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Preparation and Decarboxylation of C-Acylated β-Methylglutaconic Anhydrides[1]

BY RICHARD H. WILEY AND NEWTON R. SMITH

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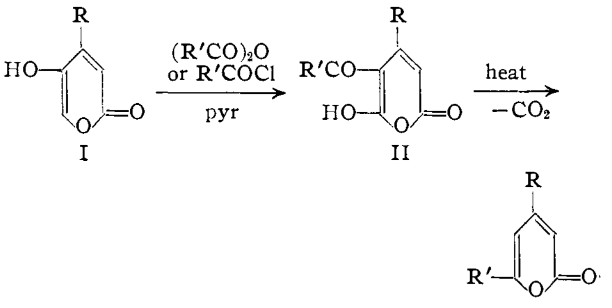
β-Methylglutaconic anhydride (I, R is methyl) has been C-acylated with acetyl, propionyl and butyryl chlorides or the corresponding anhydrides in pyridine to three new α-acyl derivatives (II, R′ is methyl, ethyl or propyl). These have been decarboxylated by heating to 4-methyl-6-alkyl-2-pyrones (III). The mechanism of the decarboxylation is considered.

It has been shown[2] that β-aryl glutaconic anhydrides (I, R is aryl) react with acyl halides in pyridine to give C-acylated derivatives (II) and that these products decarboxylate on heating to form 2-pyrones (III). The results reported here extend this reaction for the first time to a series of β-methyl (I, II, III, R is methyl, R′ is methyl, ethyl or propyl) analogs and establish with further certainty the course of the reaction by isolation of the well-known dimethyl-2-pyrone (III, R and R′ are methyl) in one series of reactions.

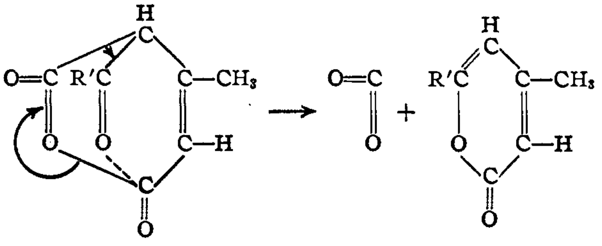


I II III

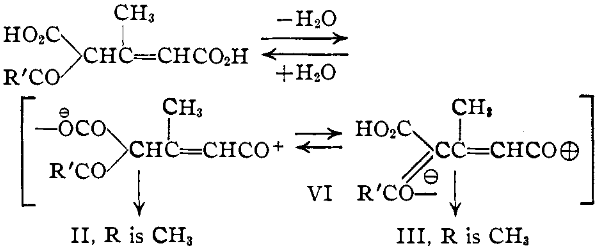
The pyridine acylation occurs exothermally on adding the acyl halide or anhydride to a pyridine solution of the β-methylglutaconic anhydride. The products were isolated by acidification of the reaction mixture and purification through the water soluble sodium salt in yields of 42–68%.

The pyrolytic decarboxylation takes place on distillation at atmospheric pressure. The products are distilled from the reaction vessel in yields of 57–72%. 4,6-Dimethyl-2-pyrone was characterized by comparison of its 3-bromo derivative with a sample prepared from the pyrone obtained by decarboxylation of isodehydroacetic acid.[3,4] The 4-methyl-6-ethyl- and 4-methyl-6-propyl-2-pyrones are hygroscopic liquids which color rapidly on exposure to air. Conversion to 3-bromo derivatives gives stable, recrystallizable solids.

A simple picture of the mechanism of this reaction is one of a concerted reaction in which the glutaconic anhydride ring is broken simultaneously with the formation of the new α-pyrone ring. The transformation may be visualized in the usual fashion as shown in formula IV leading to carbon dioxide and the α-pyrone (V), perhaps *via* a no-bond resonance structure intermediate as suggested for other decarboxylations.[5] Modification of this concept of the reaction may be necessary if acid or base catalysis of the reaction is demonstrated, to accommodate alternative mechanisms involving either conjugate acids such as are postulated as intermediates in the presumably acid-catalyzed decarboxylation of paraconic acids[6] or resonance stabilized anion structures previously suggested as contributing to the strong acidity of glutaconic anhydrides. It is also possible that some ionic form, such as VI, may function as an intermediate and under appropriate conditions be converted to either a glutaconic anhydride (II) or a pyrone (III).



