

obtained 5 g. (85%) of pure product, pale yellow crystals from ethanol, m. p. 154–155°.

Anal. Calcd. for $C_{19}H_{17}NO_6$: C, 64.2; H, 4.8. Found: C, 64.5; H, 4.7.

Ethyl 2-Hydroxy-6-methoxy[1]benzopyrano[4,2-de]-quinoline-1-carboxylate, XV.—From 4 g. of XIV, with 450 ml. of 1% alcoholic sodium ethoxide, there was obtained 3.4 g. (89%) of product, yellow needles from alcohol, m. p. 272–274°.

Anal. Calcd. for $C_{19}H_{15}NO_5$: C, 67.6; H, 4.5. Found: C, 67.5; H, 4.4.

Ethyl 2-Chloro-6-methoxy[1]benzopyrano[4,2-de]-quinoline-1-carboxylate, XVI.—From 2 g. of XIV, treated with 10 ml. of phosphorus oxychloride, there was obtained 1.7 g. of product, yellow crystals from benzene-ligroin, m. p. 161–162°.

Anal. Calcd. for $C_{19}H_{14}ClNO_4$: C, 64.1; H, 4.0. Found: C, 63.8; H, 4.0.

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Chemical Degradation of Isotopic Succinic Acid¹

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In connection with biochemical studies it was necessary to determine the distribution of isotopic carbon in samples of succinic acid isolated from biological sources. It has been found that pyrolysis of the barium salt in a high vacuum at 500° results in a satisfactory conversion of the carboxyl carbon of succinic acid to barium carbonate. The course of this reaction is uncertain. In addition to barium carbonate and some carbon, products such as carbon dioxide, carbon monoxide, methane, ethane, ethylene and hydrogen were identified by mass-spectrometric analysis.

The accompanying table, giving the results of the pyrolysis of carboxyl- and methylene-labeled succinates, shows that the barium carbonate satisfactorily represents the carboxyl carbon. Evidently there is some contamination of the carboxyl carbon by methylene carbon, but this is so small as to introduce only a negligible error. This slight enrichment of C^{13} in the non-labeled carboxyl position was not an artifact, since non-isotopic barium succinate invariably yielded barium carbonate with the normal C^{13} abundance. This enrichment may be due to oxidation of the methylene carbon by traces of oxygen; or possibly, to transfer of oxygen between barium carbonate and the accompanying residual carbon.

TABLE I

C^{13} DISTRIBUTION IN SYNTHETIC LABELED SUCCINIC ACIDS

	Atom % C^{13} excess	Carboxyl carbon	
		Over-all	Calcd. Found
Carboxyl-labeled	2.41	4.82	4.80
Methylene-labeled	3.10	0.00	0.04 ± 0.02
Unlabeled	0.00	.00	.00 ± .01

(1) This work was sponsored by the Sun Oil Company and aided by a grant from the National Cancer Institute, U. S. Public Health Service.

Experimental

Preparation of Isotopic Succinic Acids.—Carboxyl-labeled succinic acid was prepared by refluxing ethylene dibromide with isotopic potassium cyanide, according to the procedure of Vanino.² The dinitrile was saponified with alkali without isolation, and after removal of neutral substances by extraction with ether, the succinic acid was isolated by acidification and continuous ether extraction. Yields ranged between 85 and 95%.

The methylene-labeled acid was prepared by a 4-step process giving an over-all yield of about 40%. Barium carbonate was reduced to the carbide according to the procedure of Cramer and Kistiakowsky³ and the acetylene obtained therefrom reduced to ethylene by a modification of the method of Patterson and du Vigneaud.⁴ This was converted to ethylene dibromide by addition of bromine and the former converted to succinic acid by the same procedure used for the carboxyl-labeled acid.

Preparation and Pyrolysis of Barium Salts.—About 20 mg. of the acid is dissolved in 1 ml. of water, 1 ml. of 20% barium chloride is added, and the solution brought to neutrality with dilute ammonia. Two volumes of 95% ethanol are added and the precipitated barium salt centrifuged, washed successively with alcohol and ether, and dried thoroughly in a vacuum.

The barium salt is transferred to a small glass tube, which is then sealed to the vacuum line or attached by means of a standard taper joint. After evacuation to a low pressure the salt is heated to 500° in an electric furnace. After about an hour the tube is cooled, the dark-colored residue is treated with dilute sulfuric acid and the evolved carbon dioxide collected for mass-spectrographic analysis.⁵ It is important to avoid even traces of oxygen in this degradation since in its presence some of the methylene carbon will be oxidized to carbon dioxide and contaminate the carboxyl carbon.

