Synthesis of 5-Substituted Uracils and 2,4-Dimethoxypyrimidines by Wittig Olefination

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A variety of new 5-alkenyluracils has been prepared in high yields by Wittig olefination of 5-formyl-1-octyluracil, 5-formyl-1,3-dioctyluracil and 5-formyl-2,4-dimethoxy pyrimidine with stabilized and semistabilized phosphorus ylides. The conformation of the products is discussed on the basis of ^{1}H NMR spectral data.

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Introduction.

The introduction of substituents at the C-5 position of uracil is of great practical interest for both purposes of labelling and synthesis of new biological active compounds. The C-5 pyrimidine position is usually the position of choice for labelling since it is not involved in the Watson-Crick base pairing and furthermore C-5 substituted pyrimidines are compatible with polymerase enzymes [1]. On the other hand suitably C-5 substituted uracils and uridines are included among the most active and selective antiviral agents [2]. Structure -activity relationships have shown that the antiviral activity is enhanced when the C-5 substituent is unsaturated in conjugation with the pyrimidine ring, has *E*-stereochemistry and includes an hydrophobic electronegative function [2b,2c,2h]. The above structural features resulting in the enhancement of the electrophilic character of the carbon-6 of the pyrimidine ring are reasonably understood on the basis of the thymidylate synthetase mechanism [3].

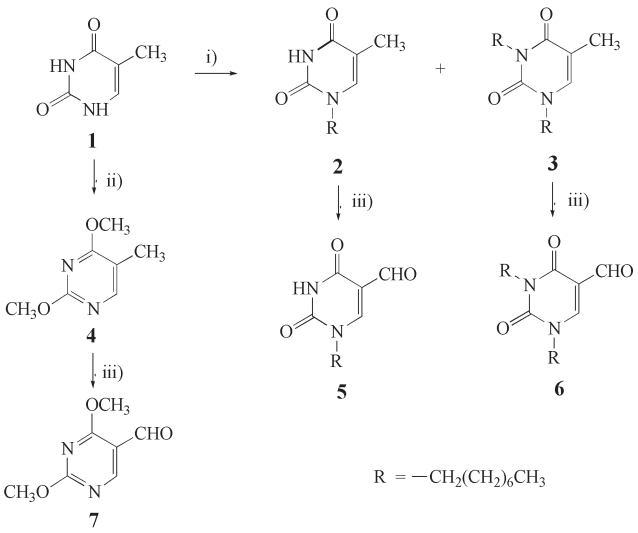
The most already applied method for the introduction of unsaturated substituents into the 5-position of pyrimidines is the palladium-catalysed addition of alkenes to either 5-halogenated or 5-mercury derivatives [2a,2b,2c,2d,2f,2h,2j,4]. Surprisingly the widely used general and effective Wittig olefination has been found a rather limited application and only a few cases are referred to give some satisfactory results [5].

In connection with our former studies on nucleic bases modifications [1c,6], we studied in this paper the Wittig reactions of mono and disubstituted formyluracils **5** and **6** and dimethoxyformylpyrimidine **7**. The octyl substituted derivatives **5** and **6** have been chosen for purposes of higher solubility and hydrophobicity, whereas compound **7** is a protected derivative of 5-formyluracil. As ylides we have chosen the stabilized and semistabilized ylides **8a-d** which have an electronegative hydrophobic function and satisfy one of the basic structure requirements for antiviral activity.

Results and Discussion.

The aldehydes **5**, **6** and **7** were prepared by oxidation of the corresponding 5-methylderivatives according to Scheme 1. The 1-octyl and 1,3-dioctylthymines **2** and **3** were obtained by alkylation of thymine with sodium hydride and octyl bromide. By varying the ratio of the alkylating agent to thymine, mono or disubstituted derivatives are obtained as the main products. For the oxidation of the methyl group a procedure described in the literature [7] for analogous derivatives was followed, which after optimisation of the reaction conditions gave the desired aldehydes in satisfactory yields (60 – 72 %).

Scheme 1



Reagents and conditions: i) n-octylbromide, NaH, DMF, 80 °C, 5 hours; ii) $POCl_3$, reflux 5 hours and then CH_3ONa / CH_3OH; iii) $K_2S_2O_8$, $CuSO_4$, 2,6-lutidine, H_2O / CH_3CN, 80 °C, 1 hour.

The ylides **8** were prepared by dehydrohalogenation of the corresponding phosphonium salts and reacted with the aldehydes **5**, **6**, **7** to give the alkene derivatives **9**, **10**, **11** according to Scheme 2. The reactions with the stabilized ylides were carried out after the isolation of the ylide in dichlomethane and methanol solutions. In the reactions with the semistabilized ylides **8c** and **8d** the formation of the ylide was made *in situ* by potassium *tert*-butoxide in benzene or under biphasic conditions in dichloromethane/

aqueous NaOH solution. In all cases the ylide was used in excess (1.5:1) and the reactions were carried out at room temperature and were monitored by TLC until consumption of the aldehyde. The yields of the reaction products after their isolation by column chromatography were very satisfactory ranging between 77 – 98 %. The reaction con-

Scheme 2

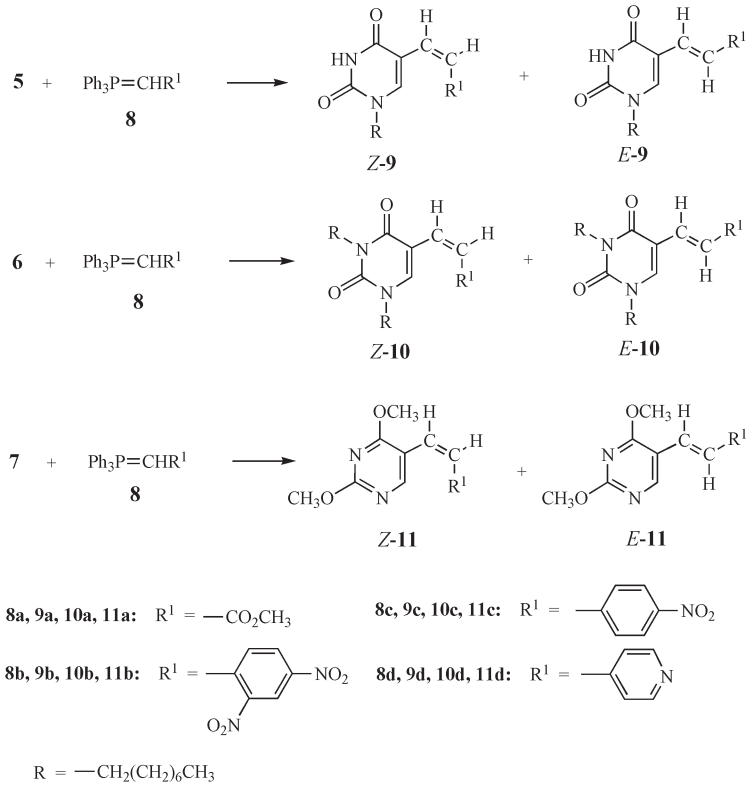


Table 1

Reaction conditions, yields and ratio of the (*Z*)/(*E*)- isomers of the reactions of ylides **8** with aldehydes **5**, **6**, **7**.

