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6-ALKYL AND 5,6-DIALKYL-2-METHOXY-4(3H)-PYRIMIDINONES IN THE TRANSFORMATIONS OF PYRIMIDINES—2†

SYNTHESIS AND CONVERSION INTO ALKYLURACILS AND 2-ALKOXY-4(3H)-PYRIMIDINONES‡

M. BOTTA*, M. CAVALIERI, D. CECI, F. DE ANGELIS, G. FINIZIA and R. NICOLETTI*
Department of Chemistry, University "La Sapienza", P. le A. Moro 5,00185, Rome, Italy

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Abstract—The synthesis of 6-alkyl and 5,6-dialkyl-2-methoxy-4(3H)-pyrimidinones **3** is described. Their versatility to be transformed into 6-alkyl and 5,6-dialkyluracils **4(a–h)**, 6-alkyl and 5,6-dialkyl-3-methyluracils **7(a,e,f)** and 6-alkyl and 5,6-dialkyl-2-alkoxy-4(3H)-pyrimidinones **5(a–i)** is also shown.

In connection with an analytical study on biological materials, we needed some pyrimidines and uracils for comparison purposes. A review of the literature showed that several synthetic routes are described for these important biological active materials.[1]

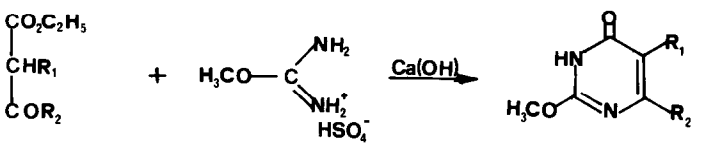
One of the most reliable synthesis of pyrimidine derivatives (e.g. uracils, isocytosines), involves the condensation of thiourea or alkylisothioureas with β-ketoesters.[2–4] However, the subsequent removal of the S atom, in order to obtain uracils, is not always a simple step, involving severe conditions.[5] Similarly, the substitution of the thioalkyl group, affording substituted pyrimidines, is not very useful owing to the extreme difficulties found in removing this group from the pyrimidine nucleus.[6] For this reason uracils are always used as starting materials for the synthesis of substituted pyrimidines.

The direct condensation of urea with β-ketoesters is described only for the synthesis of 6-methyluracil[7] and, actually, it failed in our hands when ethyl-β-ketovalerate was used instead of ethyl acetoacetate.

We have found that O-methylisourea smoothly reacts with β-ketoesters in H_2O/EtOH solution to afford the 6-alkyl and 5,6-dialkyl-2-methoxy-4(3H)-pyrimidinones **3** which in turn can be hydrolyzed, in acidic medium, to the corresponding alkyluracils **4(a–h)** in very good yields (Scheme 1).

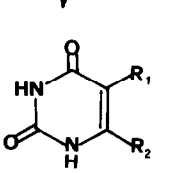
There are no records in the literature prior to our communication[8] of the use of O-methylisourea in the synthesis of uracils. Only Reese reported the use of this urea-derivative (whose bisulfate is commercially available) as a condensing agent in the synthesis of a 5,6-dihydropyrimidine.[9]

Synthesis of 6 - *alkyl and* 5,6 - *dialkyl* - 2 - *methoxy* - 4(3*H*) - *pyrimidinones and conversion into* 6 - *alkyl and* 5,6 - *dialkyluracils*. The appropriate β-ketoester **1(a–h)** reacts slowly with O-methylisourea generated *in situ* from its bisulfate **2** by adding an excess of



1[a–h] 2 3[a–h]

compd	R_1	R_2
1,3,4 a	H	CH_3
b	H	C_2H_5
c	H	n-C_5H_{11}
d	H	c-C_6H_{11}
e	CH_3	CH_3
f	$-CH_2(CH_2)_2CH_2-$	
g	$-CH_2CH=CH_2$	CH_3
h	n-C_8H_{17}	CH_3



4[a–h]

Scheme 1.

†See Ref. 17.

‡Work presented in part at the ESOC III, Canterbury, England, 5–9 Sept. 1983.

