sodium sulfate. Distillation afforded 44.7 g. (88%) of (+)-1, 1-dimethyl-2-phenylpropan-1-ol, b.p. 78–84° (5 mm.) n^{23}_{D} 1.5147 (lit.[7] n^{22}_{D} 1.5162), α^{23}_{D} +8.62° (1 = 1 dm.).

Preparation and decomposition of 1,1-dimethyl-2-phenylpropyl hypochlorite. A solution of 10.0 g. (0.0606 mole) of III in 50 ml. of carbon tetrachloride was stirred with 1200 ml. of 0.3 *M* hypochlorous acid solution[8] for 3 hr. at 0°. The yellowish-green carbon tetrachloride solution was separated, washed with water, and dried over calcium chloride. The carbon tetrachloride was removed under reduced pressure. The infrared spectrum of the carbon tetrachloride solution indicated the presence of a carbonyl compound, presumably acetone. The residue was distilled to yield 4.5 g. of material, b.p. 73–78° (11 mm.), n^{23}_{D} 1.5248, α^{26}_{D} +0.69° (1 = 1 dm.) (lit.[9] α^{25}_{D} 126°). The infrared spectrum of this material was identical to that of a known sample of α-phenethyl chloride.

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A Convenient Synthesis of α-Methyltropic Acid

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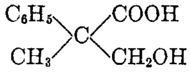
A synthesis of α-methyltropic acid (I) has been recently reported by Zaugg and DeNet.[1]

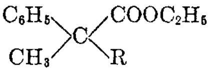


I

However, according to these authors, when α-phenylpropionic acid was treated with formaldehyde under the conditions of the Ivanov reaction, α-methyltropic acid was obtained in only trace amounts. Dimethyldiphenylsuccinic anhydride was the main end product, although yields were generally poor.

An attempted synthesis by the action of nitrous acid on ethyl β-amino-α-methyl-α-phenylpropionate[2] failed to give the expected compound, since rearrangement occurred with formation of α-benzyllactic acid.[3]

We have now ascertained that α-methyltropic acid may be prepared in reasonable yield through a way already described by Fusco and Testa for α-ethyltropic acid.[4] The starting compound was diethyl phenylmethylmalonate[5] (II), which was partially hydrolyzed to the monoester (III) in an alcohol solution of potassium hydroxide at room temperature. The monoester was then converted into the ester-chloride (IV) by reaction with thionyl chloride. Reduction of the acyl chloride with sodium borohydride gave the alcohol-ester (V), which was finally hydrolyzed to the free acid.



II. R = $COOC_2H_5$
III. R = COOH
IV. R = COCl
V. R = CH_2OH

The over-all yields ranged between 26 and 28%, based on the starting diethyl phenylmethylmalonate.

EXPERIMENTAL

Monoethyl phenylmethylmalonate (III). To a solution of 37.8 g. of potassium hydroxide in 250 ml. of water and 700 ml. of ethyl alcohol, 117.6 g. of diethyl phenylmethylmalonate was added quickly with stirring and the mixture was allowed to stand for about 100 hr. at room temperature. After this time hydrochloric acid was added to *p*H about 7.0, the ethyl alcohol was distilled off under reduced pressure, and the residue was diluted with an equal volume of water. After extraction with ethyl ether of some unreacted diethyl ester, the water layer was made acidic to *p*H 3–3.5 with hydrochloric acid. The separated oil was extracted with ethyl ether and the solvent removed *in vacuo;* the residue was sufficiently pure for the following step.

α-Phenyl-α-carbethoxypropionyl chloride (IV). The above crude ester (81 g.) was mixed cautiously with 81 ml. of thionyl chloride and refluxed for 2 hr. The excess thionyl chloride was then removed under reduced pressure. Distillation of the residue yielded 57.5 g. (66% based on the crude monoester) of IV, b.p. 135–136° (5 mm.).

Ethyl α-phenyl-α-hydroxymethylpropionate (V). To a well stirred suspension of 13.4 g. of sodium borohydride in 135 ml. of anhydrous dioxane a solution of 57.5 g. of IV in 250 ml. of anhydrous dioxane was added slowly in about 1 hr. Then the mixture was refluxed for 2.5 hr. on an oil bath. After cooling the mixture was cautiously poured into 500 ml. of ice water, taking care that the temperature did not exceed 25°. Hydrochloric acid was added to *p*H about 4, then the mixture was extracted with four 200-ml. portions of ethyl ether. The combined ether extracts were washed to neutral reaction and the solvent was removed *in vacuo*. The residue was distilled in a Claisen flask collecting at 130–132° (2 mm.); clear colorless oil. Yield 36 g. (72%).

α-Methyltropic acid (I). The above ester V (36 g.) was hydrolyzed by refluxing it for 5 hr. under rapid stirring with 720 ml. of 10% aqueous sodium hydroxide. After cooling the mixture was extracted with ethyl ether, the aqueous layer was made acidic to Congo red with hydrochloric acid, and the separated oil was extracted with ethyl ether. The solvent was removed *in vacuo* and the oily residue dissolved in equal volume of anhydrous benzene. The benzene solution was poured with stirring and cooling into 5 volumes of petroleum ether. An oil precipitated which crystallized after prolonged stirring and cooling. The white crystals were collected, washed with petroleum ether, and dried *in vacuo*. Yield 21.5 g. (70%); m.p. 86–87°.

