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SYNTHESIS OF 3- AND 5-ALKYL-6-ALKYL(ARYL)TETRAHYDROPYRAN-2,4-DIONES BY THE CONDENSATION OF β-OXO ACID ESTERS WITH ALDEHYDES AND KETONES

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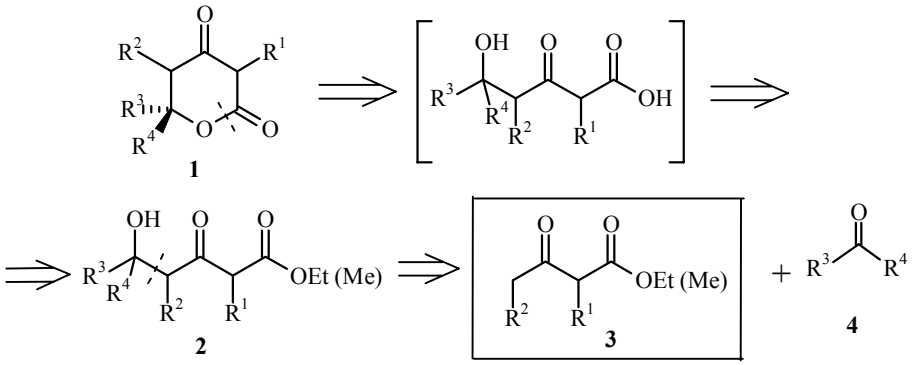
A method is proposed for obtaining 3- and 5-alkyl-6-alkyl(aryl)tetrahydropyran-2,4-diones based on the condensation of the dianion of alkyl(dialkyl)acetoacetic ester with aldehydes and ketones.

Keywords: dihydro-2-pyrones, carbonyl compounds, tetrahydropyrandiones, condensation, lactonization.

Natural and synthetic alkyl(aryl)tetrahydropyran-2,4-diones attract attention because of their diverse biological properties [1,2]. A large number of approaches has been developed for the preparation of 6-alkyl(aryl)pyran-2,4-diones, but only individual publications have been devoted to the synthesis of 3,6- and 5,6-substituted derivatives [3,4].

As in the case of other cyclic β-dicarbonyl compounds the introduction of an alkyl substituent by alkylating the anion of tetrahydropyran-2,4-dione is ineffective since O-alkylation predominates [5-9]. We have therefore investigated the possibility of introducing an alkyl substituent at the stage of forming the acyclic precursor to lead to the desired 3(5)-alkyltetrahydropyran-2,4-dione. As shown by retrosynthetic analysis of compounds **1** (see Scheme 1) the precursors are substituted esters of the 5-hydroxy-3-oxo acids **2**, the products of aldol condensation of the readily available esters of the 3-oxo acids **3** [10-14] with carbonyl compounds **4** [13,15-19].

Scheme 1



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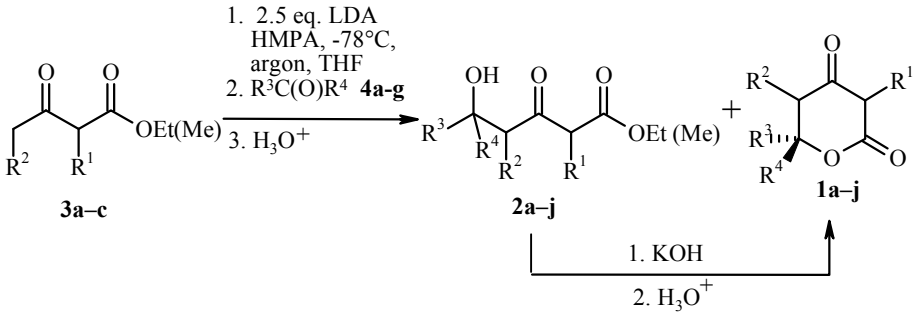
Results are given in the present work on the development of a general procedure for condensing substituted compounds **3** and **4**. In the first step of the reaction the appropriate dianion is obtained by treating ester **3** with 2.5 equivalents of lithium diisopropylamide. The dianion is then treated with aldehyde or ketone. Analysis of the reaction mixtures by TLC showed the presence of the desired tetrahydropyrandione **1** and its precursor, the ester of 5-hydroxy-3-oxo acid **2**. For complete conversion of the latter into product **1** the unseparated mixture was in each case saponified with aqueous KOH solution. Dione **1** forms a salt under the action of KOH, which is relatively inert to alkali, but ester **2** is converted into a salt of the 5-hydroxy-3-oxo carboxylic acid, which on acidification is spontaneously lactonized into the desired product **1** (see Scheme 2).

