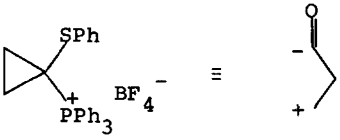
Tetrahedron Letters No. 51, pp 4531 - 4534, 1975. Pergamon Press. Printed in Great Britain.

1-PHENYLTHIOCYCLOPROPYLTRIPHENYLPHOSPHONIUM FLUOBORATE: A NEW SYNTHON FOR CYCLOPENTANONE SYNTHESIS[1]

J. P. Marino* and Robert C. Landick
Department of Chemistry, University of Michigan,
Ann Arbor, Michigan 48104

(Received in USA 13 September 1975, received in UK for publication 13 November 1975)

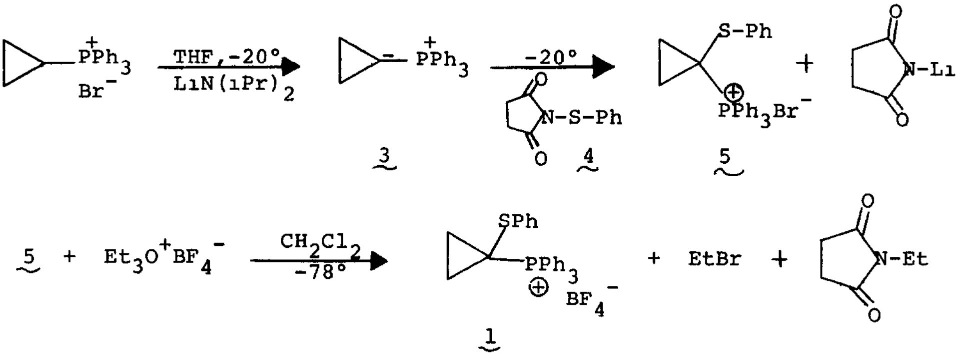
In recent years, there has been considerable interest in developing new and efficient synthetic methods for the formation of cyclopentanes and oxocyclopentanes.[2] One of the most efficient approaches to five-membered rings involves initial nucleophilic attack on activated cyclopropanes with subsequent intramolecular ring closure.[3] In this paper, we wish to report the preparation and reactions of a new three carbon synthon, 1-phenylthiocyclopropyltriphenylphosphonium fluoborate **1**, which is synthetically equivalent to the acyl zwitterion **2**.



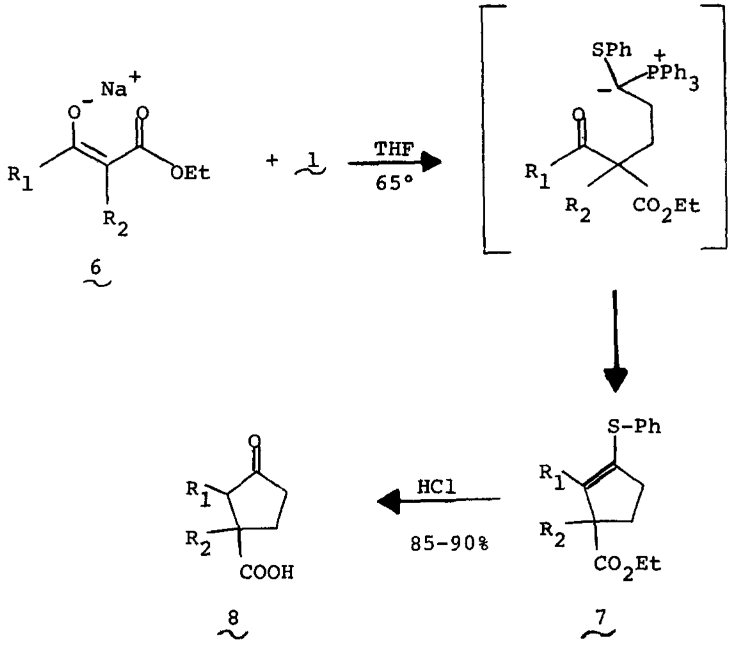
1 **2**

The doubly-activated cyclopropane **1** would be expected to suffer nucleophilic ring-opening regiospecifically, with the concomitant generation of an α-phenylthiophosphorylide moiety. Intramolecular Wittig reaction of the incipient phosphorous ylide should give rise to a vinyl sulfide, a well-known carbonyl precursor.

The preparation of the cyclopropyl salt **1** can be conveniently accomplished *via* the sulfenylation of triphenylphosphonium cyclopropylide **3**. A THF solution of the ylide **3** (prepared from lithium diisopropylamide at -20°)[4] was added dropwise to a THF solution of one equivalent of N-phenylthiosuccinimide[5] 4 at -20°. During the addition of 3, a white solid, which was believed to be the expected phosphonium bromide 5 and succinimide salt, precipitated. The hygroscopic salt was filtered in an inert atmosphere and washed with ether. Further purification of the bromide 5 was not carried out at this time, since the less nucleophilic fluoborate salt was desired. The anion exchange was affected by treating a methylene chloride suspension of 5 and the succinimide salt with an excess of triethyloxonium fluoborate at -78°C. As the oxonium salt was added to the suspension, the bromide was converted to the soluble ethyl bromide and the succinimide salt was converted to the soluble N-ethylsuccinimide. The resulting cyclopropylphosphonium fluoborate 1 was also soluble in methylene chloride at room temperature. Removal of the solvent and trituration of the residue with anhydrous ether removed the non-salt by-products. The pure white fluoborate 1 (m.p. 201.5-202.5)[6] was recrystallized from chloroform - THF mixtures [NMR (δ,$CHCl_3$) - 1.44-2.14 (m,4H); 6.89-7.29 (m,5H); 7.61-7.84 (m,15H)]. The overall yield of fluoborate 1 from cyclopropyltriphenylphosphonium bromide was in the range of 50-60%.



