at intervals to hold it in excess. After bromine removal by aeration, the reaction mixture was poured slowly into 125 ml. of ice and water and the acid was neutralized in the cold with barium carbonate. The precipitate was removed by filtration and triturated with 30 ml. of 1% aqueous potassium hydroxide and again filtered. The combined filtrates were neutralized with acetic acid and concentrated under reduced pressure at 30–40° to a sirup which was treated with 80 ml. of a 1% solution of hydrogen chloride in anhydrous methanol and again concentrated under reduced pressure to a sirup. The sirup was extracted with 30 ml. of absolute ethanol, filtered and again concentrated to a sirup under reduced pressure. This sirup was dissolved in 4 ml. of water and the solution brought to *ca.* pH 7 with solid potassium bicarbonate. Glacial acetic acid (4 ml.) was added and the solution was maintained at 15° overnight. Crystals formed which were removed by filtration and were recrystallized by dissolving in aqueous potassium bicarbonate and adding an equal volume of glacial acetic acid; yield 50 mg., $[\alpha]^{24}\text{D}$ +10° (*c* 1.8 as the dipotassium salt). The rotation was assayed by solution in water containing an equivalent (to phenolphthalein) quantity of potassium bicarbonate and was in agreement with the previously recorded[4] value (+10°). X-Ray powder diffraction data were in exact agreement with those produced by an authentic specimen of potassium acid D-glucarate (D-glucosaccharate): 4.439 (1), 3.934 (3), 3.302 (5), 2.771 (2), 2.392 (4).[7]

On repeating the above procedure with omission of the bromine oxidant, no potassium acid D-glucarate was isolable.

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[7] Interplanar spacing in Å. of the five most intense lines; estimated visually; 1 = strongest; λ = 1.5418 Å.

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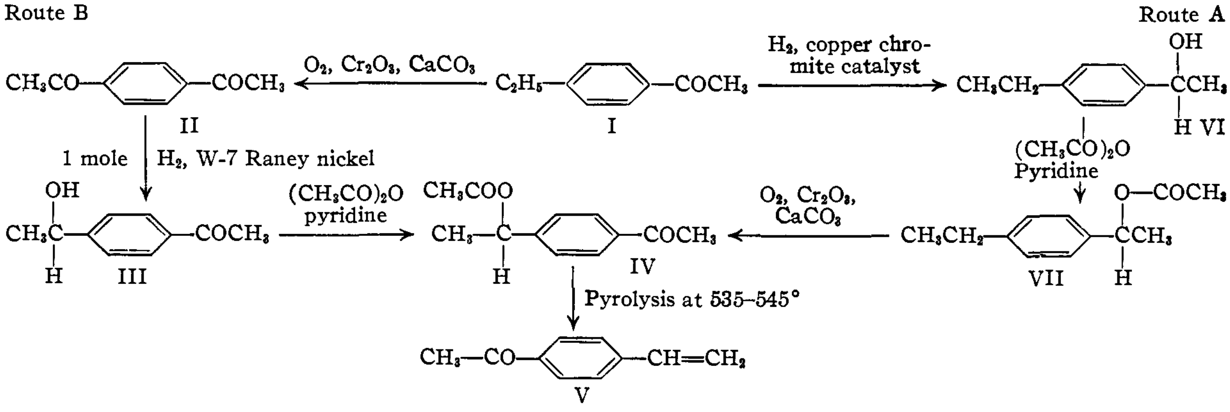
p-Vinylacetophenone: The Disproportionation of *p*-Acetophenylmethylcarbinol[1]

BY J. L. R. WILLIAMS

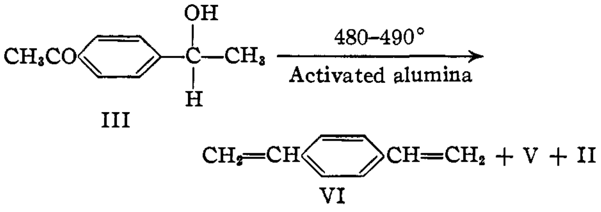
RECEIVED JANUARY 29, 1953

Two routes for the preparation of *p*-vinylacetophenone from *p*-ethylacetophenone which have been found are shown below.