Scheme 2



3a–c **2a–j** **1a–j**

1a-c, **3a**, **4a-c** $R^1 = CH_2CH{=}CH_2$, $R^2 = R^3 = H$, **a** $R^4 = CH_3$, **b** $R^4 = C_4H_9$, **c** $R^4 = C_6H_4OCH_3$-4;**1d**, **3b** $R^1 = R^3 = H$, $R^2 = C_6H_{13}$, $R^4 = C_6H_4OCH_3$-4; **1e-j**, **3c**, **4d-g** $R^1 = R^2 = R^3 = H$, **1e** $R^4 = C_4H_9$, **1f** $R^4 = C_6H_4OCH_3$-4, **1g**, **4d** $R^4 = C_6H_5$, **1h**, **4e** $R^4 = C_6H_4(OCH_3)_2$-4, **1i**, **4f** $R^3 = R^4 = CH_3$, **1j**, **4g** $R^3{+}R^4 = (CH_2)_8$

The synthesis of 3-alkyl derivatives of tetrahydropyrandione was effected using as an example α-allylacetoacetic ester **3a**, which was readily obtained from allyl bromide and acetoacetic ester **3c** in the presence of sodium methylate [20]. By condensing ester **3a** with acetaldehyde **4a**, butyraldehyde **4b**, and 4-methoxybenzaldehyde **4c**, the corresponding 3,6-disubstituted tetrahydropyrandiones **1a-c** were synthesized. The 5-alkyl derivative of tetrahydropyrandione **1d** was synthesized from aldehyde **4c** and octanoylacetic acid ester **3b**, the product of methanolysis of the octanoyl derivative of Meldrum's acid [14,21]. This is formed in quantitative yield under mild conditions from the readily available Meldrum's acid and octanoyl chloride. In addition, by the interaction of acetoacetic ester **3c** with aldehydes **4b,c**, benzaldehyde **4d**, 3,4-dimethoxybenzaldehyde **4e**, and acetone **4f**, the products **1e-j** respectively were obtained containing no substituent in positions 3 and 5. The use of cyclononanone **4g** in this reaction leads to the spiro compound **1j**. The yields of products **1** and their physicochemical properties are given in Table 1.

As might have been expected, the steric obstacles caused by the alkyl substituent in ester **3d** introduced a certain contribution to the fall in yield of the 5-hexyl derivative **1d**, which was isolated only as the *trans* isomer. The presence of an allyl substituent in ester **3a** and the structure of carbonyl compounds **4a-c** did not significantly influence the yield of the desired products.

The tetrahydropyrandiones **1**, according to data of ^{1}H NMR spectra, are predominantly in the dioxo form, though exchange of protons in position 3 by deuterium occurs in CD_3OD solution due to enolization. For a more precise assignment of the proton signals of the two tautomers of compound **1** we obtained derivatives of the enol form, certain of them being the substituted dihydropyrones **5** and **6** (see Scheme 3). The physicochemical properties of products **5** and **6** are given in Table 2.