Starting aldehyde	Starting ylide	Solvent, Reaction time	Product	Yield %	Ratio of Z/*E* isomers
5	**8a**	CH_2Cl_2, 6 hours	**9a**	96	0.8/1
5	**8a**	CH_3OH, 6 hours	**9a**	94	1.4/1
6	**8a**	CH_2Cl_2, 6 hours	**10a**	88	1/1
6	**8a**	CH_3OH, 6 hours	**10a**	90	1/1
7	**8a**	CH_2Cl_2, 6 hours	**11a**	93	0.2/1
7	**8a**	CH_3OH, 6 hours	**11a**	95	2/1
5	**8b**	CH_2Cl_2, 3 days	**9b**	80	0.2/1
5	**8b**	CH_3OH, 8 hours	**9b**	80	1.1/1
6	**8b**	CH_2Cl_2, 3 days	**10b**	81	1/1
6	**8b**	CH_3OH, 8 hours	**10b**	88	1/1
7	**8b**	CH_2Cl_2, 3 days	**11b**	85	2/1
7	**8b**	CH_3OH, 8 hours	**11b**	79	5/1
5	**8c**	*t*-BuOK, C_6H_6, 2 hours	**9c**	78	2.2/1
5	**8c**	NaOH/CH_2Cl_2, 2 hours	**9c**	85	1.2/1
6	**8c**	*t*-BuOK, C_6H_6, 2 hours	**10c**	88	11/1
6	**8c**	NaOH/CH_2Cl_2, 2 hours	**10c**	98	2.6/1
7	**8c**	*t*-BuOK, C_6H_6, 2 hours	**11c**	80	2/1
7	**8c**	NaOH/CH_2Cl_2, 2 hours	**11c**	90	2/1
6	**8d**	*t*-BuOK, C_6H_6, 2 hours	**10d**	90	4/1
6	**8d**	NaOH/CH_2Cl_2, 2 hours	**10d**	77	18/1
7	**8d**	*t*-BuOK, C_6H_6, 2 hours	**11d**	80	3/1
7	**8d**	NaOH/CH_2Cl_2, 2 hours	**11d**	85	4/1

ditions, the yields of the products and the ratio of the (*Z*)/(*E*)- isomers are given in Table 1. It should be mentioned that in the case of the reaction of the ylide **8d** with the aldehyde **5** it was not possible to isolate any product although there were indications for the formation of the expected alkenes in the ^{1}H NMR of the crude reaction mixture.

As it comes out from Table 1 the semistabilized ylides **8c** and **8d** showed almost the same reactivity in both the reaction conditions applied. The stabilized ylide **8a** showed also almost the same reactivity in both methanol and dichloromethane solutions, whereas reactions with ylide **8b** were faster in methanol solutions. In regard with the regioselectivity of the reactions no severe regularities were observed. It is known that Wittig reactions of stabilized ylides with aldehydes lead stereoselectively to the preferential formation of (*E*)-alkenes, whereas reactions with the non-stabilized ylides lead to the formation of the thermodynamically less favourable (*Z*)-alkenes and semistabilized ylides with moderate activity afford mixtures of (*Z*)-alkenes and (*E*)-alkenes [8]. Furthermore in the reactions of the stabilized ylides the proportion of (*Z*)-isomer is increased in protic solvents [8]. In our case however reactions with the stabilized ylides **8a** and **8b** gave mixtures of (*Z*)- and (*E*) isomers even in aprotic solvents, whereas an increase of the ratio of (*Z*)-isomer was observed in the reactions with the aldehydes **5** and **7** in methanol. In the reaction with the semi-stabilized ylides **8c** and **8d** the formation of (*Z*)-isomer is favoured in all cases.

The structure assignment of the obtained alkenes **9**, **10** and **11** was based on their elemental analysis and spectral data. In the mass spectra they give peaks corresponding to the molecular ion and in the ^{1}H NMR and ^{13}C NMR give the expected chemical shifts. The distinction between (*E*)- and (*Z*)- isomers was easily made on the basis of the olefinic protons coupling constant value ranging between 11.6–13.2 Hz for (*Z*)-isomers and 16.0–16.7 Hz for (*E*)-isomers. A feature worth mentioning in the ^{1}H NMR of the obtained products is the chemical shift of 6-H pyrimidine ring proton, which permits some suggestions about the preferred conformation of the alkenyl chain in the (*Z*)-isomers. The chemical shifts values of 6-H pyrimidine ring protons of (*E*)- and (*Z*)-isomers and their differences are given in Table 2. Assuming that the variations in the chemical shift of H-6 are governed mainly by the electron withdrawing effect of the R^1 substituent, H-6 is expected to be more downfield shifted in the (*E*)-isomers compared to the (*Z*)-isomers since conjugation works more effectively in the less sterically hindered (*E*)-isomers. Indeed when R^1 is aromatic (entries 4 – 11 of Table 2), the H-6 chemical shift of (*E*)-isomer is larger than that of (*Z*)-isomer. On the contrary when R^1 is carboxymethyl (entries 1 – 3 of Table 2), the 6-H of the (*Z*)-isomer is more shifted than the 6-H of the (*E*)-isomer, especially in the uracil derivatives **9a** and **10a**. These observations are in accordance with a preferred conformation [A] between the two possible conformations [A] and [B] for the (Z)-isomers as depicted in Figure 1. In the less hindered conformation [A] the H-6 undergoes the neighbouring group effect of R^1 substituent, which is shielding for R^1 = aromatic and deshielding for R^1 = CO_2CH_3, as it comes out from molecular models.

Table 2
Chemical shifts of 6-H pyrimidine protons.

	Compound	δ H-6 of (*Z*)-isomer	δ H-6 of (*E*)-isomer	Δδ [(*Z*) - (*E*)]
1	**9a**	9.27	7.33	1.94
2	**10a**	9.10	7.37	1.73
3	**11a**	8.66	8.29	0.37
4	**9b**	6.90	7.49	-0.59
5	**10b**	6.82	7.50	-0.68
6	**11b**	7.77	8.45	-0.68
7	**9c**	6.97	7.38	-0.41
8	**10c**	6.96	7.37	-0.41
9	**11c**	7.96	8,43	-0.47
10	**10d**	6.95	7.38	-0.33
11	**11d**	7.97	8.42	-0.45

Conformation [A] is further supported by NOE measurements carried out on compound (*Z*)-**9a**. Thus upon saturation of 6-H both olefinic protons substain positive NOE effect almost of the same magnitude. The mutual NOE enhancement of 6-H upon saturation of either olefinic proton is also positive and of the same magnitude. For conformation [B] the mutual NOE effect between H-6 and H_b having an almost linear arrangement with H_a is expected to be negative.

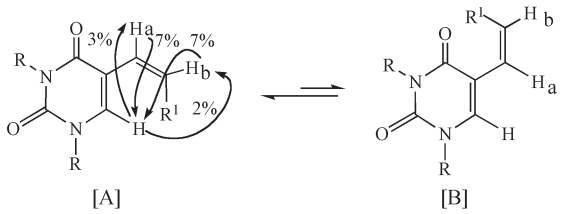


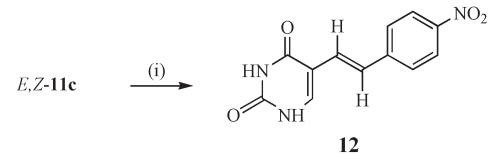
Figure 1

The proposed preferred conformation [A] explains to some degree the observed reduced antiviral reactivity of 5-[(*Z*)-alkenyl]-uracils [2b,2c,2h], since in this conformation the 6-position of uracil is too hindered to be attacked by the nucleophile cysteine group according to the thymidylate synthetase mechanism.

The dimethoxyderivatives **11** are protected forms of uracils from which the last can be obtained after the removal of the methyl groups under several conditions [9].

