A General Synthesis of Ketones and Aldehydes[1]

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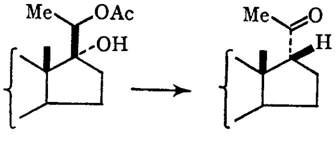
THE Serini reaction, well known in the steroid series,[2] consists of subliming 17,20-diol 20-monoacetates from zinc dust or heating them under reflux with zinc in toluene or xylene. It results in the formation of a 20-ketone *via* a 20 → 17 hydride shift, with inversion at C-17.

This reaction, which was used by us previously in some cyclic systems with *cis*-related oxygen-containing functions,[3] has been extended now to include the acyclic diol acetates listed in the Table and therefore is defined as a general synthetic method.

The following procedure is typical: a mixture of pure 2-methylheptane-2,3-diol 3-acetate (0·5 g.)†



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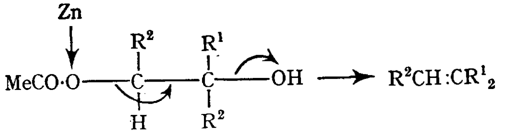
† The purity of diol acetates and the activation of zinc are essential conditions for satisfactory results.

and freshly activated zinc dust[4] (12·5 g.) was introduced into a glass tube connected with an ice-cooled trap for eventual volatile fractions. The tube was immersed in an oil bath and kept under nitrogen for 3·5 hr. at 154°. The product was isolated with ether and the solvent eliminated, by use of a Vigreux column. The yield of 2-methylheptan-3-one (68%) is based on the preparation of the semicarbazone (m.p. 111—112°), whereas g.l.c. analysis (10% SE-30 on Chromosorb W) points to the ketone as the only product, present except for 9% of 2-methylhept-2-ene. Formation of analogous olefins in yields around 10% was observed also in other similar reactions leading to ketones (but not to aldehydes) and might be represented as a zinc-promoted reductive elimination:‡



The alternative synthesis of ketones and aldehydes, starting from the corresponding primary–tertiary and secondary–tertiary diols, consists of treatment with a mineral acid,[5] and leads to undesired results when acid-sensitive functions are present. The formation of a positively charged intermediate by this latter method can involve also the migration of an aryl or alkyl group, instead of hydrogen, *via* a pinacol rearrangement. Thus, 2-methyl-3-phenylpropane-2,3-diol is converted by acid into dimethylphenylacetaldehyde or 3-phenylbutan-2-one,[6] whereas treatment of the corresponding 3-acetate with zinc led mainly to methylpropiophenone:§

TABLE

Diol acetate	Reaction time (min.)	Reaction temp.	Product[a]	Yield (%)[b]
C_5H_{11}·MeC(OH)·CH_2OAc	165	156°	2-Methylheptan-1-aldehyde..	62
Me_2C(OH)·CH(OAc)·$[CH_2]_3$·Me	210	154°	2-Methylheptan-3-one	68
Ph_2C(OH)·CH_2OAc	150	160°	Diphenylacetaldehyde	66
Ph_2C(OH)·CH(OAc)·$[CH_2]_3$·Me	180	160°	1,1-Diphenylhexan-2-one	76
Me_2C(OH)·CH(OAc)Ph	180	170°	β-Methylpropiophenone	64

[a] Identified by i.r. and n.m.r. spectroscopy and by comparison with authentic samples.
[b] Based on chromatographic separation and on n.m.r. and g.l.c. analysis.

It is considered that the more populous *gauche* arrangement of the oxygen-containing functions, expected on steric and statistical grounds, facilitates the formation of the cyclic orthoester intermediate,[7] and thus ensures the satisfactory outcome of the described reactions. Elaboration of the assumed pathway by which the hydride shift occurs will be given elsewhere. It is noteworthy that the suggestion of a radical mechanism[7b] has been disproved on the basis of e.s.r. measurements made by us during these studies.

(*Received, September 20th,* 1968; *Com.* 1282.)

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‡ More information on the type of transition state for this elimination will be provided by a stereochemical investigation of the olefins formed from diastereoisomeric diol acetates.

§ Some additional polar material (15%) remains unidentified.

[1] Part of a series on "Heterogeneous Reactions with Zinc."

[2] A. Serini, W. Logemann, and W. Hildebrand, *Ber.*, 1939, **72**, 391; for complete references on this reaction see N. L. Wendler in "Molecular Rearrangements," Part II, ed. P. de Mayo, Interscience, New York and London, 1964, p. 1039.

[3] E. Ghera, M. Gibson, and F. Sondheimer, *J. Amer. Chem. Soc.*, 1962, **84**, 2953; E. Ghera and F. Sondheimer, *Tetrahedron Letters*, 1964, 3887; E. Ghera, *J. Org. Chem.*, 1968, **33**, 1042.

[4] *Cf.* M. B. Rubin and E. C. Blossey, *Steroids*, 1963, **1**, 453.

[5] *Cf.* M. B. Green and W. J. Hickinbottom, *J. Chem. Soc.*, 1957, 3262.

[6] J. Levy, *Bull. Soc. chim. France*, 1921, **29**, 320.

[7] (a) S. S. Wagle, Dissertation, Harvard University, 1949; (b) T. Goto and L. F. Fieser, *J. Amer. Chem. Soc.*, 1961, **83**, 251.