TABLE 1. Characteristics of Alkyl(aryl)pyrane-2,4-diones

Compound	Name	Empirical formula	Found, % / Calculated, % C	Found, % / Calculated, % H	mp. °C (ether)	IR spectrum*, ν, cm^{-1}	Solvent	^{1}H NMR spectrum, δ, ppm, CC (*J*), Hz	Yield, %
1	2	3	4	5	6	7	8	9	10
1a	3-Allyl-6-methyltetrahydro-pyrane-2,4-dione	$C_9H_{12}O_3$	64.08 / 64.27	7.09 / 7.19	96-97		$CDCl_3$	1.45 (3H, d, ^3J = 6.5, CH_3); 2.35-2.77 (4H, m, CH_2CH= and $CHCH_2CO$); 3.54 (1H, t, ^2J = 6.0, $CHCH_2C$=); 4.52 (1H, m, $CHCH_3$); 5.10 (2H, m, $=CH_2$); 5.90 (1H, m, =CH)	77
1b	3-Allyl-6-butyltetrahydro-pyrane-2,4-dione	$C_{12}H_{18}O_3$	68.68 / 68.55	8.65 / 8.63	126-128	755, 800,875, 915, 930, 1000, 1135, 1165, 1220, 1270, 1320, 1360, 1380, 1595, 2640, 2960	$CDCl_3$	0.94 (3H, t, ^3J = 7.0, CH_3); 1.20-1.50 (4H, m, $CH_3(CH_2)_2$); 1.60-1.75 (2H, m, $OCHCH_2CH_2$); 2.32-2.83 (4H, m, $=CHCH_2$ and $OCHCH_2$); 3.55 (1H, t, ^3J = 6.0, $CHCH_2$); 4.70 (1H, m, CHO); 5.03-5.22 (2H, m, $=CH_2$); 5.92 (1H, m, =CH)	71
1c	3-Allyl-6-(4-methoxy-phenyl)tetrahydropyrane-2,4-dione	$C_{15}H_{16}O_4$	69.08 / 69.22	6.12 / 6.20	156-158	735, 920, 1010, 1040, 1080, 1130, 1180, 1255, 1305, 1390, 1525, 1615 br.	$CDCl_3$ + CD_3OD	2.63 (1H, dd, ^3J = 12.5, ^2J = 17.0, $CHCH_AH_BCO$); 2.92 (1H, dd, ^3J = 12.5, ^2J = 17.0, $CHCH_AH_B$); 3.09 (2H, dd, ^3J = 6.0, 1.0, $=CHCH_2$); 3.34 (1H, t, ^3J = 1.0, $CHCH_2CH$=); 3.82 (3H, s, OCH_3); 5.00 (2H, m, $=CH_2$); 5.38 (1H, dd, ^3J = 4.0, 12.0, ArCH); 5.90 (1H, m, =CH); 6.93 and 7.37 (2H and 2H, two d, ^3J = 8.9, *o*- and *m*-H_{Ar})	82
1d	*trans*-5-Hexyl-6-(4-methoxyphenyl)-tetrahydropyrane-2,4-dione	$C_{18}H_{24}O_4$	70.92 / 71.03	7.96 / 7.95	86-87	840, 900, 1040, 1190, 1220, 1265, 1525, 1595, 1665, 2865, 2935	$CDCl_3$	0.86 (3H, t, ^3J = 6.0, CH_3CH_2); 1.20 (10H, m, $CH_3(CH_2)_5$); 2.73 (1H, m, $CHCH_2$); 3.40 (1H, d, ^2J = 19, $CH_AH_BCO_2$); 3.58 (1H, d, ^2J = 19.0, $CH_AH_BCO_2$); 3.84 (3H, s, OCH_3); 5.37 (1H, d, ^3J = 7.8, ArCH); 6.93 and 7.15 (2H and 2H, two d, ^3J = 8.5, *o*- and *m*-H_{Ar})	38
1e	6-Butyltetrahydropyrane-2,4-dione	$C_9H_{14}O_3$	63.60 / 63.51	8.31 / 8.29	Oil	1230, 1405, 1455, 1640, 2890, 2960	$CDCl_3$	0.95 (3H, t, ^3J = 7.0, CH_3); 1.20-1.90 (6H, m, 6-$(CH_2)_3$); 2.30 (1H, dd, ^3J = 4.0, ^2J = 17.0, 5-H_A); 2.46 (1H, dd, ^3J = 12.0, ^2J = 17.0, 5-H_B); 3.75 (2H, s, 3-H_2); 4.30 (1H, m, 6-H)	76

TABLE 1 (continued)

