Tetrahedron Letters, Vol.31, No.21, pp 3063-3066, 1990
Printed in Great Britain

0040-4039/90 $3.00 + .00
Pergamon Press plc

"AN EFFICIENT AND MILD ENTRY TO 1,4-DICARBONYL COMPOUNDS VIA PHOTOCHEMICAL ADDITION OF ACYL RADICAL TO ELECTRON-DEFICIENT OLEFINS"

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SUMMARY: Photochemical addition of acetaldehyde to electron-deficient olefins in the presence of molecular oxygen provides an efficient and mild method for the synthesis of 1,4-functionalized compounds. Some considerations about the mechanism and the substituent effects are outlined.

It is well known that aldehydes can be added to double bonds in the presence of radical initiators. On these reactions, the polar effects are important, so yields are increased when electron-withdrawing substituents are present on the olefin [1-3]. In the case of α,ß-unsaturated carbonyl substrates, the 1,4-dicarbonyl species obtained from these additions are useful synthetic intermediates [4].

However, the high temperatures requires for thermal initiation and the presence of the initiator in the reaction mixture constitute serious disadvantages which limit the synthetic potentiality of these reactions. To overcome these difficulties other methods involving sensitizers as benzophenone [5] or low temperature initiators [6] have been reported, but the overall yields were not very high.

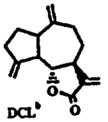
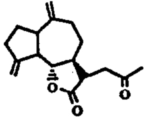
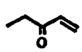
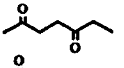
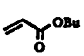
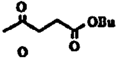
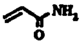
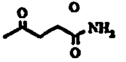
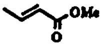
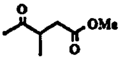
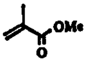
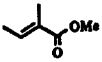
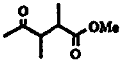
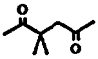
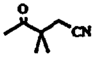
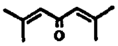
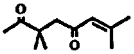
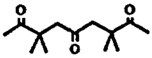
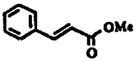
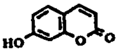
In the course of our studies directed towards the synthesis of 11,13-oxetane sesquiterpene lactones, we reported a photochemical conjugate addition-acylation of an α,ß-unsaturated γ-lactone by acetaldehyde [7].

The high yields obtained compared with those of the previously reported procedures [8,9] prompted us to undertake the present research to further evaluate the scope of the reaction. A summary of the results is given in Table I. The typical procedure was: 5 mmol of the substrate in freshly distilled acetaldehyde (100 ml) is placed in a Hanovia reactor and irradiated with a medium pressure mercury lamp using a Ni(II), Co(II) filter [10]. Vigorous stirring was maintained and the reaction was monitored by GC. Small amounts of cyclohexane were added to the reaction mixture to remove the acetic acid produced [11]. The solution was evaporated at low pressure and the residue chromatographed on silica gel to give the corresponding 1,4-dicarbonyl compound.

The use of this Ni(II) and Co(II) filter provides very clean reactions without formation of photoreduction products and generally no secondary products are detected.

The best yields were obtained with substrates bearing an unsubstituted conjugated double bond (entries 1-11). It is worth noting that the photolysis of a substrate with a methyl substituent at the α position to the electron-withdrawing group did not give the corresponding 1,4-dicarbonyl compound (entry 6) or gave a very poor yield (entry 7a).

Table I

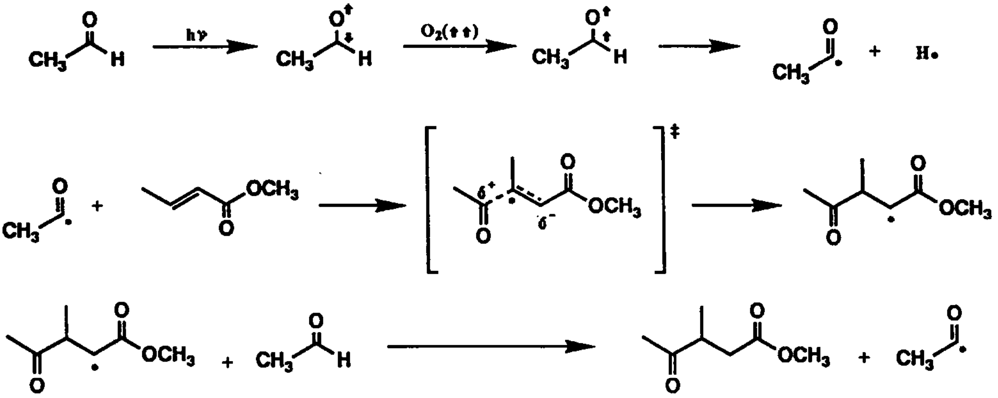
Substrate[a]	Entry	Medium	t(h)	T(°C)	Yield (%)	Product*
 DCL[b]	1a	air	1	25	70 (I) 8 (II)	 I
	1b	N_2	1	25	<5 (I)	C_{13}-Methyl alcohol II
	2	air	2.5	25	95 (III)	 III
	3	air	2.5	25	99 (IV)	 IV
	4	air	2.5	25	93 (V)	 V
	5	air	3	25	81 (VI)	 VI
	6a	air	3	25	—	—
	6b	N_2	3	25	—	—
	7a	air	3	25	16 (VII)	 VII
	7b	O_2	8	25	52 (VII)	
	7c	O_2	1	50	<5 (VII)	
	7d	O_2	2	0	<5 (VII)	
	8a	air	3	25	10 (VIII)	 VIII
	8b	O_2	8	25	49 (VIII)	
	9a	air	3	25	6 (IX)	 IX
	9b	O_2	8	25	27 (IX)	
	10a	air	3	25	30 (X) 12 (XI)	 X
	10b	O_2	8	25	27 (X) 39 (XI)	 XI
	10c	O_2	1	60	<1 (X)	
	11a	air	2.5	25	—	—
	11b	N_2	2.5	25	—	—
	12	air	2.5	25	—	—