The utilization of synthon 1 in the synthesis of five-membered rings was demonstrated by its reaction with sodium enolates of β-keto esters. When equimolar amounts of 1 and enolates derived from substituted acetoacetic esters 6 were refluxed in THF for an average of 72 hrs, good yields[7] of the cyclopentenyl sulfides, 7a, b, c, were isolated. The yields of 7a, b, c, were much lower when dimethylformamide or HMPA is used as the reaction solvent, while good yields were obtained with acetonitrile. The conversions of the vinyl sulfides to the corresponding keto-acids 8 were made using hydrolysis conditions of 20% HCl/dioxane at 60°C.[8]

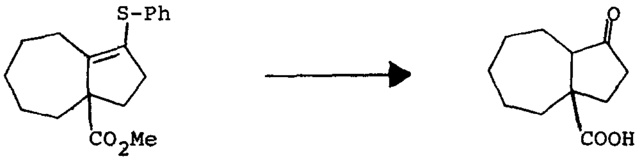


a - R_1=CH_3 (75%)
R_2=H

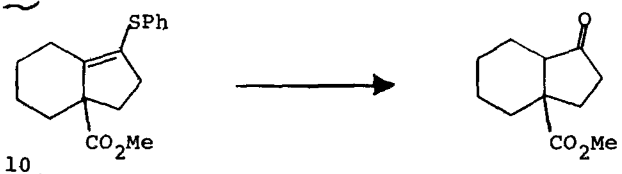
b - R_1=CH_3 (80%)
R_2=CH_2Ph

c - R_1=Ph (75%)
R_2=H

One of the most useful synthetic operations available with synthon 1 is the direct annelation of a five-membered ring onto a cyclic ketone. This approach also allows for the simultaneous introduction of an angular functionalized methyl group beta to the ketone moiety. The following examples of cyclic β-dicarbonyl compounds illustrate the utility of our approach for the hydroazulenone and hydrindanone ring systems which are quite prevalent in natural products. Thus, vinyl sulfides 9 and 10 can be isolated in 80-85% yields under the aforementioned reaction conditions and their respective hydrolyses to the keto-acids[9] can be affected in 90% yield.

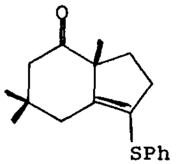


9

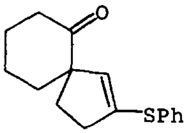


10

The reactions of 1 with enolates of 2-methyldimedone and 2-formyl cyclohexanone gave disappointingly low yields of the expected annelated products 11 (40%) and 12 (20%).



11



12

The efficiency with which reagent 1 provides a cyclopentane ring containing a masked carbonyl group should render this approach useful in the synthesis of a large variety of natural products containing five-membered rings.

References and Footnotes

1. A preliminary report of this work was presented at the 170th National Meeting of the American Chemical Society on August 25th, 1975, in Chicago, Ill., ORGN 27.
2. (a) For a review on oxocyclopentane syntheses, see R. A. Ellison, Synthesis, 397 (1973).
   (b) J. P. Marino and Wm. Mesbergen, J. Amer. Chem. Soc., 96, 4050 (1974).
   (c) B. M. Trost and S. Kurozumi, Tetrahedron Lett., 1929 (1974).
   (d) R. H. Schlessinger and R. F. Romanet, J. Amer. Chem. Soc., 96, 3701 (1974).
   (e) E. J. Corey and S. W. Walinsky, *ibid.*, 94, 8932 (1972).
   (f) I. Kawamoto, S. Muramatsu and Y. Yura, Tetrahedron Lett., 4223 (1974).
3. (a) S. Danishefsky, J. Dynak, E. Hatch and M. Yamamoto, J. Amer. Chem. Soc., 96, 1256 (1974).
   (b) P. Fuchs, *ibid.*, 96, 1607 (1974).
   (c) W. G. Dauben and D. J. Hart, *ibid.*, 97, 1622 (1975).
4. E. E. Schweizer, C. J. Berninger and J. G. Thompson, J. Org. Chem., 33, 336 (1968).
5. K. H. Buchel and A. Conte, Chem. Ber., 106, 1248 (1967).
6. All new compounds gave satisfactory elemental analyses (± 0.25%) and possessed spectral data consistent with the structures indicated.
7. The yields stated are isolated yields after preparative layer chromatography
8. Milder hydrolysis conditions involving mercuric salts were completely unsatisfactory.
9. The products derived from 9 and 10 were assumed to be a mixture of *cis-trans* stereoisomers.