In a representative experiment we have transformed quantitatively dimethoxyderivative **11c** to uracil derivative **12** by heating in acetic acid with sodium iodide according to Scheme 3. It was observed that under the applied conditions (*Z*)- to (*E*)- isomerization also takes place. Thus, treatment of a mixture of *Z*, *E*-**11c** gave the (*E*)-uracil **12**.

Scheme 3



12

(i) CH_3COOH, NaI, 1h, 90 °C.

The effectiveness of the applied conditions for the purposes of isomerization was also tested to other than methoxy derivatives. Thus dioctylderivative *Z*-**10e** was quantitatively transformed to *E*-**10e** after heating one hour in acetic acid in the presence of sodium iodide. It should be mentioned that prolonged heating in acetic acid without sodium iodide did not result in any change of the ratio of the isomers. Alternatively, a mixture *E*,*Z*-**11a** was also transformed to *E*-**11a** by treatment with thiophenol in the presence of 2,2'-azobis(2-methylpropionitrile) (AIBN) according to a procedure previously described in the literature [10]. Thus the lack of the stereoselectivity or the performed Wittig reactions with the predominance of (*Z*)-isomers in most cases does not reduce their utility for the synthesis of the most promising for biological purposes (*E*)-isomers.

In conclusion, Wittig olefination has been proved to be a very simple, effective and convenient procedure for the synthesis of a variety of 5-substituted uracils in high yields avoiding expensive and toxic metal catalysed procedures.

EXPERIMENTAL

Mp's are uncorrected and were determined on a Kofler hot-stage microscope. ^{1}H nmr spectra were recorded at 300 MHz on a Bruker 300 AM spectrometer and ^{13}C nmr spectra at 75.5 MHz on the same spectrometer and are quoted relative to tetramethylsilane as internal reference, in deuteriochloroform solutions, unless otherwise stated. Values of J are given in Hz. Mass spectra were performed on a VG-250 spectrometer with ionization energy maintained at 70 eV. Microanalyses were performed on a Perkin-Elmer 2400-II element analyser. Column chromatography was carried out on Merck Kieselgel (particle size 0.063-0.200 mm) and solvents were distilled before use. The ylides **8a** and **8b**, 4-nitrobenzylltriphenylphosphonium chloride and 4-pyridinylmethyltriphenylphosphonium chloride, precursors of the ylides **8c** and **8d** respectively, were prepared according to previously reported procedures [8b,11]. 2,4-Dimethoxy-5-methylpyrimidine **4** was prepared as described in the literature [12].

Preparation of 1-Octylthymine (**2**) and 1,3-Dioctylthymine (**3**).

A mixture of thymine (2.46 g, 20 mmoles) and sodium hydride (0.88 g 60% oil dispersion, 22 mmoles) in dry DMF (30 ml) was stirred at 80° under argon atmosphere for 1 hour. Then octylbromide (3.45 ml, 20 mmoles) was added and the reaction mixture was heated at 80° for another 4 hours. After that the reaction mixture was poured into methylene chloride/water and the organic layer was extracted three times with water to remove the DMF. After drying with sodium sulfate and evaporation of the solvent the residue was chromatographed on a silica-gel column with hexane-ethyl acetate (4:1) as the eluent. From the column they were obtained in order of elution 0.77 g (11 %) of **3** and 3.10 g (65 %) of **2**. In a repeated procedure using sodium hydride and octylbromide in 2 equivalence compounds **3** and **2** were isolated in 50 and 20 % yields respectively. The ^{1}H NMR spectrum of compound **2** was in agreement with the literature data [13].

1,3-Dioctylthymine (**3**).

This compound was obtained as an oil; ^{1}H nmr: δ 0.87 (m, 6H, CH_3), 1.26-1.30 (m, 20H, $CH_2CH_2(CH_2)_5CH_3$), 1.64 (m, 4H, $CH_2CH_2(CH_2)_5CH_3$), 1.92 (s, 3H, CH_3), 3.69 (t, J = 7.4 Hz, 2H, $CH_2CH_2(CH_2)_5CH_3$), 3.93 (t, J = 7.4 Hz, 2H, $CH_2CH_2(CH_2)_5CH_3$), 6.95 (s, 1H, 6-H); ^{13}C nmr: δ 13.0 and 14.0 (CH_3), 22.5, 26.4, 26.6, 27.5, 29.0, 29.2, 31.6 and 31.7 ($CH_2(CH_2)_6CH_3$), 41.4 and 49.4 ($CH_2(CH_2)_6CH_3$), 109.5 (C-5), 138.2 (C-6), 151.3 (C-2), 163.7 (C-4); ms: m/z 350 (M^+, 25% rel. int.).
Anal. Calcd. for $C_{21}H_{38}N_2O_2$: C, 71.95; H, 10.93; N, 7.99. Found: C, 71.57; H, 11.23; N, 7.80.

General Procedure for the Oxidation of Methyl Derivatives (**2**, **3**, **4**).

A solution of the methyl pyrimidine (10 mmoles) and 2,6-lutidine (4.1 ml, 35 mmoles) in acetonitrile (40 ml) was added to a solution of $K_2S_2O_8$ (5.4 g, 20 mmoles) and $CuSO_4.5H_2SO_4$ (1g, 4 mmoles) in water (40 ml). The reaction mixture was heated in an oil bath at 80° and the reaction mixture was monitored by TLC. After 1 hour TLC showed only traces of the starting methyl derivative and the heating was stopped. Applying longer reaction times at the same temperature or at lower temperatures side products were formed lowering the yield of the reaction. After cooling the reaction mixture was concentrated to half the initial volume and the remaining solution was extracted with ethyl acetate. The organic layer was successively washed with water then aqueous 5 % EDTA. The combined water layers were extracted with chloroform then the organic layers were combined, dried over sodium sulfate and concentrated. The residue was chromatographed on a silica gel column with hexane-ethyl acetate (4:1 for **5**, 8:1 for **6** 2:1 for **7**) as the eluent. Compounds **5**, **6** and **7** were obtained in 71 %, 60 % and 72 % yields respectively. The dimethoxy derivative **7** showed the same spectral characteristics with those given in the literature [14].

5-Formyl-1-octyluracil (**5**).

This compound was obtained as a white solid mp 108-110°; ^{1}H nmr: δ 0.81 (t, J = 6.4 Hz, 3H, CH_3), 1.23 (m, 10H, $CH_2CH_2(CH_2)_5CH_3$), 1.64 (m, 2H, $CH_2CH_2(CH_2)_5CH_3$), 3.77 (t, J = 7.6 Hz, 2H, $CH_2CH_2(CH_2)_5CH_3$), 8.03 (s, 1H, 6-H), 9.14 (s, 1H, NH), 9.95 (s, 1H, CHO); ^{13}C nmr: δ 14.0 (CH_3), 22.3, 26.3, 29.0, 29.1 and 31.7 ($CH_2(CH_2)_6CH_3$), 50.2

($CH_2(CH_2)_6CH_3$), 110.9 (C-5), 149.2 (C-6), 149.7 (C-2), 162.1 (C-4), 186.1 (CHO); ms: m/z 252 (M^+, 22% rel. int.).
Anal. Calcd. for $C_{13}H_{20}N_2O_3$: C, 61.88; H, 7.99; N, 11.10. Found: C, 61.57; H, 8.02; N, 11.20.

5-Formyl-1,3-dioctyluracil (**6**).