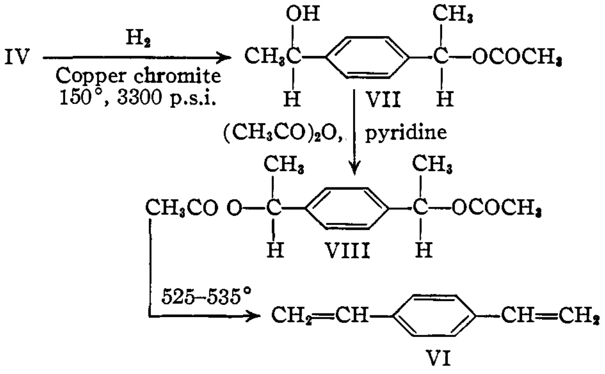


In route A, *p*-ethylacetophenone (I) was hydrogenated to *p*-ethylphenylmethylcarbinol (VI) which was acetylated and oxidized to *p*-acetophenylmethylcarbinol acetate (IV). By route B, *p*-ethylacetophenone was oxidized to *p*-diacetylbenzene (II) which was hydrogenated over W-7 Raney nickel to *p*-acetophenylmethylcarbinol (III) and then converted by acetylation to *p*-acetophenylmethylcarbinol acetate (IV). *p*-Acetophenylmethylcarbinol acetate from both routes was pyrolyzed at 530–545° over glass beads to yield *p*-vinylacetophenone (V).

p-Acetophenylmethylcarbinol (III) was alternately prepared by de-esterification of *p*-acetophenylmethylcarbinol acetate (IV) using sodium methoxide and methanol. Vapor-phase dehydration of *p*-acetophenylmethylcarbinol over activated alumina yielded not only *p*-vinylacetophenone but also *p*-diacetylbenzene (II) and *p*-divinylbenzene (VI) by disproportionation.



p-Divinylbenzene was also prepared from *p*-acetophenylmethylcarbinol acetate by the following scheme



Experimental

p-Ethylphenylmethylcarbinol Acetate (VII), Route A.—A mixture of 250 g. (1.69 moles) of *p*-ethylacetophenone and 25 g. of copper chromite catalyst (Harshaw Cu-X-649-57-P) was hydrogenated in the usual way at 125° and 4500 p.s.i. until 1.69 moles of hydrogen had been absorbed. The resulting material was heated on the steam-cone for 16 hours with 250 cc. of acetic anhydride and 5 cc. of pyridine. Distillation through a 12-in. Vigreux column yielded 220 g. (66% of theory) of *p*-ethylphenylmethylcarbinol acetate, b.p. 79° (0.9 mm.), $n^{25}\text{D}$ 1.4956.

p-Acetophenylmethylcarbinol Acetate (IV), Route A.—In a liquid phase oxidizing apparatus consisting of a large test-tube equipped with a gas disperser, and a water take-off and reflux condenser, there was placed 220 g. (1.15 moles) of *p*-ethylphenylmethylcarbinol acetate, 1 g. of chromium sesquioxide and 15 g. of calcium carbonate. Air was forced through the disperser, and the temperature of the reaction mixture was maintained at 130–140° for 28 hours by means

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[1] Communication No. 1535 from the Kodak Research Laboratories.

of an electrically heated oil-bath. The reaction mixture was filtered free from catalyst and heated at 110° for two hours after the addition of 100 cc. of acetic anhydride and 25 g. of sodium acetate. The cooled reaction mixture was washed with two 500-cc. portions of water and the organic material was dried over anhydrous magnesium sulfate. Distillation through a 12-in. Vigreux-type column yielded the following fractions: (1) 98 g., b.p. 71–105° (0.25 mm.), $n^{25}\text{D}$ 1.4962; (2) 58 g., b.p. 105° (0.25 mm.), $n^{25}\text{D}$ 1.5150. On considering fraction (1) as recovered *p*-ethylphenylmethylcarbinol acetate, fraction (2) represented a 44.5% yield of *p*-acetophenylmethylcarbinol acetate.

Anal. Calcd. for $C_{12}H_{14}O_3$: C, 69.9; H, 6.8. Found: C, 69.7; H, 6.9.

The 2,4-dinitrophenylhydrazone of *p*-acetophenylmethylcarbinol acetate melted at 223–224°.

