trioxide oxidation of the dextropimarinal-containing carbonyls proceeded readily. A dilute solution of the acids so obtained, in 1% aqueous sodium hydroxide, precipitated the crystalline sodium salt of dextropimaric acid. The formation of a crystalline sodium salt from dilute aqueous solution strongly suggested that the acid in question was dextropimaric acid. This was confirmed by the generation of the free resin acid ($[\alpha]^{25}D$ +75°) which showed no depression of melting point when mixed with an authentic sample of dextropimaric acid. The infrared absorption curves of the carbonyl-derived dextropimaric acid and the authentic sample were indistinguishable.

Attempts were made to repeat the isolation of isodextropimarinal exactly as described by Harris,[2] using dilute aqueous sodium hydroxide to extract the resin acids from an ether solution of rosin, distillation of the neutral portion so obtained, isolation of isodextropimarinal from the neutrals by means of the semicarbazone and oxidation of the aldehyde to isodextropimaric acid. This general outline was followed although it was found necessary to make certain modifications. In particular it was necessary to modify the procedure for the first extraction of the resin acids and the final isolation of isodextropimaric acid. It is presumed that Harris and Sanderson fractionally distilled the neutral fraction in order to obtain concentrated aldehydic cuts. In this work the distillation was used simply to separate the moderately volatile neutral components from non-volatile or very high boiling components. It was felt that recrystallization of later products would be a more effective method of purification than fractional distillation. Prolonged distillation of the neutral fraction might well concentrate isodextropimarinal by decomposition of less stable components or isomerization of them to pimaric-type aldehydes. It has been found in this Laboratory that the neutral fraction with high ultraviolet absorption distils to give aldehydic cuts with high absorption. However, if the reflux ratio is adjusted so as to give appreciable fractionation,

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

(2) G. C. Harris and T. F. Sanderson, THIS JOURNAL, **70**, 3870 (1948).

(3) N. A. Sörensen and T. Bruun, *Acta Chem. Scand.*, **1**, 112 (1947).

(4) D. H. R. Barton, T. Bruun and N. A. Sörensen, *Acta Chem. Scand.*, **5**, 1356 (1951).

(5) (a) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," John Wiley and Sons, Inc., New York, N. Y., 1954, pp. 133-136; (b) A. Pozefsky and N. D. Coggeshall, *Anal. Chem.*, **23**, 1611 (1951).

the ultraviolet absorption is destroyed and cannot be found in any of the fractions.[6]

The oxidation of isodextropimarinal to isodextropimaric acid was carried out as described by Harris. However, as previously indicated, the starting material was considered to be a carbonyl mixture rather than pure isodextropimarinal. In connection with this, it should be noted that Harris[2] recovered 71.5% of the original isodextropimarinal sample after the oxidation. The oxidation was carried out under very mild conditions but nevertheless in the presence of over 500% of the calculated amount of chromium trioxide needed. This seems to be an unreasonably high percentage of a pure aldehyde to survive such treatment. Under identical conditions 46.4% of the isodextropimarinal-containing carbonyl mixture, reported here, was recovered unchanged after the oxidation. During the course of the isolation of isodextropimaric acid, a very small quantity of crystals, presumably sodium dextropimarate, formed exactly as previously observed in the isolation of dextropimaric acid. Crystalline isodextropimaric acid was isolated and purified using the 2-amino-2-methyl-1-propanol and cyclohexylamine salts.

The isolated carbonyl fractions were found to comprise 0.88–1.3% of gum rosin, the former figure being obtained by following the Harris[2] procedure and the latter being based on the yield of carbonyl material obtained using Girard P reagent. Neither procedure would be expected to be quantitative. The crude yield of isodextropimaric acid reported here indicates isodextropimarinal to be present in gum rosin to the extent of 0.13%. This figure, being based on the actual isolations, represents a minimal percentage and can only be considered an approximation. Harris[2] estimated gum rosin to be 0.43% isodextropimarinal. This estimate was based on the amount of 2,4-dinitrophenylhydrazone formed from the total neutral fraction. Considering the other carbonyl material present, one would expect Harris' figure to be high, although the solubilities of the 2,4-dinitrophenylhydrazones in the presence of the total neutral fraction might well be such as to yield mainly a single 2,4-dinitrophenylhydrazone. Dextropimarinal, as reported here, represents 0.08% of gum rosin. The amount of dextropimarinal present is probably considerably greater than this inasmuch as Girard reagents were used in the isolation. Girard reagent hydrazones form readily with aldehydes, but their customary resistance to hydrolysis would be expected to lead to low yields of free aldehydes.