IV V



VI

II, R is CH_3 III, R is CH_3

Experimental[7]

Materials.—β-Methylglutaconic anhydride was prepared from acetoacetic ester by condensation of the latter to ethyl isodehydroacetate with dry hydrogen chloride,[4,8] hydrolysis with hot sodium hydroxide[9] and cyclization with acetyl chloride.[10] The over-all yield was 40% of slightly impure anhydride, m.p. 86°. The pyridine was dried over potassium hydroxide before use; the acid chlorides and anhydrides were commercial materials which were used without further purification.

Acylation.—The acylation was carried out using both acid chlorides and anhydrides in the presence of pyridine. These acylations were always accompanied by formation of materials varying in color from green to red. This color disappeared on purification through the soluble sodium salt. Best yields were obtained using stoichiometric quantities of the reacting materials.

When benzoyl chloride was used, an oil was obtained which

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[2] G. R. Gogte, *Proc. Indian Acad. Sci.*, **7A**, 214 (1938); *J. Univ. Bombay*, **8**, Pt. 3, 208 (1939).

[3] R. H. Wiley and N. R. Smith, THIS JOURNAL, **73**, 1383 (1951).

[4] R. H. Wiley and N. R. Smith, *ibid.*, **73**, 3531 (1951).

[5] W. v. E. Doering and V. Z. Pasternack, *ibid.*, **72**, 143 (1950).

[6] W. S. Johnson and R. H. Hunt, *ibid.*, **72**, 935 (1950).

[7] All melting points are corrected. Microanalyses by Micro-Tech Laboratories, Skokie, Illinois.

[8] F. R. Goss, C. K. Ingold and J. F. Thorpe, *J. Chem. Soc.*, **123**, 348 (1923).

[9] F. Feist, *Ann.*, **345**, 69 (1906).

[10] N. Bland and J. F. Thorpe, *J. Chem. Soc.*, **101**, 856 (1912).

could not be induced to solidify. This was not investigated further. Maleic anhydride reacted violently producing a resinous material, while succinic anhydride produced a resinous product.

Typical procedures are given below:

3-Acetyl-4-methyl-6-hydroxy-2-pyrone was prepared both from the acid chloride and anhydride.

Method A.—Five grams (0.04 mole) of β-methylglutaconic anhydride was dissolved in 10 ml. of pyridine and cooled in an ice-bath. Then 3.1 g. (0.04 mole) of acetyl chloride was added dropwise with shaking and the semisolid reaction mixture allowed to stand at room temperature for one-half hour. After decomposition with 15 ml. of concd. hydrochloric acid and 25 g. of ice, the mixture was cooled and filtered. The dark residue was washed with cold, dilute hydrochloric acid and suspended in 40 ml. of water. Solid sodium bicarbonate was added cautiously with stirring until solution was complete and 2 g. of Norite added with stirring. After filtering, the filtrate was acidified with an excess of concentrated hydrochloric acid with cooling in an ice-bath. The precipitate was filtered and washed with dilute hydrochloric acid. This purification was repeated three times and the product finally washed with a little cold water and dried in a vacuum desiccator. The yield was 2.8 g. (42%) of 3-acetyl-4-methyl-6-hydroxy-2-pyrone, m.p. 131–132°.

Anal. Calcd. for $C_8H_8O_4$: C, 57.16; H, 4.75. Found: C, 57.07; H, 4.93.

Method B.—To 5 g. (0.04 mole) of β-methylglutaconic anhydride was added a mixture of 10 ml. of pyridine and 4.1 g. (0.04 mole) of acetic anhydride. The reaction was moderated by cooling under a water tap. When the reaction had subsided, it was allowed to stand at room temperature for one hour. The mixture was worked up as described under method A. The yield was 4.5 g. (68%) of the acetylated glutaconic anhydride, m.p. 131–132°.