Table 1. Synthesis of 6-alkyl and 5,6-dialkyl-2-methoxy-4(3H)-pyrimidinones **3(a,b,e,f)** and of 6-alkyl and 5,6-dialkyl-uracils **4(a–h)**

compd	R_1	R_2	Reaction Conditions					Yield % 3	Overall Yield % 4	m.p.°C 3 (solv.)	m.p.°C 4 (solv.)	(rep.)
			solv.	condensation time (h.)	condensation temp. °C	hydrolysis time (h.)	hydrolysis temp. °C					
3,4 a	H	CH_3	H_2O	24	r.t.	12	70	95	79	207 (EtOH)	300dec. (AcOH)	300dec.[7]
3,4 b	H	C_2H_5	H_2O/EtOH 1:1	48	40	24	70	70	66	210 (EtOH)	310dec. (AcOH)	204-5[21]
4 c	H	n-C_5H_{11}	H_2O/EtOH 1:1	72	40	48	70		65		280dec. (AcOH)	171-2[22]
4 d	H	c-C_6H_{11}	H_2O/EtOH 1:1	96	40	48	85		62		286-7 (H_2O-EtOH)	286-7[23]
3,4 e	CH_3	CH_3	H_2O/EtOH 5:1	72	r.t.	48	70	78	60	198 (EtOH)	300dec. (H_2O)	296dec.[24]
3,4 f	$-CH_2(CH_2)_2CH_2-$		H_2O/EtOH 5:1	72	40	48	70	72	70	215 ($CHCl_3$)	295-7 (EtOH)	295-7[25]
4 g	$-CH_2CH=CH_2$	CH_3	H_2O/EtOH 1:1	48	40	24	70		54		230dec. (EtOH)	130-2[26]
4 h	n-C_8H_{17}	CH_3	H_2O/EtOH	72	40	24	70		42		159-160 ($CHCl_3$-n-hexane)	

$Ca(OH)_2$ in water or water–ethanol solution. A slightly basic medium is necessary for the condensation and the ethanol content must be choosen according to the solubility of β-ketoesters. Filtration of the reaction mixture and solvent removal *in vacuo* gave the 12-methoxy-4(3H)-pyrimidinones **3** as crystalline materials.

Not commercially available β-ketoesters **1b** and **1c** were prepared following the Weiler procedure[10] *via* the dianion of ethyl acetoacetate, **1d** through decarboxylation of ethyl, t-buthyl-hexa-hydrobenzylacetate,[11] while **1g** and **1h** were prepared by alkylation of ethyl acetoacetate in the presence of sodium ethoxide.[12]

The 6-alkyl and 5,6 - dialkyl - 2 - methoxy - 4(3H)-pyrimidinones **3** can be easily hydrolyzed to the corresponding uracils **4(a–h)** in very good yields (Table 1).

Isolation of **3** was not necessary in the case that uracils are the desired products. The reaction mixtures were acidified with 2N H_2SO_4 at pH = 2 as soon as the condensation was complete and then were heated for additional 14–18 hr, according to the nature of the substrate, at 70–80°. Uracils **4(a–h)** were obtained by filtration of the inorganic salts and solvent removal *in vacuo*.

This condensation did not show any appreciable limitation, with the possible exception of aroylacetates. Actually no reaction was observed in the conditions reported when ethyl benzoylacetate was used.

Physical properties of the uracils **4(a–h)** and the relative overall yields are reported in Table 1: for the sake of comparison, some literature data are reported.

In three instances, the m.ps found are higher than those reported in the literature; therefore, for uracils **4b,4c,4g** some considerations are necessary. **4b** has been synthetized by us through an independent route following the condensation method of Fulkuda[13] and we have found for it the same m.p. alone or in a mixture with a sample prepared with the method here described. The reported m.p. of **4g** (130–2°)[26] appears to be very low for a quite simple uracil derivative. In addition, it is claimed that it crystallized from petroleum ether. Such unusual properties strongly suggest that the reported structure is not correct. The difference in the m.p. of **4c** can be justified by a different purity of the samples. Incidentally, the m.p. here reported appears more coherent as compared to those of the other uracils.

The 2-methoxy-4(3H)-pyrimidinones **3(a,b,e,f)** have been isolated and in Table 1 their physical properties and yields are reported.

