Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

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Version of record first published: 23 Sep 2006.

To cite this article: T. Ben Ayed & H. Amri (1995): A Convenient Synthesis of α-Functional Alkyl Vinyl Ketones, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 25:23, 3813-3819

To link to this article: http://dx.doi.org/10.1080/00397919508011455

SYNTHETIC COMMUNICATIONS, 25(23), 3813-3819 (1995)

A CONVENIENT SYNTHESIS OF α-FUNCTIONAL ALKYL VINYL KETONES

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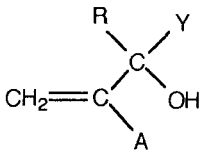
Abstract: *Reaction of 2-functional alkyl-1,3-diketones with 30% aqueous formaldehyde using aqueous 6-10M potassium carbonate solution as base, afforded α-functional alkyl vinyl ketones in good yields.*

Introduction of functional group to the sp^2-hybridized α-position of acrylic compounds (esters, ketones and nitriles) is an important operation to reach to the corresponding α-functional substrates **1** which are considered as potential intermediates in organic synthesis (scheme 1). Several methods have been used for their preparation consisting mainly in the alkylation of α-vinyl acrylic esters[1], α-alkylation of α,β-unsaturated enones through Michael addition[2], Wittig-Horner reaction of various phosphonates and aqueous formaldehyde under heterogeneous conditions[3], coupling reaction of aldehydes with acrylic compounds in the presence of DABCO as catalyst[4-11], aldol condensation[12] and alkoxyalkylation in α-position of methyl vinyl ketones[13], and α-hydroxyalkylation via a cross coupling acrylonitrile and aldehydes in the presence of trialkyl phosphine or $(nBu)_3P$-Et_3Al as catalysts[14,15].

*To whom correspondence should be addressed.



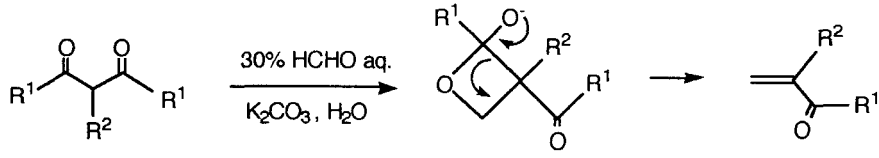
1

Y = H , Me
R = alkyle, COOEt, COMe
A = COMe , COEt, COOEt, CN

Scheme 1

In this context, condensation of various active methylene compounds with formaldehyde has been described as key methods available to prepare simple α-alkylated vinyl esters, ketones, nitriles[16] and sulfones[17]. However these methods suffer from two major drawbacks : the requirement and use of expensive chemicals and particular experimental conditions (gas HCHO, LDA, solvents, heating...).

In extension of our work on the synthesis of vinyl substrates **1**, we wish to communicate herein a simple and straightforward synthesis of α-functional vinyl ketones **3** via a deacylative condensation of monoalkylated 1,3-diketones **2** with 30% aqueous formaldehyde under heterogeneous liquid-solid conditions using highly concentrated (6-10 molar) aqueous solution of potassium carbonate at room temperature in the absence of an organic solvent (scheme 2).



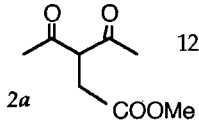
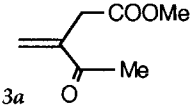
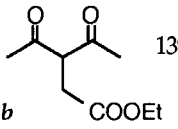
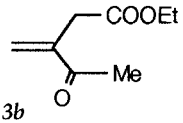
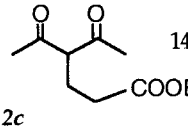
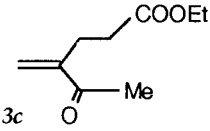
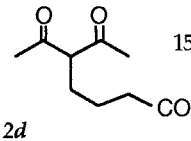
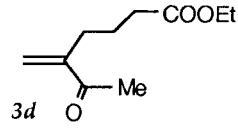
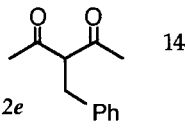
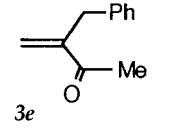
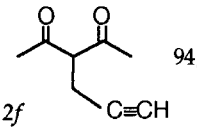
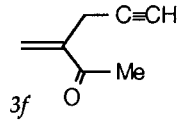
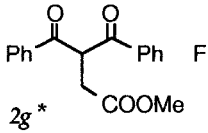
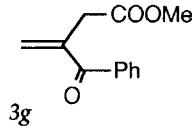
2a-h **3a-h**

Scheme 2

The 1,3-diketones employed in this work included commercially available pentane-2,4-dione and 1,3-diphenylpropanedione while the reaction of their alkali metal salts with simple or functional alkyl halide, according to the known procedure[18], leads to the corresponding diketones **2**. Yields of the new α-functionalized α,β-enones **3a-h** ranged from 46-81% (Table).

