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ACID CATALYZED RING CLOSURE REACTIONS OF ELECTROPHILIC ALKENES[1]

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Abstract—Treatment of α-acyl-α,β-unsaturated ketones with sulfuric acid or dimethylformamide-hydrogen chloride or *p*-toluenesulfonic acid gave rise to 3-acyl-2-alkyl-4,5-dihydrofurans. Similar cyclization of α-acyl-α,β-unsaturated esters initially afforded 3-alkoxycarbonyl-2-alkyl-4,5-dihydrofurans which were transformed into 2-acylbutanolides on further reaction with sulfuric acid.

This acid catalyzed cyclization is strongly dependent upon the substitution pattern of the electrophilic alkenes, the acid used and reaction conditions.

During the course of our investigations concerning the reactivity of double activated allyl halides, mainly producing electrophilically disubstituted cyclopropanes upon reaction with a variety of nucleophiles,[4-7] it was observed that on bromination of Knoevenagel condensation products of aldehydes with β-ketoesters minor amounts of cyclic by-products were formed.

Therefore attempts were made to identify these products and to elucidate the mechanism of their formation. The purpose of this report is to present a new synthesis of dihydrofuran derivatives and lactones by treatment of electrophilic alkenes with various acids. The electrophilic alkenes were prepared by a Knoevenagel condensation of aliphatic aldehydes with β-diketones and β-ketoesters, respectively, at room temperature in the presence of catalytic amounts of piperidine.[8,10] Originally only the α,β-unsaturated dicarbonyl compounds **1A** were formed but after distillation or on standing substantial amounts of the isomeric β,γ-unsaturated compounds **1B** were produced in combination with the geometric isomers and the corresponding dienols **1C**.

In analogy with our recent synthesis of γ-butyrolactones[11] by reactions of alkylidenemalonates with sulfuric acid, similar treatment of the unseparable mixture of unsaturated β-diketones (**1A,B,C**; $R^3 = R^4 = Me$) with concentrated sulfuric acid at room temperature afforded 3-acetyl-2-methyl-4,5-dihydrofurans **5** in high yields (Table 1).

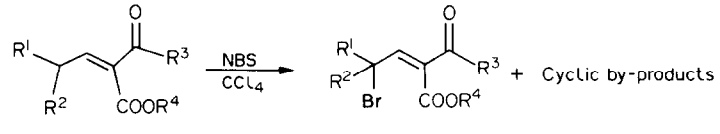
A similar ring closure was briefly mentioned in a study dealing with the UV spectra of substituted β-diketones. The spectra in concentrated sulfuric acid of propenyl- and allylacetylacetone and 1,1 - diacetyl - 2 - methylcyclopropane were identical with those of 3 - acetyl - 2,5 - dimethyl - 4,5 - dihydrofuran (**5a**) which could be obtained from the former products by treatment with sulfuric acid.[12] Other entries to the 3 - acyl - 4,5 - dihydrofuran system consist of the coupling reaction of olefins with 2,4-pentanedione in the presence of thallic (III) acetate,[13] lead (IV) acetate,[14] manganese (III) acetate[15-17] and silver (II) and lead (IV) oxides.[18] The yields were only satisfactory in the case of aryl substituted alkenes giving rise to 4- and or 5-phenyl substituted 4,5-dihydrofurans dependent upon the reagent used and the reaction conditions. 3 - Acetyl - 4,5 - dihydrofurans were also generated, although most of all in minor amounts next to other compounds, by the acid catalyzed rearrangement of 1,1-diacetylcyclopropanes,[12] the reaction of S-ethenylsulfoximine derivatives[19] and oxymercurials[20] with 2,4-pentanedione, by thermolysis of 3,3-diacetylpyrazolines[21] and by electrochemical oxidative addition of sodium acetylacetonate to olefins.[22]

The dihydrofuran formation described here was strongly dependent upon the nature of the R^1 and/or R^2 functions. Complications arose when one of the R^1 or R^2 groups consisted of a phenyl function where a rearrangement of the phenyl group occurred during the ring closure of **1g** providing a mixture of the isomeric furans **5f** and **5g** (ratio 7/3).

In other cases where the possibility existed that the double bond is able to migrate to the γ,δ-position such as in the propylidene derivative **1h** and the isobutylidene derivative **1i**, dihydropyran compounds **6, 7** were isolated next to the expected dihydrofurans **5h,i**. In addition, a rearrangement took place in the case of **1i** giving rise to the dihydrofuran **5c**.

The dihydrofuran formation was not limited to acetyl compounds. Also the cyclization of 6 - methyl - 4 - propionyl - 4 - hepten - 3 - one (**1j**) readily occurred affording 2 - ethyl - 5,5 - dimethyl - 3 - propionyl - 4,5 - dihydrofuran (**8**).

However cyclization of Knoevenagel condensation products derived from unsymmetrical β-diketones (e.g. **1k**) gave rise to a mixture of isomers **9** and **10** which could not be separated, even by GLC.



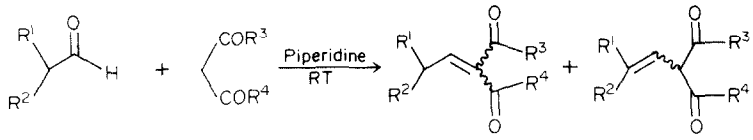
1 2

Table 1. Synthesis and spectrometric properties of 3-acetyl-2-methyl-4,5-dihydrofurans **5**