Anal. Calcd. for $C_{18}H_{18}O_6N_4$: C, 56.0; H, 4.7; N, 14.5. Found: C, 56.1; H, 4.8; N, 15.0.

p-Vinylacetophenone (V), Route A.—A mixture of 52 g. (0.25 mole) of *p*-acetophenylmethylcarbinol acetate and 60 cc. of thiophene-free benzene was passed at a rate of one drop per second through a 25-mm. o.d. Pyrex tube packed for a distance of 30 inches with glass beads and maintained at 535–545° by means of an electrically controlled furnace. The reactants and products were flushed through the tube by a slow stream of nitrogen into a Dry-Ice trap. Six grams of polymer formed in the cooler portion of the reaction tube during pyrolysis. The trapped products were washed with two 100-cc. portions of water, dried over anhydrous magnesium sulfate, and distilled to yield 20 g. of material, b.p. 63–78° (0.31 mm.), m.p. 20–25°. Recrystallization from 25 cc. of hexane gave 15 g. (40.8% of theory) of *p*-vinylacetophenone, m.p. 34–35°. A sample recrystallized twice from hexane had m.p. 37–37.5°.

Anal. Calcd. for $C_{16}H_{10}O$: C, 82.3; H, 6.9. Found: C, 81.9; H, 6.7.

The 2,4-dinitrophenylhydrazone melted at 225–226.5°.

Anal. Calcd. for $C_{16}H_{13}O_4N_4$: C, 59.1; H, 4.0; N, 17.2. Found: C, 59.5; H, 4.6; N, 17.0.

The oxime melted at 118–119°.

Anal. Calcd. for $C_{10}H_{11}ON$: C, 75.1; H, 6.9; N, 8.7. Found: C, 74.6; H, 6.7; N, 9.2.

p-Acetophenylmethylcarbinol Acetate (IV), Route B.—*p*-Diacetylbenzene was prepared by catalytic oxidation of *p*-ethylacetophenone, using chromium sesquioxide according to the method of Hochwalt.[2]

In a Parr low-pressure hydrogenation apparatus there was placed 64.8 g. (0.4 mole) of *p*-diacetylbenzene, 32 g. of freshly prepared, alcohol-washed W-7 Raney nickel,[3] and 175 cc. of methanol (Eastman Kodak Co., White Label). The reaction vessel was evacuated and flushed three times with hydrogen in the usual way and pressured to 50 p.s.i. After shaking for 32 minutes, the pressure drop was 30 pounds (theory 29 lb.), at which time shaking was stopped. The catalyst was removed and the reaction mixture evaporated at the water pump. At this stage the reaction mixture presumably consisted of *p*-ethylacetophenone, 1,4-bis-(α-hydroxyethyl)-benzene, and the desired product. No attempt was made to separate the products, but the reaction mixture was acetylated by heating with 150 cc. of acetic anhydride and 5 cc. of pyridine on the steam-cone for 16 hours. Distillation through a 6-in. Vigreux-type column resulted in the following fractions: (1) 1 g., b.p. 97–100° (0.2 mm.); (2) 2.0 g., b.p. 100–101° (0.2 mm.); (3) 15 g., b.p. 100–103° (0.2 mm.); (4) 50 g., b.p. 103–107° (0.2 mm.), $n^{25}\text{D}$ 1.5168. Fraction (4) represented 60.5% of the theoretical yield of *p*-acetophenylmethylcarbinol acetate.

p-Vinylacetophenone (V), Route B.—A solution of 41 g. (0.22 mole) of fraction (4) (*p*-acetophenylmethylcarbinol acetate) in 50 cc. of thiophene-free benzene was pyrolyzed as described above for route A. Distillation yielded the following fractions: (1) 3.0 g., b.p. 60° (0.3 mm.); (2) 5.0 g., b.p. 60–63° (0.29 mm.); (3) 14 g., b.p. 63–67° (0.29 mm.), m.p. 36–38° (porous plate). Fraction (3) represented 42.5% of the theoretical yield of *p*-vinylacetophenone. The 2,4-dinitrophenylhydrazone melted at 225°. A mixture of 1.1 g. of fraction (3) and 0.05 g. of benzoyl peroxide was heated at 65° for 16 hours to yield a clear, hard polymer.

p-Acetophenylmethylcarbinol (III).—A mixture of 100 g. (0.48 mole) of *p*-acetylphenylmethylcarbinol acetate, prepared as above for route A, 250 cc. of methanol (Eastman Kodak Co., White Label) and 1.0 g. of sodium methoxide (Mathieson Chemical Corp.) was allowed to stand at room temperature (28°) for one-half hour. The reaction mixture was made acidic with 5% hydrogen chloride in methanol. The excess hydrogen chloride was removed at the water pump and the liquid distilled at atmospheric pressure to give 34 cc. of methyl acetate, b.p. 54–59°.