1	2	3	4	5	6	7	8	9	10
1f	6-(4-Methoxyphenyl)-tetrahydropyrane-2,4-dione	$C_{12}H_{12}O_4$	65.65 65.45	5.52 8.29	131-132	830, 920, 955, 1010, 1040, 1070, 1180, 1260, 1295, 1350, 1525, 1620, 1720, 1740 br.	$CDCl_3$ $CDCl_3$ + CD_3OD	2.92 (2H, d, ^3J = 8.5, CHC$\underline{H}_2$); 3.50 (1H, d, ^2J = 20.0, CH$_A\underline{H}_B$CO$_2$); 3.70 (1H, d, ^2J = 20.0, C$\underline{H}_A$H$_B$CO$_2$); 3.84 (3H, s, C$\underline{H}_3$); 5.67 (1H, t, ^3J = 7.0, ArC$\underline{H}$); 6.95 and 7.17 (2H and 2H, two d, ^3J = 8.5, *o*- and *m*-H_{Ar}) 2.57 (1H, dd, ^2J = 17.5, ^3J = 4.0, CHCH$_A\underline{H}_B$); 2.84 (1H, dd, ^2J = 17.5, ^3J = 12.0, CHC$\underline{H}_A$H$_B$); 3.37 (less than 2H due to exchange of D, s, C$\underline{H}_2$CO$_2$); 3.84 (3H, s, CH$_3$); 5.40 (1H, dd, ^3J = 4.0, 12.0, ArC$\underline{H}$); 6.93 and 7.35 (2H and 2H, two d, ^3J = 8.5, *o*- and *m*-H_{Ar})	82
1g	6-Phenyltetrahydropyrane-2,4-dione	$C_{11}H_{10}O_3$	69.62 69.46	5.30 5.30	132-134 [15]	1250, 1310, 1345, 1635, 1715, 1735	$CDCl_3$ + CD_3OD	2.36 (1H, dd, ^3J = 4.5, ^2J = 17.0, CHCH$_A\underline{H}_B$); 2.59 (1H, dd, ^3J = 12.0, ^2J = 17.0, CHC$\underline{H}_A$H$_B$); 3.09 (2H, s, C$\underline{H}_2$CO$_2$); 5.20 (1H, dd, ^3J = 4.5, ^2J = 12.0, PhC$\underline{H}$); 7.14 (5H, m)	87
1h	6-(2,4-Dimethoxyphenyl)-tetrahydropyrane-2,4-dione	$C_{13}H_{14}O_5$	62.45 62.39	5.65 5.64	Oil	660, 675, 740, 775, 820, 860, 1030, 1140, 1270, 1470, 1525, 1595, 1710, 1740	$CDCl_3$	2.76 (1H, dd, ^2J = 17.0, ^3J = 4.5, CHCH$_A\underline{H}_B$); 2.91 (1H, dd, ^2J = 17.0, ^3J = 12.0, CHC$\underline{H}_A$H$_B$); 3.40 (2H, s, C$\underline{H}_2$CO$_2$); 3.84 and 3.80 (6H, two s, two CH$_3$); 5.00 (1H, dd, ^3J = 4.0, 8.5, ArC$\underline{H}$); 5.84 (1H, s, 2'-H); 6.75 (2H, two s, 5'- and 6'-H)	77
1i	6,6-Dimethyltetrahydro-pyrane-2,4-dione	$C_7H_{10}O_3$	59.10 59.14	7.06 7.09	127-128	1020, 1115, 1190, 1210, 1245, 1290, 1330, 1355, 1580, 1660	CD_3OD	1.53 and 1.48 (6H, two s, two CH$_3$); 2.47 (1H, s, (CH$_3$)$_2$CCH$_A\underline{H}_B$); 2.72 (1H, s, (CH$_3$)$_2$CC$\underline{H}_A$H$_B$)*[2]	84
1j	1-Oxaspiro[5,8]tetradecane-2,4-dione	$C_{13}H_{20}O_3$	69.50 69.61	9.00 8.99	120-122	860, 1000, 1030, 1220, 1265, 1320, 1480, 1610, 1675, 2930	$CDCl_3$	1.35-1.85 (14H, m, 7 CH$_2$); 2.13 (2H, m, CC$\underline{H}_2$CH$_2$); 2,70 (2H, s, CCH$_2$CO); 3.43 (2H, s, C$\underline{H}_2$CO$_2$)	75

* The spectra of compounds **1e** and **1h** were taken with a film of substance, the remainder in KBr disks.