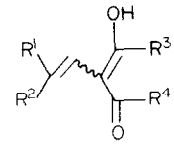
Compound	R_1	R_2	B.p. °C/mmHg	Yield[a] (%)	IR (cm^{-1})	NMR $\delta(CCl_4)$	MS m/e
a	Me	H	88-91/13 (95/13)[12]	74	1675 1620 1595	1.30(3H,d,J=6.2Hz,$\underline{CH_3}$-CH) 2.03(3H,s,CO$\underline{CH_3}$) 2.09(3H,t,J=1.8Hz,$\underline{CH_3}$-C=C) 2.27-3.23(2H,m,$\underline{CH_2}$-C=C) 4.39-5.00(1H,m,$\underline{CH}$-O)	140(M^+, 24), 125(34), 107(6), 97(6), 83(20), 79(5), 55(7), 43(100), 41(6)
b	Me	Me	95-97/14	81	1670 1620 1600	1.33(6H,s,$(\underline{CH_3})_2$) 2.02(3H,s,CO$\underline{CH_3}$) 2.10(3H,t,J=1.0Hz,$\underline{CH_3}$-C=C) 2.67(2H,q,J=1.0Hz,$\underline{CH_2}$-C=C)	154(M^+, 20), 139(17), 121(10), 111(5), 97(8), 94(9), 93(8), 55(7), 43(100), 41(7)
c	Me	Et	115-118/15	71	1665 1595	0.93(3H,t,J=7.2Hz,$\underline{CH_3}CH_2$) 1.32(3H,s,$\underline{CH_3}$) 1.62(2H,q,J=7.2Hz,$CH_3\underline{CH_2}$) 2.09(3H,s,$\underline{CH_3}$CO) 2.15(3H,t,J=1.7Hz,$\underline{CH_3}$-C=C) 2.66(2H,q,J=1.7Hz,$\underline{CH_2}$-C=C)	168(M^+, 7), 153(4), 139(3), 135(4), 108(6), 107(5), 97(4), 55(6), 43(100), 41(6)
d	Et	Et	121-125/13	81	1670 1620 1595	0.85(6H,b,J=7.0Hz,$(\underline{CH_3}CH_2)_2$) 1.63(4H,q,J=7.0Hz,$(CH_3\underline{CH_2})_2$) 2.05(3H,s,$COCH_3$) 2.14(3H,t,J=1.6Hz,$\underline{CH_3}$-C=C) 2.66(2H,q,J=1.6Hz,$\underline{CH_2}$-C=C)	182(M^+, 9), 167(3), 153(9), 149(6), 139(2), 122(6), 121(11), 107(6), 67(4), 57(6), 55(9), 43(100), 41(8)
e	cyclohex		98-101/0.1	84	1670 1620 1595	1.5-2.0(10H,m,$(CH_2)_5$) 2.05(3H,s,$COCH_3$) 2.14(3H,t,J=2.0Hz,$\underline{CH_3}$-C=C) 2.61(2H,q,J=2.0Hz,$\underline{CH_2}$-C=C)	195(M^+, 6), 179(3), 176(2), 161(8), 133(30), 113(5), 105(8), 91(7), 81(5), 67(8), 55(9), 53(7), 43(100), 41(14)
f	Me	C_6H_5	-	GLC	1670 1625 1600	1.63(3H,s,CH_3) 2.03(3H,s,$\underline{CH_3}$CO) 2.27(3H,t,J=2.0Hz,$\underline{CH_3}$-C=C) 3.10(2H,q,J=2.0Hz,$\underline{CH_2}$-C=C) 7.23(5H,s, broad, Ar-H)	216(M^+, 2), 174(2), 173(4), 155(5), 131(3), 115(3), 91(3), 77(4), 51(3), 43(100)

g	Me	H	-	GLC	1665 1610 1590	1.37(3H,d,J=6.4Hz,$\underline{CH_3}$CH) 1.70(3H,s,$\underline{CH_3}$CO) 2.28(3H,d,J=1.8Hz,$\underline{CH_3}$-C=C) 3.84(1H,dxd,J=6.2Hz,J=1.8Hz, $\underline{CH}$-C_6H_5) 4.40(1H,qxd,J=6.4Hz,J=6.2Hz, O$\underline{CH}$-CH_3) 7.17(5H,s, broad, Ar-H)	216(M^+, 2), 201(2), 156(5), 155(2), 129(5), 128(3), 91(3), 77(3), 51(3), 43(100)
h	Et	H	-	GLC	1670 1625 1600	0.94(3H,t,J=7.1Hz,$\underline{CH_3}CH_2$) 1.37-1.91(2H,m,$CH_3\underline{CH_2}CH$) 2.03(3H,s,CO$\underline{CH_3}$) 2.05(3H,t,J=2.0Hz,$\underline{CH_3}$-C=C) 2.20-3.15(2H,m,$\underline{CH_2}$-C=C) 4.15-4.70(1H,m,$\underline{C}$HO-)	154(M^+, 1), 139(1), 115(2), 112(7), 97(5), 71(7), 69(6), 61(5), 58(11), 55(9), 43(100), 43(100), 41(10)
i	Me	i-Pr	-	GLC	1675 1625 1600	0.90(3H,d,J=6.0Hz,$\underline{CH_3}$CH) 0.92(3H,d,J=6.0Hz,$\underline{CH_3}$CH) 1.47-1.85(1H,m,$(CH_3)_2\underline{CH}$) 2.03(3H,s,$COCH_3$) 2.10(3H,t,J=2.0Hz,CH_3-C=C) 2.31-3.03(2H,m,CH_2-C=C) 4.03-4.47(1H,m,OCH)	168(M^+, 15), 153(14), 135(5), 125(13), 113(12), 97(16), 56(16), 55(13), 43(100), 41(12)
j	3-cyclo- hexenyl		87-91/0.1	54 (DMF)	1660 1590	1.55-1.95(2H,m,CH_2) 2.-2.3(4H,m,$(CH_2)_2$) 2.03(3H,s,CH_3CO) 2.14(3H,t,J=1.7Hz,CH_3-C=C) 2.63(2H,q,J=1.7Hz,CH_2-C=C) 5.35-5.72(2H,m,HC=CH)	192(M^+, 20), 139(10), 138(7), 132(26), 111(8), 99(10), 95(10), 91(9), 80(34), 79(18), 71(4), 67(6), 55(7), 53(9), 43(100), 41(17)

(a) All compounds gave satisfactory microanalyses (C $\pm$ 0.21, H $\pm$ 0.09)

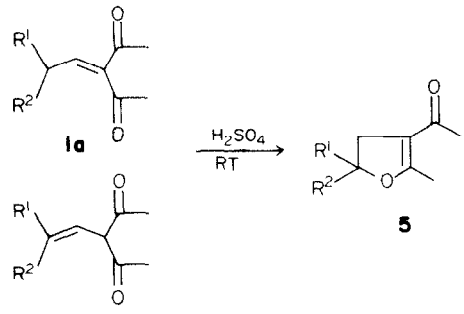


3 **4** **1a** **1b**



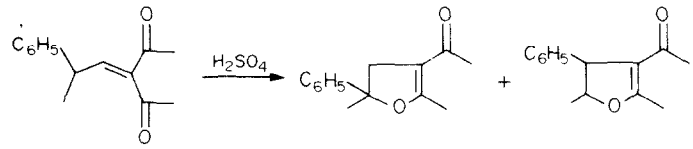
1c

a : R^1=H, R^2=R^3=R^4=Me
b : R^1=R^2=R^3=R^4=Me
c : R^1=Me, R^2=Et, R^3=R^4=Me
d : R^1=R^2=Et, R^3=R^4=Me
e : R^1, R^2 : 3-cyclohexenyl, R^3=R^4=Me
f : R^1; R^2 : cyclohexyl, R^3=R^4=Me
g : R^1=Ph, R^2=R^3=R^4=Me
h : R^1=H, R^2=Et, R^3=R^4=Me
i : R^1=H, R^2=*i*-Pr, R^3=R^4=Me
j : R^1=R^2=Me, R^3=R^4=Et
k : R^1=R^2=Me; R^3=Et, R^4=n-Pr
l : R^1=R^2=R^3=Me, R^4=OMe
m : R^1=R^2=R^3=Me, R^4=OEt
n : R^1=R^2=Me, R^3=Ph, R^4=OMe
o : R^1=R^2=Et, R^3=Me, R^4=OMe
p : R^1; R^2=3-cyclohexenyl, R^3=Me, R^4=OMe
q : R^1, R^2=cyclohex., R^3=Me, R^4=OMe
r : R^1=H, R^2=R^3=Me, R^4=OMe
s : R^1=H, R^2=Et, R^3=Me, R^4=OMe
t : R^1=H, R^2=Et, R^3=Me, R^4=OEt