In conclusion, the practical and convenient route to the uncommonly vinyl ketones **3a-h** which compares favourably in terms of brevity, use of simple

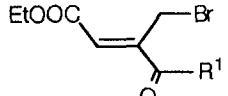
Table: α-Functional vinyl ketones **3** from 2-alkylated-1,3-aliphatic diketones **2**.

2-Alkylated 1,3-diketone 2*	b.p °C/mmHg	Yield(%)	α-Functional Vinyl ketone 3	b.p °C/mmHg	Yield(%)
 *2a*	128/14	71,5	 *3a*	98/22	78
 *2b*	139/20	69	 *3b*	108/20	66
 *2c*	149/16	52	 *3c*	109/12	81
 *2d*	153/10	79	 *3d*	141/35	73
 *2e*	148/11	59	 *3e*	112/10	58
 *2f*	94/11	41	 *3f*	124/37	46
 *2g* *	F:132	71	 *3g*	115/1	75

(*) *Products* ***2a-h*** *showed spectral data (IR, NMR) in accordance to theirs expected structure.*

(**) *Reaction of solid 2-alkylated-1,3-diketone* ***2g*** *is carried in the presence of ethyl acetate as solvent.*

reagents and overall yield with the majority of the previously reported synthesis of analogous samples. Some specific enones can be used in a one pot type synthesis of (Z)-β-bromomethyl-γ-ketoesters **4**. Work in this direction is in progress in our laboratory.



4 R^1 : Me, Ph

Experimental section

Reaction progress and purity of products were monitored on an Intersmat 20M gas chromatograph using a 3mx3mm column packed with 10% SE 30 and by TLC on silica gel plates (Fluka Kieselgel $60F_{254}$). IR spectra were taken on Perkin-Elmer 257 spectrophotometer. ^1H and ^{13}C Nuclear Magnetic Resonance were recorded on a Jeol C-HL 60MHz, FX 90MHz and Bruker 300MHz instruments in $CDCl_3$ solution with TMS as the internal standard.

Preparation of α-functional vinyl ketones 3a-f

General procedure

To a magnetically stirred mixture of 2-alkylated-1,3-diketone **2a** (3.44g, 20mmol) and 30% aqueous formaldehyde (4mL) is added at room temperature gelatinous solution of potassium carbonate (5.52g, 40mmol) diluted in water (4mL). The heterogeneous reaction mixture is stirred overnight at room temperature then treated with water(40mL). The solution is then extracted with ether (5x30mL). The combined organic layers are dried over anhydrous magnesium sulfate, filtered and concentrated. The residue obtained is distilled under reduced pressure.

Methyl 3-methylene-4-oxopentanoate 3a

IR($CHCl_3$,vcm^{-1}): 1730(C=O) ; 1680(C=O) ; 1635(C=C).

^1H NMR($CDCl_3$,TMS): 2.33(s,3H,CH_3CO) ; 3.26(s,2H,CH_2-CO) ; 3.67(s,3H,$COOCH_3$) ;

5.93 and 6.16(2s,2H.CH_2=). ^{13}C NMR($CDCl_3$,TMS): 25.33($\underline{C}H_3$-CO) ; 36.52($\underline{C}H_2$-CO) ; 51.99($\underline{C}H_3$-O) ; 128.45(CH_2=) ; 142.34(CH_2=$\underline{C}$) ; 171.55(-COO-) ; 198.66(CH_3-$\underline{C}$O).

Ethyl 3-methylene-4-oxopentanoate 3b

IR($CHCl_3$,vcm^{-1}): 1725(C=O) ; 1680(C=O) ; 1635(C=C).

^1H NMR($CDCl_3$,TMS): 1.26(t,3H, J=6,5Hz, CH_3) ; 2.36(s,3H,CH_3CO) ; 3.25(s,2H,CH_2-CO) ; 4.08(q,2H, J=6,5Hz, CH_2-O) ; 5.98 and 6.15(2s,2H,CH_2=). ^{13}C NMR($CDCl_3$,TMS): 15.10($\underline{C}H_3$-CH_2) ; 25.36($\underline{C}H_3$-CO) ; 36.81($\underline{C}H_2$-CO) ; 60.83(-CH_2O-) ; 128.11(CH_2=); 142.54(CH_2=$\underline{C}$) ; 171.05(-COO-) ; 198.58(CH_3-$\underline{C}$O).