The pyrimidinones are formulated as 4(3H)-pyrimidinones: however their structures could correspond to 4(1H)-pyrimidinones. In view of the tautomeric equilibrium between these two structures, this aspect has not been considered.

The easy access to the substituted 2-methoxypyrimidinones like **3** prompted us to study a possible use of these compounds as starting materials for the preparation of other pyrimidines.

It is well known, in fact, that the 2,4-dimethoxypyrimidines are used in the synthesis of N(1)-pyrimidine-bases (e.g. uridine, thimidine),[14] and, in general, methoxyls are introduced as good leaving groups, in view of further transformations.[15] Nevertheless, to the best of our knowledge, a straightforward route to obtain 2-methoxypyrimidinones like **3** has not already been reported. The reported methylation of uracils *via* chlorination–methoxylation[16] always affords mixtures of 2- or 4- or 2,4-dimethoxypyrimidinones.

Therefore, we focused our attention towards selective substitutions at C-2 and C-4 atoms suffered by substrates **3(a,e,f)**.

We have already published[17] the transformation of the 2-methoxy-4(3H)-pyrimidinones **3(a,e,f)**, operated by the conjugate base of an (aryl) alkylamine, and also the selective chlorination at C(4) with the Vilsmeier complex.[18]

We wish to report here some other possible uses of the substrates **3** (Scheme **2**).

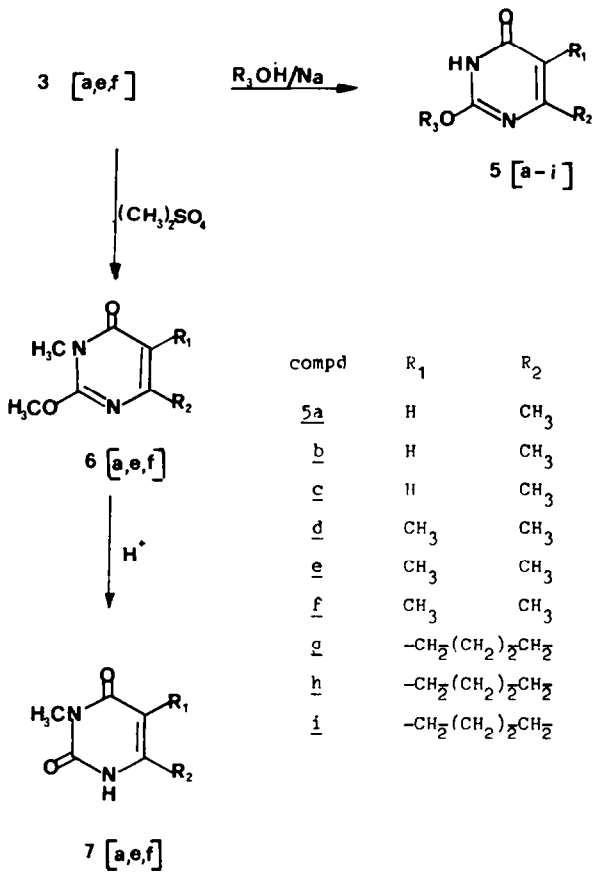
Synthesis of 6-alkyl and 5,6-dialkyl-2-alkoxy-4(3H)-pyrimidinones. 6-alkyl and 5,6 - dialkyl - 2 - methoxy - 4(3H) - pyrimidinones **3(a,e,f)** can be transformed into various 2-alkoxy-4(3H)-pyrimidinones **5(a–i)** (Scheme 2). They react with an excess of primary and secondary alkoxides in alcoholic solution; the substitution products could be isolated in excellent yields.[19] Nine examples employing three different substrates are given in Table 2.

Such alkoxides exchanges at pyrimidinone nucleus have not been previously reported.

