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1,3-Dipolar cycloaddition approach to isoxazole, isoxazoline and isoxazolidine analogues of *C*-nucleosides related to pseudouridine

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Abstract—Isoxazole, isoxazoline and isoxazolidine analogues of *C*-nucleosides related to pseudouridine have been synthesized by 1,3-dipolar cycloaddition reactions of nitrile oxides and nitrones derived from mono and disubstituted uracil-5-carbaldehydes and 2,4-dimethoxypyrimidine-5-carbaldehyde. The dimethoxy derivatives have been easily deprotected to the corresponding uracils bearing the heterocyclic ring instead of a sugar moiety. The regio and stereoselectivity of the reactions are discussed.
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1. Introduction

Since the latter part of the 1980s unnatural nucleoside analogues have played an important role as anticancer and antiviral agents.[1] Consequently, several variations have been made to both the heterocyclic base and the sugar moiety in the search for effective and selective derivatives. Due to the need for the base moiety to preserve the base-pairing functionalities, only minor modifications of the base are usually found in biologically active nucleosides analogues. The C-5 position is usually the position of choice for the introduction of substituents in pyrimidine nucleosides since it is not involved in the Watson–Crick base-pairing.[2] On the contrary, a lot of variations have been made in the sugar part replacing it by acyclic moieties or carbo or other heterocyclic rings. Among them, isoxazoline and isoxazolidine nucleosides have emerged as an important class of nucleoside analogues and several approaches for their synthesis have been reported.[3]

Besides the variations in the sugar and base moieties a crucial modification results from varying their connection, as in the *C*-nucleosides, which have a carbon–carbon linkage instead of an hydrolyzable carbon–nitrogen bond between the sugar and the aglycon. The most abundant natural *C*-nucleoside is pseudouridine a C-5 linked uridine. Pseudouridine is the first *C*-nucleoside found in nature and has attracted the interest of organic chemists and biochemists since its discovery in 1957.[4] The occurrence of pseudouridine in highly conserved regions of RNA indicates that certain physicochemical properties of pseudouridine are critical to the biological function of RNA molecules.

Thus the biological significance of pseudouridine has resulted in studies aimed at the incorporation of synthetic pseudouridine analogues with modified sugar moieties.[5] Recently, the synthesis of isoxazoline analogues of pseudouridine by 1,3-dipolar cycloaddition reactions of 5-uracil nitrones has been described.[6]

During recent years and in connection with our interests to induce nucleoside modifications,[7] we have also attempted to apply the convenience and diversity of 1,3-dipolar cycloaddition reactions to the synthesis of pseudouridine analogues. However, our initial attempts to isolate cycloaddition products via the in situ formation of nitrile oxides from 5-uracilcarbaldehyde oxime or 1-monosubstituted 5-uracilcarbaldehyde oximes were unsuccessful even in the presence of very active dipolarophiles such as methyl acrylate. On the contrary these oximes gave mixtures of isoxazolidines from the reaction of intermediate nitrones.[8a] Nitrone generation from oximes via a 1,2-prototropic process or an 1,3-azaprotiocyclotransfer is a well known reaction established by Grigg,[8b,c] and it has been also described by us for other oximes.[8d] The last findings indicated that nitrone cycloaddition can work with uracil nitrones barrying free NH bonds. This has been also shown recently by the work of Chiacchio et al.[6]

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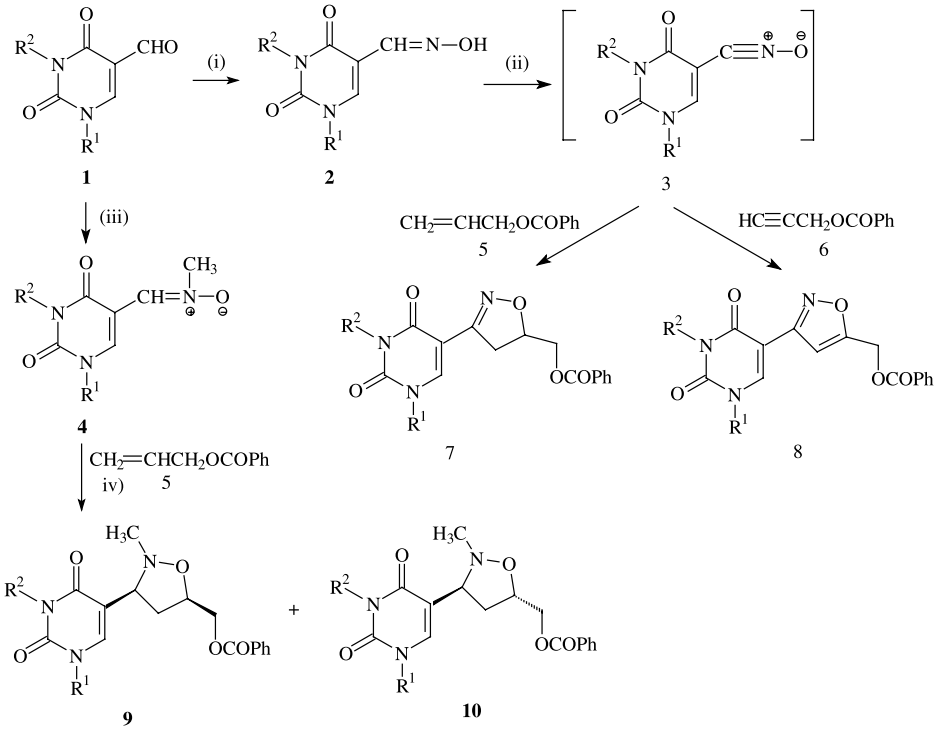
However, nucleoside analogues with restricted conformational flexibility induced by a second ring or by unsaturation are the target compounds in many cases, since they are potent inhibitors of HIV-1 reverse transcriptase.[3k,o,9] Thus, in order to expand the use of 5-uracil dipoles for the formation of both saturated and unsaturated rings, we report in this paper, the application of cycloaddition reactions of both nitrile oxides and nitrone uracil dipoles by applying monosubsituted, disubstituted and protected uracil derivatives.