1a **1b** **5**

a : R^1=Me; R^2=H
b : R^1=R^2=Me
c : R^1=Et; R^2=Me
d : R^1=R^2=Et
e : R^1; R^2=cyclohexyl

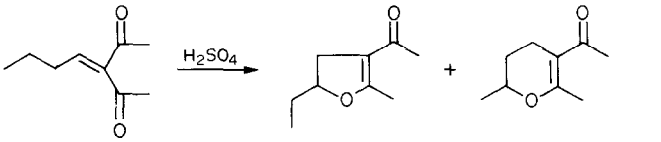


1g **5f** **5g**

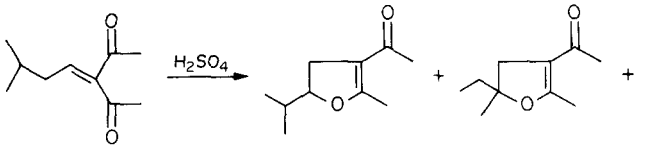
Attempts were carried out to perform the cyclization in other acidic media. Heating of **1** in a 20% solution of gaseous hydrogen chloride in dry dimethylformamide at 140° afforded the same 3 - acetyl - 4,5 - dihydrofurans **5**, but in lower yields due to side-reactions such as formation of α,β- and β,γ-unsaturated ketones. The synthesis of spirofuran **5** could only be performed in DMF–HCl starting from the cyclohexenyl compound **1e** as cyclization in sulfuric acid resulted in tar formation. In addition, minor amounts of 2 - acetyl - 1 - methylindan **11** were produced in the former reaction.

The reaction took a completely different course with these compounds where one of the R^1 or R^2 groups consisted of hydrogen. A diacetylcyclohexenone **12** was isolated when **1a** was heated in DMF–HCl at 120° for 48 h. The cyclohexenone **12** was formed by an addition of 2,4-pentanedione (generated by decomposition of **1a** on heating) to the unsaturated diketone followed by ring closure and dehydration.

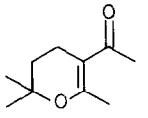
On the other hand, when the reaction was carried out in boiling xylene in the presence of *p*-toluenesulfonic acid, benzofuran derivatives **13**, **14** were formed by



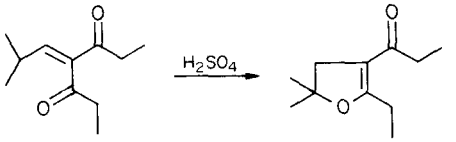
1h **5h** (45%) **6** (55%)



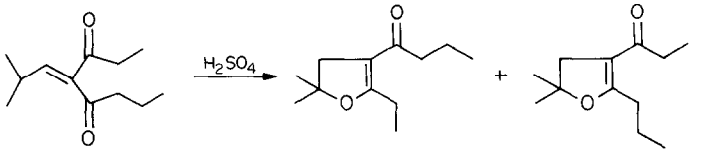
1i **5i** (21%) **5c** (19%)



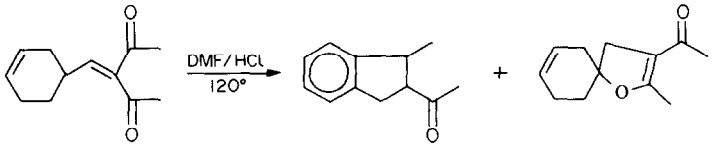
7 (60%)



1j **8**



1k **9** **10**



1e **11** **5j**

further condensation and aromatization of **1b** with respectively acetone and 5-methyl-4-hexen-2-one (formed by decomposition of **1b**) with **5b**.

The mechanism of the dihydrofuran formation must involve a migration of the double bond followed by protonation of the double bond leading to a carbonium ion and subsequent intramolecular O-alkylation. The dihydropyran formation is explained by a double migration of the double bond as outlined in the following scheme.

This proposed mechanism has been substantiated by the fact that ring closure in deuterated sulfuric acid gave rise to the formation of the monodeuterated dihydrofuran derivative. A pathway which proceeds via a hydride shift during the cyclization step (as observed during the ring closure of alkylidene malonates) would give a non deuterated compound and can be ruled out.

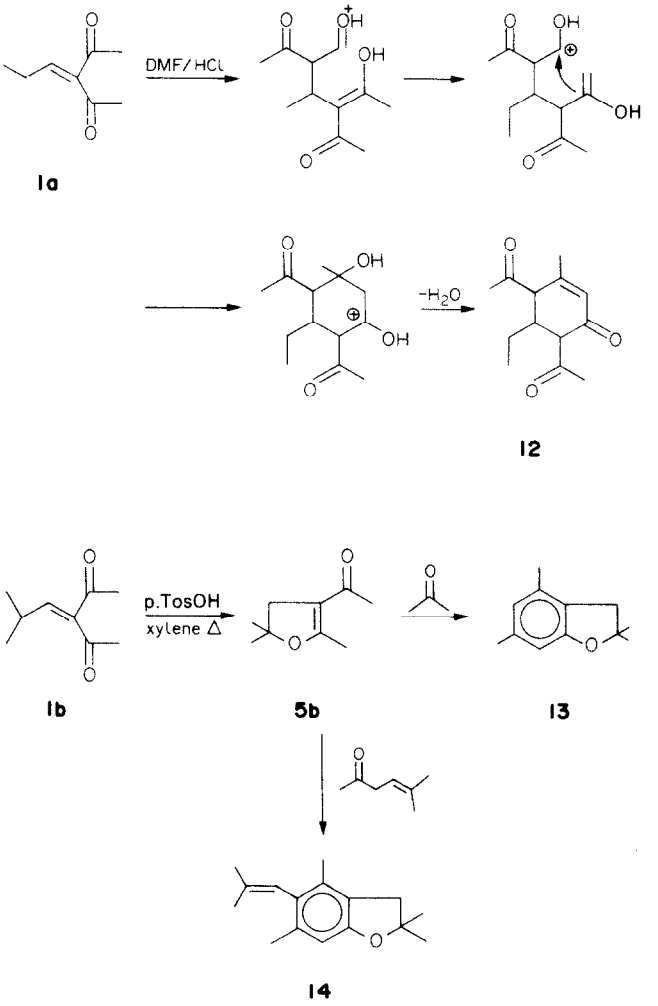
Also the acid catalyzed ring closure of the Knoevenagel addition products derived from aldehydes and β-ketoesters proceeded very smoothly, but the nature of the reaction products varied upon the acid and the reaction time.