Anal. Calcd. for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71. Found: C, 66.28; H, 6.80.

Acidimetric assay: 99%. The infrared spectrum was entirely consistent with the formula. After a further crystal-

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lization from ligroin the product melted at 91–92°. Mixed melting point with an authentic sample of α-benzyllactic acid (m.p. 98°) was depressed to 67–68°.

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Zinc Complex of Toluene-3,4-dithiol as a Reagent for Ketose Sugars

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Aliphatic and aromatic aldehydes and ketones react readily with 1,2-dimercapto compounds to form cyclic derivatives which are often intensely colored or easily oxidized to intensely colored compounds. Thus 1,2-dimercaptobenzene, I, condenses with benzaldehyde to give II which, in turn, is easily oxidized to salts of the cation III.[2] Similarly, 1,2-dimercaptoethane is a well recognized reagent for ketones.[3,4] In view of these facts it might be expected that the commercially available toluene-3,4-dithiol ("dithiol"), IV, would likewise afford a useful reagent for aldehydes and ketones.[5]

The poor keeping qualities of dithiol make it a difficult reagent to use. Recently, however, it has been found that its colorless zinc derivative, "zinc dithiol," V (or possibly VI), is surprisingly stable.[6] This is now available[1] as a very bulky pure white powder, the marked non-wettability of which appears to protect it from attack even on considerable exposure to acid vapors. It can generally be used in place of free dithiol and has application in the testing for trace quantities of numerous cations.[7]

It has been found that most common aldehydes do in fact react to give yellow colorations, or oily precipitates, when warmed with zinc dithiol in acid solution. Of immediate interest, however, is a reaction which occurs with sugars. When fructose or sorbose in dilute hydrochloric acid solution is heated to boiling with zinc dithiol a strong yellow color begins to develop within a few seconds and, after about 60 seconds, an oily yellow or orange precipitate separates. With sucrose a similar color develops, but much more slowly, doubtless owing to hydrolysis with formation of fructose. Among the sugars it appears that the reaction is given only by ketoses. In $4N$ hydrochloric acid none of the following available sugars or related compounds was found to give a reaction: arabinose, citric acid, galactose, glucose, inositol, lactose, mannitol, mannose, raffinose,[8] rhamnose, tartaric acid, xylose. Furfural gave a pale yellow color, much less intense than that given by the ketoses. In $2N$ acid the same distinction was observed, but the rate of development of color with fructose and sorbose was rather slow.

The reaction affords a quick and easy method by means of which ketoses may be immediately distinguished from aldoses. For example, fructose may be distinguished from glucose, or may be detected in the presence of the latter. The test is easily applied to qualitative work since neither the exact concentration of the acid nor the relative proportions of the reactants are critical. Since, under the conditions of the experiment, dithiol does not combine with such sugars as glucose, and since the excess of dithiol present may readily be titrated with mercuric chloride in presence of pyridine with a trace of a cobalt salt as indicator,[6] it appears that the reaction could be adapted to the quantitative estimation of ketoses.

This method was compared with others previously described for the detection of ketose sugars (8, 9). Although the anthrone reagent of Johanson is effective for developing chromatograms, and in spot test analysis, for qualitative identification in solution it was found to be inferior to dithiol. For example, addition of anthrone reagent to a dilute solution of fructose required three minutes for the color to develop, whereas less than 25 seconds was required for a strong yellow coloration employing the zinc complex of IV. The final color intensity and the sensitivity appeared to be of the same order of magnitude for both methods.

EXPERIMENTAL

General procedure for sugar analysis. To 0.25 ml. of dilute hydrochloric acid[10] was added 0.3–0.5 mg. (or more) of the sugar to be tested together with approximately the same amount of zinc dithiol. The mixture was heated to boiling, with shaking, and held at the boiling point for 30–60 sec. In presence of a ketose the liquid begins to become yellow within a few seconds, with deposition of a yellow or orange-yellow precipitate within 0.5–2.0 min., depending upon the concentration. With sucrose the color develops more slowly but is easily visible within 30–60 sec. The precipitate is readily visible when formed in a 0.2% fructose solution.

Comparison of anthrone with zinc dithiol in detection of fructose. Anthrone reagent was prepared by the method of Johanson.[9] Three min. was required for color to develop when fructose (1.0 mg.) was added to 0.25 ml. of reagent. Using zinc dithiol a strong yellow color developed within 25 sec. in presence of 0.5 mg. fructose. The final color intensities and sensitivities appeared to be comparable for both rea-

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(1) Reprints of this article, diacetyl-3,4-dithiol, dibenzoyl-3,4-dithiol, and the zinc complex of toluene-3,4-dithiol are available from Dr. Roy G. Neville, 783 Cereza Drive, Palo Alto, Calif.

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