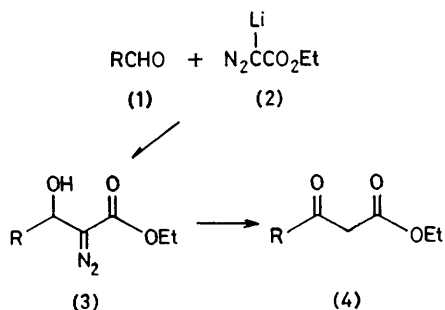


β-Keto esters from the Rhodium(II) Acetate Catalysed Conversion of α-Diazo-β-hydroxy esters

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Summary A new and efficient procedure for the transformation of α-diazo-β-hydroxy esters into the corresponding β-keto esters, which involves the use of Rh₂(OAc)₄, is described.

WE report that rhodium(II) acetate¹ catalyses the conversion of α-diazo-β-hydroxy esters into the corresponding β-keto esters. The operational simplicity of this procedure, which gives the product in high yield, enhances the synthetic importance of the sequence represented in the Scheme.



SCHEME

The first step involving the aldol-type condensation of ethyl lithiodiazoacetate (2) with aldehydes (1) to give α-diazo-β-hydroxy esters (3) has been improved.² Heating to reflux in the presence of hydrogen chloride or vacuum thermolysis³ are the only available methods for the conversion of α-diazo-β-hydroxy esters (3) into the corresponding β-keto esters (4). Both methods, however, are

unsatisfactory when sensitive functionality is present in the R group. The formation of rearrangement products³ is avoided in the present method which is also superior in that it gives better yields and purification and scale-up requirements are simpler. Addition of a catalytic amount of rhodium(II) acetate to a stirring solution of (3) at room temperature results in rapid and quantitative evolution of nitrogen with the formation of β-keto esters (4). Removal of the catalyst by filtration followed by evaporation of the solvent gives the crude product which is ready for synthetic applications without any further purification. A variety of β-keto esters have been prepared by this method and the results are summarised in the Table.‡

TABLE. Rh₂(OAc)₄ catalysed conversion of α-diazo-β-hydroxy esters (3)^a into β-keto esters (4).^b

Entry	R	Reaction time/min	Yield of (4) ^c /%
1	Pr ⁿ	1	100 ^d
2	Pr ⁱ	1	100 ^e
3	Ph ₂ CH	1	100 ^f
4	CH ₂ =CH	60	97 ^g
5	PhCH=CH	60	(90) ^h
6	Ph	1	92 ⁱ

^a Prepared from the corresponding aldehydes (1) according to the procedure in refs 2d, g. ^b The reaction mixture consisted of 0.5 mmol of (3), 4 ml of solvent and 2–5 mg of the catalyst. All the reactions were carried out in dimethoxyethane (DME) unless otherwise indicated. Slightly inferior yields (3–5%) were observed when EtOH was used as solvent. ^c All yields by g.l.c. except for entry 5. Yields are based on the initial amount of (3). ^d W. Wierenga and H. I. Skulnick, *J. Org. Chem.*, 1979, **44**, 310. ^e See ref. 2b. ^f R. Huisgen, L. A. Feiler, and P. Otto, *Chem. Ber.*, 1969, **102**, 3405. ^g See ref. 3. ^h Isolated yield. J. English and L. J. Lapidus, *J. Amer. Chem. Soc.*, 1943, **65**, 2466. ⁱ Reaction performed in pentane. With DME the yield was 86%. See ref. 2b.

‡ Particularly noteworthy are the results of the catalysed decomposition of α-diazo-β-hydroxy-γ,δ-unsaturated esters (e.g., Table, entries 3 and 4). These highly reactive compounds give very complex reaction mixtures when treated with acids; when pyrolysed at 285 °C and 0.25 Torr pressure they give the corresponding β-keto esters in low yields (ref. 3).

The products which would have been expected to arise as a result of the initial formation of a metal carbenoid complex, such as dimers and insertion products, were not detected in the reaction mixtures. These results therefore confirm that the presence of an hydroxy group α to the

diazo group alters the general reactivity observed for alkyl diazoketones.

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¹ P. Legzdins, R. W. Mitchell, G. L. Rempel, J. D. Ruddick, and G. Wilkinson, *J. Chem. Soc. (A)*, 1970, 3322; $\text{Rh}_2(\text{OAc})_4$ has been previously employed as catalyst (a) for the insertion of carbenes into activated H-bonds: R. Paulissen, H. Reimlinger, E. Hayez, A. J. Hubert, and P. Teyssie, *Tetrahedron Letters*, 1973, 2233; (b) for the cyclopropanation of alkenes with alkyl diazoacetates: A. J. Hubert, A. F. Noels, A. J. Anciaux, and P. Teyssie, *Synthesis*, 1976, 600; (c) for the formation of sulphonium ylides with diazomalonic esters: R. J. Gillespie, J. Murray-Rust, P. Murray-Rust, and A. E. A. Porter, *J.C.S. Chem. Comm.*, 1979, 366, and references cited therein.

² The best yields of (**3**) are obtained when ethyl lithiodiazoacetate (LiEDA) is generated *in situ* by adding to a mixture of the aldehyde and EDA in THF at -78°C a solution of lithium di-isopropylamide in THF. For previous work see: (a) U. Schollkopf and H. Frasnelli, *Angew. Chem.*, 1970, **82**, 291; (b) E. Wenkert and C. A. McPherson, *J. Amer. Chem. Soc.*, 1972, **94**, 8084; (c) N. F. Woolsey and M. H. Khalil, *J. Org. Chem.*, 1972, **37**, 2405; (d) U. Schollkopf, B. Bahhidai, H. Frasnelli, R. Meyer, and H. Beckaus, *Annalen*, 1974, 1767; (e) N. F. Woolsey and M. H. Khalil, *J. Org. Chem.*, 1975, **40**, 3521; (f) D. A. Evans, L. K. Truesdale, and K. G. Grimm, *ibid.*, 1976, **41**, 3335; (g) R. Pellicciari, E. Castagnino, and S. Corsano, *J. Chem. Research (S)*, 1979, 76.

³ E. Wenkert, P. Ceccherelli, and R. A. Fugiel, *J. Org. Chem.*, 1978, **43**, 3983.