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SYNTHESIS OF FOUR-MEMBERED RING ACYLOINS AND α-DIKETONES

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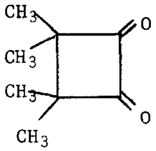
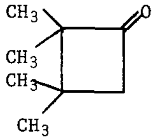
The very recent report by Bloomfield (1) that four-membered ring acyloins can be conveniently synthesised *via* intermediate enediolates as their trimethylsilyl ether derivatives prompts us to communicate some of our results in this field. For some time, we have been attempting to synthesise 3,3,4,4-tetramethylcyclobutanedione (I) (2) as part of our studies on the photochemistry of α-diketones (5), and the synthesis of small ring compounds.

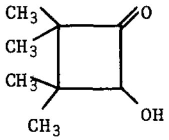
2,2,3,3-Tetramethylcyclobutanone (II) (6) and the acyloin 2-hydroxy-3,3,4,4-tetramethylcyclobutanone (III) seemed to be attractive intermediates for the preparation of (I). Not unexpectedly, attempted synthesis of (III) from dimethyl tetramethylsuccinate under the usual conditions of the acyloin synthesis (e.g., sodium in toluene and xylene, sodamide in ether, and liquid ammonia/ether) was unsuccessful. The use of sodium/potassium alloy (7), however, led to a fair yield (35%) of the acyloin (III), m.p. 96-98°. When dimethyl tetramethylsuccinate was treated with sodium in toluene in the presence of chlorotrimethylsilane (8), a high yield (84%) of the compound (IV), b.p. 105-106°/20 mm was obtained. Hydrolysis of (IV) with hydrochloric acid in tetrahydrofuran (8,9) gave the desired acyloin (72%). The overall yield of (III) from the starting ester was 60%, thus demonstrating, as also found by Bloomfield (1), the superiority of this method over that using sodium/potassium alloy. As reported by Bloomfield (1), we had also found that diethyl succinate and *cis*-1,2-dicarbomethoxycyclohexane are converted in high yields to the corresponding cyclic derivatives by the use of sodium in toluene containing chlorotrimethylsilane. An attempt to convert dimethyl phthalate to the compound (V) was unsuccessful; only intractable tar was obtained.



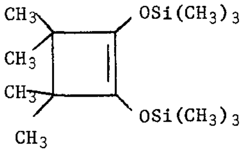
(I)



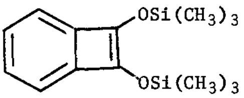
(II)



(III)



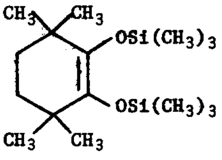
(IV)



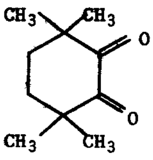
(V)

All attempts to oxidise the pure acyloin (III) to the diketone (I) have been unsuccessful. Oxidants used have included chromic oxide in pyridine, acetic acid and acetone/sulphuric acid, cupric acetate in various media, ferric chloride, lead tetra-acetate in pyridine, activated manganese dioxide, ruthenium tetroxide/sodium metaperiodate, dimethylsulphoxide/acetic anhydride, dimethylsulphoxide/benzene/pyridine/trifluoroacetic acid, and dimethylsulphoxide/pyridine-sulphur trioxide complex. Efforts to convert the ketone (II) to the diketone (I) by the action of selenium dioxide in various media have been unsuccessful. The failures to oxidise (II) and (III) to (I) are in direct contrast to the ready oxidation of the corresponding derivatives having five and six-membered rings.

On one occasion only, hydrolysis of the compound (IV) with hydrochloric acid in ether containing anhydrous ferric chloride (3 equivs) led to the isolation of a very small quantity (5% yield) of an unstable red-brown powder. Its infrared spectrum (in chloroform) (strong absorption at 1780 cm^{-1} and a doublet at 1385 and 1365 cm^{-1}) was consistent with that predicted for the desired α-diketone. Despite many attempts, it has not been possible to repeat the above experiment. It is pertinent to mention that, under the same conditions, the compound (VI) is converted almost quantitatively to 3,3,6,6-tetramethylcyclohexane-1,2-dione (VII) (11).



(VI)



(VII)

Further attempts to convert (II) and (III) to (I), as well as alternate routes to (I), are currently under investigation.

REFERENCES

1. J.J. Bloomfield, *Tetrahedron Letters*, 587 (1968).
2. Except for the special case in which the substituents are halogens (F, Cl or Br) (3), examples of saturated 3,3,4,4-tetrasubstituted cyclobutane-1,2-diones do not seem to have been reported. 3-Phenylcyclobutane-1,2-dione, the only reported example of a less substituted saturated cyclobutane-1,2-dione exists as the enol (4).
3. D.C. England, *J.Amer.Chem.Soc.*, *83*, 2205 (1961); D.C. England, *Chem.Abst.*, *56*, P1363a, 1962; *61*, P2987e, 1964.
4. E.F. Silversmith and J.D. Roberts, *J.Amer.Chem.Soc.*, *80*, 4083 (1958).
5. G.E. Gream, J.C. Paice and C.C.R. Ramsay, *Aust.J.Chem.*, *20*, 1671 (1967); and papers in preparation.
6. We are indebted to Dr. H. Bestian, Farbwerke Hoechst AG, Frankfurt, for a very generous gift of compound (II).
7. J.J. Bloomfield and J.R.S. Irelan, *J.Org.Chem.*, *31*, 2017 (1966).
8. U. Schräpler and K. Rühlmann, *Chem.Ber.*, *97*, 1383 (1964), and references therein.
9. It is advisable to use the compound (IV) soon after its preparation. On one occasion, it was found that considerable decomposition had occurred in a sample which had been kept at 0° under nitrogen for three months.

To obtain a maximum yield of the acyloin, it is essential that the hydrolysis be carried out under pure nitrogen, and in tetrahydrofuran which has been distilled from $LiAlH_4$ followed by purging with pure nitrogen immediately before use. Otherwise, appreciable yields of tetramethylsuccinic anhydride can be obtained.

10. Since compound (VI) is produced in a yield of 94% from diethyl α,α,α',α'-tetramethyladipate, the present method of synthesis of (VII) is markedly superior to that previously described (11). It is probable that the modified synthesis of (VII) can be extended to the synthesis of other α-diketones.

11. D. Klenberg, *Ann.Acad.Sci.Fennicae*, Ser AII, No. 118, 1962.