This compound was obtained as a white solid mp 49-51°; ^{1}H nmr: δ 0.79 (m, 6H, CH_3), 1.19-1.24 (m, 20H, $CH_2CH_2(CH_2)_5CH_3$), 1.56-1.96 (m, 4H, $CH_2CH_2(CH_2)_5CH_3$), 3.80 (t, J = 7.3 Hz, 2H, $CH_2CH_2(CH_2)_5CH_3$), 3.87 (t, J = 6.1 Hz, 2H, $CH_2CH_2(CH_2)_5CH_3$), 8.04 (s, 1H, 6-H), 9.94 (s, 1H, CHO); ^{13}C nmr: δ 14.1 (CH_3), 22.6, 26.4, 26.9, 27.5, 29.0, 29.2, 31.7 and 31.8 ($CH_2(CH_2)_6CH_3$), 41.6 and 51.0 ($CH_2(CH_2)_6CH_3$), 110.3 (C-5), 146.9 (C-6), 150.4 (C-2), 161.8 (C-4), 187.1 (CHO); ms: m/z 364 (M^+, 23% rel. int.).
Anal. Calcd. for $C_{21}H_{36}N_2O_3$: C, 69.19; H, 9.95; N, 7.68. Found: C, 69.12; H, 9.85; N, 7.86.

General Procedure for the Wittig Reaction of Aldehydes **5**, **6** and **7** with the Stabilized Ylides **8a** and **8b**.

A mixture of the aldehyde (1 mmole) and the ylide (1.5 mmoles) in dry methylene chloride (10 ml) or dry methanol (10 ml) was stirred at room temperature until the aldehyde was consumed, as indicated by TLC. The solvent was then evaporated and the residue was chromatographed on a silica gel column with hexane-ethyl acetate (2:1 for the reactions of **5**, 5:1 the for reactions of **6**, 3:1 for the reactions of **7**) as the eluent. With the exceptions of *E,Z*-**10a** which was obtained as a mixture and *Z*-**9b** which was obtained only as a mixture with the (*E*)-isomer, in the other cases it was possible to isolate from the column fractions with separated pure (*E*)- and (*Z*)-isomers.

General Procedure for the Wittig Reaction of Aldehydes **5**, **6** and **7** with the Semistabilized Ylides **8c** and **8d**.

I) To a stirred suspension of 4-nitrobenzylltriphenylphosphonium chloride or 4-pyridinylmethyltriphenylphosphonium chloride (1.5 mmole) in dry benzene (5 ml) under argon atmosphere was added potassium *tert*-butoxide (0.224 g, 2 mmoles). After stirring for 1 hour, 1 mmole of the corresponding aldehyde was added and the mixture was stirred for additional 2 hours. The reaction mixture was diluted with water and extracted with ether. The organic layers were combined, dried over sodium sulfate and concentrated. The residue was chromatographed on a silica gel column with hexane-ethyl acetate (2:1 for the reactions of **5**, 5:1 for the reactions of **6**, 3:1 for the reactions of **7**) as the eluent. In all cases it was possible to isolate from the column fractions with separated pure (*E*)- and (*Z*)-isomers.

II) 4-Nitrobenzylltriphenylphosphonium chloride or 4-pyridinylmethyltriphenyl phosphonium chloride chloride (1.5 mmoles) and aldehyde (1mmole) were dissolved in methylene chloride (5 ml) and the solution was stirred with an aqueous 10 % NaOH solution (5 ml) at room temperature until consumption of the aldehyde. The two layers were separated and the aqueous layer was extracted with methylene chloride. The combined organic layers were extracted once with water, dried over sodium sulfate and concentrated. The residue was treated as in procedure I.

5-[(*E*)-3-Methoxy-3-oxo-1propenyl]-1-octyluracil (*E*-**9a**).

This compound was obtained as a white solid mp 116-118°; ^{1}H nmr: δ 0.80 (t, J = 6.4 Hz, 3H, CH_3), 1.23 (m, 10H, $CH_2CH_2(CH_2)_5CH_3$), 1.65 (m, 2H, $CH_2CH_2(CH_2)_5CH_3$), 3.70 (s, 3H, OCH_3), 3.74 (t, J = 7.2 Hz, 2H, $CH_2CH_2(CH_2)_5CH_3$), 6.93 (d, J = 16.2 Hz, 1H, CH=CH), 7.22 (d, J = 16.2 Hz, 1H, CH=CH), 7.33 (s, 1H, 6-H), 8.99 (br s, 1H, NH); ^{13}C nmr: δ 14.0 (CH_3), 22.6, 26.3, 26.4, 29.1, 29.7 and 31.7 ($CH_2(CH_2)_6CH_3$), 49.4 ($CH_2(CH_2)_6CH_3$), 51.6 ($COOCH_3$), 109.8 (C-5), 119.3 and 135.9 (CH=CH), 146.3 (C-6), 149.5 (C-2), 161.4 (C-4), 167.9 ($COOCH_3$); ms: m/z 308 (M^+, 17% rel. int.).
Anal. Calcd. for $C_{16}H_{24}N_2O_4$: C, 62.32; H, 7.84; N, 9.08. Found: C, 62.28; H, 7.81; N, 8.90.

5-[(*Z*)-3-Methoxy-3-oxo-1propenyl]-1-octyluracil (*Z*-**9a**).

This compound was obtained as a white solid mp 110-112°; ^{1}H nmr: δ 0.87 (t, J = 6.6 Hz, 3H, CH_3), 1.30 (m, 10H, $CH_2CH_2(CH_2)_5CH_3$), 1.75 (m, 2H, $CH_2CH_2(CH_2)_5CH_3$), 3.73 (s, 3H, OCH_3), 3.82 (t, J = 7.2 Hz, 2H, $CH_2CH_2(CH_2)_5CH_3$), 5.91 (d, J = 13.2 Hz, 1H, CH=CH), 7.02 (d, J = 13.2 Hz, 1H, CH=CH), 9.27 (s, 1H, 6-H), 9.58 (br s, 1H, NH); ^{13}C nmr: δ 14.1 (CH_3), 22.6, 26.4, 29.1, 29.7 and 31.8 ($CH_2(CH_2)_6CH_3$), 49.6 ($CH_2(CH_2)_6CH_3$), 51.6 ($COOCH_3$), 108.3 (C-5), 116.9 and 134.6 (CH=CH), 148.5 (C-6), 150.1 (C-2), 163.1 (C-4), 167.3 ($COOCH_3$); ms: m/z 308 (M^+, 38% rel. int.).
Anal. Calcd. for $C_{16}H_{24}N_2O_4$: C, 62.32; H, 7.84; N, 9.08. Found: C, 62.15; H, 7.58; N, 8.89.

5-[(*E,Z*)-3-Methoxy-3-oxo-1propenyl]-1,3-dioctyluracil (*E,Z*-**10a**).

This mixture of isomers was obtained as an oil; ^{1}H nmr: δ 0.80 (m, CH_3), 1.20 (m, $CH_2CH_2(CH_2)_5CH_3$), 1.54-1.63 (m, $CH_2CH_2(CH_2)_5CH_3$), 3.68-3.78 (m, $CH_2CH_2(CH_2)_5CH_3$ and $COOCH_3$), 3.91 (t, J = 6.8 Hz, $CH_2CH_2(CH_2)_5CH_3$), 5.81 (d, J = 12.8 Hz, CH=CH of (*Z*)-isomer), 6.97 (d, J = 16.1 Hz, CH=CH of (*E*)-isomer), 7.12 (d, J = 12.8 Hz, CH=CH of (*Z*)-isomer), 7.26 (d, J = 16.1 Hz, CH=CH of (*E*)-isomer), 7.37 (s, 6-H of (*E*)-isomer), 9.10 (s, 6-H of (*Z*)-isomer); ^{13}C nmr: δ 13.9 (CH_3), 22.5, 26.3, 26.9, 27.4, 28.8, 29.0, 29.05, 29.1, 31.6, 31.7 41.6 and 47.0 (($CH_2)_7CH_3$ and $COOCH_3$), 107.3 and 108.8 (C-5), 116.3, 118.3 135.7 and 136.8 (CH=CH), 144.3 and 146.3 (C-6), 150.1 and 151.2 (C-2), 160.9 and 162.1 (C-4), 167.2 and 168.0 ($COOCH_3$); ms: m/z 420 (M^+, 38% rel. int.).
Anal. Calcd. for $C_{24}H_{40}N_2O_4$: C, 68.54; H, 9.59; N, 6.66. Found: C, 68.47; H, 9.36; N, 7.06.