The literature preparation of these 2-alkoxy deriv-

Table 2. Synthesis of 6-alkyl and 5,6-dialkyl-2-alkoxy-4(3H)-pyrimidinones **5(a–i)**

compd.	R_1	R_2	R_4	yield%	m.p.°C	reaction time (hr)
5a	H	CH_3	C_2H_5	85	197–9	48
5b	H	CH_3	n-C_4H_9	77	87–8	70
5c	H	CH_3	c-C_6H_{11}	81	103–5	24
5d	CH_3	CH_3	C_2H_5	92	129–131	50
5e	CH_3	CH_3	n-C_4H_9	87	99–101	70
5f	CH_3	CH_3	c-C_6H_{11}	70	163–5	36
5g	$-CH_2(CH_2)_2CH_2-$		C_2H_5	84	160–1	120
5h	$-CH_2(CH_2)_2CH_2-$		n-C_4H_9	87	115–7	50
5i	$-CH_2(CH_2)_2CH_2-$		c-C_6H_{11}	73	150–2	24



compd	R_1	R_2	R_3
5a	H	CH_3	C_2H_5
b	H	CH_3	n-C_4H_9
c	H	CH_3	c-C_6H_{11}
d	CH_3	CH_3	C_2H_5
e	CH_3	CH_3	n-C_4H_9
f	CH_3	CH_3	c-C_6H_{11}
g	$-CH_2(CH_2)_2CH_2$		C_2H_5
h	$-CH_2(CH_2)_2CH_2$		n-C_4H_9
i	$-CH_2(CH_2)_2CH_2$		c-C_6H_{11}

Scheme 2.

atives are based on the direct condensation of O-alkylisoureas (which are not easily obtainable) with ethyl acetoacetate,[3] and there is also an example of substitution of a thiomethyl group with n-butanol in the presence of $HgCl_2$.[6]

The reaction here described gives an easy access to a broad variety of 2 - alkoxy - 4(3H) - pyrimidinones without problems of selectivity between the two oxygens like those encountered starting from uracils by oxygen-halogen exchange.[16]

Synthesis of 6-alkyl and 5,6-dialkyl-3-methyluracils. Finally we tried some selective alkylation at N(3) and C(4) atoms. These experiments were not successful since we obtained, under several conditions, mixtures of N(3) and O(4)-alkyl derivatives. However, the alkylation of **3(a,e,f)** with dimethyl sulfate in alkaline solution gave the 3-methyl derivatives as the sole product (Scheme 2). From them it was possible to obtain, by mild hydrolysis (see experimental), the 6-alkyl and 5,6-dialkyl-3-methyluracils **7(a,e,f)** in very good yields (see Table 3).

This method appears to be superior to others described in the patent literature for the preparation of 3-methyluracils.[20]

EXPERIMENTAL

M.ps are uncorrected. IR spectra were recorded on Perkin–Elmer 257 and 298 instruments, with CCl_4, $CHCl_3$ or Nujol as solvents, or in KBr pellets. NMR spectra were determined at 60 MHz on a Varian EM 360 A instrument ($CDCl_3$, Py-d_5 and DMSO-d_6 as solvents, and TMS as internal standard were used). Mass spectra were recorded at 70 eV on an AEI MS 12 spectrometer.

Preparative and analytical TLC were performed on precoated Merck Kieselgel 60 F_{254} plates. Revelation was performed with UV light. Column chromatography was performed using Merck Kieselgel 60 (70–230 mesh ASTM).

Table 3. Synthesis of 6-alkyl and 5,6 - dialkyl - 2 - methoxy - 3 - methyl - 4 - pyrimidinones **6(a,e,f)**, and of 6-alkyl and 5,6-dialkyl-3-methyluracils **7(a,e,f)**

compd.	R_1	R_2	yield% 6	yield% 7 (a)	m.p.°C 7	reported m.p.°C 7
6,7 a	H	CH_3	99	100	262–3	262[2]
6,7 e	CH_3	CH_3	78	70	220–1	220[2]
6,7 f	$-CH_2(CH_2)_2CH_2$		72	68	225–6	

(a) hydrolysis from 6 to 7.