2. Results and discussion

As starting materials for the formation of the dipoles we have chosen the mono and disubstituted aldehydes **1a** and **1b** and the dimethoxy-5-formyl pyrimidine **11** (Schemes 1 and 2). The octyl derivatives **1a** and **1b** have been chosen for purposes of higher solubility and enhanced hydrophobicity, whereas aldehyde **11** is a protected form of 5-formyluracil. The above aldehydes were prepared according to the procedures we have previously described.[10] The oximes **2a**, **2b**, **12** as well as the nitrones **4a**, **4b** and **14** were prepared from the corresponding aldehydes applying conventional procedures. As dipolarophiles, we have used allylic or propargylic alcohol derivatives in order to ensure the presence of a 5′-hydroxymethyl group in the final product, which potentially allows enzymatic phosphorylation for antiviral expression or incorporation into automatic solid phase synthesis.

Nitrile oxide **3b** was generated in situ from the corresponding oxime in the presence of the dipolarophile in a biphasic methylene chloride/aqueous bleach system. Generation of nitrile oxide **3a** following the same procedure was unsuccessful. As we have already mentioned, in our initial attempts we failed to isolate nitrile oxide cycloaddition products from 1-substituted uracil aldoximes. Thus, as well as the above standard procedure for the generation of the nitrile oxide **3a** from the oxime **2a**, several other alternative procedures using *N*-chlorosuccinimide, and several variations in the reaction time, temperatures and work up were also tested without success. Nitrile oxide **3b** reacted with both allylic benzoate (**5**) and propargylic benzoate (**6**) to give the isoxazoline **7b** and the isoxazole **8b**, respectively, in good yields (70–80%). The reactions were regioselective and only 5-substituted cycloadducts were isolated. The reactions of nitrones **4** with the alkene **5** took place under reflux in xylene to give isoxazolidines **9** as the main products in satisfactory yields (70–72%). The reactions were regio and stereoselective. In both cases only 5-substituted derivatives with a cis arrangement of the 3′ and 5′ substituents (structure **9**) were isolated, although in the crude reaction mixture, traces of compounds with structure **10** were also detected on the basis of some ^{1}H NMR chemical shifts (Table 1).

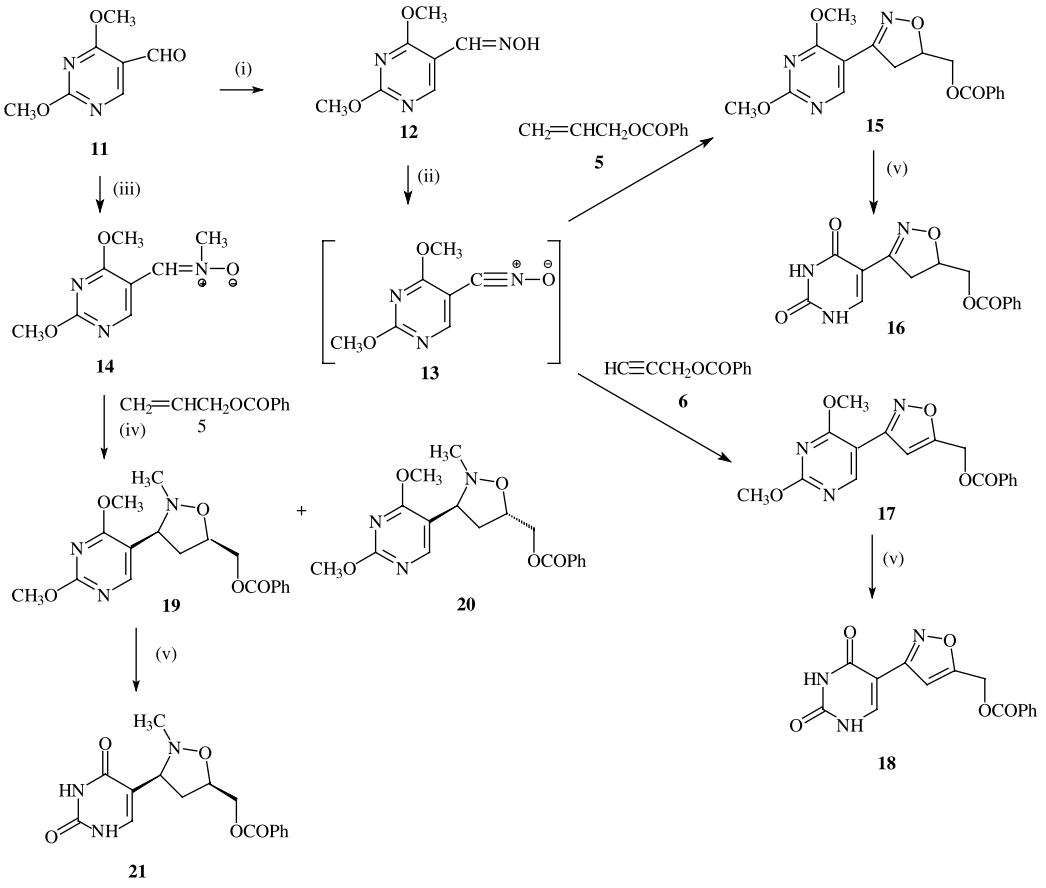
Dimethoxypyridine dipoles **13** and **14** showed analogous behaviour. Nitrile oxide **13** generated in situ from the oxime **12** reacted regioselectively with **5** to give the isoxazoline derivative **15**. The reaction of **13** with the alkyne derivative



1a, **2a**, **4a**, **9a**, **10a** $R^1 = CH_3(CH_2)_6CH_2$, $R^2 = H$

1b, **2b**,**3b**, **4b**, **7b**, **8b**, **9b**, **10b** $R^1 = R^2 = CH_3(CH_2)_6CH_2$

Scheme 1. Reagents and conditions: (i) $NH_2OH \cdot HCl$, Na_2CO_3, $EtOH/H_2O$, 20 °C, 24 h; (ii) NaOCl, CH_2Cl_2/H_2O, 0–20 °C, 24 h; (iii) $CH_3NHOH \cdot HCl$, Na_2CO_3, $EtOH/H_2O$, 20 °C, 24 h; (iv) Xylene, reflux, 48 h.