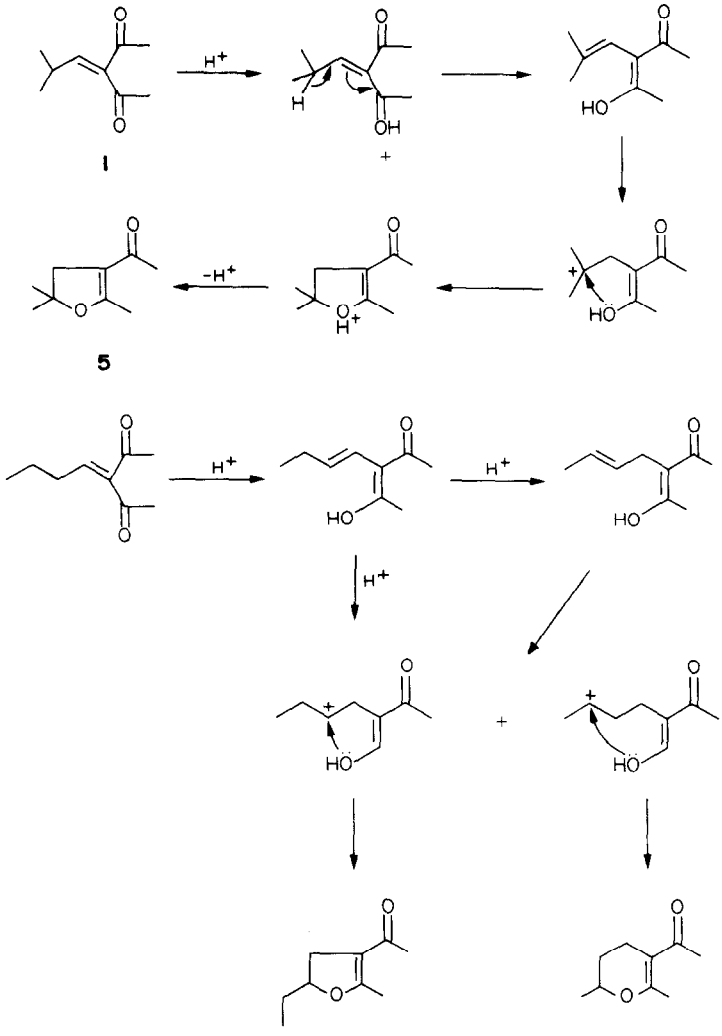
Treatment of the electrophilic alkenes **1** (**l**, **m**, **n**, **o**, **p**, **q**) with concentrated sulfuric acid for a short period (maximum 30 min afforded 3 - alkoxycarbonyl - 4,5 - dihydrofurans **15** (Table 2).

On standing in concentrated sulfuric acid for a longer period of time (12 h) the dihydrofurans **15** were transformed into 2-acyllactones **16**; except when R^3 is a phenyl function and the dihydrofuran **15d** is isolated next to minor amounts of 4,4-dimethyltetralone (**17**). The dihydrofurans were also formed when the reaction was carried out in the presence of DMF–HCl or *p*-TosOH in boiling xylene; in the latter cases only traces of 2-acyllactones were detected. It should be noted that in the case of the 3-cyclohexenyl compound **1p** only reaction in DMF–HCl gave rise to the corresponding 4,5-dihydrofuran **15f** next to small amounts of 1-methylindan (**18**) and 4 - (1 - cyclohexenyl) - 3 - buten - 2 - one (**19**). In the literature 3 - alkoxycarbonyl - 4,5 - dihydrofurans were synthesized by an acid catalyzed rearrangement of α-acyllactones[23,24] and α-thioacyllactones[25] in alcohol, the oxidative coupling of olefins with β-ketoesters,[15–17,26] reaction of sodium carboxylates with carbethoxycyclopyltriphenyltetrafluoroborate,[27] aluminium oxide assisted rearrangement of 1 - acylcyclopropanecarboxylates[28] and the condensation of 1,2 - dibromoethanes with β-ketoesters (next to 1 - acylcyclopropanecarboxylates).[29]

2-Acyllactones were easily prepared by ester condensation with lactones[30] and by reaction of substituted oxiranes with β-ketoesters.[31–33]

The 3 - alkoxycarbonyl - 4,5 - dihydrofurans **15** are





formed via an identical mechanism as proposed for the 3-acyl compounds **5**, while the 2-acyllactones **16** are generated by protonation of **15** followed by ring opening and subsequent intramolecular transesterification.

This lactonization is the reverse reaction of the well-known acyllactone rearrangement[23] and concentrated sulfuric acid is necessary to perform the transformation **15**→**16**.

However, the dihydrofuran formation was limited to these compounds where R^1 or R^2 are different from hydrogen, otherwise cyclohexenones **20** are mainly produced next to α,β- and β,γ-unsaturated ketones **20**, **21**. Also appreciable amounts of cyclohexenone derivatives **20** were formed when the esters **1** (R^1,R^2 = alkyl) were heated in DMF–HCl for a long period (12–24 h).

EXPERIMENTAL

IR spectra were obtained with a Perkin–Elmer 257 spectrometer. NMR spectra were recorded on a Varian T60 apparatus. Mass spectra were determined on an AEI MS20 instrument coupled with a Pye Unicam 104 gas chromatograph (SE-30, 5%, 1.5 m) at an ionizing voltage of 70 eV.

General procedure for the preparation of the electrophilic alkenes **1**

A mixture of **3** (0.1 mol) and 1,3-diketone or β-ketoesters (0.1 mol) was treated with 1 ml piperidine at room temp. After stirring for 24 h the mixture was triturated with 100 ml CH_2Cl_2 and the soln was successively washed with 50 ml dil HCl (5%) and water. After drying ($MgSO_4$) and evaporation of the solvent, the alkenes **1** were obtained by fractional distillation.

The spectral data of **1** ($R^1 = R^2 = R^3 = R^4$ = Me) and **1** ($R^1 = R^2 = R^3$ = Me, R^4 = OMe are representative for all other compounds.

2 - *Acetyl* - 4 - *methyl* - 2 - *pentenone* (**1A,b**). B.p. 92–94°/15 mmHg; Yield 63%. IR (NaCl): 1710, 1670 (C=O); 1630 cm^{-1} (C=C). NMR δ (CCl_4): 1.06 (6H, d, J = 7.4 Hz, $(CH_3)_2$); 2.22 (3H, s, $COCH_3$); 2.25 (3H, s, $COCH_3$); 2.28–2.90 (1H, m, CH–C=C); 6.35 (1H, d, J = 10.2 Hz, =CH). Mass spectrum *m/e*: 154(M^+, 21); 139(8); 136(14); 121(13); 112(13); 97(13); 94(12); 79(7); 67(7); 43(100); 41(10).

2 - *Acetyl* - 4 - *methyl* - 3 - *pentenone* (**1C,b**). NMR δ (CCl_4): 1.60 (3H, d, J = 1.8 Hz, CH_3–C–C); 1.82 (3H, d, J = 1.8 Hz, CH_3–C=C); 2.27 (6H, s, $(COCH_3)_2$); 5.76 (1H, m, =CH); 15.75 (1H, s broadened, enol OH).