Ethyl 4-methylene-5-oxohexanoate 3c

IR($CHCl_3$,vcm^{-1}):1725(C=O) ; 1675(C=O) ; 1635(C=C).

^1H NMR($CDCl_3$,TMS): 1.27(t,3H, J=7Hz, CH_3) ; 2.37(s,3H,CH_3CO) ; 2.53(m,4H,CH_2-CH_2-CO) ; 4.01(q,2H, J=7Hz, CH_2-O) ; 5.83 and 6.01(2s,2H,CH_2=). ^{13}C NMR($CDCl_3$,TMS): 14.03($\underline{C}H_3$-CH_2) ; 25.60(-$\underline{C}H_2$-CH_2-CO) ; 26.05($\underline{C}H_3$-CO) ; 32.92($\underline{C}H_2$-CO) ; 60.15(-CH_2O-) ; 125.84(CH_2=) ; 147.24(CH_2=$\underline{C}$) ; 172.64(-COO-) ; 199.05(CH_3-$\underline{C}$O).

Ethyl 5-methylene-6-oxoheptanoate 3d

IR($CHCl_3$,vcm^{-1}):1725(C=O) ; 1675(C=O) ; 1630(C=C).

^1H NMR($CDCl_3$,TMS): 1.21(t,3H,J=6.5Hz,$C\underline{H}_3CH_2$) ; 1.51-2.43(m,6H,3CH_2) ; 4.08(q,2H,J=6.5Hz,CH_2O) ; 5.76 and 6.00(2s,2H,CH_2=). ^{13}C NMR($CDCl_3$,TMS): : 13.83($\underline{C}H_3$-CH_2) ; 23.26(-$\underline{C}H_2$-CH_2-CO) ; 25.42($\underline{C}H_3$-CO) ; 29.53($\underline{C}H_2$-CO) ; 33.34(-$\underline{C}H_2$-CH_2-CH_2-CO) ; 59.88(-CH_2O-) ; 125.31(CH_2=) ; 147.82(CH_2=$\underline{C}$) ; 173.08(-COO-) ; 199.17(CH_3-$\underline{C}$O).

3-Methylene-4-phenyl butan-2-one 3e

IR($CHCl_3$,vcm^{-1}):1710(C=O) ; 1630(C=O) ; 1610(C=C).

^1H NMR($CDCl_3$,TMS): 2.30(s,3H,CH_3-CO) ; 3.56(s,2H,$C\underline{H}_2$-Ph) ; 5.58 and 6.01(2s,2H,CH_2=) ; 7.16(s,5H,Ph). ^{13}C NMR($CDCl_3$,TMS) : 25.91 ($\underline{C}H_3$-CO) ; 36.70 (-$\underline{C}H_2$-Ph); 126.47(CH_2=) ; (Ph) : 126.21; 126.47 ; 128.14 ; 128.35 ; 129.79 ; 130.52 ; 148.62(CH_2=$\underline{C}$) ; 199.12(CH_3-$\underline{C}$O).

3-Methylene hex-5-yn-2-one 3f

IR($CHCl_3$,vcm^{-1}): 3310(C≡C) ; 1710(C=O) ; 1630(C=C).

^{1}H NMR($CDCl_3$,TMS): 2.26(d,H,J=2,6Hz,H-C≡C) ; 2.38(s,3H,CH_3-CO) ; 3.15(d,2H,J=2,6Hz,CH_2-C≡C) ; 6.25(m,2H,CH_2=). ^{13}C NMR($CDCl_3$,TMS): 21.05(-$\underline{C}H_2$-C≡C) ; 25.73($\underline{C}H_3$-CO) ; 72.35(-$\underline{C}$≡CH) ; 89.79(-C≡$\underline{C}$H) ; 126.95(CH_2=) ; 143.33(CH_2=$\underline{C}$); 198.47(CH_3-$\underline{C}$O).

Methyl 3-methylene-4-oxo-4-phenylbutanoate 3g

IR($CHCl_3$,νcm^{-1}):1735(C=O) ; 1690(C=O) ; 1630(C=C)1600(C=C).

^{1}H NMR($CDCl_3$,TMS): 3.50(s,2H,CH_2-CO) ; 3.63(s,3H,$COOCH_3$) ; 5.72 and 5.93(2s,2H,CH_2=). ^{13}C NMR($CDCl_3$,TMS): 37.85($\underline{C}H_2$-CO) ; 51.93($\underline{C}H_3$-O) 128.45(CH_2=) ; (Ph) : 128.33 ; 128.76 ; 129.66 ; 129.77 ; 132.33;137.33 ; 141.30(CH_2=$\underline{C}$) ; 171.33(-COO-) ; 196.89(-$\underline{C}$O-Ph).

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(Received in The Netherlands 19 May 1995)