Scheme 2. Reagents and conditions: (i) $NH_2OH\cdot HCl$, Na_2CO_3, $EtOH/H_2O$, 20 °C, 24 h; (ii) NaOCl, CH_2Cl_2/H_2O, 0–20 °C, 24 h; (iii) $CH_3NHOH\cdot HCl$, Na_2CO_3, $EtOH/H_2O$, 20 °C, 24 h; (iv) Xylene, reflux, 48 h; (v) CH_3COOH, NaI, 90 °C, 1 h.

Table 1. Selected values for proton chemical shifts and coupling constants of compounds **9**, **10**, **19**, **20**

Compound	4′-Ha	4′-Hb	3′-H
9a	2.10 (dt, $J_{4'a,4'b}=12.2$ Hz, $J_{3',4'a}=J_{4'a,5'}=5.1$ Hz)	3.02 (ddd, $J_{4'a,4'b}=12.2$ Hz, $J_{3',4'b}=7.3$ Hz, $J_{4'b,5'}=8.4$ Hz)	4.03 (dd, $J_{3',4'a}=5.1$ Hz, $J_{3',4'b}=7.3$ Hz)
9b	2.05 (dt, $J_{4'a,4'b}=13.6$ Hz, $J_{3',4'a}=J_{4'a,5'}=5.1$ Hz)	3.02 (ddd, $J_{4'a,4'b}=13.6$ Hz, $J_{3',4'b}=7.8$ Hz, $J_{4'b,5'}=8.4$ Hz)	3.99 (dd, $J_{3',4'a}=5.1$ Hz, $J_{3',4'b}=7.8$ Hz)
19	2.05 (dt, $J_{4'a,4'b}=12.8$ Hz, $J_{3',4'a}=J_{4'a,5'}=6.4$ Hz)	2.89 (ddd, $J_{4'a,4'b}=12.8$ Hz, $J_{3',4'b}=8.4$ Hz, $J_{4'b,5'}=7.7$ Hz)	3.85 (dd, $J_{3',4'a}=6.4$ Hz, $J_{3',4'b}=8.4$ Hz)
20	2.41 (ddd, $J_{4'a,4'b}=14.2$ Hz, $J_{3',4'a}=5.7$ Hz, $J_{4'a,5'}=7.7$ Hz)	2.55 (ddd, $J_{4'a,4'b}=14.2$ Hz, $J_{3',4'b}=3.9$ Hz, $J_{4'b,5'}=8.9$ Hz)	4.24 (dd, $J_{3',4'a}=5.7$ Hz, $J_{3',4'b}=3.9$ Hz)
10a	2.29–2.37 (m)	2.60–2.69 (m)	4.22 (dd, $J_{3',4'a}=6.0$ Hz, $J_{3',4'b}=4.1$ Hz)
10b	2.25–2.35 (m)	2.60–2.69 (m)	4.22 (dd, $J_{3',4'a}=5.2$ Hz, $J_{3',4'b}=3.8$ Hz)

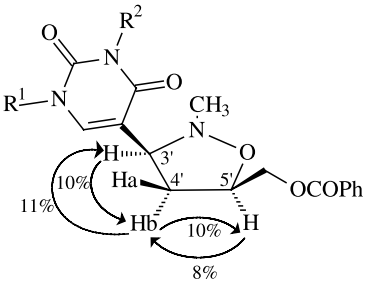
6 was also regioselective affording the 5′-substituted isomer **17**. The reaction of the nitrone **14** with the alkene **5** was also regioselective, but less stereospecific than that of nitrones **4** resulting in the formation of the two 5′-substituted stereoisomes **19** and **20** in a ratio 1.5:1.

The structure elucidation of the obtained cycloadducts was made on the basis of their elemental analysis and their spectral data. All the compounds give molecular ion peaks in the mass spectra and the expected chemical shifts in the ^1H and ^{13}C NMR spectra. The differentiation between stereoisomers **9** and **10** and between **19** and **20** was less obvious and was based on observed coupling constants and NOE measurements carried out on compound **9b**. The protons assignment was confirmed by decoupling experiments and selected chemical shifts and coupling constants of diagnostic value for compounds **9**, **10**, **19** and **20** are given in Table 1.

In **9a**, **9b**, and **19**, the one of 4′-H (4a′-H) appears at a higher field, and exhibits smaller coupling constants with both 3′-H and 5′-H than the other 4′-H (4b′-H), indicating a trans topological relationship with both of them. On the contrary, in compound **20** each of the 4′-H exhibits one large and one small coupling constant indicative that is trans to one and cis to the other. An interesting feature also in the ^1H NMR spectra is the difference in the chemical shifts of the two 4′-H protons, which is remarkably larger in the stereoisomers **9a**, **9b**, and **19** with a cis arrangement of the 3′ and 5′ substituents than in **20** with a trans arrangement probably as a result of the shielding effect of both substituents to the same proton. Also, the chemical shift of 3′-H is higher in

the trans isomer than in the cis. Thus the presence of multipets in the ^{1}H NMR of the crude reaction mixtures at the regions 2.25–2.37 and 2.60–269 as well as a dd at δ 4.22 are indicative for isomers **10a** and **10b**.

The proposed stereochemistry for the isolated cycloadducts was further supported by NOE measurements carried out on compound **9b**. As depicted in Figure 1, the mutual large NOE enhancements observed upon saturation of 3′-H, 5′-H and 4b′-H are in accordance with their cis arrangement.