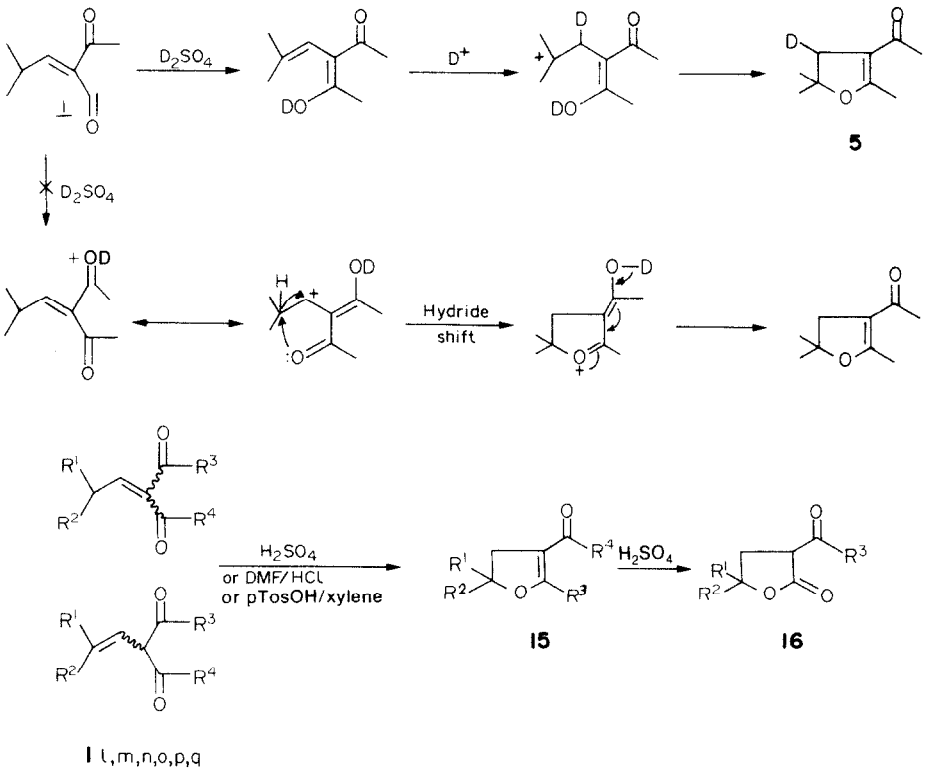
Methyl 2 - *acetyl* - 4 - *methyl* - 2 - *pentenoate* (**1A,l**). B.p. 107–110°/18 mmHg; Yield 81%. IR (NaCl): 1740 (COOMe); 1680 (CO); 1640 cm^{-1} (C=C). NMR δ (CCl_4) (Z): 1.09 (6H, d, J = 6.2 Hz, $(CH_3)_2$); 2.23 (3H, s, $COCH_3$); 2.68 (1H, septet × d, J = 6.2 Hz, J = 9.0 Hz, CH); 3.79 (3H, s, $COOCH_3$); 6.53 (1H, d, J = 9.0 Hz, =CH). (E): 1.07 (6H, d, J = 7.0 Hz, $(CH_3)_2$); 2.26 (3H, s, $COCH_3$); 2.70 (1H, septet × d, J = 7.0 Hz, J = 100.0 Hz, CH); 3.69 (3H, s, $COOCH_3$); 6.60 (1H, d, J = 10.0 Hz, =CH). Mass spectrum *m/e*: 170 (M^+, 6); 139(13); 138(44); 128(70); 123(20);

Table 2. Synthesis and spectrometric properties of 3-alkoxycarbonyl-4,5-dihydrofurans **15**

Compound	R_1	R_2	R_3	R_4	B.p. °C/mmHg	Yield[a] %	IR cm^{-1}	NMR δ(CCl_4)	MS m/e
a	Me	Me	Me	OMe	95-97/17 81-82/12[30]	73	1705	1.25(6H,s,$(CH_3)_2$) 2.11(3H,t,J=1.5Hz,$\underline{CH_3}$-C=C) 2.63(2H,q,J=1.5Hz,CH_2-C=C) 3.63(3H,s,$COOCH_3$)	170(M^+, 37), 139(35), 138(59), 123(21), 120(25), 96(38), 95 (25), 81(11), 73(11), 67(12), 55(13), 43(100), 41(14)
b	Me	Me	Me	OEt	107-109/13	67	1695 1640	1.20(3H,t,J=6.8Hz,$\underline{CH_3}CH_2O$) 1.32(6H,s,$(CH_3)_2$) 2.07(3H,t,J=1.1Hz,CH_3-C=C) 2.56(2H,q,J=1.1Hz,CH_2-C=C) 4.06(2H,q,J=6.8Hz,$CH_3\underline{CH_2}O$)	184(M^+, 30), 139(46), 138(55), 123(25), 120(30), 97(45), 96 (27), 43(100), 41(21)
c	Et	Et	Me	OMe	68-71/0.1	78	1700 1640	0.89(6H,t,J=7.0Hz,$(\underline{CH_3}CH_2)_2$ 1.60(4H,q,J=7.0Hz,$(CH_3\underline{CH_2})_2$ 2.13(3H,t,J=3.1Hz,CH_3-C=C) 2.58(2H,q,J=3.1Hz,CH_2-C=C) 3.61(3H,s,$COOCH_3$)	198(M^+, 4), 169(8), 167(6), 166(8), 151(11), 137(10), 124(11), 123(13), 109(8), 97(10), 95(12), 81(6), 69(5), 59(12), 57(12), 55(25), 53(9), 43(100), 41(21)