*[2] The signal of the protons of the CH_2CO_2 grouping is not observed due to exchange of these protons with deuterium.

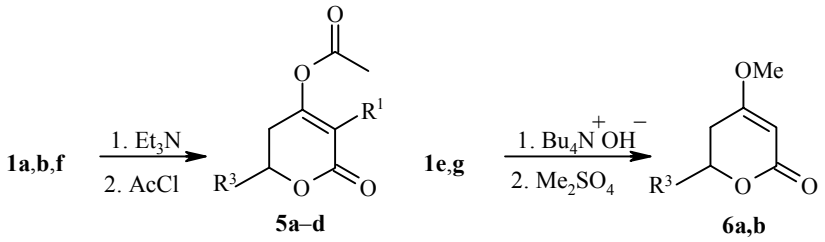
TABLE 2. Characteristics of Derivatives of the Enol Forms of Alkyl(aryl)pyrane-2,4-diones*

Compound	Name	Empirical formula	Found, % / Calculated, % C	Found, % / Calculated, % H	IR spectrum, ν, cm^{-1}	^{1}H NMR spectrum, δ, ppm, CC (*J*), Hz*2	Yield, %
5a	4-Acetoxy-3-allyl-6-methyl-5,6-dihydro-2-pyrone	$C_{11}H_{14}O_4$	62.97 / 62.85	6.72 / 6.71		1.42 (3H, d, ^3J = 7.0, 6-CH_3); 2.20 (3H, s, C(O)C$\underline{H}_3$); 2.46 (1H, dd, ^2J = 11.5; ^3J = 4.0, CHC$H_A\underline{H}_B$); 2.66 (1H, dd, ^2J = 11.5, ^3J = 17.0, CHC$\underline{H}_AH_B$); 3.00 (2H, m, C$\underline{H}_2$CH=); 4.58 (1H, m, CH_3C$\underline{H}$); 5.00 (2H, m, =CH_2); 5.70 (1H, m, =CH)	94
5b	4-Acetoxy-3-allyl-6-(4-methoxyphenyl)-5,6-dihydro-2-pyrone	$C_{17}H_{18}O_5$	67.44 / 67.54	5.99 / 6.00	750, 825, 910, 930, 1015, 1040, 1075, 1130, 1205, 1255, 1290, 1315, 1330, 1380, 1430, 1470, 1525, 1600, 1625, 1650, 1690, 1730, 1765, 2820, 2870	2.21 (3H, s, C(O)CH_3); 2.62 (1H, dd, ^3J = 4.0, ^2J = 18.0, $CH_A\underline{H}_B$); 3.03 (3H, m, C$\underline{H}_AH_B$ and =CHC$\underline{H}_2$); 3.78 (3H, s, OCH_3); 5.02 (2H, m, =CH_2); 5.36 (1H, dd, ^3J = 4.0, 13.0, ArC$\underline{H}$); 5.76 (1H, m, =CH); 6.83 and 7.28 (2H and 2H, two d, ^3J = 8.5, *o*- and *m*-H_{Ar})	93
5c	4-Acetoxy-6-(4-methoxyphenyl)-5,6-dihydro-2-pyrone	$C_{14}H_{14}O_5$	64.18 / 64.12	5.39 / 5.38	915, 935, 970, 1160, 1185, 1205, 1260, 1290, 1310, 1385, 1435, 1470, 1525, 1625, 1670, 1720, 1775	2.26 (3H, s, C(O)CH_3); 2.64 (1H, dd, ^3J = 3.5, ^2J = 18.0, $CH_A\underline{H}_B$); 3.00 (1H, ddd, ^3J = 12.0, ^2J = 18.0, ^4J = 1.5, C$\underline{H}_AH_B$); 3.83 (3H, s, OCH_3); 5.45 (1H, dd, ^3J = 3.5, 12.0, ArC$\underline{H}$); 6.00 (1H, d, ^4J = 1.5, =C$\underline{H}$CO); 6.90 and 7.33 (2H and 2H, two d, ^3J = 8.5, *o*- and *m*-H_{Ar})	95
6a	6-Butyl-4-methoxy-5,6-dihydro-2-pyrone	$C_{10}H_{16}O_3$	65.04 / 65.19	8.74 / 8.75	745, 830, 880, 970, 1010, 1050, 1135, 1180, 1230, 1290, 1400, 1460 br., 1630, 1720, 2885, 2965	0.95 (3H, t, ^3J = 7.0, C$\underline{H}_3$CH$_2$); 1.20-1.95 (6H, m, CH_3(C$\underline{H}_2$)$_3$); 2.27 (1H, dd, ^2J = 17.0, ^3J = 4.0, $CH_A\underline{H}_B$); 2.46 (1H, ddd, ^2J = 17.0, ^3J = 12.0, ^4J = 1.5, C$\underline{H}_AH_B$); 3.75 (3H, s, OCH_3); 4.32 (1H, m, CH_2C$\underline{H}$); 5.07 (1H, d, ^4J = 1.5, =C$\underline{H}$)	94
6b	4-Methoxy-6-phenyl-5,6-dihydro-2-pyrone	$C_{12}H_{12}O_3$	70.47 / 70.58	5.91 / 5.92		2.67 (1H, dd, ^2J = 18.0, ^3J = 4.0, $CH_A\underline{H}_B$); 3.00 (1H, ddd, ^2J = 18.0, ^3J = 12.0, ^4J = 1.5, C$\underline{H}_AH_B$); 3.83 (3H, s, OCH_3); 6.03 (1H, d, ^4J = 1.5, OC=CH); 7.15 (5H, m, H_{Ph})	89