[a] Reactions were carried out dissolving 5 mmol of substrate in 100 mL of acetaldehyde (freshly distilled) under vigorous stirring, using a medium pressure mercury lamp (125 W).

[b] 1 mmol of substrate was used.

This behaviour can be explained assuming that the transition state has the polar character shown in Scheme 1. Thus, an alkyl substitution at the α position may cause an increase of the activation energy of such transition state.

Scheme 1



The introduction of two methyl substituents at the carbon atom of the more remote double bond from the electron-withdrawing group resulted in a decrease of the yields (entries 7a-10a). This fact suggest that hindrance factors may be also involved in the transition state.

A key point for the success of this photoaddition is the presence of molecular oxygen in our reaction conditions. We believe that the singlet oxygen acts as sensitizer facilitating the intersystem crossing (Scheme 1). In accordance with this hypothesis, the photoaddition practically does not occur when the α,ß-unsaturated substrates were irradiated under N_2 atmosphere (entries 1b,6b,11b). On the other hand, the decreasing yields obtained when temperatures higher than 25 °C are used might be related to a lower solubility of the oxygen in the aldehyde (entries 7c, 10c).

Substrates bearing a double bond conjugated to a benzene ring failed to give detectable amount of the photoadduct (entries 11,12), perhaps a consequence of the implicit lost of conjugation in the reaction product.

Acknowledgements

This research was supported by Direccion General de Investigacion Cientifica y Tecnica, Spain (DGICYT, Project PB-87 n 0965). J.M.G.M. thanks the Ministerio de Educacion y Ciencia, Spain, for a predoctoral fellowship.

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11.- B.P. of Acetic acid, Cyclohexane azeotrope: 81.8 °C.

* All compounds had satisfactory spectroscopic data. The most significative data are the following:Compound I, ^{1}H NMR (200 MHz,DCCl$_3$): 5.14 (d,J=1.5Hz,H-15); 4.98 (d,J=1.5Hz,H-15'); 4.80 (brs,H-14); 4.71 (brs,H-14'); 3.90 (dd,J=9.5Hz,H-6); 2.88 (dd,J=6.0Hz,H-13,H-13'); 2.79 (m,H-5); 2.67 (m,H-1); 2.19 (s,H-17). IR (HCCl$_3$,cm^{-1}): 1725 (CO-Me). Compound II, ^{1}H NMR (200 MHz,DCCl$_3$): 5.12 (d,J=1.9Hz,H-15); 4.98 (d,J=1.9Hz,H-15'); 4.82 (d,J=1.7Hz,H-14); 4.72 (d,J=1.7Hz,H-14'); 4.14 (m,H-16); 3.93 and 3.90 (dd,J=10.0Hz,H-6); 2.80 (m,H-1); 2.77 (brd,J=10.0Hz,H-5); 2.02 (m,H-11); 1.17 (d,J=4.0,H-17). IR(HCCl$_3$,cm^{-1}): 3670 (OH). Compound IV,^{1}H NMR (80 MHz,DCCl$_3$): 4.13 (t,J=6.0Hz,H-1'); 2.78 (t,J=6.0Hz,H-2); 2.60 (t,J=6.0Hz,H-3); 2.17 (s,H-5); 0.98 (t,J=6.0Hz,H-4'). IR (neat,KBr,cm^{-1}): 1740 sh (COOMe); 1714 (CO-Me). Compound VII, ^{1}H NMR (200 MHz,DCCl$_3$): 3.68 and 3.66 (s,OMe); 2.21 and 2.19 (s,H-5); 2.15 and 2.14 (d,J=7.0Hz,H-7); 1.11 and 1.10 (d,J=7.0Hz,H-6). Compound IX, ^{1}H NMR (80 MHz,DCCl$_3$): 2.48 (s,H-2); 2.15 (s,H-5); 1.32 (s,H-6). IR (neat,KBr,cm^{-1}): 2250 (CN); 1701 (CO-Me). Compound XI, ^{1}H NMR (80 MHz,DCCl$_3$): 2.78 (s,H-4,H-6); 2.22 (s, H-1,H-9); 1.23 (s, H-10,H-11,H-12,H-13). IR (neat,KBr,cm^{-1}): 1697 (CO-Me).

(Received in UK 3 April 1990)