A Novel α-Acrylate Anion Equivalent: A Useful Synthon for α-Substituted Acrylic Esters

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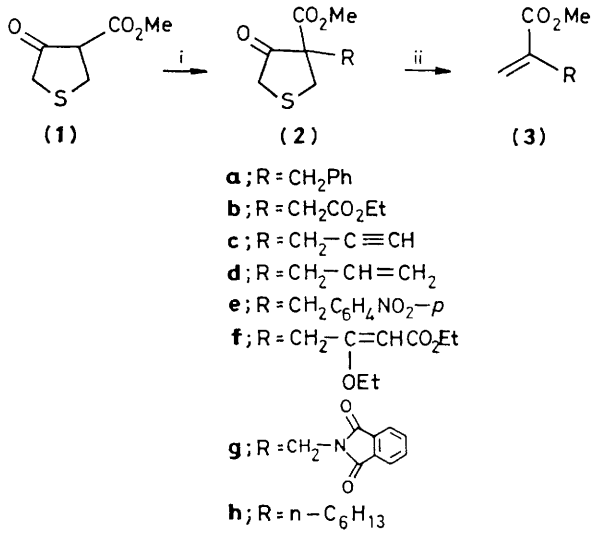
An efficient preparation of α-substituted acrylic esters is described, based on the Dieckmann–Michael retrograde reactions of the C-alkylation products of 4-methoxycarbonylthiolan-3-one (**1**).

Esters of α-substituted acrylic acids are important sub-units in a variety of natural products. Moreover, because of their acceptor and dienophile properties, they are valuable intermediates in the construction of complex organic molecules. This is reflected in the number of methods which have been developed for their preparation.[1,2]

In this communication we describe a new method for the synthesis of α-substituted acrylic esters involving a tandem of reverse reactions, namely, a retrograde Dieckmann–Michael strategy.



Scheme 1. i, RX, K_2CO_3, Me_2CO; ii, 5% NaOH.

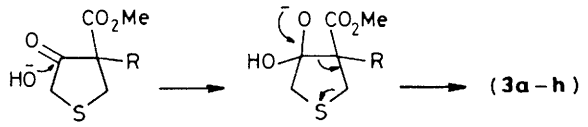
The starting material was 4-methoxycarbonylthiolan-3-one (**1**), a member of a class of compounds widely used in the synthesis of heteropolycyclic compounds. Compound (**1**) was obtained easily[3] in good yield by Dieckmann cyclization, under well defined conditions, of the unsymmetrical diester which was derived from Michael addition of methyl thioglycolate to methyl acrylate in the presence of catalytic quantities of piperidine.[4]

Alkylation of (**1**) with a variety of alkyl halides was readily accomplished in the presence of anhydrous potassium carbonate in refluxing acetone,[5] producing excellent yields of the

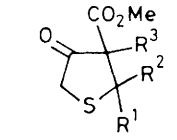
Table 1. Results of the alkylation of compound (**1**) with a variety of alkyl halides to give the C-alkylated products (**2a—h**) and the acrylate esters (**3a—h**).

	Yield of (**2**)/%[a]	Yield of (**3**)/%[b]
a	80	81
b	85	78
c	79	76
d	81	78
e	86	90
f	79	75
g	63	39[c]
h	50	80

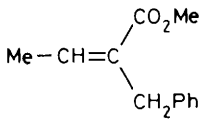
[a] Yields are given for the isolated products after flash-chromatography to remove any O-alkylated products. [b] Yields refer to the isolated product after bulb to bulb distillation, except for (**3g**) (m.p. 99—100 °C) which is after crystallization. [c] The low yield of (**3g**), the methyl ester of the phthaloyl-derivative of the toxic amino-acid α-methylene-β-alanine, isolated from a Red Sea sponge *Fasciospongia cavernosa* (M. B. Yunker and P. J. Scheuer, *Tetrahedron Lett.*, 1978, 4651), may be accounted for by the concomitant base promoted opening of the phthaloyl moiety.



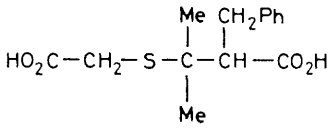
Scheme 2



(**4**) R^1=H; R^2=Me; R^3=H
(**5**) R^1=R^2=Me; R^3=H
(**6**) R^1=H; R^2=Me; R^3=CH_2Ph
(**7**) R^1=R^2=Me; R^3=CH_2Ph



(**8**)



(**9**)

C-alkylated products (**2a**—**h**) (Table 1).†‡ Treatment of compounds (**2a**—**h**) with 5% aqueous NaOH in biphasic diethyl ether solution at room temperature smoothly generated the acrylate esters (**3a**—**h**) (Scheme 1, Table 1) through a base promoted fragmentation, probably occurring as shown in Scheme 2.

The reaction times (30—60 min) were only slightly reduced by addition of a phase transfer catalyst ($PhCH_2$)$Et_3N^+Cl^-$ (TEBA) and hydrolysis of the ester function was negligible. Use of aqueous ammonia as the base gave rise to products derived exclusively from a reverse Dieckmann reaction.

The overall process can be considered formally as an α-alkylation of methyl acrylate under mild conditions, and therefore (**1**) can be considered as a useful synthon for α-substituted acrylic esters. The failure of the anion of (**1**) to react with less reactive alkylating agents such as epoxides precluded a direct approach to α-methylene lactones. However, these have already been obtained by roundabout routes starting from suitably substituted acrylates (**3**).[1,6,7]

In order to extend the range of the method, we have also investigated the use of the substituted parent compounds (**4**)[8] and (**5**), as potential anion equivalents of methyl crotonate and methyl β,β-dimethyl acrylate respectively. The model compounds (**6**) and (**7**), obtained in 70 and 40% yields, respectively, by the alkylation of (**4**) and (**5**) using standard methods were submitted to the action of 5% aqueous NaOH in a biphasic diethyl ether solution as described above. Compound (**6**) underwent base promoted fragmentation in the same manner as the related unsubstituted compounds (**2a**—**h**), although the reaction took 18 h at room temperature to complete and required the presence of a phase transfer catalyst (TEBA). An 80% yield of a mixture (9:1) of the *E*/*Z* isomers of (**8**) resulted. Compound (**4**) is therefore a promising tool for the α-alkylation of methyl crotonate.

Compound (**7**), not unexpectedly, behaved differently, since only the reverse Dieckmann reaction took place producing the dicarboxylic acid (**9**) as the main reaction product. The retrograde Michael reaction probably suffers from the normal restriction of the forward Michael reaction in that *geminal*-substitution of the acceptor β- to the electron-withdrawing groups inhibits the reaction. It may be noted that in this case hydrolysis of the ester function occurred completely, owing to the long exposure to basic conditions in an attempt to induce the reverse Michael reaction in addition to the reverse Dieckmann reaction.

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† Satisfactory analytical and spectral data were obtained for all new compounds.

‡ The reaction course must be carefully monitored by t.l.c. and stopped when (**1**) has disappeared in order to avoid the occurrence of fragmented products.