3-Propionyl-4-methyl-6-hydroxy-2-pyrone was obtained by method A as a colorless solid, m.p. 114–115°. The yield was 54%.

Anal. Calcd. for $C_9H_{10}O_4$: C, 59.33; H, 5.53. Found: C, 59.47; H, 5.56.

3-Butyryl-4-methyl-6-hydroxy-2-pyrone was obtained in a 61% yield by method B. It was a tan solid melting at 67° and decomposing to a reddish, oily solid on standing for several weeks.

Anal. Calcd. for $C_{10}H_{12}O_4$: C, 61.24; H, 6.17. Found: C, 61.23; H, 6.25.

Thermal Decomposition.—A typical preparation of 4,6-dimethyl-2-pyrone by the thermal decomposition of the acetylated anhydride is given. The other acylated anhydrides were decomposed in a similar manner. All the alkylpyrones were hygroscopic and discolored on standing in air.

4,6-Dimethyl-2-pyrone.—In a 10 × 150 mm. glass tube, sealed at one end and bent at a right angle, was placed 3 g. of 3-acetyl-4-methyl-6-hydroxy-2-pyrone. The anhydride was melted with the free flame of a bunsen burner and cautiously distilled into a receiver cooled in ice. The solid distillate (2.0 g.) was redistilled under reduced pressure yielding 1.6 g. (72%) of 4,6-dimethyl-2-pyrone, melting at 45–47°, reported 51.5°.[11]

4-Methyl-6-ethyl-2-pyrone.—This compound was prepared in a 68% yield by thermal decomposition of 3-propionyl-4-methyl-6-hydroxy-2-pyrone. The pyrone was a colorless liquid, b.p. 100–115° (4 mm.); $n^{25}D$ 1.5176. It did not solidify on standing in an ice-box overnight. Satisfactory analyses were obtained only on samples carefully protected from the atmosphere.

Anal. Calcd. for $C_8H_{10}O_2$: C, 69.52; H, 7.29. Found: C, 69.41; H, 7.57.

4-Methyl-6-propyl-2-pyrone.—Thermal decomposition of 3-butyl-4-methyl-6-hydroxy-2-pyrone yielded on redistillation a 57% yield of 4-methyl-6-propyl-2-pyrone. A middle fraction, b.p. 110–120° (5 mm.), $n^{25}D$ 1.5094, did not solidify on standing in an ice-box. Two different preparations both analyzed low for carbon presumably because the compound is unstable.

Anal. Calcd. for $C_9H_{12}O_2$: C, 71.03; H, 7.95. Found: C, 70.24; H, 7.97.

Brominations.—The pyrones were all converted to solid derivatives by bromination. The pyrone (0.25 g.) was dissolved in 5 ml. of carbon tetrachloride and a stoichiometric quantity of bromine added. After standing overnight, the carbon tetrachloride was removed on a water-bath and the residue recrystallized from 60° petroleum ether.

3-Bromo-4,6-dimethyl-2-pyrone was obtained as a white solid, melting at 104–105°, reported 105°.[11] Its mixed melting point with a sample prepared by decarboxylation of isodehydroacetic acid[3,4] and bromination of the resulting dimethylpyrone, was 104–105°, establishing the identity of this pyrone.

3-Bromo-4-methyl-6-ethyl-2-pyrone formed white needles, m.p. 57°.

Anal. Calcd. for $C_8H_9O_2Br$: C, 44.26; H, 4.15. Found: C, 44.31; H, 4.18.

3-Bromo-4-methyl-6-propyl-2-pyrone was obtained as white needles, m.p. 65°.

Anal. Calcd. for $C_9H_{11}O_2Br$: C, 46.78; H, 4.80. Found: C, 46.73; H, 4.93.

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(11) A. Hantzsch, *Ann.*, **222**, 16 (1883).