After all of the methanol had distilled, the residual liquid was distilled *in vacuo* through a 6-in. Vigreux-type column to yield the following fractions: (1) 19 g., b.p. 118–120° (0.4 mm.), $n^{25}\text{D}$ 1.5444; (2) 34 g., b.p. 120° (0.5 mm.), $n^{25}\text{D}$ 1.5462; (3) 8 g., b.p. 122° (0.6 mm.), $n^{25}\text{D}$ 1.5452. The combined fractions weighed 61 g., representing 76.8% of the theoretical yield of *p*-acetophenylmethylcarbinol.

Anal. Calcd. for $C_{10}H_{11}O_2$: C, 73.1; H, 7.4. Found: C, 72.7; H, 7.7.

The 2,4-dinitrophenylhydrazone was prepared, and, after recrystallization from alcohol and water, it melted at 204–205°.

Anal. Calcd. for $C_{16}H_{16}N_4O_5$: C, 55.8; H, 4.7; N, 16.3. Found: C, 55.8; H, 5.0; N, 16.3.

The α-naphthylurethan of *p*-acetophenylmethylcarbinol melted at 133.5–134.5° after recrystallization from a mixture of hexane and ethyl acetate.

Anal. Calcd. for $C_{21}H_{19}O_3$: C, 75.7; H, 5.7; N, 4.2. Found: C, 75.7; H, 5.6; N, 3.9.

Disproportionation of p-Acetophenylmethylcarbinol during Dehydration over Activated Alumina.—Harshaw activated alumina (Al-0104-T-$^1/_8$ inch) was preheated in a stream of air for six hours at 550°. The catalyst was cooled to 480° and used immediately as follows.

One hundred grams (0.61 mole) of *p*-acetophenylmethylcarbinol was passed at a rate of one-half drop per second through a 25-mm. o.d. Pyrex tube packed for a distance of 1 in. with glass beads, followed by 28 in. of the above catalyst, then 1 in. of glass beads. The tube was maintained at 480–490° by means of an electrically heated furnace. The reactants and products were swept through the tube by means of dry nitrogen flowing at the rate of 6 l. per hour. Several Dry Ice traps were required to condense the gaseous products. The combined condensates were diluted with 200 cc. of benzene, 10 g. of water was separated, and the organic material dried over anhydrous magnesium sulfate. After the addition of a trace of picric acid, the benzene was removed at the water pump. An equal volume of hexane was added to the residue, and, after cooling in crushed ice, 6 g. of a white solid, m.p. 109–110°, was filtered off. This material was *p*-diacetylbenzene, as determined by a mixed melting point with an authentic sample of *p*-diacetylbenzene.

The hexane was removed from the mother liquors at the water pump, and the residue distilled *in vacuo* through a 6-in. Vigreux-type column to yield the following fractions: (1) 8.5 g., b.p. 48.5–60 (0.75 mm.), m.p. 4–10°, $n^{25}\text{D}$ 1.5770; (2) 8.6 g., b.p. 60–73° (0.75 mm.), m.p. 22.5–24°, $n^{25}\text{D}$ 1.5791; (3) 15.5 g., b.p. 73–83° (0.75 mm.), m.p. 24–28°, $n^{25}\text{D}$ 1.5720.

One-gram portions of the above fractions were titrated for unsaturation by the standard bromide–bromate technique, using $^1/_{12}$ *M* solution:

	Bromide–bromate, cc.
Fraction (1)	46.7
Fraction (2)	26.19
Fraction (3)	24.57
Pure *p*-vinylacetophenone	28.0

These titrations indicated that fraction (1) contained considerable divinylbenzene, although it was not isolated in pure form. Fractions (2) and (3), when recrystallized from 20 cc. of hexane, gave 18.6 g. of *p*-vinylacetophenone (20.9% of the theoretical yield).

p-(α-Hydroxyethyl)-phenylmethylcarbinol Acetate (VII).—A mixture of 54.6 g. (0.3 mole) of *p*-acetophenylmethylcarbinol acetate (IV) and 5 g. of copper chromite catalyst in a cyclohexane solution of 150 cc. total volume was hydrogenated at 150° and 3300 p.s.i. until 0.3 mole of hydrogen

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[2] C. A. Hochwalt, U. S. Patent 2,390,368 (Dec. 4, 1945); *C. A.*, **40**, 1878 (1946).