***** Compounds **5a-c, 6a** were oils, compound **6b** had mp 101-102°C (ether).

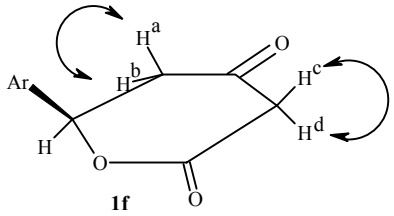
*2 The spectrum of compound **5c** was taken in a $CDCl_3$–CCl_4 mixture, the remainder in $CDCl_3$.

Scheme 3



5a $R^1 = CH_2CH{=}CH_2$, $R^3 = CH_3$; **b** $R^1 = CH_2CH{=}CH_2$, $R^3 = C_6H_4OCH_3$-4; **c** $R^1 = H$, $R^3 = C_6H_4OCH_3$-4; **6a** $R^3 = C_4H_9$; **b** $R^3 = C_6H_5$

The shape of the signals of the protons in positions 3 and 5 of compound **1** depends on the substituents in the ring and on the solvent (see Tables 1 and 3). The latter is probably explained by the change in dynamics of the conformational transitions on forming methanolic solvates.



Two racemic pairs of γ-hydroxy-β-oxo esters **2a-c** must formally be formed from the aldol condensation leading to the corresponding racemic pairs of tetrahydropyrandiones **1a-c** with two chiral atoms at $C_{(3)}$ and $C_{(6)}$. As a result of keto-enol tautomerism observed in the β-dicarbonyl fragment of diones **1** there is possibly a spontaneous change in configuration at atom $C_{(3)}$. The equilibrium of this reaction is displaced towards the thermodynamically most stable racemic pair (starting from general considerations the most preferred seem to be the isomers in which the alkyl substituents occupy equatorial positions).

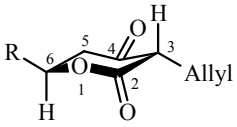
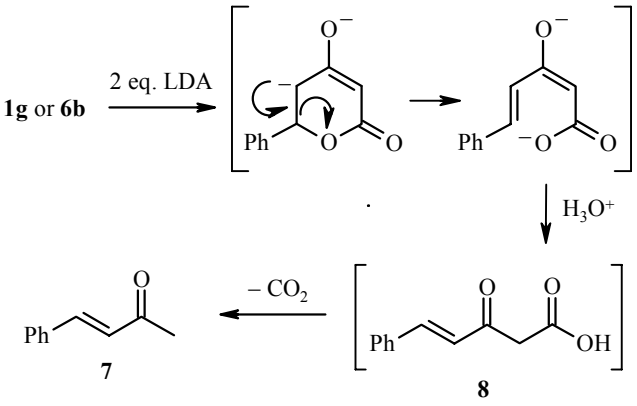