Acknowledgment.—The authors express their appreciation to the Sun Oil Company for its support and interest, and to Mr. Arthur Kent for the C^{13} analyses.

(2) Vanino, "Handb. d. prep. Chem.," 3, p. 263.

(3) Cramer and Kistiakowsky, *J. Biol. Chem.*, **137**, 549 (1941).

(4) Patterson and du Vigneaud, *ibid.*, **123**, 327 (1938).

(5) "Preparation and Measurement of Isotopic Tracers," Edwards Brothers, Ann Arbor, Mich., 1946, p. 43.

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Methoxyacetone

BY RAYMOND P. MARIELLA AND JOHN L. LEBCH

In continuing our investigations of unsymmetrical ketones, it became necessary to prepare a large quantity of methoxyacetone.

It was found that the wet oxidation of the inexpensive and easily-available 1-methoxy-2-propanol (Dowanol 33B) with chromic acid at room temperature goes conveniently in one step to give methoxyacetone. The present method is adapted from that of Petrov¹ and gives methoxyacetone in much shorter time than other published methods^{2–5} although in a somewhat lower yield.

(1) Petrov, *J. Gen. Chem., U. S. S. R.*, **16**, 1206 (1946); *cf. C. A.*, **41**, 3051 (1947).

(2) Henry, *Ann. chim.*, [8] **16**, 318 (1908).

(3) Henze and Rigler, *THIS JOURNAL*, **56**, 1350 (1934).

(4) Leonardi and diFranchis, *Gazz. Chim. Ital.*, **33**, I, 319 (1903)

(5) Traetta, Masca and Preti, *ibid.*, **31**, II, 275 (1921).

The dry catalytic dehydrogenation of 1-methoxy-2-propanol was also investigated, but no ketone could be isolated. Various attempts to prepare methoxyacetone from chloroacetone using a non-polar solvent also failed.

Two derivatives of methoxyacetone were easily obtained; the 2,4-dinitrophenylhydrazone and the *p*-nitrophenylhydrazone, but the semicarbazone did not form. Attempts to prepare the semicarbazone gave a very insoluble substance, which was proved to be the disemicarbazone of pyruvaldehyde. In addition, the osazone of pyruvaldehyde was prepared from phenylhydrazine and methoxyacetone.

Methoxyacetone gave a positive Benedict test (basic medium),⁶ a positive Schiff test (acid medium) and a positive test with Tollens reagent (basic medium). Apparently then, methoxyacetone is not too stable in either acid or basic media in the presence of oxidizing agents. This accounts for the rather low yield (28%) in its preparation from Dowanol 33B.

It is probably the rapidity of the reaction of methoxyacetone with 2,4-dinitrophenylhydrazine and *p*-nitrophenylhydrazine, and the insolubility of the resulting derivatives that make their isolation feasible. It is interesting to note that methoxyacetaldehyde also did not give the expected semicarbazone.⁷ The product obtained was probably the disemicarbazone of glyoxal.

The authors wish to express their thanks to the Graduate School for providing some funds, to Misses Guy, Hines and Hobbs, for the microanalyses, and to the Dow Chemical Company for a generous sample of Dowanol 33B.

Experimental

Methoxyacetone from 1-Methoxy-2-propanol.—To a solution of 375 g. of sodium dichromate and 202 g. of 1-methoxy-2-propanol (b. p. 118–120° at 745 mm.) in 200 cc. of water was added dropwise over a period of six hours, a solution of 450 g. of sulfuric acid in 115 g. of water. The reaction mixture was stirred during the addition and the temperature kept between 20–25°. After standing at room temperature all night, the green mixture was extracted four times with 200-cc. portions of ether. The ether extract was dried with anhydrous potassium carbonate, the ether removed, and the product fractionated; b. p. 112–116° at 750 mm.; yield 55.5 g. There was also isolated 10 g. of unreacted alcohol. The ketone was carefully refractionated, and the liquid, b. p. 114.5–115.0° at 756 mm., collected; n_D^{20} 1.3982, d_4^{20} 0.9494.

The *p*-nitrophenylhydrazone⁸ was isolated as yellow-orange plates from alcohol, m. p. 110–111°.

Anal. Calcd. for C₁₀H₁₃N₃O₃: N, 18.9. Found: N, 19.2.