Table 4.

compd	MS[a] m/z	IR (cm^{-1}) (Nujol) ν C=O	IR (cm^{-1}) (Nujol) δ C=N[b]	^{1}H NMR δ ($CDCl_3$)
3a	140	1660	1610	5,83(1H,s,C_5H);3,90(3H,s,+OCH_3); 2,14(3H,s,C_6CH_3).
3b	154	1650	1600[d]	6,03(1H,s,C_5H);4,00(3H,s,-OCH_3); 2,5-2,3(2H,q,-CH_2CH_3,J=6Hz);1,3-1,1(3H,t,-CH_2CH_3,J=6Hz).
3e	154	1660	1610	3,90(3H,s,-OCH_3);2,23(3H,s,C_5CH_3); 2,00(3H,s,C_6CH_3).
3f	180	1650	1610	(c) 3,87(3H,s,-OCH_3);3,3-3,2(1H,bs, -NH-);2,5-2,2(4H,m,-$(CH_2)_2$);1,8-1,6(4H,m,-$(CH_2)_2$).

[a] 70 eV,150°C,direct injection. [b] C=N cyclic conjugated sistem. [c] NMR spectrum performed in DMSO-d_6. [d] IR spectrum performed in KBr.

Elemental Analyses for compounds 3(a,b,e,f)

compd		Found %			Required %		
		C	H	N	C	H	N
3a	$C_6H_8N_2O_2$	51,40	5,78	20,01	51,42	5,75	19,99
3b	$C_7H_{10}N_2O_2$	54,54	6,54	18,20	54,53	6,54	18,17
3e	$C_7H_{10}N_2O_2$	54,50	6,56	18,18	54,53	6,54	18,17
3f	$C_9H_{12}N_2O_2$	59,97	6,73	15,56	59,98	6,71	15,55

Table 5.

compd	MS[a] m/z	IR (cm^{-1}) (KBr) ν NH	IR (cm^{-1}) (KBr) ν C=O	^{1}H NMR δ ($Py-d_5$)
4a	126		1730,1660	5,85(1H,s,C_5H);2,30(3H,s,C_6CH_3).
4b	140		1730,1670	5,57(1H,s,C_5H);2,5-2,2(2H,q,-CH_2CH_3, J=6Hz);1,2-1,0(3H,t,-CH_2CH_3,J=6Hz).
4c	182	3420	1740,1670	5,60(1H,s,C_5H);2,4-2,2(2H,t,C_6CH_2,J= 7Hz);1,3-1,1(9H,m,-$(CH_2)_3CH_3$).
4d	194		1740,1650	5,65(1H,s,C_5H);1,9-1,1(11H,m,c-C_6H_{11}).
4e	140	3420	1720,1670[b]	2,05(3H,s,C_5CH_3);1,95(3H,s,C_6CH_3).
4f	166		1720,1650	2,4-2,2(4H,m,-$(CH_2)_2$);1,6-1,4(4H,m, -$(CH_2)_2$).
4g	166	3400	1730,1670[b]	5,2-4,9(3H,m,-$CH=CH_2$);3,3-3,1(2H,d, -$CH_2CH=CH_2$,J=6Hz);2,12(3H,s,C_6CH_3).
4h	238	3400	1730,1670[b]	(c) 4,1-3,9(2H,t,-$CH_2(CH_2)_6CH_3$,J=6Hz); 2,28(3H,s,C_6CH_3);1,4-1,0(12H,m,-$CH_2(CH_2)_6CH_3$);0,9-0,8(3H,m,-$(CH_2)_7CH_3$).

[a] 70 eV,150°C,direct injection. [b] IR spectrum performed in $CHCl_3$. [c] NMR spectrum performed in $Py-d_5$+$CDCl_3$.

Elemental Analysis for 4h, $C_{13}H_{22}N_2O_2$: found % C=65,44;H=9,29;N=11,78. Required %:C=65,41;H=9,31;N=11,76.

Elemental analyses were kindly furnished by ACRAF laboratories, Rome, Italy.

Anhydrous alcohols were prepared by distillation from sodium.

General procedure for the synthesis of 6-alkyl and 5,6 - dialkyl - 2 - methoxy - 4(3H) - pyrimidinones **3(a,b,e,f)**. In a typical experiment, 1 mol of O-methylisourea bisulfate and 1,1 mol of $Ca(OH)_2$ (basic pH) were dissolved in water under vigorous stirring, then 1 mol of the appropriate β-ketoester and ethanol were added. The H_2O/EtOH ratio depends on the alkyl groups R_1 and R_2 (Table 1). When the reaction was finished (TLC analysis: $CHCl_3$–MeOH = 9:1), the reaction mixture was filtered, the solid phase was washed twice with EtOH, then the combined solvents were evaporated *in vacuo*. The residue was crystallized from $CHCl_3$ or EtOH, as shown in Table 1. Spectroscopic data are given in Table 4.