TABLE 3. Effect of Exchanging the Solvent on the Coupling Constants of the Protons at $C_{(3)}$ and $C_{(5)}$ in 6-(4-Methoxy)tetrahydropyran-2,4-dione **1f**

H	$CDCl_3$			$CDCl_3 + CD_3OD$		
	δ, ppm	shape of signal	J_{ab} or J_{cd}	δ, ppm.	shape of signal	J_{ab} or J_{cd}
a	2.92	d	~0	2.57	dd	17.5
b	2.92	d	~0	2.84	dd	17.5
c	3.50	d	19	3.37	s	~0
d	3.70	d	19	3.37	s	~0

In order to obtain 5-alkyl derivatives of tetrahydropyran-2,4-dione of the type of **1d** in good yield it was logical to apply an alternative method, *viz*. the alkylation of tetrahydropyran-2,4-dione **1g** dianion or the anion of its 4-methoxy derivative **6b**. However this reaction proceeded to benzylideneacetone in 80% yield (see Scheme 4). Probably destruction of the dianion leads to the formation of the unstable acid **8** clearly shown by TLC (like the hydroxy ester **2**, 3-oxoacid **8** was colored brown by the action of alcoholic $FeCl_3$ solution).

Scheme 4



EXPERIMENTAL

The ^{1}H NMR spectra were recorded on a Bruker AC spectrometer (operating frequency 200 MHz) in $CDCl_3$ and CD_3OD solution, internal standard was TMS. The IR spectra were recorded on a UR 20 spectrometer in KBr disks or as a film of compound. Melting points were determined on a Kofler block. Silufol UV 254 plates were used for TLC eluting with the following mixtures: chloroform–methanol [for pyrandiones **1** and 3,5-dioxo esters **2**; R_f (**1**)/R_f(**2**) approx. 4], ether–hexane (for enol acetates **5** and enol esters **6**). Column chromatography was carried out on silica gel 60 (70-230 μ), eluent was chloroform. The derivatives of acetoacetic ester **3** and carbonyl compounds **4** were redistilled before reaction. The spectral characteristics of benzylidenacetone **7** were identical to the literature data of [22].

Condensation of Esters of β-Oxo Carboxylic Acids 3 with Aldehydes and Ketones 4 (General Procedure). Ester **3** (0.01 mol) was added with stirring in an atmosphere of argon to a solution of lithium diisopropylamide (0.025 mol), obtained from butyllithium (0.025 mol), diisopropylamine (2.53 g, 0.025 mol), and hexamethylphosphoramide (1.63 g, 0.01 mol), in absolute tetrahydrofuran (50 ml) at -78°C. After 20 min the aldehyde or ketone **4** (0.012 mol) was added, the mixture stirred for 30 min, and treated with 2 N HCl (60 ml). The organic layer was separated, combined with ether extracts (2 × 100 ml) of the aqueous layer, and evaporated. The residue was dissolved in 1 N KOH (100 ml), the solution stirred for 5 h, cooled to 0°C, and cold aqueous 6 N HCl solution added to pH 0. Product **1** precipitated as a solid, was filtered off, and washed with cold water. An additional quantity of product **1** was obtained by extraction of the aqueous layer after separating product **1** with ether (2 × 100 ml), drying the extract with sodium sulfate, and evaporating the solvent. Column chromatography on silica gel (eluent chloroform) was used to isolate the 5-hexyl derivative **1d**. Analytical samples were obtained by recrystallization of the products from ether.