The 2,4-dinitrophenylhydrazone was easily formed as yellow-orange needles from alcohol, m. p. 162.5–163°.

Anal. Calcd. for C₁₀H₁₃N₄O₅: N, 20.9. Found: N, 20.6.

When 1.0 g. of methoxyacetone, 1.2 g. of semicarbazide hydrochloride and 0.9 g. of sodium acetate were refluxed in 10 cc. of water for three hours, on cooling, 0.6 g. of a

white solid was formed. It was insoluble in all common solvents. A sample was recrystallized with great difficulty from a very large volume of water, m. p. 250–254° (dec.). Wohl and Lange⁸ noted the insolubility of the disemicarbazone of pyruvaldehyde, and reported a m. p. of 254°, which was not sharp.

Anal. Calcd. for C₅H₁₁N₃O₂ (monosemicarbazone of methoxyacetone): N, 29.2. Calcd. for C₅H₁₀N₄O₂ (disemicarbazone of pyruvaldehyde): N, 45.1. Found: N, 45.3.

When 1.0 g. of methoxyacetone, 5.0 g. of phenylhydrazine hydrochloride and 7.0 g. of sodium acetate in 40 cc. of water were refluxed for three hours, on cooling, a very viscous dark liquid was formed. This material was easily separated from the water layer by decantation. Crystallization of this liquid from alcohol-water slowly deposited 0.6 g. of an orange solid. Several recrystallizations produced an orange-brown solid, m. p. 147°.⁹

Anal. Calcd. for C₁₀H₁₄N₂O (phenylhydrazone of methoxyacetone): N, 15.7. Calcd. for C₁₅H₁₆N₄ (osazone of pyruvaldehyde): N, 22.2. Found: N, 21.7.

Methoxyacetone turned Benedict solution green in ten minutes and a small red precipitate was visible in one-half hour. When a few drops of methoxyacetone were added to 2 cc. of Schiff reagent, a deep purple color was produced immediately. With Tollens reagent, methoxyacetone developed a faint turbidity at room temperature in fifteen minutes, and gave a visible silver mirror in five minutes when heated on a steam-bath.

Attempted Catalytic Dehydrogenation of 1-Methoxy-2-propanol.—1-Methoxy-2-propanol (110 cc.) was passed over brass turnings at a rate of 1.2 cc. per minute. The gas evolution was almost negligible at 400°, increased slightly at 450°, and at 500° the evolution was rapid at first, but then decreased after the first fifteen minutes. At 500°, for instance, 3100 cc. of gas was collected. The product was fractionated and was for the most part unreacted starting material. No 2,4-dinitrophenylhydrazone of methoxyacetone could be isolated from any of the material.

Reactions with Chloroacetone.—Freshly distilled chloroacetone was added to sodium methoxide in benzene and, in another experiment, sodium methoxide was added to chloroacetone in benzene. In both cases, a brown sticky mass was obtained and no methoxyacetone could be isolated.

(8) Wohl and Lange, *Ber.*, **41**, 3615 (1908).

(9) Knopfer reports a m. p. of 148° for the osazone of pyruvaldehyde [*Monatsh.*, **32**, 767 (1911)].

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The Sulfonation of *m*-Aminophenol

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The sulfonation of *m*-aminophenol has been reported to yield 2-amino-4-hydroxybenzenesulfonic acid by Oehler.⁴ The reference to Oehler's work in Beilstein⁵ describes the product as the isomeric 4-amino-2-hydroxybenzenesulfonic acid. Other workers^{6,7} who have used the Oehler pro-

(1) Present address: Celanese Corp. of Amer., Summit, N. J.
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(3) Deceased.

(4) Oehler, German Patent 70,788; *Fydl.*, **3**, 59.

(5) Beilstein, "Handbuch der organischen Chemie," Vol. XIII, 1st ed., Julius Springer, Berlin, 1930, p. 402.

(6) Jacobs, Heidelberger and Rolfe, *THIS JOURNAL*, **41**, 471 (1919).

(7) Thorpe and Williams, *Biochem. J.*, **35**, 61 (1941).

(6) This result is similar to that obtained with α,α' -diethoxyacetone, which also gave a positive Fehling test; Grimaux and LeFèvre, *Bull. soc. chim.*, [3] **1**, 12 (1889).

(7) Drake, *et al.*, *THIS JOURNAL*, **60**, 73 (1938).