2,4-Dimethoxy-5-[(*E*)-3-methoxy-3-oxo-1propenyl]pyrimidine (*E*-**11a**).

This compound was obtained as a white solid mp 118-120°; ^{1}H nmr: δ 3.72 (s, 3H, OCH_3), 3.95 (s, 3H, OCH_3), 4.01 (s, 3H, OCH_3), 6.52 (d, J = 16.0 Hz, 1H, CH=CH), 7.52 (d, J = 16.0 Hz, 1H, CH=CH), 8.29 (s, 1H, 6-H); ^{13}C nmr: δ 51.6, 54.2 and 55.1 (OCH_3), 110.3 (C-5), 119.0 and 136.0 (CH=CH), 159.6 (C-6), 165.3, 167.4 and 168.9 (C-2, C-4 and $COOCH_3$); ms: m/z 224 (M^+, 84% rel. int.).
Anal. Calcd. for $C_{10}H_{12}N_2O_4$: C, 53.57; H, 5.39; N, 12.49. Found: C, 54.19; H, 5.69; N, 12.29.

2,4-Dimethoxy-5-[(*Z*)-3-methoxy-3-oxo-1-propenyl]pyrimidine (*Z*-**11a**).

This compound was obtained as a white solid mp 87-90°; ^{1}H nmr: δ 3.71 (s, 3H, OCH_3), 4.01 (s, 3H, OCH_3), 4.02 (s, 3H, OCH_3), 5.99 (d, J = 12.7 Hz, 1H, CH=CH), 6.91 (d, J = 12.7 Hz, 1H, CH=CH), 8.66 (s, 1H, 6-H); ^{13}C nmr: δ 51.4, 54.1 and 55.0 (OCH_3), 109.9 (C-5), 120.0 and 134.3 (CH=CH), 159.5 (C-6),

165.2, 166.3 and 168.4 (C-2, C-4 and *C*OOCH$_3$); ms: m/z 224 (M$^+$, 74% rel. int.).

Anal. Calcd. for $C_{10}H_{12}N_2O_4$: C, 53.57; H, 5.39; N, 12.49. Found: C, 53.23; H, 5.79; N, 12.19.

5-[(*E*)-2-(2,4-Dinitrophenyl)ethenyl]-1octyluracil (*E*-**9b**).

This compound was obtained as a yellow solid mp 147- 150°; ^{1}H nmr: δ 0.87 (t, J = 6.4 Hz, 3H, CH$_3$), 1.28 (m, 10H, CH$_2$CH$_2$(C*H*$_2$)$_5$CH$_3$), 1.74 (m, 2H, CH$_2$C*H*$_2$(CH$_2$)$_5$CH$_3$), 3.62 (t, J = 7.4 Hz, 2H, C*H*$_2$CH$_2$(CH$_2$)$_5$CH$_3$), 7.01 (d, J = 16.1 Hz, 1H, CH=CH), 7.49 (s, 1H, 6-H), 7.85 (d, J = 16.1 Hz, 1H, CH=CH), 7.89 (d, J = 6.4 Hz, 1H, Ar-H), 8.40 (dd, J = 6.4, 1.4 Hz, 1H, Ar-H), 8.67 (br s, 1H, NH), 8.79 (d, J = 1.4 Hz, 1H, Ar-H); ^{13}C nmr: δ 14.0 (CH$_3$), 22.6, 26.4, 29.1, 29.2, 29.7 and 31.7 (CH$_2$(*C*H$_2$)$_6$CH$_3$), 49.1 (*C*H$_2$(CH$_2$)$_6$CH$_3$), 110.9 (C-5), 120.7, 121.9, 127.1, 128.4, 128.9 (CH=CH and C-Ar), 138.7 (C-Ar), 143.2 (C-6), 146.3 and 147.4 (C-Ar), 149.4 (C-2), 161.5 (C-4); ms: m/z 416 (M$^+$, 35% rel. int.).

Anal. Calcd. for $C_{20}H_{24}N_2O_6$: C, 57.69; H, 5.81; N, 13.45. Found: C, 57.29; H, 5.81; N, 13.05.

5-[(*Z*)-2-(2,4-Dinitrophenyl)ethenyl]-1octyluracil (*Z*-**9b**).

This compound was obtained only as a solid mixture with the (*E*)-isomer. Its proton nmr chemical shifts were assigned from the ^{1}H nmr of the mixture; ^{1}H nmr: δ 0.87 (m, CH$_3$), 1.28 (m, CH$_2$CH$_2$(C*H*$_2$)$_5$CH$_3$), 1.60 (m, CH$_2$C*H*$_2$(CH$_2$)$_5$CH$_3$), 3.57 (t, J = 7.1 Hz, C*H*$_2$CH$_2$(CH$_2$)$_5$CH$_3$), 6.60 (d, J = 12.2 Hz, CH=CH), 6.90 (s, 6-H), 6.97 (d, J = 12.2 Hz, CH=CH), 7.57 (d, J = 8.3 Hz, Ar-H), 8.45 (dd, J = 6.4, 1.6 Hz, Ar-H), 8.45 (br s, NH), 8.94 (d, J = 1.6 Hz, Ar-H).

5-[(*E*)-2-(2,4-Dinitrophenyl)ethenyl]-1,3-dioctyluracil (*E*-**10b**).

This compound was obtained as a yellow solid mp 131-133°; ^{1}H nmr: δ 0.87 (m, 6H, CH$_3$), 1.27-1.32 (m, 20H, CH$_2$CH$_2$(C*H*$_2$)$_5$CH$_3$), 1.63-1.75 (m, 4H, CH$_2$C*H*$_2$(CH$_2$)$_5$CH$_3$), 3.83 (t, J = 7.4 Hz, 2H, C*H*$_2$CH$_2$(CH$_2$)$_5$CH$_3$), 3.97 (t, J = 7.4 Hz, 2H, C*H*$_2$CH$_2$(CH$_2$)$_5$CH$_3$), 7.08 (d, J = 16.1 Hz, 1H, CH=CH), 7.50 (s, 1H, 6-H), 7.84 (d, J = 16.1 Hz, 1H, CH=CH), 7.90 (d, J = 9.0 Hz, 1H, Ar-H), 8.37 (dd, J = 9.0, 1.6 Hz, 1H, Ar-H), 8.76 (d, J = 1.6 Hz, 1H, Ar-H); ^{13}C nmr: δ 14.0 (CH$_3$), 22.6, 26.4, 26.9, 27.4, 29.0, 29.1, 29.2, 31.6 and 31.7 (CH$_2$(*C*H$_2$)$_6$CH$_3$), 41.8 and 50.4 (*C*H$_2$(CH$_2$)$_6$CH$_3$), 110.0 (C-5), 120.6, 120.9, 126.9, 128.7, 129.7 and 138.9 (CH=CH and C-Ar), 141.4 (C-6), 146.0 and 147.2 (C-Ar), 150.2 (C-2), 161.4 (C-4); ms: m/z 528 (M$^+$, 35% rel. int.).