Acetylation of the Alkyl Derivatives of Tetrahydropyran-2,4-dione 1 (General Procedure). Triethylamine (1.4 ml, 0.01 mol) was added with stirring to tetrahydropyran-2,4-dione **1** (0.01 mol) in absolute dichloromethane (50 ml). After complete solution of dione **1**, acetyl chloride (0.78 ml, 0.01 mol) in dichloromethane (15 ml) was added dropwise. After 1 h the mixture was acidified with 0.2 N HCl (15 ml). The

organic layer was separated, washed with saturated NaCl solution (2 × 50 ml), dried with sodium sulfate, and evaporated. To remove contaminating starting materials the solid was applied to a small layer of Al_2O_3 and eluted with chloroform.

Synthesis of 4-Methoxy-5,6-dihydro-2-pyrones 6 (General Procedure). Calcined finely ground potassium carbonate (2.76 g, 0.02 mol) and dimethyl sulfate (1.39 g, 0.011 mol) were added to a solution of the appropriate tetrahydropyran-2,4-dione **1** (0.01 mol) in acetone. The mixture was boiled for about 4 h, after which the solid inorganic salt was filtered off, and washed thoroughly with acetone. The washings were combined with the filtrate. After evaporating the acetone the residue was recrystallized from ether.

REFERENCES

1. E. F. Steinmetz, *Piper methysticum (Kava), Famous Drug Plant of the South Sea Islands*, Elsevier, Amsterdam (1960).
2. W. B. Morc, M. T. Magalhaes, and O. R. Gottlieb in L. Zechmeister (editor), *Progress in the Chemistry of Organic Natural Products*, Vol. 20, Springer-Verlag, Berlin (1962).
3. B. Eistert and G. Heck, *Justus Liebigs Ann. Chem.*, **681**, 123 (1965).
4. R. M. Carlson, A. R. Oyler, and J. R. Peterson, *J. Org. Chem.*, **40**, 1610 (1975).
5. A. A. Akhrem, F. A. Lakhvich, L. G. Lis, V. A. Khripach, N. A. Fil'genkov, V. A. Kozinets, and F. S. Pashkovskii, *Dokl. Akad. Nauk SSSR*, **311**, 1381 (1990).
6. J. M. McIntosh and P. M. Beaumier, *Can. J. Chem.*, **51**, 843 (1979).
7. H. Stetter and W. Dierichs, *Chem. Ber.*, **85**, 1061 (1952).
8. H. O. House, *Modern Synthetic Reactions*, Benjamin, New York (1972). p. 511.
9. D. N. Kursanov, Z. N. Parnes, M. I. Kalinkin, and N. M. Loim, *Ionic Hydrogenation* [in Russian], Khimiya, Moscow (1979), p. 192.
10. M. W. Rathke and J. Deitch, *Tetrahedron Lett.*, 2953 (1971).
11. I. Shahak and Y. Sasson, *Tetrahedron Lett.*, 4207 (1973).
12. R. M. Carlson and J. L. Isidor, *Tetrahedron Lett.*, 4819 (1973).
13. S. N. Huckin and L. Weiler, *Tetrahedron Lett.*, 1082 (1974).
14. M. Sato, J. Sakaki, K. Takayama, S. Kobayashi, M. Suzuki, and C. Kaneko, *Chem. Pharm. Bull.*, **38**, 94 (1990).
15. J. R. Petersen, T. J. Winter, and C. P. Miller, *Synth. Commun.*, **18**, 949 (1988).
16. I. Paterson, D. J. Wallace, and C. J. Cowden, *Synthesis*, 639 (1998).
17. D. Seebach and K. Meyer, *Angew. Chem.*, **86**, 40 (1974).
18. T. Reffstrup and P. M. Boll, *Acta Chem. Scand.*, **B30**, 613 (1976).
19. J. F. Wolfe, T. M. Harris, and C. R. Hauser, *J. Org. Chem.*, **29**, 3249 (1964).
20. *Organicum* [Russian translation], Vol. 2, Mir, Moscow (1979), p. 176.
21. M. Sato, H. Ogasawara, K. Oi, and T. Kato, *Chem. Pharm. Bull.*, **31**, 1896 (1983).
22. C. Pouchert, *Alrich Library of NMR Spectra,* Ed. 2, Vol. 2, Aldrich Chem. Co. Inc. (1983), p. 53D; *Aldrich Library of IR Spectra*, Ed. 3, Aldrich Chem. Co. Inc. (1981), p. 852D.