9b

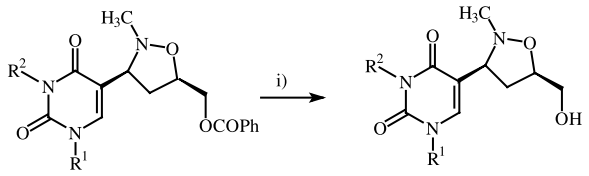
Figure 1.

It should be mentioned that the stereoselectivity of the reactions leading preferentially to cycloadducts with a cis arrangement of 3′ and 5′ substituents is favorable, since cis cycloaaducts match more the natural analogues. On the contrary, trans cycloadducts were referred as the main products of the reactions of unsubstituted uracil nitrones.[6] The observed stereoselectivity of the reactions can be explained via an *endo* approach of the dipolarophile assuming *Z*-configuration of the nitrone as it has been proved for aldonitrones.[6,11] Secondary interactions that favor an *endo* approach obviously prevail in the reactions of octyl and dioctyl substituted nitrones **4**, leading almost exclusively to the formation of cis cycloadducts **9**. In the reaction of the dimethoxy nitrone **14**, competition between steric factors and secondary interactions leads to the formation of a substantial amount of the minor trans isomer **20** as a product of the *exo* approach of the dipolarophile.

The dimethoxy derivatives **15**, **17** and **19** were readily transformed to uracil derivatives **16**, **18** and **21**, respectively, in satisfactory yields (67–72%) and without loss of the heterocyclic ring moiety, by heating in acetic acid in the presence of sodium iodide. The obtained uracils, besides the disappearance of the methoxy chemical shifts and the presence of NH resonances, exhibits in their NMR almost the same characteristics with their precursors.

The removal of the benzoyl group from the obtained cycloadducts can be also done easily by alkaline hydrolysis. In a representative experiment compounds **9a** and **9b** were transformed quantitatively to the corresponding hydroxy derivatives **22a** and **22b** with potassium hydroxide in aqueous methanol solution (Scheme 3).

In conclusion, cycloaddition reactions of nitrones or nitrile oxides derived from suitably substituted uracils or dimethoxy pyrimidines can be used as versatile procedures for the synthesis of modified pseudouridine analogues



9 **22**

9a, 22a $R^1 = CH_3(CH_2)_6CH_2$, $R^2 = H$

9b, 22b $R^1 = R^2 = CH_3(CH_2)_6CH_2$

Scheme 3. Reagents and conditions: (i) KOH, MeOH/H_2O, 20 °C, 24 h.

bearing isoxazole, isoxazoline or isoxazolidine rings instead of a sugar unit. The case of dimethoxy pyrimidine derivatives is significant in the sense that they could be deprotected without affecting the heterocyclic ring moiety. The presence of substituents differentiates the stereoselectivity of the reactions favoring those more close related to the natural products (cis cycloadducts) as a result of enhanced secondary interactions.

3. Experimental

3.1. General

Mps are uncorrected and were determined on a Kofler hot-stage microscope. IR spectra were recorded on a Perkin-Elmer 297 spectrometer. ^{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. Mass spectra (EI) were performed on a VG-250 spectrometer with ionization energy maintained at 70 eV. High resolution mass spectra (HRESI) were obtained with a 7 T APEX II spectrometer. 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 preparation of the aldehydes **1** and **11** was made according to previously described procedures.[10]

3.2. Synthesis of oximes 2 and 12

General procedure. An aqueous solution (2.5 ml) of hydroxylamine hydrochloride (2.25 mmol) and sodium carbonate (1.5 mmol) were added to an ethanolic solution (5 ml) of the aldehyde **1** or **11** (1 mmol) and the reaction mixture was stirred at room temperature for 24 h. After that the ethanol was evaporated, water was added and the mixture was extracted with methylene chloride. The organic layer was dried over sodium sulfate and after evaporation of the solvent the oximes were obtained as white solids and they were used without further purification.

3.2.1. 1-Octyl-5-uracilcarbaldehyde oxime (2a). This compound was obtained in 90% yield as a white solid, mp 173–176 °C; IR (Nujol): ν_{max} 3300, 3150, 3040, 1680, 1600 cm^{-1}; ^{1}H NMR (DMSO-d_6+$CDCl_3$)): δ 0.87 (t, J= 7.2 Hz, 3H, CH_3), 1.27–1.31 (m, 10H, $CH_2CH_2(CH_2)_5CH_3$), 1.68 (br t, 2H, $CH_2CH_2(CH_2)_5CH_3$), 3.74 (t, J=7.2 Hz, 2H,

$CH_2CH_2(CH_2)_5CH_3$), 7.82 and 7.95 (two s, 2H, CH=N and 6-H), 10.79 and 11.45 (two br s, 2H, NH and OH); ^{13}C NMR (DMSO-d_6+$CDCl_3$): δ 12.9 (CH_3), 21.2, 25.0, 27.7, 27.8 and 30.3 ($CH_2(CH_2)_6CH_3$), 47.6 ($CH_2(CH_2)_6CH_3$), 105.8 (C-5), 139.6 and 140.1 (C=N and C-6), 149.3 (C-2), 161.2 (C-4); MS (EI): *m/z* (%) 267 (M^+, 84). Anal. Calcd for $C_{13}H_{21}N_3O_3$: C, 58.41; H, 7.92; N, 15.72. Found: C, 58.41; H, 7.86; N, 15.35.