One flask synthesis of 6-alkyl and 5,6-dialkyluracils **4(a–h)**. 1 mol of **1(a–h)** was added to a stirred mixture of O-methylisourea bisulfate (1 mol) and $Ca(OH)_2$ (1,1 mol) in the appropriate solvent (Table 1). The mixture was stirred at the temp shown in Table 1 until TLC analysis ($CHCl_3$/MeOH = 9/1) indicated the absence of the β-ketoester. The mixture was then acidified to pH = 2 with 2N H_2SO_4 and stirred at 70°. When the reaction was finished, mixture was filtered and the solvents were evaporated *in vacuo*, affording the crystalline compounds **4(a–h)**.

Spectroscopic data are given in Table 5.

Synthesis of 6-alkyl and 5,6-dialkyl - 2 - alkoxy - 4(3H) - pyrimidinones **5(a–i)**. 25 ml of anhyd alcohol and 400 mg of Na were mixed and warmed, under vigorous stirring. When the Na was completely dissolved, 500 mg of 6-alkyl or 5,6-dialkyl 2 methoxy - 4(3H) - pyrimidinone were added and the mixture was refluxed until the substrate disappeared (TLC analysis: $CHCl_3$–MeOH = 9:1). The mixture was then diluted with $CHCl_3$, neutralized with 2N HCl, and extracted with $CHCl_3$. The organic layer was dried over Na_2SO_4 and the solvent was evaporated *in vacuo*. The residue was purified over preparative TLC, then crystallized from *n*-hexane or $CHCl_3$ as shown in Table 2. Spectroscopic data are given in Table 6.

Synthesis of 6-alkyl and 5,6-dialkyl-3-methyluracils **7(a,e,f)**. 500 mg of 6-alkyl or 5,6 - dialkyl - 2 - methoxy - 4 (3H) - pyrimidinone were dissolved in 5 ml of NaOH 5%;

Table 6.

compd	MS[a] m/z	IR (cm^{-1}) ($CHCl_3$) νNH	νC=O	^{1}H NMR ($CDCl_3$) δ
7a	154	3400	1660	5,90(1H,s,C_5H);4,6-4,2(2H,q,-O-$\underline{CH_2}CH_3$,J=6Hz);3,6-3,5(1H,bs,-NH-);2,20(3H,s,C_6CH_3);1,5-1,3(3H,t,-O-$CH_2\underline{CH_3}$,J=6Hz).
7b	182	3400	1650	5,87(1H,s,C_5H);4,4-4,2(2H,t,-O-$\underline{CH_2}C_3H_7$,J=6Hz);2,20(3H,s,C_6CH_3);1,7-1,2(4H,m,-O-CH_2($\underline{CH_2}$)$_2$$CH_3$);1,0-0,8(3H,m,-O-$(CH_2)_3\underline{CH_3}$).
7c	208	3400	1670	5,87(1H,s,C_5H);5,1-4,9(1H,bs,-NH-);2,20(3H,s,C_6CH_3);2,0-1,2(11H,m,-O-$\underline{C_6H_{11}}$).
7d	168	3400	1650[b]	4,5-4,1(2H,q,-O-$\underline{CH_2}CH_3$,J=7Hz);2,20(3H,s,C_5CH_3);2,00(3H,s,C_6CH_3);1,5-1,2(3H,t,-O-$CH_2\underline{CH_3}$,J=7Hz).
7e	196	3400	1660	4,3-4,1(2H,t,-O-$\underline{CH_2}C_3H_7$,J=6Hz);3,5-3,4(1H,bs,-NH-);2,18(3H,s,C_5CH_3);1,93(3H,s,C_6CH_3) 1,7-1,2(4H,m,-O-$CH_2(\underline{CH_2})_2CH_3$);1,0-0,8(3H,m -O-$(CH_2)_3\underline{CH_3}$).
7f	222	3400	1650	(c) 5,1-4,9(1H,bs,-NH-);2,13(3H,s,C_5H);1,93(3H,s,C_6CH_3);1,8-1,2(11H,m,-O-$\underline{C_6H_{11}}$).
7g	194	3400	1660	4,5-4,2(2H,q,-O-$\underline{CH_2}CH_3$,J=7Hz);2,7-2,4(4H,m,-$(\underline{CH_2})_2$);1,9-1,6(4H,m,-$(\underline{CH_2})_2$);1,5-1,3 3H,t,-O-$CH_2\underline{CH_3}$,J=7Hz).
7h	222	3400	1660	4,3-4,1(2H,t,-O-$\underline{CH_2}C_3H_7$,J=6Hz);3,5-3,4(1H bs,-NH-);2,6-2,3(4H,m,-O-$CH_2(\underline{CH_2})_2CH_3$);1,0-0,8(3H,m,-O-$(CH_2)_3\underline{CH_3}$).
7i	248	3400	1660	5,1-4,9(1H,bs,-NH-);2,6-2,3(4H,m,-$(\underline{CH_2})_2$);1,9-1,6(4H,m,-$(\underline{CH_2})_2$);1,5-1,1(11H,m,-O-$\underline{C_6H_{11}}$).