Anal. Calcd. for $C_{28}H_{40}N_4O_6$: C, 63.62; H, 7.63; N, 10.60. Found: C, 63.87; H, 7.30; N, 10.27.

5-[(*Z*)-2-(2,4-Dinitrophenyl)ethenyl]-1,3-dioctyluracil (*Z*-**10b**).

This compound was obtained as a yellow solid mp 107-110°; ^{1}H nmr: δ 0.89 (m, 6H, CH$_3$), 1.12-1.42 (m, 24H, CH$_2$(C*H*$_2$)$_6$CH$_3$), 3.56 (t, J = 7.1 Hz, 2H, C*H*$_2$CH$_2$(CH$_2$)$_5$CH$_3$), 3.89 (t, J = 7.4 Hz, 2H, C*H*$_2$CH$_2$(CH$_2$)$_5$CH$_3$), 6.67 (d, J = 11.8 Hz, 1H, CH=CH), 6.82 (s, 1H, 6-H), 6.88 (d, J = 11.8 Hz, 1H, CH=CH), 7.58 (d, J = 8.4 Hz, 1H, Ar-H), 8.32 (dd, J = 8.4, 2.5 Hz, 1H, Ar-H), 8.92 (d, J = 2.5 Hz, 1H, Ar-H); ^{13}C nmr: δ 14.0 (CH$_3$), 22.5, 22.6, 26.2, 26.5, 26.9, 27.0, 27.4, 29.0, 29.1, 29.2, 31.7 and 31.8 (CH$_2$(*C*H$_2$)$_6$CH$_3$), 41.8 and 50.0 (*C*H$_2$(CH$_2$)$_6$-CH$_3$), 108.9 (C-5), 125.5, 126.1, 127.1, 127.5, 132.8 and 139.9 (CH=CH and C-Ar), 141.7 (C-6), 146.7 and 148.0 (C-Ar), 150.4 (C-2), 161.4 (C-4); ms: m/z 528 (M$^+$, 31% rel. int.).

Anal. Calcd. for $C_{28}H_{40}N_4O_6$: C, 63.62; H, 7.63; N, 10.60. Found: C, 63.22; H, 7.81; N, 10.28.

2,4-Dimethoxy-5-[(*E*)- 2-(2,4-dinitrophenyl)ethenyl]pyrimidine (*E*-**11b**).

This compound was obtained as a yellow solid mp 170-173°; ^{1}H nmr: δ 4.05 (s, 3H, OCH$_3$), 4.13 (s, 3H, OCH$_3$), 7.21 (d, J = 16.1 Hz, 1H, CH=CH), 7.78 (d, J = 16.1 Hz, 1H, CH=CH), 7.96 (d, J = 7.0 Hz, 1H, Ar-H), 8.43 (dd, J = 7.0, 1.9 Hz, 1H, Ar-H), 8.45 (s, 1H, 6-H), 8.82 (d, J = 1.9 Hz, 1H, Ar-H); ^{13}C nmr: δ 54.5 and 55.2 (OCH$_3$), 111.6 (C-5), 120.7, 122.5, 127.1, 129.1, 128.8, 139.0, 146.2 and 147.3 (CH=CH and C-Ar), 158.3 (C-6), 165.1 (C-4), 168.5 (C-2): ms: m/z 332 (M$^+$, 45% rel. int.).

Anal. Calcd. for $C_{14}H_{12}N_4O_6$: C, 50.61; H, 3.64; N, 16.86. Found: C, 50.63; H, 4.04; N, 16.59.

2,4-Dimethoxy-5-[(*Z*)- 2-(2,4-dinitrophenyl)ethenyl]pyrimidine (*Z*-**11b**).

This compound was obtained as a yellow solid mp 145-148°; ^{1}H nmr: δ 3.91 (s, 3H, OCH$_3$), 3.94 (s, 3H, OCH$_3$), 6.79 (d, J = 11.6 Hz, 1H, CH=CH), 6.98 (d, J = 11.6 Hz, 1H, CH=CH), 7.42 (d, J = 8.4 Hz, 1H, Ar-H), 7.77 (s, 1H, 6-H), 8.25 (dd, J = 8.4, 1.9 Hz, 1H, Ar-H), 8.92 (d, J = 1.9 Hz, 1H, Ar-H); ^{13}C nmr: δ 54.1 and 55.0 (OCH$_3$), 110.2 (C-5), 120.5, 125.5, 126.1, 127.2, 132.8, 139.7, 146.8 and 147.7 (CH=CH and C-Ar), 158.3 (C-6), 164.9 (C-4), 168.4 (C-2): ms: m/z 332 (M$^+$, 28% rel. int.).

Anal. Calcd. for $C_{14}H_{12}N_4O_6$: C, 50.61; H, 3.64; N, 16.86. Found: C, 50.91; H, 3.76; N, 16.70.

5-[(*E*)-2-(4-Nitrophenyl)ethenyl]-1-octyluracil (*E*- **9c**).

This compound was obtained as a yellow solid mp 173-176°; ^{1}H nmr: δ 0.87 (t, J = 6.5 Hz, 3H, CH$_3$), 1.28 (m, 10H, CH$_2$CH$_2$(C*H*$_2$)$_5$CH$_3$), 1.64 (m, 2H, CH$_2$C*H*$_2$(CH$_2$)$_5$CH$_3$), 3.81 (t, J = 7.3 Hz, 2H, C*H*$_2$CH$_2$(CH$_2$)$_5$CH$_3$), 6.90 (d, J = 16.4 Hz, 1H, CH=CH), 7.38 (s, 1H, 6-H), 7.57 (d, J = 8.7 Hz, 2H, Ar-H), 7.64 (d, J = 16.4 Hz, 1H, CH=CH), 8.20 (d, J = 8.7 Hz, 2H, Ar-H), 8.71 (br s, 1H, NH); ^{13}C nmr: δ 14.0 (CH$_3$), 22.6, 26.4, 29.1, 29.2, 29.7 and 31.7 (CH$_2$(*C*H$_2$)$_6$CH$_3$), 49.3 (*C*H$_2$(CH$_2$)$_6$CH$_3$), 111.4 (C-5), 124.1, 126.7, 127.7, 129.3, 142.8, 143.9 and 146.8 (CH=CH, C-6 and C-Ar), 149.4 (C-2), 161.7 (C-4); ms: m/z 371 (M$^+$, 51% rel. int.).

Anal. Calcd. for $C_{20}H_{25}N_3O_4$: C, 64.67; H, 6.78; N, 11.31. Found: C, 64.47; H, 6.38; N, 11.15.

5-[(*Z*)-2-(4-Nitrophenyl)ethenyl]-1-octyluracil (*Z*- **9c**).

This compound was obtained as a yellow solid mp 108-110°; ^{1}H nmr: δ 0.87 (t, J = 6.8 Hz, 3H, CH$_3$), 1.32 (m, 10H, CH$_2$CH$_2$(C*H*$_2$)$_5$CH$_3$), 1.43 (m, 2H, CH$_2$C*H*$_2$(CH$_2$)$_5$CH$_3$), 3.54 (t, J = 7.4 Hz, 2H, C*H*$_2$CH$_2$(CH$_2$)$_5$CH$_3$), 6.53 (d, J = 12.2 Hz, 1H, CH=CH), 6.68 (d, J = 12.2 Hz, 1H, CH=CH), 6.97 (s, 1H, 6-H), 7.49 (d, J = 8.6 Hz, 2H, Ar-H), 8.19 (d, J = 8.6 Hz, 2H, Ar-H), 9.38 (br s, 1H, NH); ^{13}C nmr: δ 14.0 (CH$_3$), 22.5, 26.2, 29.0, 29.2, 29.7 and 31.7 (CH$_2$(*C*H$_2$)$_6$CH$_3$), 48.9 (*C*H$_2$(CH$_2$)$_6$CH$_3$), 109.9 (C-5), 123.7, 124.1, 129.1, 129.3, 142.9, 143.8 and 146.7 (CH=CH, C-6 and C-Ar), 150.0 (C-2), 162.8 (C-4); ms: m/z 371 (M$^+$, 48% rel. int.).

