The Synthesis of 2-Methyl-cyclopenta-1,3-dione

by

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A Thesis Describing Chemical Research in Ch 80

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Gentlemen:

The stated purpose of the research described in the following thesis is the synthesis of the synthetically useful molecule 2-methyl-cyclopenta-1,3-dione. The success or failure of any such synthetic problem is not the intended goal of undergraduate research, in my opinion however. In any final evaluation of undergraduate education, laboratory experience is a considerable factor. To gain such experience then is the real goal of my undergraduate research effort. The synthetic problem described here is then merely a vehicle in the persuit of the more elusive goal.

The confidence and ability of an undergraduate student are directly dependent upon his fortune and the influence of the co-workers around him. The eventual success of this project was predictable: good fortune. The contact with graduate level education and laboratory experience was also inevitable: better fortune. When I consider the greater gain obtained from the many associations, the actual synthetic success seems superficial. To be involved, however slightly, in the workings of a graduate-professional level research program, to be aware and attentive in an atmosphere of challenge and invention, and to be stimulated by such an environment are the true "good fortunes". It is with this hope and consideration that I entered the undergraduate research program. It is with this accomplishment that I leave.

Sincerely,

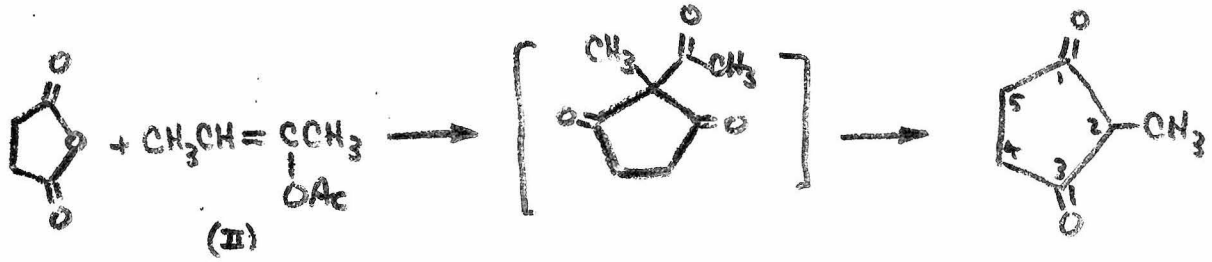
Craig McAllister

Abstract

The preparative synthesis of 2-methyl-cyclopenta-1,3-dione from 2-buten-2-ol acetate and succinic anhydride is described. The synthesis of the enol acetate precursor is summarized. Final yields of product are enumerated.

The synthetically useful molecule, 2-methyl-cyclopenta-1,3-dione (I), is interesting for at least two reasons. The structural properties of such a molecule suggest many opportunities for its use in adding a carbonyl-activated and methyl-substituted ring or 5-carbon chain to a parent molecule. With the cleavage of the C_1-C_2 bond and the presumed destruction of one of the carbonyls, the residue retains the C_2-methyl group as well as the second carbonyl group for activation. Thus, in the proper circumstances, this molecule provides an activated product of synthesis. The second source of interest is the stereochemistry of the 2-methyl group in synthetic reactions. Both of these factors combine to provide sufficient interest in this molecule to warrent its synthesis.

A recently published article by V. J. Grenda et. al.[1] suggests a one-step route to this molecule from 2-buten-2-ol acetate and succinic anhydride. The synthesis of the enol



acetate (II) had to be performed before the Grenda method could be attempted. With the synthetic scheme illustrated above, Grenda obtained a crystalline product (I) directly upon quenching

1. V.J. Grenda, et.al., JOC 32:1236 (1967).

with water. Dry nitrobenzene was the solvent of his choice. In his work, the reaction was performed in two main stages, as suggested above. The first stage is one of strict control and low temperatures (5-10°C.), to prevent O→C acyl migration in the enol acetate (II); the second stage is forcing, requiring heating to 110°C. and aging.[2]

Preparation of Reagents

Except for the enol acetate required for this reaction, all the other chemicals were available in large, pure quantities. The synthesis of the 2-buten-2-ol acetate was performed using an adaptation of the work of H. O. House and V. Kramer.[3] The starting materials were 2-butanone (methyl-ethyl-ketone) and acetic anhydride. Although House's work describes the synthesis and characteristic properties of homologs of this enol acetate, there was no exact literature reference to (II). The largest adaptation of House's work was a more strict control of the reaction temperatures. With:

83 ml. (0.918 mole) of 99% 2-butanone

175 ml. (1.940 mole) of 99% acetic anhydride

1.20 gm. (6.98 mmole) of p-toluene sulfonic acid as catalyst

the reaction vessel was heated to 70°C. for 50 hours. (In preliminary experiments it was found that excessive heating and/or short reaction times reduced the yield of the enol acetate. A molar ratio of 2:1, Ac_2O:2-butanone was found to be satisfactory. The use of p-TsOH was found to be another acceptable adaptation of the work by House and Kramer.) The crude mixture was cooled

2. Ibid.
3. H.O. House and V. Kramer, JOC 28:3362 (1963).

to room temperature, and slowly poured, with stirring, into an ice cold mixture of saturated $NaHCO_3$ and pentane. Distillation of the dry organic phase yielded a crude fraction. BP 118-125°C. A second distillation yielded 21 gm. of 99% pure (II). BP 118-121°C. This product is actually an isomeric mixture of the cis and trans forms. Since both isomers are synthetically useful, a VPC was taken only for qualitative inspection.

Commercial grade 2-buten-2-ol acetate was also obtained as a limited sample, for comparison studies. Both samples of (II) performed identically.

The Synthesis of 2-Methyl-cyclopenta-1,3-dione (I):

204 gm. (1.54 mole) of dry aluminum chloride
380 ml. of redistilled dry nitrobenzene
44 gm. (0.44 mole) succinic anhydride
75 gm. (0.66 mole) of 99% enol acetate (II)

To a 1-liter, 3-necked flask, fitted with a magnetic stirrer, thermometer, condensor, and protected from moisture with a dry N_2 atmosphere, the aluminum chloride was added to the nitrobenzene. With the addition of the succinic anhydride, the temperature was allowed to rise from 25 to 65°C. The solution was heated at 110° for 30 minutes to facilitate the formation of the aluminum chloride complexes. After cooling this mixture to room temperature, the enol acetate was added, dropwise with continuous stirring. There was no immediate change in temperature. After approximately 15 minutes, the temperature was allowed to rise to 50°C. With additional cooling, the remaining portion of the enol acetate was allowed to mix dropwise. The mixture appeared deep red in color. After aging the mixture at 25°C. for 30

minutes, the flask was heated slowly until the evolution of HCl gas became obvious, and then maintained at such a temperature to produce gas evolution (40-70°C.). After the completion of all HCl evolution, the mixture was aged for 2 hours at 70°C. After cooling to 5°C. in an ice bath, the reaction mixture was quenched with 500 ml. of cold (5°C.) water. The two-phase mix was aged at 5° for 72 hours.

The solid obtained upon filtration of the quenched mixture was washed twice with 50 ml. portions of nitrobenzene, and then with 25 ml. of dry pentane. The crude solid weighed 48.4 gm. This solid was dissolved in 1500 ml. of hot (90°C.) water, and stirred with 6.0 gm. of activated charcoal (Norite A). Upon filtration over Celite, white crystals formed immediately in the cooling water. From the cold (5°) solution clear-white crystals were obtained. 25.52 gm. MP 210.1-211.4°C. (Lit. 210-212°C.). Further purifications and crystallizations yielded a total of 3.27 gm. of additional product, for an overall yield from the enol acetate of 46.8%.

In the course of several such preparations of the product (I), the total amount of various reagents used was:

320 gm. aluminum chloride
630 ml. nitrobenzene (BP 208-210°C.)
69 gm. succinic anhydride
118 gm. 99% 2-buten-2-ol acetate (BP 118.5-121.5°C.)

The overall yield for all the preparations was 48.4 gm. of (I), for a 43.2% yield. In all cases, spectral analysis and melting point determinations conformed to literature values.

See the Research Notebook #2087 for details and notes.

In this particular series of experiments, the need for strict economy of procedure was minimal. At the time, there was a large need for the methyl diketone (I), and an available surplus of precursor materials. Thus, a yield of only 43% was satisfactory. That this yield was not higher was due to the nature of the conditions: only the purest, first-crop of crystalline product was necessary. Elaborate concentration and purification techniques were not attempted. Thus, it is not surprising to find more than one adaptation of the literature procedure to fit existing conditions and chemical availabilities.

A second factor which was important in the evaluation of this project was the amount of information and experience to be gained by a continuation of the work. Since this project was a vehicle rather than the goal itself, elaboration of a particular technique was considered to be extravagant. Thus, this procedure did not involve parameter variations, etc. The importance of such a decision cannot be over-emphasized.

The goals of this experiment were met. The purposes of this project were followed in a satisfactory manner: there <u>was</u> a great deal of interchange between the "resident" graduate staff and the "transitory" undergraduate. A measure of maturity (although often a trite word) was gained in regard to organic chemistry. The outcome of this effort then was an understanding of the modern organic research organization, the problems, and the means of solution.