3.2.2. 1,3-Dioctyl-5-uracilcarbaldehyde oxime (2b). This compound was obtained in 87% yield as a white solid, mp 128–130 °C; IR (Nujol): ν_{max} 3290, 3040, 1685, 1620, 1590 cm^{-1}; ^{1}H NMR: δ 0.83–0.87 (m, 6H, CH_3), 1.27–1.32 (m, 20H, $CH_2CH_2(CH_2)_5CH_3$), 1.62–1.71 (m, 4H, $CH_2CH_2(CH_2)_5CH_3$), 3.78 (t, J=7.3 Hz, 2H, CH_2CH_2-$(CH_2)_5CH_3$), 3.95 (t, J=7.1 Hz, 2H, $CH_2CH_2(CH_2)_5CH_3$), 7.66 and 8.13 (two s, 2H, CH=N and 6-H), 8.80 (br s, 1H, OH); ^{13}C NMR: δ 14.0 (CH_3), 22.6, 26.4, 26.9, 27.5, 29.0, 29.2, 31.7 and 31.8 ($CH_2(CH_2)_6CH_3$), 41.8 and 50.4 ($CH_2(CH_2)_6CH_3$), 106.1 (C-5), 139.6 (C=N), 143.8 (C-6), 150.7 (C-2), 161.2 (C-4); MS (EI): *m/z* (%) 379 (M^+, 11). Anal. Calcd for $C_{21}H_{37}N_3O_3$: C, 66.46; H, 9.83; N, 11.07. Found: C, 66.45; H, 9.42; N, 10.79.

3.2.3. 2,4-Dimethoxy-5-pyrimidinecarbaldehyde oxime (12). This compound was obtained in 87% yield as a white solid, mp 150–154 °C; IR (Nujol): ν_{max} 3200, 3010, 1580, 1550 cm^{-1}; ^{1}H NMR: δ 4.04 (s, 3H, OCH_3), 4.06 (s, 3H, OCH_3), 8.19 and 8.56 (two s, 2H, 6-H and CH=N), 8.85 (br s, 1H, OH); ^{13}C NMR: δ 54.3 and 55.1 (OCH_3), 107.7 (C-5), 143.2 (C=N), 156.9 (C-6), 161.7 and 168.3 (C-2 and C-4); HRESIMS for $C_7H_9N_3O_3$ $(M+Na)^+$: calcd 206.0536, found 206.0536.

3.3. Synthesis of nitrones 4 and 14

General procedure. An aqueous solution (2.5 ml) of methylhydroxylamine hydrochloride (2 mmol) and sodium carbonate (1.5 mmol) were added to an ethanolic solution (5 ml) of the aldehyde **1** or **11** (1 mmol) and the reaction mixture was stirred at room temperature for 24 h. After that the ethanol was evaporated, water was added and the mixture was extracted with methylene chloride. After drying and evaporation of the solvent from the organic layer the residue nitrones were used without further purification.

3.3.1. *N*-Methyl-*C*-(1-octyl-5-uracil) nitrone (4a). This compound was obtained in 84% yield as a white solid, mp 190–193 °C; IR (Nujol): ν_{max} 3180, 3110, 3040, 1670, 1590 cm^{-1}; ^{1}H NMR (45 °C): δ 0.89 (br, 3H, CH_3), 1.29–1.34 (m, 10H, $CH_2CH_2(CH_2)_5CH_3$), 1.75 (br t, 2H, $CH_2CH_2(CH_2)_5CH_3$), 3.76–3.80 (m, 5H, $CH_2CH_2(CH_2)_5CH_3$ and N–CH_3), 7.56 (s, 1H, 6-H), 8.81 (br s, 1H, NH), 9.90 (s, 1H, CH=N(O)); ^{13}C NMR (45 °C): δ 13.8 (CH_3), 22.5, 26.5, 29.0 and 31.7 ($CH_2(CH_2)_6CH_3$), 47.6 ($CH_2(CH_2)_6CH_3$), 53.5 (*N*–CH_3), 106.5 (C-5), 127.6 (CH=N(O)), 144.3 (C-6), 149.8 (C-2), 161.8 (C-4); MS (EI): *m/z* (%) 281 (M^+, 86). Anal. Calcd for $C_{14}H_{23}N_3O_3$: C, 59.77; H, 8.24; N, 14.93. Found: C, 59.87; H, 8.07; N, 14.89.

3.3.2. *N*-Methyl-*C*-(1,3-dioctyl-5-uracil) nitrone (4b). This compound was obtained in 87% yield as a white solid, mp 70–72 °C; IR (Nujol): ν_{max} 3070, 3030, 1695, 1630, 1590 cm^{-1}; ^{1}H NMR: δ 0.85–0.89 (m, 6H, CH_3), 1.26–1.32 (m, 20H, $CH_2CH_2(CH_2)_5CH_3$), 1.58–1.67 (m, 4H, $CH_2CH_2(CH_2)_5CH_3$), 3.79 (t, J=7.3 Hz, 2H, $CH_2CH_2(CH_2)_5CH_3$), 3.81 (s, 3H, *N*–CH_3), 3.96 (t, J=7.4 Hz, 2H, $CH_2CH_2(CH_2)_5CH_3$), 7.62 (s, 1H, 6-H), 9.83 (s, 1H, CH=N(O)); ^{13}C NMR: δ 14.0 (CH_3), 22.5, 26.4, 26.9, 27.5, 29.0, 29.1, 29.2, 31.7 and 31.8 ($CH_2(CH_2)_6CH_3$), 41.8, 50.6 and 53.5 ($CH_2(CH_2)_6CH_3$ and *N*–CH_3), 105.6 (C-5), 128.5 (CH=N(O)), 142.5 (C-6), 150.1 (C-2), 161.4 (C-4); MS (EI): *m/z* (%) 393 (M^+, 26). Anal. Calcd for $C_{22}H_{39}N_3O_3$: C, 67.14; H, 9.99; N, 10.68. Found: C, 67.50; H, 9.58; N, 10.53.