Anal. Calcd. for $C_{20}H_{25}N_3O_4$: C, 64.67; H, 6.78; N, 11.31. Found: C, 65.02; H, 6.99; N, 10.98.

5-[(*E*)-2-(4-Nitrophenyl)ethenyl]-1,3-dioctyluracil (*E*-**10c**).

This compound was obtained as an oil; ^{1}H nmr: δ 0.88 (m, 6H, CH$_3$), 1.26-1.34 (m, 20H, CH$_2$CH$_2$(C*H*$_2$)$_5$CH$_3$), 1.66-1.75 (m, 4H,

$CH_2CH_2(CH_2)_5CH_3$), 3.82 (t, J = 7.1 Hz, 2H, CH_2CH_2-$(CH_2)_5CH_3$), 4.00 (t, J = 7.7 Hz, 2H, CH_2CH_2-$(CH_2)_5CH_3$), 6.94 (d, J = 16.7 Hz, 1H, CH=CH), 7.37 (s, 1H, 6-H), 7.55 (d, J = 16.7 Hz, 1H, CH=CH), 7.63 (d, J = 9.0 Hz, 2H, Ar-H), 8.19 (d, J = 9.0 Hz, 2H, Ar-H); ^{13}C nmr: δ 14.0 (CH_3), 22.6, 26.5, 27.0, 27.5, 29.1, 29.2, 29.3, 29.7, 31.7, 31.8, and 31.9 ($CH_2(CH_2)_6CH_3$), 41.8 and 50.3 ($CH_2(CH_2)_6CH_3$), 110.5 (C-5), 124.1, 125.1, 126.6, 126.9, 141.0, 144.2 and 146.6 (CH=CH, C-6 and C-Ar), 150.2 (C-2), 161.6 (C-4); ms: m/z 483 (M^+, 100% rel. int.).

Anal. Calcd. for $C_{28}H_{41}N_3O_4$: C, 69.54; H, 8.54; N, 8.69. Found: C, 69.51; H, 8.58; N, 9.04.

5-[(*Z,*)-2-(4-Nitrophenyl)ethenyl]-1,3-dioctyluracil (*Z*-**10c**).

This compound was obtained as an oil; ^{1}H nmr: δ 0.88 (m, 6H, CH_3), 1.26-1.34 (m, 20H, $CH_2CH_2(CH_2)_5CH_3$), 1.44-1.62 (m, 4H, $CH_2CH_2(CH_2)_5CH_3$), 3.55 (t, J = 7.1 Hz, 2H, $CH_2CH_2(CH_2)_5$-CH_3), 3.96 (t, J = 7.7 Hz, 2H, $CH_2CH_2(CH_2)_5CH_3$), 6.53 (d, J = 12.2 Hz, 1H, CH=CH), 6.64 (d, J = 12.2 Hz, 1H, CH=CH), 6.96 (s, 1H, 6-H), 7.49 (d, J = 8.4 Hz, 2H, Ar-H), 8.18 (d, J = 8.4 Hz, 2H, Ar-H); ^{13}C nmr: δ 14.0 (CH_3), 22.5, 22.6, 26.2, 26.9, 27.5, 29.1, 28.9, 29.1, 29.2, 31.6, and 31.7 ($CH_2(CH_2)_6CH_3$), 41.7 and 49.7 ($CH_2(CH_2)_6CH_3$), 109.0 (C-5), 123.9, 124.7, 128.3, 129.3, 140.8, 144.0 and 146.5 (CH=CH, C-6 and C-Ar), 150.5 (C-2), 162.1 (C-4); ms: m/z 483 (M^+, 100% rel. int.).

Anal. Calcd. for $C_{28}H_{41}N_3O_4$: C, 69.54; H, 8.54; N, 8.69. Found: C, 69.64; H, 8.78; N, 8.34.

2,4-Dimethoxy-5-[(*E*)- 2-(4-nitrophenyl)ethenyl]pyrimidine (*E*-**11c**).

This compound was obtained as a yellow solid mp 137-140°; ^{1}H nmr: δ 4.04 (s, 3H, OCH_3), 4.12 (s, 3H, OCH_3), 7.18 (d, J = 16.7 Hz, 1H, CH=CH), 7.25 (d, J = 16.7 Hz, 1H, CH=CH), 7.62 (d, J = 9.0 Hz, 2H, Ar-H), 8.22 (d, J = 9.0 Hz, 2H, Ar-H) 8.43 (s, 1H, 6-H); ^{13}C nmr: δ 54.3 and 55.1 (OCH_3), 112.0 (C-5), 124.1, 124.3, 126.8, 127.4, 129.2 and 144.0 (CH=CH and C-Ar), 157.0 (C-6), 164.7 (C-4), 168.4 (C-2): ms: m/z 287 (M^+, 45% rel. int.).

Anal. Calcd. for $C_{14}H_{13}N_3O_4$: C, 58.53; H, 4.56; N, 14.63. Found: C, 58.43; H, 4.59; N, 14.66.

2,4-Dimethoxy-5-[(*Z*)- 2-(4-nitrophenyl)ethenyl]pyrimidine (*Z*-**11c**).

This compound was obtained as a yellow solid mp 118-120°; ^{1}H nmr: δ 3.98 (s, 6H, OCH_3), 6.61 (d, J = 12.2 Hz, 1H, CH=CH), 6.71 (d, J = 12.2 Hz, 1H, CH=CH), 7.37 (d, J = 9.0 Hz, 2H, Ar-H), 7.96 (s, 1H, 6-H), 8.12 (d, J = 9.0 Hz, 2H, Ar-H); ^{13}C nmr: δ 54.1 and 54.9 (OCH_3), 110.9 (C-5), 123.8, 124.2, 128.3, 129.2, 129.3 and 143.8 (CH=CH and C-Ar), 157.8 (C-6), 164.7 (C-4), 168.6 (C-2): ms: m/z 287 (M^+, 48% rel. int.).

Anal. Calcd. for $C_{14}H_{13}N_3O_4$: C, 58.53; H, 4.56; N, 14.63. Found: C, 58.29; H, 4.50; N, 14.38.

1,3-dioctyl-5-[(*E*)-2-(4-pyridinyl)ethenyl]uracil (*E*-**10d**).

This compound was obtained as a oil; ^{1}H nmr: δ 0.91 (t, J = 6.4 Hz, 6H, CH_3), 1.30-1.36 (m, 20H, $CH_2CH_2(CH_2)_5CH_3$), 1.68-1.74 (m, 4H, $CH_2CH_2(CH_2)_5CH_3$), 3.84 (t, J = 7.3 Hz, 2H, $CH_2CH_2(CH_2)_5CH_3$), 4.02 (t, J = 7.7 Hz, 2H, CH_2CH_2-$(CH_2)_5CH_3$), 7.00 (d, J = 16.1 Hz, 1H, CH=CH), 7.32 (d, J = 4.8 Hz, 2H, Pyr-H), 7.38 (s, 1H, 6-H), 7.50 (d, J = 16.1 Hz, 1H, CH=CH), 8.56 (d, J = 4.8 Hz, 2H, Pyr-H); ^{13}C nmr: δ 14.1 (CH_3), 22.6, 26.3, 26.5, 27.0, 27.6, 29.1, 29.2, 29.3, 31.7 and 31.8 ($CH_2(CH_2)_6CH_3$), 41.8 and 50.3 ($CH_2(CH_2)_6CH_3$), 110.0 (C-5), 120.6, 125.0, 126.6, 140.8, 145.0 and 150.1 (CH=CH, C-Pyr. and C-6), 150.3 (C-2), 161.6 (C-4); ms: m/z 439 (M^+, 48% rel. int.).

