Pergamon

Tetrahedron Letters, Vol. 37, No. 11, pp. 1899-1900, 1996
Copyright © 1996 Published by Elsevier Science Ltd
Printed in Great Britain. All rights reserved
0040-4039/96 $15.00 + 0.00

S0040-4039(96)00147-5

A New Approach to 4-Hydroxy-cyclopent-2-en-1-ones by Horner-Wadsworth-Emmons Olefination of 1,2-Diketones

Francesco Bonadies[a] *, Arrigo Scettri[b] *, Concetta Di Campli[a]

[a] Centro di Studio CNR per la Chimica delle Sostanze Organiche Naturali, Dipartimento di Chimica, Università "La Sapienza",
P.le A. Moro 5 00185 Roma, ITALY.

[b] Dipartimento di Chimica, Università degli Studi di Salerno, 84081 Baronissi (Salerno), Italy

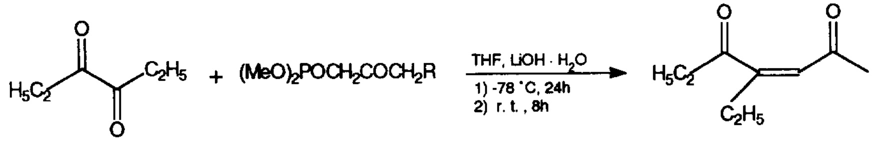
Abstract: 4-hydroxycyclopent-2-en-1-ones 4 are easily available by a one-pot procedure involving a stereoselective Z-olefination of 1,2-diketones with stabilized lithium phosphonates and subsequent intramolecular aldol condensation of the resulyting Z-enedicarbonyl compounds.

Cyclopentenone nucleus represents the main structural feature of some classes of natural and synthetic products characterized by important biological activities, such as rethrolones, prostaglandins. One of the typical procedures for the synthesis of 4-hydroxycyclopentenones involves the previous preparation of Z-enedicarbonyl compounds[1,2] achievable, for example, through controlled hydrolysis of 2,5-dialkoxy-2,5-dihydrofurans[3] or chemical[4], and photochemical[5] oxidation of furan derivatives.

Previous investigations on the reactivity of stabilized lithium phosphonates towards ketones or aldehydes bearing additional functions[6,7] suggested the possibility of an easy access to enedicarbonyl compounds by treatment of 1,2-diketones with Horner-Wadsworth-Emmons (HWE) reagents of type **2**.

In fact we have found that when 3,4-hexanedione **1a** was submitted at -78°C in anhydrous THF solution, to the action of lithium dimethyl 2-oxopropyl phosphonate **2a** (R=H), generated in situ through the employment of lithium hydroxide as base, the formation of the expected enedicarbonyl compound **3** occurred in good yield (Scheme 1) and very satisfactory degree of Z-stereoselectivity (Z/E > 95/5).

SCHEME 1



1 **2** a: R= H Yield 62% **Z-3**

More interestingly (Scheme 2), when the olefination was performed in methanolic solution under the conditions given in table, the usual formation of Z-**3** was followed by a base-catalyzed intramolecular aldol condensation leading to cyclopentenone derivatives **4**.

Scheme 2

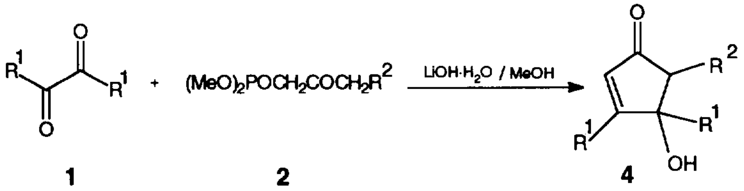


Table- HWE Olefination of 1,2-Diketones in MeOH Solution [a]

Entry	R^1	R^2	Temp. (°C)	React. time (h)	Yields (%) [b]
a	Et	H	-20	14	52
b	Ph	H	r. t.	12	64
c	2-furyl	H	r. t.	4	80
d	2-furyl	n-Bu	r. t.	3	75 [c]
e	Ph	n-Bu	r. t.	20	60 [c]

a) All the reactions have been performed using 1/1/1.2 1,2-diketones/phosphonate/LiOH molar ratio. b) All the yields refer to isolated, chromatographically pure compounds, which have been characterized by IR, ^{1}H-NMR, ^{13}C-NMR and mass spectral data. c) Obtained as 1/1 diastereoisomeric mixtures which were not separated.

It has to be noted that, on the ground of previous reports[3], in entry **a** we would have expected the formation of the regioisomeric product of intramolecular aldol condensation, deriving from the thermodynamically favoured enolate; therefore, the isolation of the corresponding hydroxycyclopentenone of type **4** points out a very unusual process of cyclization, involving the kinetic enolate.

In conclusion, this methodology has proven to be of synthetic value since it affords olefination products in very high stereoselectivity (in THF solution) and furthermore, allows an easy and direct approach to cyclopentenone derivatives.

Experimental: in a typical experimental procedure a mixture of 1,2-diketone (1 mmole), phosphonate **2** (1 mmole) and $LiOH·H_2O$ (1.2 mmole) in 10 ml. of methanol is stirred at room temperature (-20°C for **1a**) and the reaction is monitored on TLC. The crude product, after evaporation of methanol, is purified by column chromatography (silica gel, 1:1 hexane : ether as eluent).

REFERENCES:

1) Floyd M.B., *J. Org. Chem.* **1978**, *43*, 1641-1643
2) Shono T.; Hamaguchi H.; Aoki K., *Chem. Lett.*, **1977**, 1053-1056
3) Shono T.; Matsumura Y.; Hamaguchi H.; Nakamura K., *Chem. Lett.*, **1976**, 1249-52
4) Williams P.D.; Le Goff E. J., *Tetrahaedron Lett.*, **1985**, *26*, 1367-70 and references therein
5) Feringa B.L., *Recl. Trav. Chim. Pays-Bas,* **1987**, *106*, 469-488
6) Bonadies F.; CardilliA.; Lattanzi A.; Orelli L.; ScettriA., *Tetrahedron Lett.*, **1994**, *35*, 3383-86;
7) Bonadies F.; Cardilli A.; Lattanzi A.; Pesci S.; Scettri A., *Tetrahedron Lett.*, **1995**, *36*, 2839-2840.

(*Received in UK* 19 *December* 1995; *revised* 24 *January* 1996; *accepted* 26 *January* 1996)