3.3.3. *N*-Methyl-*C*-(1,3-dimethoxy-5-pyrimidine) nitrone (14). This compound was obtained in 75% yield as a white solid, mp 168–170 °C; IR (Nujol): ν_{max} 3040, 1585, 1570, 1540 cm^{-1}; ^{1}H NMR: δ 4.04, 4.05 and 4.12 (three s, 9H, OCH_3 and *N*–CH_3), 7.57 (s, 1H, 6-H), 10.19 (s, 1H, CH=N(O)); ^{13}C NMR: δ 53.9, 54.2 and 54.9 (OCH_3 and *N*–CH_3), 107.2 (C-5), 126.4 (CH=N(O)), 157.5 (C-6), 164.8 and 167.6 (C-2 and C-4); MS (EI): *m/z* (%) 197 (M^+, 100). Anal. Calcd for $C_8H_{11}N_3O_3$: C, 48.73; H, 5.62; N, 21.31. Found: C, 48.62; H, 5.53; N, 21.71.

3.4. Formation of nitrile oxides 3 and 13 and reactions with the dipolarophiles 5 and 6

General procedure. A solution of the aldoxime **2** or **12** (0.5 mmol) and the dipolarophile **5** or **6** (1 mmol) in methylene chloride (5 ml) was cooled to 0 °C and commercial bleach (4 ml) was added. The reaction mixture was warmed to room temperature and allowed to react overnight with stirring. The reaction mixture was extracted with methylene chloride and the organic layer was dried over sodium sulfate. After evaporation of the solvent the residue was chromatographed on a silica gel column with hexane–ethyl acetate (3/1 for the reactions of **2b**, 2/1 for reactions of **12**) as the eluent.

3.4.1. 5-(5′-Benzoyloxymethyl-isoxazolin-3′-yl)-1,3-dioctyluracil (7b). This compound was obtained in 70% yield as an oil; IR (liquid film): ν_{max} 3060, 1710–1640, 1595, 1575 cm^{-1}; ^{1}H NMR: δ 0.87–0.89 (m, 6H, CH_3), 1.26–1.31 (m, 20H, $CH_2CH_2(CH_2)_5CH_3$), 1.61–1.70 (m, 4H, $CH_2CH_2(CH_2)_5CH_3$), 3.44 (dd, J=18.0, 7.1 Hz, 1H, 4′-H), 3.65 (dd, J=18.0, 10.9 Hz, 1H, 4′-H), 3.78 (t, J=7.4 Hz, 2H, $CH_2CH_2(CH_2)_5CH_3$), 3.93 (t, J=7.4 Hz, 2H, $CH_2CH_2(CH_2)_5CH_3$), 4.38–4.49 (m, 2H, CH_2OCOPh), 4.98–5.10 (m, 1H, 5′-H), 7.42 (t, J=7.6 Hz, 2H, Ph-H), 7.56 (t, J=7.6 Hz, 1H, Ph-H), 7.88 (s, 1H, 6-H), 8.04 (d, J=7.6 Hz, 2H, Ph-H); ^{13}C NMR: δ 14.1 (CH_3), 22.7, 26.5, 26.9, 27.1, 27.2, 27.3, 27.5, 29.1, 29.2, 29.3, 31.7 and 31.8 ($CH_2(CH_2)_6CH_3$), 39.0 (C-4′), 41.9 and 50.5 ($CH_2(CH_2)_6CH_3$), 65.4 (CH_2OCOPh), 78.5 (C-5′), 103.5 (C-5), 128.4, 129.7, 129.8 and 133.2 (C-Ph), 141.7 (C-6), 150.6 and 152.8 (C-2 and C=N), 161.0 (C-4), 166.3 (C=O); MS (EI): *m/z* (%) 539 (M^+, 8). Anal. Calcd for $C_{31}H_{45}N_3O_5$: C, 68.99; H, 8.40; N, 7.79. Found: C, 69.27; H, 8.57; N, 7.99.

3.4.2. 5-(5′-Benzoyloxymethyl-isoxazol-3′-yl)-1,3-dioctyluracil (8b). This compound was obtained in 80% yield as a white solid, mp 47–49 °C; IR (Nujol): ν_{max} 3050, 1710,

1650, 1595 cm^{-1}; ^1H NMR: δ 0.85–0.89 (m, 6H, CH_3), 1.26–1.32 (m, 20H, $CH_2CH_2(CH_2)_5CH_3$), 1.62–1.78 (m, 4H, $CH_2CH_2(CH_2)_5CH_3$), 3.83 (t, J=7.4 Hz, 2H, $CH_2CH_2(CH_2)_5CH_3$), 3.99 (t, J=7.4 Hz, 2H, $CH_2CH_2(CH_2)_5CH_3$), 5.46 (s, 2H, CH_2OCOPh), 7.13 (s, 1H, 4′-H), 7.46 (t, J=7.4 Hz, 2H, Ph-H), 7.60 (t, J=7.4 Hz, 1H, Ph-H), 8.05 (s, 1H, 6-H), 8.07 (d, J=7.4 Hz, 2H, Ph-H); ^{13}C NMR: δ 14.0 (CH_3), 22.5, 26.4, 26.8, 26.9, 27.5, 29.0, 29.1, 29.2, 31.7 and 31.8 ($CH_2(CH_2)_6CH_3$), 41.9 and 50.5 ($CH_2(CH_2)_6CH_3$), 56.9 (CH_2OCOPh), 102.4 (C-5), 104.5 (C-4′), 128.4, 129.1, 129.9 and 133.5 (C-Ph), 141.6 (C-6), 150.6 (C-2), 156.8 (C=N), 161.9 (C-4), 165.7 and 166.3 (C=O and C-5′); HRESIMS for $C_{31}H_{43}N_3O_5$ $(M+Na)^+$: calcd 560.3095, found 560.3098.

