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SYNTHESIS OF FURANS BY CARBENE INSERTION

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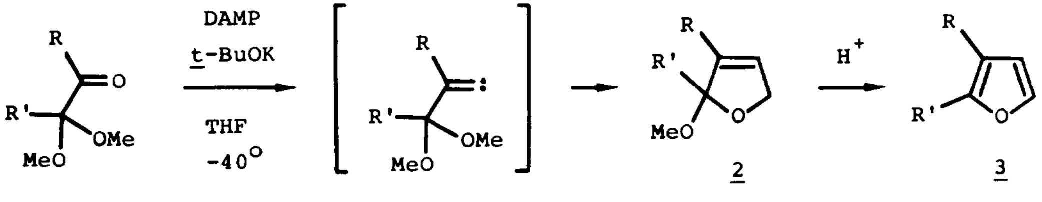
Summary: Reactions of α,α-dimethoxy ketones with diethyl diazomethylphosphonate proceed initially to dihydrofurans, probably through C-H insertion of a carbene intermediate; subsequent elimination of methanol affords the corresponding furans in good overall yields.

The furan ring is a structural feature of many natural products which exhibit interesting biological activity.[1] Synthetic methods leading to this ring system are therefore of considerable interest. We wish to report a simple route to furan derivatives starting from α-keto acetals.

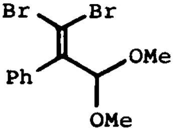
The reaction of 2,2-dimethoxycyclohexanone (1a)[2] with diethyl diazomethylphosphonate (DAMP)[3] and potassium t-butoxide in THF at -40°C gave as the primary product the bicyclic dihydrofuran derivative 2a.[4] Attempted distillation of this caused elimination of methanol, resulting in a 72% yield of 5,6,7,8-tetrahydrobenzofuran (3a).[5] Similarly, the homologue 3b[5] was obtained in 70% yield from 1b.[2] As expected, the elimination reaction is acid catalyzed.

This method is not limited to cyclic α-keto acetals. Thus, treatment of 1,1-dimethoxyhexan-2-one (1c)[6] with DAMP afforded 3-butylfuran (3c)[7] in 67% yield without isolation of the intermediate dihydrofuran derivative 2c. On the other hand, a similar reaction of α,α-dimethoxyacetophenone (1d)[8] gave rise to a 75% yield of the corresponding dihydrofuran 2d[4], which in the presence of hydrochloric acid at room temperature was converted almost quantitatively to 3-phenylfuran (3d).[9] Compound 2d was also obtained in similar yield by treatment of the dibromomethylene derivative 4[10] with methyllithium.



1 5 2 3

	a	b	c	d
R	$(CH_2)_4$	$(CH_2)_3$	Bu	Ph
R'			H	H



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From evidence in the literature both reactions of ketones with DAMP[11] and dibromomethylene derivatives with alkyllithium[12] generate alkylidenecarbenes as reactive intermediates. Carbenes are known to insert intramolecularly into C-H bonds, particularly when these are 1,5 related and adjacent to oxygen atoms.[13] Hauske *et al.*[14] have recently reported the formation of a dihydrofuran derivative from an α-methoxy ketone and DAMP. We regard the first step in the present sequence to be a selective intramolecular insertion of the carbenic carbon of 5 into a C-H bond of the methoxy group as indicated in the Scheme.

In the open-chain alkylidenes there is no apparent steric restriction to a close approach between the carbenic carbon and the appropriate C-H bonds, and in the case of the cyclic ketones the equatorial methoxy groups of the carbene derived from 1a is ideally positioned for insertion. The subsequent ready elimination of methanol is easily conceived. Furthermore, the conjugative effect of the phenyl group explains the stability of the dihydrofuran 2d.

The simplicity and mild conditions of the present 'one-pot' process may prove to be an asset when compared with many of the methods already available for the preparation of furans.

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REFERENCES

1. F.M. Dean and M.V. Sargent in 'Comprehensive Heterocyclic Chemistry', vol 4, p. 531 eds. A.R. Katritzky and C.W. Rees, Pergamon Press, Oxford 1984; P. Crews and S. Naylor, Progr. Chem. Org. Nat. Prod. 1985, 48, 203.
2. F. Huet, M. Pellet, A. Lechevallier, and J.-M. Conia, J. Chem. Research (M), 1982, 2528.
3. M. Regitz, A. Liedhegener, U. Eckstein, M. Martin, and W. Anschütz, Liebigs Ann. Chem., 1971, 748, 207.
4. All compounds were fully characterized by spectral data.
5. H.-D. Scharf and E. Wolters, Chem. Ber., 1978, 111, 639.
6. E.E. Royals and A.G. Robinson, J. Am. Chem. Soc., 1956, 78, 4161.
7. S.W. Pelletier, Z.Djarmati, S.D. Lajsic, I.V. Micovic, and D.T.C. Yang, Tetrahedron, 1975, 31, 1659.
8. K.R. Henery-Logan and T.L. Fridinger, J. Chem. Soc., Chem. Commun., 1968, 130.
9. D. Miller, J. Chem. Soc., C, 1969, 12.
10. G.H. Posner, G.L. Loomis, and H.S. Sawaya, Tetrahedron Lett., 1975, 1373.
11. J.C. Gilbert, U. Weerasooriya, and D. Giamalva, Tetrahedron Lett., 1979, 4619; J.C. Gilbert and U. V Weerasooriya, ibid., 1980, 21, 2041; J.C. Gilbert and B.K. Blackburn, ibid., 1984, 25, 4067, J. Org. Chem., 1986, 51, 3656; J.C. Gilbert, D. Giamalva and M.E. Baze, J.Org. Chem., 1985, 50 2557; J.C. Gilbert and B.K. Blackburn, ibid. 1986, 51, 3656.
12. H.D. Hartzler, J. Am. Chem. Soc., 1964, 86, 526.
13. W. Kirmse, 'Carbene Chemistry', 2nd. Ed., Academic Press, New York 1971; J. Arct, L. Skattebøl and Y. Stenstrøm, Acta Chem. Scand., 1983, B37, 681 and refs. therein.
14. J.R. Hauske, M. Guadliana, and K. Desai, J. Org. Chem., 1982, 47, 5019.

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