[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

2,5-Dimethoxy-3,4,6-trimethylbenzoic Acid

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Any method of oxidizing 2,5-dimethoxy-3,4,6-trimethylbenzaldehyde[1] so far tried, yields none of the corresponding acid. This aldehyde also shows other abnormalities: thus it does not undergo the benzoin condensation, nor the Cannizzaro reaction. Staudinger[2] has studied a number of aldehydes which are oxidized to the corresponding acids only with difficulty, or not at all, and he has generalized that "only aldehydes easily oxidized to acids may be expected to undergo the benzoin condensation."

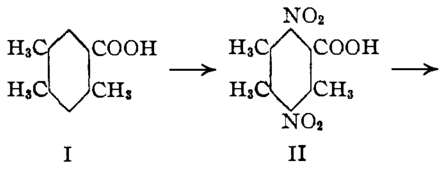
It was of interest, therefore, to synthesize and study the behavior of the corresponding acid, 2,5-dimethoxy-3,4,6-trimethylbenzoic acid, toward oxidizing agents, since the failure to obtain it by oxidizing the aldehyde might be due either to a resistance of the aldehyde group to oxidation, or to an instability of the acid itself toward oxidizing agents.

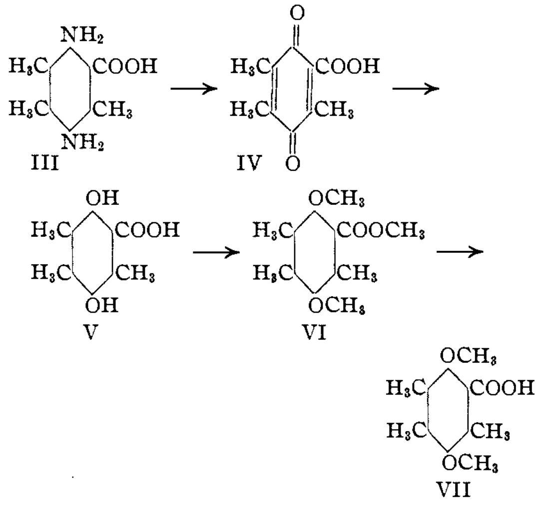
The acid, a white solid stable at its melting point (100–101°), decomposes only slowly at 200°. But like the aldehyde, the acid decolorizes permanganate, giving only small amounts of oily products and, again like the aldehyde, gives trimethylnitroquinone with nitric acid.

It is therefore reasonable to suppose that the aldehyde can be oxidized to the acid, since the action of nitric acid on the aldehyde and on the acid yields the same product. However, in view of the other peculiar properties of the aldehyde, it seems likely that the oxidation is a difficult one, and any combination of reagents so far tried which brings it about also destroys any of the acid as fast as it is formed.

Experimental

The route to the acid involved the following steps





Durylic acid (I) was prepared from acetylpseudocumene.[3]

Dinitrodurylic acid (II)[4] was prepared in 87% yield as previously described.

Diaminodurylic Acid (III).—The *pure* nitro acid of m. p. 210–212° (38.1 g. = 0.15 mole) is dissolved in 200 cc. of warm 0.75 *N* sodium hydroxide, and 20 cc. of 50% acetic acid is added. This hot solution is added slowly to a boiling mixture of 50 g. of iron powder (20 mesh), 150 cc. of water, and 10 cc. of glacial acetic acid. When the mixture becomes too thick to shake well, 200 cc. of hot water is added. After adding all the nitro compound and boiling for fifteen minutes, some sodium bisulfite is added and the mixture made alkaline to litmus. The hot solution is filtered, the iron slime boiled first with 2% sodium hydroxide, then with water, the washings and filtrates combined (volume about 2 liters) and concentrated to about 600 cc., filtering off any iron hydroxide which precipitates. The resulting clear orange liquid is cooled to 0° and acidified with acetic acid. The precipitate is filtered and washed two or three times with cold water, then with alcohol followed by ether; white needles, wt. 28 g. (96%), m. p. 218–220° (dec.).[5]

Trimethylquinonecarboxylic Acid (IV).[6]—Diaminodurylic acid (5 g.) is dissolved in 20 cc. of water and 5 cc. of concentrated hydrochloric acid, the solution cooled to 0°, and a cold solution of 50 g. of ferric chloride in 50 cc. of water is added. After standing at 0° for an hour, the reaction mixture is extracted with ether, the combined ethereal solutions washed with ice water until free from iron, filtered, and the ether allowed to evaporate at room

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[1] Smith and Dobrovolny, THIS JOURNAL, **48**, 1693 (1926); Smith, *ibid.*, **56**, 472 (1934).

[2] Staudinger, *Ber.*, **46**, 3535 (1913); see also Raiford and Talbot, THIS JOURNAL, **54**, 1092 (1932).