3.4.3. 5-(5′-Benzoyloxymethyl-isoxazolin-3′-yl)-2,4-dimethoxypyrimidine (15). This compound was obtained in 65% yield as a white solid, mp 132–133 °C; IR (Nujol): ν_{max} 3030, 1710, 1595, 1535 cm^{-1}; ^1H NMR: δ 3.32 (dd, J=17.4, 6.8 Hz, 1H, 4′-H), 3.57 (dd, J=17.4, 10.9 Hz, 1H, 4′-H), 4.01 (s, 3H, OCH_3), 4.04 (s, 3H, OCH_3), 4.43–4.56 (m, 2H, CH_2OCOPh), 5.08–5.17 (m, 1H, 5′-H), 7.41 (t, J=7.6 Hz, 2H, Ph-H), 7.55 (t, J=7.6 Hz, 1H, Ph-H), 8.02 (d, J=7.6 Hz, 2H, Ph-H), 8.65 (s, 1H, 6-H); ^{13}C NMR: δ 39.0 (C-4′), 54.2 and 54.4 (OCH_3), 65.4 (CH_2OCOPh), 78.0 (C-5′), 105.2 (C-5), 128.3, 129.4, 129.5 and 133.1 (C-Ph), 151.5 (C=N), 158.1 (C-6), 165.7, 166.1 and 167.9 (C-2, C-4 and C=O); MS (EI): m/z (%) 343 (M^+, 9%). Anal. Calcd for $C_{17}H_{17}N_3O_5$: C, 59.47; H, 4.99; N, 12.44. Found: C, 59.34; H, 4.89; N, 12.39.

3.4.4. 5-(5′-Benzoyloxymethyl-isoxazol-3′-yl)-2,4-dimethoxypyrimidine (17). This compound was obtained in 90% yield as a white solid, mp 98–100 °C; IR (Nujol): ν_{max} 3050, 1715, 1590, 1550 cm^{-1}; ^1H NMR: δ 4.07 (s, 3H, OCH_3), 4.11 (s, 3H, OCH_3), 5.48 (s, 2H, CH_2OCOPh), 6.82 (s, 1H, 4′-H), 7.47 (t, J=7.4 Hz, 2H, Ph-H), 7.58 (t, J=7.4 Hz, 1H, Ph-H), 8.09 (d, J=7.4 Hz, 2H, Ph-H), 8.85 (s, 1H, 6-H); ^{13}C NMR: δ 54.4 and 55.2 (OCH_3), 56.7 (CH_2OCOPh), 104.7 (C-5), 104.9 (C-4′), 128.5, 129.5, 129.9 and 133.6 (C-Ph), 156.6 (C=N), 158.1 (C-6), 163.5, 165.8, 166.7 and 168.1 (C-2, C-4, C-5′ and C=O); MS (EI): m/z (%) 341 (M^+, 23). Anal. Calcd for $C_{17}H_{15}N_3O_5$: C, 59.82; H, 4.43; N, 12.31. Found: C, 59.60; H, 4.53; N, 12.51.

3.5. Reactions of nitrones 4 and 14 with the dipolarophile 5

General procedure. A solution of the nitrone **4** or **14** (0.5 mmol) and the dipolarophile **5** (1 mmol) in xylene (5 ml) was heated to reflux and the reaction was monitored by TLC until the consumption of the nitrone. After 2 days only traces of the nitrone were detected in the TLC. The heating was stopped and after evaporation of the solvent the residue was chromatographed on a silica gel column with hexane–ethyl acetate (1/1 for the reaction of **4a**, 3/1 for the reaction of **4b**, 2/1 for the reaction of **14**) as the eluent.

3.5.1. (3′*RS*,5′*SR*)-5-(5′-Benzoyloxymethyl-isoxazolidin-3′-yl)-1-octyluracil (9a). This compound was obtained in 72% yield as an oil; IR (liquid film): ν_{max} 3190, 3060, 1715–1650, 1595, 1575 cm^{-1}; ^1H NMR: δ 0.87 (t, J=8.5 Hz, 3H, CH_3), 1.15–1.40 (m, 10H, $CH_2CH_2(CH_2)_5CH_3$), 1.50–1.65 (m, 2H, $CH_2CH_2(CH_2)_5CH_3$), 2.10 (dt, J=12.2, 5.1 Hz, 1H, 4′-H), 2.73 (s, 3H, N–CH_3), 3.02 (ddd, J=12.2, 8.4, 7.3 Hz, 1H, 4′-H), 3.48–3.76 (m, 2H, $CH_2CH_2(CH_2)_5CH_3$), 4.03 (dd, J=7.3, 5.1 Hz, 1H, 3′-H), 4.31 (dd, J=12.0, 6.0 Hz, 1H, CH_2OCOPh), 4.47 (dd, J=12.0, 3.3 Hz, 1H, CH_2OCOPh), 4.67 (dddd, J=8.4, 6.0, 5.1, 3.3 Hz, 1H, 5′-H), 7.41 (t, J=7.4 Hz, 2H, Ph-H), 7.43 (s, 1H, 6-H) 7.55 (t, J=7.4 Hz, 1H, Ph-H), 7.98 (d, J=7.4 Hz, 2H, Ph-H), 9.81 (s, 1H, NH); ^{13}C NMR: δ 13.9 (CH_3), 22.5, 26.3, 28.9, 29.0 and 31.6 ($CH_2(CH_2)_6CH_3$), 37.5 (C-4′), 44.1 and 48.7 ($CH_2(CH_2)_6CH_3$ and N–CH_3), 63.1 and 64.9 (C-3′ and CH_2OCOPh), 74.6 (C-5′), 113.6 (C-5), 128.3, 129.4, 129.6 and 133.1 (C-Ph), 141.7 (C-6), 150.5 (C-2), 163.5 (C-4), 166.1 (C=O); MS (EI): m/z (%) 443 (M^+, 10). Anal. Calcd for $C_{24}H_{33}N_3O_5$: C, 64.99; H, 7.50; N, 9.57. Found: C, 65.11; H, 7.50; N, 9.24.