Anal. Calcd. for $C_{27}H_{41}N_3O_2$: C, 73.76; H, 9.40; N, 9.56. Found: C, 73.58; H, 9.19; N, 9.90.

1,3-dioctyl-5-[(*Z*)-2-(4-pyridinyl)ethenyl]uracil (*Z*-**10d**).

This compound was obtained as a oil; ^{1}H nmr: δ 0.87 (t, J = 6.4 Hz, 6H, CH_3), 1.24-1.64 (m, 24H, $CH_2(CH_2)_6CH_3$), 3.53 (t, J = 7.1 Hz, 2H, $CH_2CH_2(CH_2)_5CH_3$), 3.96 (t, J = 7.4 Hz, 2H, $CH_2CH_2(CH_2)_5CH_3$), 6.52 (d, J = 12.2 Hz, 1H, CH=CH), 6.57 (d, J = 12.2 Hz, 1H, CH=CH), 6.95 (s, 1H, 6-H), 7.22 (d, J = 5.5 Hz, 2H, Pyr-H), 8.55 (d, J = 5.5 Hz, 2H, Pyr-H); ^{13}C nmr: δ 14.0 (CH_3), 22.6, 26.2, 26.9, 27.5, 29.0, 29.1, 29.2, 29.3, 31.6 and 31.7 ($CH_2(CH_2)_6CH_3$), 41.7 and 49.7 ($CH_2(CH_2)_6CH_3$), 108.9 (C-5), 120.0, 123.0, 124.7, 127.5, 140.7 and 145.0 (CH=CH, C-Pyr. and C-6), 150.3 (C-2), 162.2 (C-4); ms: 439 (M^+, 68% rel. int.).

Anal. Calcd. for $C_{27}H_{41}N_3O_2$: C, 73.76; H, 9.40; N, 9.56. Found: C, 73.72; H, 9.09; N, 9.60.

2,4-Dimethoxy-5-[(*E*)-2-(4-pyridinyl)ethenyl]pyrimidine (*E*-**11d**).

This compound was obtained as a white solid mp 112-114°; ^{1}H nmr: δ 4.03 (s, 3H, OCH_3), 4.10 (s, 3H, OCH_3), 7.10 (d, J = 16.7 Hz, 1H, CH=CH), 7.23 (d, J = 16.7 Hz, 1H, CH=CH), 7.37 (d, J = 6.4 Hz, 2H, Pyr-H), 8.42 (s, 1H, 6-H), 8.56 (d, J = 6.4 Hz, 2H, Pyr-H); ^{13}C nmr: δ 54.2 and 55.0 (OCH_3), 111.8 (C-5), 120.8, 124.5, 126.9, 145.3 and 149.4 (CH=CH and C-Pyr), 157.0 (C-6), 164.6 (C-4), 168.3 (C-2): ms: m/z 243 (M^+, 100% rel. int.).

Anal. Calcd. for $C_{13}H_{13}N_3O_2$: C, 64.19; H, 5.39; N, 17.27. Found: C, 63.98; H, 5.50; N, 16.99.

2,4-Dimethoxy-5-[(*Z*)-2-(4-pyridinyl)ethenyl]pyrimidine (*Z*-**11d**).

This compound was obtained as a white solid mp 88-91°; ^{1}H nmr: δ 3.95 (s, 3H, OCH_3), 3.97 (s, 3H, OCH_3), 6.57 (s, 2H, CH=CH), 7.08 (d, J = 5.1 Hz, 2H, Pyr-H), 7.97 (s, 1H, 6-H), 8.48 (d, J = 5.1 Hz, 2H, Pyr-H); ^{13}C nmr: δ 54.1 and 54.9 (OCH_3), 111.0 (C-5), 123.0, 124.4, 130.0, 144.7 and 150.1 (CH=CH and C-Pyr), 157.8 (C-6), 164.7 (C-4), 168.5 (C-2): ms: m/z 243 (M^+, 100% rel. int.).

Anal. Calcd. for $C_{13}H_{13}N_3O_2$: C, 64.19; H, 5.39; N, 17.27. Found: C, 64.02; H, 5.62; N, 17.05.

Demethylation of Compound **11c**.

A mixture of (*E*)- (*Z*)-isomers of **11c** (0.057 g, 0.2 mmoles) was heated with sodium iodide (0.1 g) in glacial acetic acid (3 ml) at 100° for 1 hour. The solvent was removed under reduced pressure and the residue was chromatographed on a silica gel column with 3% methanol in methylene chloride as the eluent. From the column 0.047 g (92 % yield) of the demethylated uracil **12** were obtained.

5-[(*E*)-2-(4-Nitrophenyl)ethenyl]uracil (**12**).

This compound was obtained as a yellow solid which does not melts up to 300°; ^{1}H nmr (DMSO-d_6): δ 7.11 (d, J = 16.5 Hz, 1H, CH=CH), 7.57 (d, J = 16.5 Hz, 1H, CH=CH), 7.62 (d, J = 8.2 Hz, 2H, Ar-H), 7.75 (s, 1H, 6-H), 8.12 (d, J = 8.2 Hz, 2H, Ar-H), 11.29 (br s, 2H, NH); ^{13}C nmr: δ 109.0 (C-5), 123.7, 124.6, 126.3, 126.4, 142.0, 144.8 and 145.6 (CH=CH, C-Ar and C-6), 150.3 (C-2), 162.8 (C-4); ms: m/z 259 (M^+, 48% rel.int.).

Anal. Calcd. for $C_{12}H_9N_3O_4$: C, 55.60; H, 3.50; N, 16.21. Found: C, 55.46; H, 3.35; N, 15.97.

Isomerization of *Z*-**10c** to *E*-**10c.**

A solution of *Z*-**10c** (0.048 g, 0.1 mmole) in glacial acetic acid (2 ml) was heated with sodium iodide (0.05 g) at 100° for 1 hour. The solvent was removed under reduced pressure and the residue taken up in diethyl ether (10 ml) and washed with water (2 x 10 ml). The organic layer was dried over sodium sulfate and concentrated to leave 0.04 g (83%) of *E*-**10c.**

Isomerization of the Mixture *E,Z*-**11a** to *E*-**11a.**

A solution of 1:1 mixture of *E,Z*-**11a** (0.067 g, 0.3 mmoles) in carbon tetrachloride (1 ml) was treated with thiophenol (0.017g, 0.15 mmoles) and 2,2'-azobis(2-methylpropionitrile) (AIBN, 0.008 g, 0.05 mmoles) at 80° for 3 hours. The reaction mixture was cooled to room temperature and taken up in ethyl acetate (10 ml) and washed with an 0.01 *N* NaOH aqueous solution (10 ml). The organic layer was dried over sodium sulfate and concentrated to leave an oil (0.07 g), which contained only (*E*)-isomer contaminated with aromatic thiol product, as it was shown by ^{1}H NMR spectrum.

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