[3] Smith and Byrkit, *ibid.*, **55**, 4306 (1933).

[4] Smith and Byrkit, *ibid.*, **55**, 4307 (1933).

[5] Nef (Ref. 6) gives the m. p. as 210°, but if the material is carefully recrystallized by dissolving it in water containing a little bisulfite and then acidifying with acetic acid, it melts at 221–222° (corr.) with decomposition.

[6] Nef., *Ann.*, **237**, 1 (1887); *Ber.*, **18**, 2801, 3496 (1885); **19**, 516 (1886).

temperature. There remains 5 g. of yellow needles, but the quality of the product varies greatly in different runs and the acid cannot be purified by recrystallization. Usually the product turns red at 110° and melts with decomposition around 120°.[7]

Trimethylhydroquinonecarboxylic Acid; 2,5-Dihydroxy-3,4,6-trimethylbenzoic Acid (V).—The quinone acid (5 g.) is finely powdered and suspended in 400 cc. of cold water saturated with sulfur dioxide, the reduction taking place without any apparent solution. The solid is filtered, washed with a little water and dried at room temperature; yield 3.5 g. (69%), m. p. 200–202° with decomposition.

Methyl 2,5-Dimethoxy-3,4,6-trimethylbenzoate (VI).—In a 500-cc. flask fitted with reflux condenser are placed 4.5 g. of the hydroquinone acid, 70 cc. of methyl alcohol, and 37 cc. of dimethyl sulfate. The solution is warmed and to it is added slowly a solution of 45 g. of potassium hydroxide in 225 cc. of methyl alcohol, after which the mixture is boiled for a few moments and then steam distilled. The distillate is extracted with ether, the ether evaporated and the crude product is recrystallized from 5 cc. of 80% methyl alcohol, giving 2.7 g. (53%) of colorless crystals of m. p. 39–41°.

Anal. Calcd. for $C_{13}H_{18}O_4$: C, 65.55; H, 7.56; OCH_3 (three), 39.74. Found: C, 65.60, 65.90; H, 7.74, 7.43; OCH_3, 39.51, 39.35.

2,5-Dimethoxy-3,4,6-trimethylbenzoic Acid, Dimethoxydurylic Acid (VII).—To 1 g. of the methyl ester is added 140 cc. of a 30% methyl alcohol solution of potassium hydroxide, and the mixture refluxed for ten hours. The hydrolysis is very slow. After completion of the reaction, the mixture is steam distilled, the residue cooled, extracted with ether, the aqueous layer acidified with hydrochloric acid and again extracted with ether. The ether extract of the acidified solution is evaporated at room temperature, leaving 0.9 g. of colorless crystals, m. p. 96–99°. Recrystallized from high boiling petroleum ether, the melting point became constant at 100–101°. The acid is stable at its melting point but decomposes slowly at 200°.

Anal. Calcd. for $C_{12}H_{16}O_4$: C, 64.28; H, 7.14; OCH_3 (two), 27.67. Found: C, 64.34, 64.15; H, 7.14, 7.05; OCH_3, 27.87, 27.21.

Silver Salt, 0.13 g. of the acid gave 0.17 g. of light gray silver salt. The silver salt, suspended in ether and treated with methyl iodide, gives a quantitative yield of the methyl ester, m. p. and mixed m. p. 39–40°.

Anal. Calcd. for $C_{12}H_{15}O_4Ag$: C, 43.53; H, 4.53; Ag, 32.63. Found: C, 43.10, 42.94; H, 4.66, 4.68; Ag (residue on combustion), 31.03, 31.66.

Oxidation of the Acid with Permanganate.—0.1 g. of the acid dissolved in 1 cc. of acetic acid and 1 drop of sulfuric acid, was treated with 2% permanganate, 0.1 cc. at a time. The permanganate was decolorized at once. After adding 12 cc. of permanganate, the reaction was interrupted although there was no indication that the oxidation was slowing up. The reaction mixture, worked up in the usual way, yielded only an exceedingly small amount of oily material.

Oxidation of the Acid with Nitric Acid.—0.1 g. of the acid was refluxed with 5 cc. of nitric acid ($d = 1.4$) for thirty minutes. The cooled diluted solution was extracted with ether and the solid so obtained was recrystallized from aqueous alcohol; light yellow plates, m. p. 108–110°; mixed m. p. of 108–111° with an authentic specimen of trimethylnitroquinone (m. p. 111–112°).

Summary

1. Dimethoxydurylic acid has been prepared and found to be a stable substance at its melting point, but it is quickly attacked by permanganate, and by nitric acid, the latter giving trimethylnitroquinone.

2. Since the acid and the corresponding aldehyde give the same results on oxidation, the failure to obtain any of the acid by oxidation of the aldehyde must mean that the aldehyde is more difficult to oxidize than the acid.

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(7) Nef gives the m. p. as 127–130° with decomposition.