[3] H. Adkins and H. R. Billica, THIS JOURNAL, **70**, 695 (1948).

had been absorbed. The cooled reaction mixture was removed from the bomb, filtered, and distilled to give 25 g. (54%) of *p*-(α-hydroxyethyl)-phenylmethylcarbinol acetate, b.p. 116–117° (0.5 mm.), $n^{25}D$ 1.5120.

Anal. Calcd. for $C_{12}H_{16}O_3$: C, 69.2; H, 7.6; acetyl, 21.3. Found: C, 69.3; H, 7.6; acetyl, 20.8.

1,4-Bis-(α-hydroxyethyl)-benzene Diacetate (VIII). Method A.—A mixture of 13.5 g. (0.065 mole) of *p*-(α-hydroxyethyl)-phenylmethylcarbinol acetate, 20 g. (0.2 mole) of acetic anhydride, and 5 drops of pyridine was heated on the steam-cone for 16 hours. Distillation of the reaction mixture yielded 21.0 g. (80%) of the diacetate, b.p. 104° (0.2 mm.), $n^{25}D$ 1.4955.

Method B.—1,4-Bis-(α-hydroxyethyl)-benzene was also prepared from *p*-diacetylbenzene. A mixture of 16.2 g. (0.1 mole) of *p*-diacetylbenzene, 8.1 g. of W-7 Raney nickel, and 200 cc. of methanol was hydrogenated in a Parr low-pressure apparatus at 50 p.s.i. The pressure drop was 13 p.s.i.; calcd., 12.8 p.s.i. After the catalyst had been filtered off, the methanol was evaporated to yield 12 g. of 1,4-bis-(α-hydroxyethyl)-benzene. A mixture of 9.0 g. (0.055 mole) of 1,4-bis-(α-hydroxyethyl)-benzene, 1.25 g. of acetic anhydride and 1 cc. of pyridine was heated on the steam-cone for 16 hours. Distillation of the reaction mixture gave 10.5 g. of 1,4-bis-(α-acetoxyethyl)-benzene, b.p. 110–112° (0.25 mm.), $n^{25}D$ 1.4932.

Anal. Calcd. for $C_{14}H_{18}O_4$: C, 67.2; H, 7.3. Found: C, 67.9; H, 7.4.

***p*-Divinylbenzene (VI).**—A solution of 21.0 g. (0.084 mole) of 1,4-bis-(α-hydroxyethyl)-benzene diacetate in 25.0 cc. of benzene was passed dropwise during the course of 1.5 hours through a 25-mm. o.d. Pyrex tube, packed for a distance of 30 inches with glass beads, and heated to 525–535° by means of an electrically controlled furnace. The reaction products were swept into a Dry Ice trap by a slow stream of nitrogen. The reaction products were melted, washed with water, and dried over anhydrous magnesium sulfate. Distillation yielded 7.7 g. (70% of the theoretical) of *p*-divinylbenzene, b.p. 34° (0.2 mm.). Titration of 0.52 g. of this material with $^1/_{12}$ *M* bromide–bromate solution required 30.2 cc., corresponding to a purity of 97.6%.

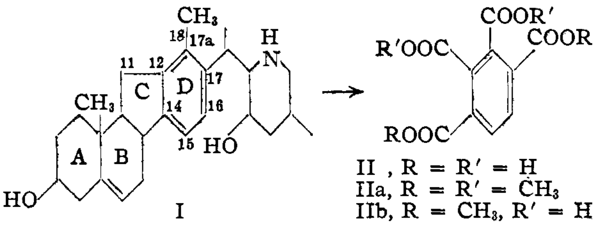
EASTMAN KODAK CO.
RESEARCH LABORATORIES
ROCHESTER, N. Y.