Experimental[7]

Isolation of Carbonyl Constituents Containing Dextropimarinal from Rosin.—A solution of 100 g. of WW rosin in 150 cc. of absolute ethanol was allowed to react with 3.60 g. of Girard P reagent[8] in the presence of 15 cc. of glacial acetic acid in a one-necked flask equipped with a reflux condenser. The solution was boiled gently for 1.5 hours. The hot reaction solution was poured with vigorous stirring into a solution of 9.20 g. of sodium hydroxide in 450 cc. of ice and water under a layer of 1600 cc. of ether. Following separation of the layers, the aqueous layer was washed with 400 cc. of ether.

Hydrolysis of the Girard adducts present in the aqueous layer was accomplished by the addition of 40 cc. of concentrated hydrochloric acid followed by storing at 5° for 40 hours.

The acidic solution was extracted with ether until the ether washings were colorless. The combined ether extracts were washed five times with 3% aqueous sodium hydroxide and three times with water and dried over sodium sulfate. Evaporation of the ether yielded 1.27 g. of a light yellow oil, having an acid number of 5.8 and showing characteristic aldehyde absorption in the infrared (2695, 1733 cm.$^{-1}$). The carbonyl fraction was stored under nitrogen in the refrigerator without appreciably altering the acid number.

Dextropimaric Acid.—A solution of 2.00 g. of the carbonyl fraction of rosin obtained above, in 18 cc. of acetic acid, was treated with 2.60 g. of chromium trioxide in 4.3 cc. of water and 8.5 cc. of acetic acid according to the procedure of Harris.[2] Both solutions were pre-cooled before combination and allowed to warm to room temperature as the reaction proceeded.

The reaction mixture was stirred vigorously for one hour, diluted with 150 cc. of water and extracted several times with ether. The ether extract was washed several times with water and extracted five times with 70-cc. portions of 1% aqueous sodium hydroxide. Storing the alkaline solution in the refrigerator overnight allowed the white crystalline sodium dextropimarate to precipitate. Filtration by means of a fritted-glass filter stick fitted with a hard filter-paper disk yielded 0.14 g. of white crystalline sodium dextropimarate, $[\alpha]^{25}D$ +53°. The product showed no appreciable absorption of ultraviolet light. Two recrystallizations of the salt, one from 2% aqueous sodium hydroxide and one from water, followed by acidification with acetic acid according to the procedure of Palkin,[9] yielded white crystalline dextropimaric acid, m.p. 212–213°, $[\alpha]^{25}D$ +75°. The product showed no melting point depression when mixed with an authentic sample of dextropimaric acid, m.p. 211–214°. The above melting points were taken in evacuated, sealed, capillary tubes. The yield of sodium dextropimarate was 0.08% based on rosin and 6.2% based on the carbonyl fraction. The total recovery from the oxidation was 1.57 g. (0.52 g. of unoxidized carbonyl compounds and 1.05 g. of carboxylic acids of which 0.13 g. was dextropimaric acid).