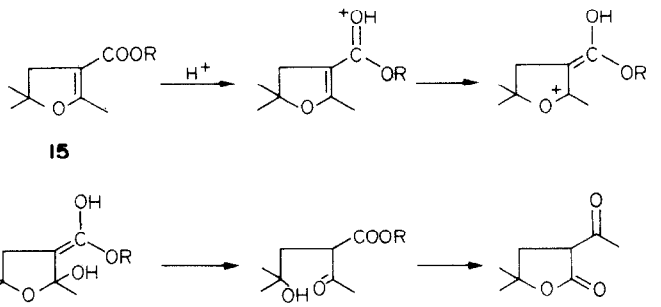
d	Me	Me	C_6H_5	OEt	93-96/0.05	44 (H_2SO_4)	1700 1625	1.14(3H,t,J=7.0Hz,$\underline{CH_3}CH_2O$) 1.40(6H,s,$(CH_3)_2$)	248(M^+, 33), 201(14), 200(16),
						70 (DMF)	1600 1570	2.84(2H,s,CH_2-C=C) 4.02(2H,q,J=7.0Hz,$CH_3\underline{CH_2}O$) 7.15-7.30(3H,m,Ar-H) 7.55-7.82(2H,m,Ar-H)	174(17), 171(10), 129(7), 122(35), 115(9), 105(100), 77(37), 51(8), 43(10)
e	cyclohex.	Me		OMe	101-106/0.2	81	1700 1640	1.5-1.8(10H,m,$(CH_2)_5$) 2.12(3H,t,J=2.0Hz,CH_3-C=C) 2.56(2H,q,J=2.0Hz,CH_2-C=C) 3.61(3H,s,$COOCH_3$)	210(M^+, 8), 179(10), 178(36), 163(10), 149(6), 136(25), 135(32), 129(7), 121(8), 107(11), 97(29), 81(10), 79(16), 67(20), 55(29), 53(11), 43(100), 41(27)
f	3-cyclo-hexenyl	Me		OMe	96-98°/0.3	34 (DMF)	1700 1645	1.60-2.90(2H,m,CH_2) 2.11(3H,t,J=2.0Hz,CH_3-C=C) 2.1-2.3(4H,m,CH_2-C=C) 2.60(2H,q,J=2.0Hz,CH_2-C=C) 3.61(3H,s,$COOCH_3$) 5.34-5.75(2H,m,HC=CH)	208(M^+, 33), 178(12), 177(17), 154(11), 153(14), 133(16), 105(18), 97(30), 91(23), 80(100), 79(51), 77(27), 70(12), 55(17), 43(79)

(a) All compounds gave satisfactory microanalysis (C $\pm$ 0.19; H $\pm$ 0.05)



l (l,m,n,o,p,q

a : $R^1=R^2=R^3=Me$; $R^4=OMe$
b : $R^1=R^2=R^3=Me$; $R^4=OEt$
c : $R^1=R^2=Et$; $R^3=Me$; $R^4=OMe$
d : $R^1=R^2=Me$; $R^3=Ph$; $R^4=OEt$
e : R^1; R^2= cyclohex ; $R^3=Me$; $R^4=OMe$
f : R^1; R^2=3−cyclohexenyl ; $R^3=Me$; $R^4=OMe$



(3H, s, $COOCH_3$); 5.97 (1H, s broadened, =CH); 14.26 (1H, s, enol OH). MS; *m/e*: 210 (M^+, 4); 167 (8), 151 (18), 140 (35), 123 (16), 112 (100), 109 (24), 107 (13), 97 (28), 82 (16), 81 (18), 79 (24), 77 (16), 67 (15), 59 (18), 55 (19), 53 (21), 43 (58), 41 (45).

Ethyl 4 - methyl - 2 - oxo - 6 - propyl - 3 - cyclohexene

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120(12); 113(13); 96(41); 95(24); 81(17); 73(13); 69(17); 68(11); 67(20); 55(15); 43(100); 41(19).

Methyl 2 - *acetyl* - 4 - *methyl* - 3 - *pentenoate* (**1B,C,I**). NMR δ (CCl_4): 1.50 (3H, d, J = 2.1 Hz, CH_3–C=C); 1.66 (3H, d, J = 2.0 Hz, CH_3–C=C); 1.80 (3H, s, broadened, CH_3CO); 3.69 (3H, s, $COOCH_3$); 4.10 (0.6 H, d, J = 9.8 Hz, $CH_3OC\underline{CH}(COOCH_3)$; 5.30–5.60 (1H, m, =CH); 13.33 (0.4 H, s broadened, enol OH).

Preparation of 2-*acetyldihydrofurans* **5**

Ring closure in sulfuric acid. H_2SO_4 (1 ml) was added dropwise to 0.1 mol of electrophilic alkene under stirring at room temp. After stirring for 12 h the mixture was treated with 100 ml CH_2Cl_2 and 100 ml water. The organic layer was separated off and the aqueous layer was extracted with 50 ml CH_2Cl_2 and the combined extracts were successively washed with sat. $NaHCO_3$aq and water. After drying ($MgSO_4$) the solvent was removed *in vacuo* and distillation yielded derivatives **5**.

Ring closure in dimethylformamide-hydrogen chloride. A soln of 0.1 mol alkene in 100 ml DMFHCl (20%) was heated at 140° for 24 h. After cooling the mixture was poured into 250 ml 2N HCl and 100 ml ether. The organic layer was separated and the aqueous phase was extracted with ether (2 × 50 ml). The combined extracts were worked-up as above.

2 - Acetyl - 4,5 - dihydro - 2,6 - dimethylpyran (**6**). IR (NaCl): 1670 (CO); 1580 cm^{-1} (C=C). NMR δ(CCl_4): 1.24 (3H, d, J = 6.0 Hz, CH_3CH); 1.64–1.84 (2H, m, CH_2); 2.10 (6H, s, $COCH_3$,CH_3–C=C); 2.2–3 (2H, m, CH_2–C=C) 3.66–4.10 (1H, m, OCH). MS: *m/e*: 154 (M^+, 7), 139 (12), 121 (4), 111 (4), 97 (15), 70 (6), 69 (4), 55 (18), 53 (4), 43 (100), 41 (5).

2 - *Acetyl* - 4,5 - *dihydro* - 2,2,6 - *trimethylpyran* (**7**). IR (NaCl): 1675 (CO); 1575 cm^{-1} (C=C). NMR: δ(CCl_4): 0.90 (6H, s, $(CH_3)_2$); 1.63 (2H, t, J = 6.5 Hz, CH_2); 2.10 (3H, s, $COCH_3$); 2.11 (3H,t J = 2.0 Hz, CH_3–C=C); 2.33 (2H, t × q, J = 6.5 Hz, J = 2.0 Hz, CH_2–C=C). MS; *m/e*: 168 (M^+, 12), 153 (6), 135 (8), 125 (8), 113 (33), 108 (10), 97 (10), 93 (5), 71 (5), 70 (5), 69 (5), 56 (36), 55 (15), 43 (100), 41 (21), 39 (10).

2 - *Ethyl* - 4,5 - *dihydro* - 5,5 - *dimethyl* - 3 - *propionylfuran* (**8**). B.p. 66–68°/0.1 Hg: Yield: 68%. IR (NaCl): 1665 (CO); 1595 cm^{-1} (C=C). NMR; δ(CCl_4): 1.03 (3H, t, J = 6.9 Hz, CH_3CH_2); 1.08 (3H, t, J = 6.9 Hz, CH_3CH_2); 1.38 (6H, s, $(CH_3)_2$); 2.32 (4H, J = 6.9 Hz, CH_2CO; CH_2–C=C); 2.72 (2 H, s broad, CH_2–C=C). MS; *m/e*: 182 (M^+, 25), 153 (90), 135 (33), 125 (6), 107 (10), 97 (12), 69 (9), 57 (100), 43 (43), 41 (28).