Degradation of Veratramine to Benzene-1,2,3,4-tetracarboxylic Acid

BY O. WINTERSTEINER, M. MOORE AND N. HOSANSKY

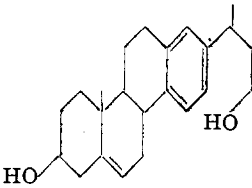
RECEIVED JANUARY 5, 1953

The structure I proposed by Tamm and Wintersteiner[1] for the secondary base veratramine from *Veratrum viride* Aiton requires that oxidative degradation of the alkaloid should result in the formation of II, benzene-1,2,3,4-tetracarboxylic acid (prehnitic acid[2]). This was indeed found to be the case. When veratramine was oxidized with hot alkaline permanganate and the mixture was worked up by the procedure described by Read and Purves[3] for the separation of the benzene polycarboxylic acids derived from coal and lignin, there was obtained a crystalline acid, m.p. 238–241°, $C_{10}H_6O_8$, identified as benzene-1,2,3,4-tetracarboxylic acid by analysis and comparison with an authentic sample.[4] The melting point of the tetramethyl ester (m.p. 128–130°) and of the (apparently slightly impure) 1,4-diester (160–167°, lit.[3] 171–172°) served to confirm this conclusion,[4] as did the identity of the infrared spectrum of the tetramethyl ester with that of an authentic specimen.

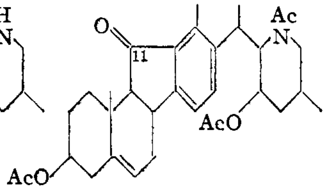


I

II , R = R' = H
IIa, R = R' = CH_3
IIb, R = CH_3, R' = H



III



IV

This result places the methyl group representing carbon atom 18 in the normal steroid skeleton into position 17a of ring D as visualized in formula I, and in conjunction with other facts[5,6] rules out the perhydrochrysene structure III proposed by Jacobs and Sato,[7] in which this carbon atom is incorporated in the ring system proper. Since there is ample evidence to show that rings A and B in veratramine are constituted as in normal steroids,[1,7] and that it is ring D which is aromatic,[1,5,7] it follows that ring C must be five-membered as postulated. These conclusions also apply to the related secondary alkaloid jervine, which has been correlated with veratramine[5] through one of its acetolysis products, the indanone IV.[6]

Experimental

The melting points were taken in capillaries and are corrected for stem exposure. The ultraviolet spectra were determined with a Cary self-recording spectrophotometer model 11-M. The infrared measurements were carried out with a Perkin–Elmer spectrophotometer model 12-B. The analytical samples were dried over phosphorus pentoxide at 110° (2 mm.).

Oxidation of Veratramine with Permanganate.—A suspension of veratramine (free base, 5 g.) in 500 cc. of water containing 8.0 g. of potassium hydroxide was brought to boiling in a vessel fitted with a reflux condenser, a separatory funnel and an air inlet tube extending to the bottom of the flask. Aqueous 3.5% potassium permanganate was added to the boiling mixture in 50-cc. portions at intervals governed by the consumption of the most of the reagent from the preceding addition. A stream of air admitted through the inlet tube served to prevent excessive bumping. When the last 50-cc. portion of a total of 1550 cc. added had remained unreduced for 5 hours (aggregate reaction time 30 hours), the contents of the flask were cooled and the excess permanganate destroyed by the addition of ethanol. The manganese dioxide was filtered off and washed thoroughly with hot water. The combined filtrate and washings were acidified to *p*H 2 with hydrochloric acid, filtered through a bed of Super-Cel, and concentrated *in vacuo* to about 200 cc. The solution was then brought to *p*H 10 by

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(1) Ch. Tamm and O. Wintersteiner, THIS JOURNAL, **74**, 3842 (1952).

(2) As pointed out by L. I. Smith and E. J. Carlson, *ibid.*, **61**, 288 (1939), the still widespread use in the contemporary literature of the trivial name mellophanic acid for this instead of for the 1,2,4,5-isomer is incorrect. We are following in this paper the suggestion of Read and Purves (ref. 3) to use the rational terms only.

(3) D. E. Read and C. B. Purves, *ibid.*, **74**, 116, 120 (1952).

(4) We wish to express our sincere thanks to Prof. C. B. Purves for making available to us samples of this acid and of its tetra and dimethyl esters.

(5) O. Wintersteiner and N. Hosansky, THIS JOURNAL, **74**, 4474 (1952).

(6) J. Fried, O. Wintersteiner, A. Klingsberg, M. Moore and B. M. Iselin, *ibid.*, **73**, 2970 (1951); O. Wintersteiner, B. M. Iselin and M. Moore, Abstracts, XIIth Internat. Congress of Chemistry, New York, N. Y., September 10–13, 1951, Medicinal Chemistry, p. 292.

(7) W. A. Jacobs and Y. Sato, *J. Biol. Chem.*, **191**, 71 (1951).