[a] 70 eV, 150°C, direct injection. [b] IR spectrum performed in CCl_4. [c] NMR spectrum performed in CCl_4.

Table 7.

compd	MS[a] m/z	IR (cm^{-1}) $\nu_{C=O}$	IR (cm^{-1}) $\delta_{C=N}$	^1H NMR ($CDCl_3$) δ
6a	154	1690	1610[b]	5,97(1H,s,C_5-H);4,00(3H,s,-OCH_3); 3,42(3H,s,N-CH_3);2,20(3H,s,C_6-CH_3).
6e	168	1680	1610[b]	4,00(3H,s,-OCH_3);3,40(3H,s,N-CH_3); 2,23(3H,s,C_5-CH_3);2,04(3H,s,C_6-CH_3).
6f	194	1670	1610[b]	4,00(3H,s,-OCH_3);3,40(3H,s,N-CH_3); 2,6-2,4(4H,m,-(CH_2)-);1,9-1,7(4H, m,-(CH_2)-).
7a	140.	1720,1670[c]		5,36(1H,s,C_5-H);3,16(3H,s,N-CH_3); 2,04(3H,s,C_6-CH_3).
7e	154	1710,1630[c]		3,34(3H,s,N-CH_3);2,18(3H,s,C_5-CH_3); 1,94(3H,s,C_6-CH_3).
7f	180	1720,1640[c]		3,30(3H,s,N-CH_3);2,5-2,3(4H,m, -(CH_2)-);1,8-1,7(4H,m,-(CH_2)-).

[a] 70 eV;150°C;direct injection; [b] IR spectrum performed in CCl_4. [c] IR spectrum performed in $CHCl_3$.

1 ml of Me_2SO_4 was added and the mixture was stirred at room temp (reaction times: see Table 3).

Isolation of the 2-methoxy derivatives **6(a,e,f)**. When the reaction was finished (TLC solvents: $CHCl_3$–MeOH = 9:1) the excess of Me_2SO_4 was destroyed by treatment with drops of conc NH_4OH and NaCl (s.s.). The mixture was then extracted with $CHCl_3$; the organic layer was dried over Na_2SO_4, and the solvent was evaporated *in vacuo*. The residue, for analytical purposes, was purified over preparative TLC and crystallized to afford the 6-alkyl and 5,6 - dialkyl - 3 - methyl - 2 - methoxy - 4 - pyrimidinones **6(a,e,f)**.

Isolation of the 6-alkyl and 5,6-dialkyl-3-methyluracils **7(a,e,f)**. When the reaction described above was finished, the mixture was acidified to pH = 2 with conc H_2SO_4 and stirred at 50 for 2 hr (TLC solvent:$CHCl_3$–MeOH = 9:1). Then the solvents were evaporated and the residue was purified over preparative TLC affording the desired 3-methyluracil. Spectroscopic data are given in Table 7.

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