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TEAF Mediated Hydroxylation of Allylic Bromide : A Facile Synthesis of 4-Methoxycarbonyl-2(5H)-Furanone

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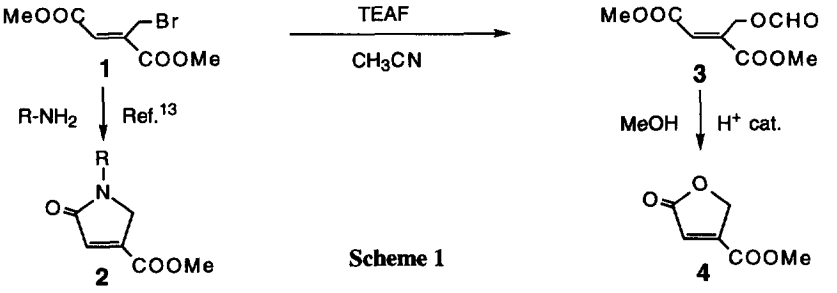
Abstract : *A simple two-step synthesis of 4-methoxycarbonyl-2(5H)-furanone consisting of formylation of dimethyl 2-(bromomethyl) fumarate, followed by acid catalysed transesterification in methanol was carried out. It led to the corresponding substituted furanone in 67% global yield.*

The 2(5H)-furanones are unsaturated γ-lactones which may be regarded as $\Delta^{\alpha,\beta}$-butenolides[1] some of which exert a specific and powerful action on the cardiac muscles of humans and animals and, are therefore, known as cardenolides[2], herbicide intermediates[3] or agrochemical fungicides[4] and they may also have a pharmacological activity[5]. Because of the very limited availability of substituted butenolides[1,6], a simple method for the preparation of 4-methoxycarbonyl-2(5H)-furanone **4** is communicated here. Several procedures are available for the synthesis of this compound[7-10] but all suffer from their complicated methodology and their low overall yields.

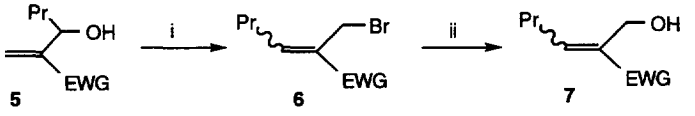
In connection with our previous studies on the carbon-heteroatom ring formation involving a two step reactions via a substitution of functional allylic bromide **1**[11-13] by primary amines, then cyclization leading to the pyrrolin-2-ones derivatives **2**[13], we have now extended this utility to provide a new and short synthesis of furanone **4** in large (10g) scale (Scheme 1).



Scheme 1

Our experiment was carried out as follows : the allylic bromide **1** was displaced with two molar equivalents of a triethylammonium formate (TEAF) reagent with the composition of $2(Et_3N)_2,5(HCO_2H)$[14-16] to

afford the corresponding allylic formate **3**[17] in (80%) yield . Stirring of **3** in methanol in the presence of two drops of concentrated hydrochloric acid undergo transesterification and gave 4-methoxycarbonyl-2(5H)-furanone **4**[18] in 67% global yield from bromide **1** as pure needles. Applied to some other functional allylic bromides like **6**, this methodology contitutes a useful route for the direct conversion of 2-(hydroxyalky) acrylic derivatives **5**[19] to the corresponding 2-(hydroxymethyl)-α,β-unsaturated ones **7** (Scheme 2).



Scheme 2. i) PBr_3, Et_2O, 0°C ; ii) TEAF, MeCN, r.t., then H^+ cat.; MeOH, r.t.

EWG	Yield of **6** (%)	Yield of **7** (%)
COOEt	80 (Z)	82 (E)
CN	79 (E,Z)	86 (E,Z)

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17. ***Preparation of formate 3 :*** (Z)-Dimethyl 2-(bromomethyl) fumarate **1** (9.48g, 40 mmol) was added to a solution of triethyl ammonium formate TEAF (14.7g, 100 mmol) in MeCN (30 mL) and the solution stirred at room temperature for 20 h. The mixture was extracted with diethyl ether (3x30 mL). The combined organic layers were dried over $MgSO_4$ and evaporated at reduced pressure to give the crude product, which was purified by column chromatography (SiO_2, hexane / ethyl acetate 8 : 2) to afford 6.46 g (80%) as a colorless oil **3 :** I.R.[ν cm^{-1}] (film): 1729 ; 1681. ^1H NMR (300 MHz, $CDCl_3$) δ 3.77 and 3.80 (2s, 6H, OCH_3) ; 5.23 (s, 2H, OCH_2) ; 6.84 (s, 1H, =CH) ; 7.96 (s, 1H, CHO). ^{13}C-NMR (75 MHz, $CDCl_3$) δ: 52.2 and 52.8 (OCH_3) ; 56.9 (OCH_2) ; 131.4 (=CH) ; 139.1 (=C-) ; 160.1 and 164.7 (COO) ; 165.3 (CHO).
18. ***Synthesis of furanone 4 :*** To a solution of formate **3** in methanol (30mL) were added two drops of concentrated hydrochloric acid and the mixture was stirred room temperature for 3h. The reaction mixture was diluted with diethyl ether and dried over $MgSO_4$, filtered and concentrated *in vacuo*. Cristallization of the residue from ether afforded **4** (3.81g, 84%) as colorless needles. m.p. 84°C (Litt[8]. 86°C). I.R.[ν cm^{-1}] (film) : 1783 ; 1737 ; 1636. ^1H NMR (300 MHz, $CDCl_3$) δ 3.91 (s, 3H, OCH_3) ; 5.04 (s, 2H, OCH_2-C=) ; 6.73 (s, 1H, =CH). ^{13}C-NMR (75 MHz, $CDCl_3$) δ : 53.3 (OCH_3); 71.0 (OCH_2) ; 126.9 (=CH); 155.0 (=C-) ; 161.5 (COO) ; 72.00 (COOCH$_2$-). MS (70eV) : m/z = 142 ($M^{+\cdot}$, 12) ; 113 (100) ; 111 (49) ; 110 (42) ; 85 (16) ; 82 (18) ; 59 (21) ; 53 (62).
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