Separation of the Total Neutral Fraction from Rosin.[2]—A solution of 750 g. of WW gum rosin in 1500 cc. of ether was stirred for 30 minutes with a solution of 90 g. of sodium hydroxide in 2800 cc. of water. Inasmuch as the components formed a solution, it was necessary to add sodium sulfate to effect phase separation. The aqueous layer was washed with ether; the combined ether extracts were washed successively with 1% aqueous sodium hydroxide and water, sodium sulfate again being used when necessary. The solvent ether was evaporated from the organic layer, water was added, and the final extractions of the neutrals were made using pentane containing 20% ether. The pentane solution was dried over sodium sulfate and evaporated to yield 40.0 g. of neutral material. Distillation at 1.5 mm. pressure using a Vigreux column yielded 24.3 g. of rosin neutrals collected at 105–189°. The infrared spectrum of the higher-boiling cuts showed absorption at 2670 and 1728 cm.$^{-1}$, indicative of the aldehyde group.

Isolation of Isodextropimarinal-containing Carbonyls from the Neutral Fraction.—The portion of the neutrals (15.77 g.) distilling at 179–189° was treated with semicarbazide hydrochloride to yield 7.35 g. of semicarbazones, m.p. 210–211.5°. The total neutral fraction gave a positive Tollens test, whereas the residual oil remaining unreacted with semicarbazide hydrochloride showed no reaction with the Tollens reagent. Regeneration of the carbonyls from the semicarbazones using sulfuric acid followed the Harris procedure[2] closely except that the final product was observed to be a mixture of carbonyls (main ultraviolet absorption peak 234 mμ, α 15.4) rather than the pure isodextropimarinal. This was the case even after several recrystallizations of the semicarbazones from dilute ethanol or ethyl acetate. The presence of aldehydes in the regenerated carbonyls was indicated by absorption in the infrared region at 2680 and 1731 cm.$^{-1}$.

(6) Albert E. Johnson, unpublished results.

(7) All reported melting points are uncorrected. The determination of infrared spectra was made by Mary N. Woodroof. Optical rotations were determined on 0.5–1% solutions in 95% ethanol.

(8) A. Girard and G. Sandulesco, *Helv. Chim. Acta*, **19**, 1095 (1936).

(9) S. Palkin and T. H. Harris, THIS JOURNAL, **55**, 3677 (1933).

Isodextropimaric Acid.—The previously described chromium trioxide oxidation procedure was used without modification to oxidize 1.40 g. of the isodextropimarinal-containing carbonyls isolated above. The resulting acids were isolated by basic extraction from ether solution as before. Evaporation of the ether solution yielded 0.65 g. of unoxidized carbonyl compounds which gave a positive test with 2,4-dinitrophenylhydrazine and a negative Tollens test. A very small quantity of white crystals which precipitated from the dilute alkaline solution was presumed to be sodium dextropimarate and discarded. Acidification of the alkaline solution with 2 *M* acetic acid followed by heptane extraction, removal of excess acetic acid by several water washings, and treatment of the heptane solution with 2-amino-2-methyl-1-propanol yielded 0.20 g. of the amine salt, $[\alpha]^{24}D$ −11.2°. Successive recrystallizations of the salt from acetone solution served to increase the negative rotation to −14.4°. The amine salt showed very low absorption in the ultraviolet, indicative of only minor amounts of contaminants: general absorption 235–275 mμ, λ_{max} 248–256 mμ (α 2.0). Conversion of the salt to the cyclohexylamine salt followed by recrystallization from acetone showed similar results. However, the cyclohexylamine salt of isodextropimaric acid was found to be concentrated in the mother liquors. Treatment of the cyclohexylamine salt, $[\alpha]^{26}D$ ±0°, with acetic acid yielded isodextropimaric acid, m.p. 161–163.5°.

OLUSTEE, FLORIDA

[CONTRIBUTION FROM THE ORGANIC CHEMISTRY LABORATORIES OF THE UNIVERSITY OF FLORIDA]

The Addition of Saturated Heterocyclic Amines to Cinnamate Esters

BY C. B. POLLARD AND G. C. MATTSON

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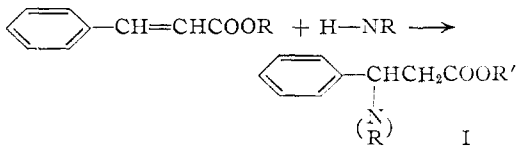
A series of esters of β-(N-heterocyclic)-β-phenylpropionic acid was prepared for pharmacological testing. The addition of saturated heterocyclic amines to cinnamate esters has been shown to be a practical method of synthesizing these compounds.