2 - Acetyl - 1 - methylindan (**11**). B.p.: 58–60°/0.1 mm Hg; Yield 30%. IR (NaCl): 1610, 1565, 1525 cm^{-1} (aromatic). NMR; δ(CCl_4): 1.33 (3H, d, J = 7.5 Hz, CH_3CH); 2.22 (3H, s, $COCH_3$); 2.85–3.55 (4H, m, CH_2–CH–CH); 7.14 (4H, m, Ar–H). MS; *m/e*: 174 (M^+, 42), 159 (70), 131 (36), 130 (92), 129 (23), 116 (14), 115 (28), 91 (22), 77 (8), 53 (8), 51 (11), 45 (12), 43 (100).

4,6 - *Diacetyl* - 5 - *ethyl* - 3 - *methyl* - 2 - *cyclohexenone* (**12**). IR (NaCl): 1670–1570 cm^{-1} (C=O, C=C). NMR; δ(CCl_4): 0.93 (3H, t, J = 6.3 Hz, CH_3–CH_2); 1.2–2 (2H, m, CH_2); 1.98 (3H, d, J = 2.0 Hz, CH_3–C=C); 2.45–3.0 (2H, m, CH); 5.97 (1H, q, J = 2.0 Hz, =CH); 15.53 (1H, s, enol OH). MS; *m/e*: 222 (M^+, 1), 193 (0.5), 179 (2), 151 (12), 137 (2), 109 (2), 53 (2), 43 (100), 41 (2).

Ring closure of 2 - *acetyl* - 4 - *methyl* - 2 - *pentenone* (**1b**) *in xylene*/*p-toluenesulfonic acid.* A soln of 0.1 mol 2 - acetyl - 4 - methyl - 2 - pentenone and 1 g *p*-toluenesulfonic acid in 100 ml xylene was heated at 140° for 12 h. After cooling the mixture was poured into 100 ml water. The organic layer was separated and the aqueous layer was extracted with toluene. The combined extracts were washed with sat $NaHCO_3$aq and water and dried ($MgSO_4$). The solvent was removed *in vacuo* and fractional distillation of the residue afforded **13** and **14**.

2,3 - *Dihydro* - 2,2,4,6 - *tetramethylbenzofuran* (**13**). B.p.: 88–94°/0.1 mm Hg; Yield: 16%. NMR; δ(CCl_4): 1.48 (6H, s, $(CH_3)_2$); 2.16 (3H, s, Ar–CH_3); 2.22 (3H, s, Ar–CH_3); 2.86 (2H, s, Ar–CH_2); 6.72 (2H, m, Ar–H). MS; *m/e*: 176 (M^+, 64), 161 (100), 135 (15), 133 (25), 115 (9), 105 (6), 91 (17), 77 (10), 43 (8), 41 (9), 39 (11).

2,3 - *Dihydro* - 2,2,4,6 - *tetramethyl* - 5 - (2 - *methyl* - 1 - *propenyl*) - *benzofuran* (**14**). B.p.: 145–150°/0.1 mm Hg; Yield: 54%. IR (NaCl): 1610, 1600 cm^{-1}/aromatic). NMR; δ(CCl_4): 1.38 (3H, s, CH_3–C=C); 1.39 (6H, s, $(CH_3)_2$); 1.82 (3H, s, CH_3–C=C); 1.97 (3H, s, Ar–CH_3); 2.06 (3H, s, Ar–CH_3); 2.86 (2H, s, Ar–CH_2); 5.95 (1H, s, broad, =CH); 6.36 (1H, s, Ar–H). MS; *m/e*: 230 (M^+, 100), 215 (29), 190 (19), 188 (16), 173 (23), 160 (12), 159 (20), 114 (14), 99 (16), 91 (14), 79 (8), 77 (10), 55 (14), 53 (8), 43 (70), 41 (28).

Preparation of 2 - *alkoxycarbonyldihydrofurans* **15**

A mixture of 0.1 ml of the α,β-unsaturated ester and 1 ml H_2SO_4 and was stirred for (0.5 h) at room temp (except for the cyclohexyl compound: reaction time 2 h) and the mixture was worked-up as in the case of **5**.

The compounds **14** could also be obtained by heating a soln of 0.1 ml ester in 100 ml DMF–HCl for 12 h.

Synthesis of 2 - *acetylbutanolides* (**16**)

A mixture of 0.1 mol of **1** and 1 ml H_2SO_4 was stirred for 24 h at room temp (cyclohexyl compound; reaction time 48 h) and the mixture was worked-up as above.

2 - *Acetyl* - 4,4 - *dimethylbutanolide* (**16**, $R^1 = R^2 = R^3$ = Me). B.p.: 137–140°/13 mm Hg (59–61/0.03);[30] Yield: 68%. IR (NaCl): 1765, 1720, 1655 cm^{-1}. NMR; δ (CCl_4): 1.36 (6H, s, $(CH_3)_2$); 1.70–2.70 (2H, m, CH_2–CH); 2.34 (3H, s, $COCH_3$); 3.55–3.84 (1H, m, CH_2–CH). MS; *m/e*: 156 (M^+, 4), 141 (8), 138 (5), 114 (50), 99 (15), 97 (6), 70 (6), 69 (15), 59 (17), 56 (8), 55 (22), 43 (100), 41 (14).

2 - *Acetyl* - 4,4 - *diethylbutanolide* (**16**, $R^1 = R^2$ = Et, R^3 = Me). B.p. 98–102°/0.2 mm Hg. Yield 41%. IR (NaCl): 1760, 1720, 1650 cm^{-1}. NMR; δ(CCl_4): 0.97 (6H, t, J = 7.0 Hz, $(CH_3CH_2)_2$); 1.72 (4H, 9, J = 7.0 Hz, $(CH_3CH_2)_2$); 1.97–2.91 (2H, m, CH_2–CH); 2.10 (3H, s, $COCH_3$); 3.63–3.94 (1H, m, CH_2–CH). MS; *m/e*: 184 (M^+, 0.5), 166 (1), 155 (9), 142 (6), 113 (13), 87 (6), 70 (6), 67 (5), 57 (16), 43 (100), 41 (11).

3 - *Acetyl* - 2 - *oxo* - 1 - *oxaspiro*[4.5]*decane* (**16**, R_1,R_2 = *cyclohex.*, R^3 = Me). Decomposition on distillation; an analytical sample was prepared by column chromatography (Al_2O_3ether–hexane 3:1). IR (NaCl): 1770, 1725, 1655 cm^{-1}. NMR; δ(CCl_4): 1.3–1.9 (10H, m, $(CH_2)_5$; 1.85–2.60 (2H, m, CH_2–CH); 2.36 (3H, s, $COCH_3$); 3.46–3.66 (1H, m, CH_2–CH). MS; *m/e*: 196 (M^+, 1); 195 (5), 181 (3), 163 (7), 137 (3), 133 (21), 119 (4), 95 (4), 81 (6), 79 (6), 67 (10), 55 (9), 53 (6), 43 (100), 41 (13).