The object of this research was to prepare β-(N-heterocyclic)-β-phenylpropionic esters (I) for pharmacological testing in the hope of obtaining a clinically useful analgesic. It was decided to attempt the formation of these compounds by the addition of saturated heterocyclic secondary amines to cinnamate esters.



The addition of amines to acrylate esters constitutes a useful method of synthesizing N-substituted β-aminopropionate esters.[1-4] However, there are few literature reports of the reaction of amines with the less reactive, substituted acrylate esters such as the cinnamate esters. In addition to the reaction of the amine with the olefinic bond, it is also possible for aminolysis of the ester group to occur. This competing reaction is known to occur and under certain conditions the amide is the only product isolated. The products of the reactions of ammonia, methylamine and diethylamine with ethyl cinnamate have been studied by Morsch.[5] The reactions of ammonia and methylamine with ethyl cinnamate gave low yields of the β-amino esters, whereas the only product isolated from the reaction of diethylamine with ethyl cinnamate was the amide, N,N-diethylcinnamide.

The reaction of saturated heterocyclic amines with cinnamate esters was effected by refluxing equimolar quantities of the reactants with or without a solvent. A marked increase in yield of β-(N-heterocyclic)-β-phenylpropionate ester was obtained either by employing tetramethylammonium hydroxide as a catalyst or by using an excess of the secondary amine. All of the products were isolated as the hydrochloride salts, by the same general procedure. The yields reported refer to purified products and are based upon the molar quantity of cinnamate ester used.

The corresponding amide may be formed by changing the conditions of the reaction and the method of isolation.

Experimental

Preparation of Intermediates.—The piperidine, pyrrolidine and morpholine were commercial grade materials and were redistilled before use. 4-Methylpiperidine was prepared by the hydrogenation of γ-picoline under 4000 pounds pressure at 200°, using a Raney nickel catalyst, according to the method used by Adams and Leonard.[4]

The cinnamate esters, other than the ethyl ester which was commercially available, were prepared by the reaction of cinnamyl chloride with the corresponding alcohol in the presence of pyridine. Cinnamyl chloride was formed by refluxing a benzene solution of cinnamic acid and thionyl chloride for 8 hr. The solvent was then removed on the steam-bath under water-pump vacuum. The cinnamyl chloride so obtained was used without further purification.

Cinnamyl chloride (0.2 mole) was added portionwise, with ice-bath cooling, to a solution of the alcohol (0.2 mole) and pyridine (0.2 mole) in 100 ml. of benzene. The reaction mixture was allowed to stand for 24 hr. It was then extracted with three 50-ml. portions of distilled water. The organic layer was separated and dried over anhydrous cal-

TABLE I

CINNAMATE ESTERS

Cinnamate	Boiling range °C.	Mm.	Yield, %	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
Methyl[b]	36[a]		75.0				
n-Propyl[b]	92–94	0.50	79.0				
n-Butyl[c]	98–100	.50	73.0				
1-Methylpropyl	87–89	.35	79.0	76.43	76.54	7.88	7.73
2-Methylpropyl[d]	90–92	.25	86.0				
n-Amyl	104–106	.50	74.0	77.03	77.40	8.30	8.02
1-Methylbutyl	102–104	.50	85.0	77.03	76.72	8.30	7.92
n-Hexyl	114–115	.45	64.0	77.55	77.68	8.68	8.57

[a] Melting point. [b] F. Weger, *Ann.*, 212, 126 (1883). [c] D. Vorlander and R. Walter, *Z. physik. Chem.*, 118, 13, 17 (1925). [d] J. J. Sudborough and K. J. Thompson, *J. Chem. Soc.*, 83, 676 (1903).

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(3) C. A. Weisel, R. B. Taylor, H. S. Mosher and F. C. Whitmore, THIS JOURNAL, **67**, 1071 (1945).
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