4,4 - *Dimethyl* - 1 - *tetralone* (**17**). B.p.: 75–80°/0.05 mm Hg; Yield: 12%. IR (NaCl): 1685 (CO); 1600 cm^{-1} (aromatic). NMR δ(CCl_4): 1.35 (6H, s(CH_3)$_2$); 1.97 (2H, t, J = 6.1 Hz, CH_2–CH_2); 2.61 (2H, t, J = 6.1 Hz, CH_2–CO); 7.1–7.5 (3H, m, Ar–H); 7.70–7.95 (1H, m, Ar–H). MS; *m/e*: 174 (M^+, 44); 159 (100), 131 (50), 118 (6), 117 (9), 116 (8), 115 (11), 105 (33), 91 (24), 77 (23), 65 (8), 64 (8), 58 (11), 51 (18), 41 (9).

1-*Methylindane* (**18**). NMR; δ(CCl_4): 1.28 (3H, d, J = 5.8 Hz, CH_3–CH); 2.15–3.3 (5H, m, CH_2–CH_2–CH); 7.2–7.5 (4H, m, Ar–H). MS; *m/e*: 132 (M^+, 30), 131 (10), 117 (100), 115 (15), 91 (8), 67 (4), 65 (4), 57 (6), 51 (5).

4 - (1 - *Cyclohexenyl*) - 3 - *buten* - 2 - *one* (**19**). IR (NaCl): 1680 (CO); 1660 cm^{-1} (C=C). NMR; δ(CCl_4): 1.65 (4H, m, $(CH_2)_2$); 2.15 (3H, s, $COCH_3$); 2.06–2.3 (4H, m, CH_2–C=C–CH_2); 5.90 (1H, d, J_{AB} = 15.5 Hz, H=CH); 6.10 (1H, m, =CH); 6.95 (1H, d, J_{AB} = 15.5 Hz, CH=CH). MS; *m/e*: 150 (M^+, 7); 149 (27), 135 (32), 121 (100), 107 (35), 95 (18), 91 (29), 59 (47), 77 (23), 57 (18), 55 (29), 53 (20), 51 (20), 43 (98), 41 (29).

Methyl 6 - *ethyl* - 4 - *methyl* - 2 - *oxo* - 3 - *cyclohexene carboxylate* **20** (R^1 = H, $R^2 = R^3$ = Me, R^4 = OMe). Reaction conditions: H_2SO_4/12 h, B.p. 107–112°/0.1 mmHg, Yield 42%. IR (NaCl): 1735 (COOMe); 1670 (CO); 1640 cm^{-1}(C=C). NMR; δ(CCl_4): 0.95 (3H, t, J = 6.0 Hz, CH_3CH_2); 1.11–1.50 (2H, m, CH_2CH_2CH); 1.90 (3H, d, J = 1.0 Hz, CH_3–C=C); 2.1–2.5 (2H, m, CH–CH_2–C=C); 2.95–3.30 (1H, m, CH_2–CH–C=C); 3.66 (3H, s, $COOCH_3$); 5.76 (1H, 9, J = 1.0 Hz, =CH); 13.75 (1H, s, broad, enol OH). MS; *m/e*: 196 (M^+, 15), 167 (9), 140 (60), 138 (33), 112 (100), 109 (18), 97 (23), 95 (14), 79 (20), 67 (14), 59 (18), 55 (18), 53 (18), 43 (27), 41 (26).

Methyl 4 - *methyl* - 2 - *oxo* - 6 - *propyl* - 3 - *cyclohexene carboxylate* **20** (R^1=H, R^2=Et, R^3=Me, R^4=OMe). Reaction conditions: H_2SO_4/12 h. B.p. 121–124°/0.1 mmHg Yield: 64%. IR (NaCl): 1730 (COOMe), 1675 (CO), 1635 cm^{-1} (C=C). NMR; δ(CCl_4): 1.02 (3H, J = 7 Hz, CH_3CH_2); 1.2–1.6 (4H, m, $(CH_2)_2$; 2.03 (3H, s broadened, CH_3CO); 2.15–2.8 (3H, m, CH_2; CH); 3.85

(3H, s, $COOCH_3$); 5.97 (1H, s broadened, =CH); 14.26 (1H, s, enol OH). MS; *m/e*: 210 (M^+, 4); 167 (8), 151 (18), 140 (35), 123 (16), 112 (100), 109 (24), 107 (13), 97 (28), 82 (16), 81 (18), 79 (24), 77 (16), 67 (15), 59 (18), 55 (19), 53 (21), 43 (58), 41 (45).

Ethyl 4 - methyl - 2 - oxo - 6 - propyl - 3 - cyclohexene carboxylate **20** (R^1 = H, R^2 = Et, R^3 = Me, R^4 = OMe). Reaction conditions: DMF/HCl-140°/5 h. B.p. 131–135°/0.2 mmHg; Yield 34%. IR (NaCl): 1730 (COOEt); 1670 (CO); 1635 cm^{-1} (C=C). NMR; $\delta(CCl_4)$: 0.96 (3H, t, J = 7 Hz, $\underline{CH_3}CH_2$); 1.30 (3H, t, J = 6.9 Hz, $\underline{CH_3}CH_2O$); 1.1–1.4 (4H, m, $(CH_2)_2$); 2.00 (3H, s, broadened, $\underline{CH_3}C$=C); 2.1–2.6 (3H, m, CH_2, CH); 2.85–3.18 (1H, m, $\underline{CH}$–COOEt); 4.22 (2H, J = 6.9 Hz, $CH_3\underline{CH_2}O$); 5.82 (1H, s broadened, =CH). MS; *m/e*: 224 (M^+, 8), 154 (80), 151 (48), 126 (70), 109 (100), 107 (19), 81 (34), 80 (19), 79 (41), 69 (15), 67 (24), 55 (30), 53 (35), 43 (37), 41 (74).

Ethyl 6 - isopropyl - 4 - methyl - 3 - oxo - 2 - cyclohexene carboxylate **20** (R^1 = H, R^2 = Et, R^3 = Me, R^4 = OMe). Reaction conditions: DMF/HCl-140°/5 h. B.p. 131–135°/0.2 mmHg—Yield 60%. IR (NaCl): 1730 (COOEt); 1670 (CO); 1635 (C=C). NMR; $\delta(CCl_4)$: 0.85 (3H, d, J = 5.3 Hz, $\underline{CH_3}CH$); 0.93 (3H, d, J = 5.3 Hz, $\underline{CH_3}CH$); 1.26 (3H, t, J = 7.0 Hz, $\underline{CH_3}CH_2$); 1.91 (3H, s, broadened CH_3–C=C); 2.0–2.6 (4H, m, CH_2, CH, CH); 3.05–3.3 (1H, m, CH_2–COOEt); 4.18 (2H, q, J = 7.0 Hz, $CH_3\underline{CH_2}O$); 5.86 (1H, s, broadened, =CH). MS; *m/e*: 224 (M^+, 10), 181 (17), 154 (55), 151 (18), 126 (46), 109 (100), 81 (15), 80 (15), 79 (23), 53 (15), 43 (25), 41 (37).

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