3.5.2. (3′*RS*,5′*SR*)-5-(5′-Benzoyloxymethyl-isoxazolidin-3′-yl)-1,3-dioctyluracil (9b). This compound was obtained in 70% yield as an oil; IR (liquid film): ν_{max} 3060, 1720–1690, 1660–1630, 1590 cm^{-1}; ^1H NMR: δ 0.85–0.92 (m, 6H, CH_3), 1.15–1.40 (m, 20H, $CH_2CH_2(CH_2)_5CH_3$), 1.50–1.70 (m, 4H, $CH_2CH_2(CH_2)_5CH_3$), 2.05 (dt, J=13.6, 5.1 Hz, 1H, 4′-H), 2.73 (s, 3H, N–CH_3), 3.02 (ddd, J=13.6, 8.4, 7.8 Hz, 1H, 4′-H), 3.49–3.75 (m, 2H, $CH_2CH_2(CH_2)_5CH_3$), 3.90 (t, J=9.3 Hz, 2H, $CH_2CH_2(CH_2)_5CH_3$), 3.99 (dd, J=7.8, 5.1 Hz, 1H, 3′-H), 4.32 (dd, J=11.9, 6.1 Hz, 1H, CH_2OCOPh), 4.43 (dd, J=11.9, 3.1 Hz, 1H, CH_2OCOPh), 4.67 (dddd, J=8.4, 6.1, 5.1, 3.1 Hz, 1H, 5′-H), 7.37 (s, 1H, 6-H), 7.41 (t, J=7.6 Hz, 2H, Ph-H), 7.56 (t, J=7.6 Hz, 1H, Ph-H), 7.97 (d, J=7.6 Hz, 2H, Ph-H); ^{13}C NMR: δ 14.0 (CH_3), 22.5, 26.4, 26.9, 27.5, 28.9, 29.0, 29.1, 31.6 and 31.7 ($CH_2(CH_2)_6CH_3$), 37.7 (C-4′), 41.4, 44.2 and 49.7 ($CH_2(CH_2)_6CH_3$ and N–CH_3), 63.7 and 65.1 (C-3′ and CH_2OCOPh), 74.5 (C-5′), 112.9 (C-5), 128.3, 129.5, 129.7 and 133.1 (C-Ph), 139.3 (C-6), 150.8 (C-2), 162.6 (C-4), 166.2 (C=O); MS (EI): m/z (%) 555 (M^+, 16). Anal. Calcd for $C_{32}H_{49}N_3O_5$: C, 69.16; H, 8.89; N, 7.56. Found: C, 69.46; H, 8.81; N, 7.25.

3.5.3. (3′*RS*,5′*SR*)-5-(5′-Benzoyloxymethyl-isoxazolidin-3′-yl)-2,4-dimethoxypyrimidine (19). This compound was obtained in 52% yield as an oil; IR (liquid film): ν_{max} 3060, 1715, 1595, 1565 cm^{-1}; ^1H NMR: δ 2.05 (dt, J=12.8, 6.4 Hz, 1H, 4′-H), 2.68 (s, 3H, N–CH_3), 2.89 (ddd, J=12.8, 8.4, 7.7 Hz, 1H, 4′-H), 3.85 (dd, J=8.4, 6.4 Hz, 1H, 3′-H), 3.97 (s, 3H, OCH_3), 4.00 (s, 3H, OCH_3), 4.37 (dd, J=11.5, 3.9 Hz, 1H, CH_2OCOPh), 4.45 (dd, J=11.5, 7.1 Hz, 1H, CH_2OCOPh), 4.61 (dddd, J=7.7, 7.1, 6.4, 3.9 Hz, 1H, 5′-H), 7.37 (s, 1H, 6-H), 7.42 (t, J=7.6 Hz, 2H, Ph-H), 7.54 (t, J=7.6 Hz, 1H, Ph-H), 8.01 (d, J=7.6 Hz, 2H, Ph-H); ^{13}C NMR: δ 38.9 (C-4′), 43.5 (N–CH_3), 53.9 (OCH_3), 54.7 (OCH_3), 64.1 and 66.0 (C-3′ and CH_2OCOPh), 74.3 (C-5′), 113.1 (C-5), 128.2, 129.6, 129.8 and 132.9 (C-Ph), 156.4 (C-6), 164.6, 166.4 and 168.7 (C-2, C-4 and C=O); MS (EI): m/z (%) 359 (M^+, 17). Anal. Calcd for $C_{18}H_{21}N_3O_5$: C, 60.16; H, 5.89; N, 11.69. Found: C, 60.28; H, 6.10; N, 11.39.

3.5.4. (3′*RR*,5′*SS*)-5-(5′-Benzoyloxymethyl-isoxazolidin-3′-yl)-2,4-dimethoxy-pyrimidine (20). This compound was obtained in 26% yield as an oil; IR (liquid film): ν_{max} 3060, 1710, 1660, 1600–1560 cm^{-1}; ^1H NMR: δ 2.41 (ddd, J=14.2, 7.7, 5.7 Hz, 1H, 4′-H), 2.55 (ddd, J=14.2, 8.9,

3.9 Hz, 1H, 4′-H), 2.69 (s, 3H, *N*–CH_3), 4.00 (s, 3H, OCH_3), 4.02 (s, 3H, OCH_3), 4.24 (dd, J=5.7, 3.9 Hz, 1H, 3′-H), 4.41 (dd, J=12.2, 6.4 Hz, 1H, CH_2OCOPh), 4.50–4.61 (m, 2H, CH_2OCOPh and 5′-H), 7.47 (t, J=7.4 Hz, 2H, Ph-H), 7.57 (t, J=7.4 Hz, 1H, Ph-H), 8.11 (d, J=7.4 Hz, 2H, Ph-H), 8.35 (s, 1H, 6-H); ^{13}C NMR: δ 38.7 (C-4′), 43.8 (*N*–CH_3), 54.0 (OCH_3), 54.7 (OCH_3), 64.0 and 65.4 (C-3′ and CH_2OCOPh), 74.8 (C-5′), 112.6 (C-5), 128.3, 129.6, 129.9 and 133.0 (C-Ph), 156.6 (C-6), 164.6, 167.6 and 169.3 (C-2, C-4 and C=O); MS (EI): *m*/*z* (%) 359 (M^+, 14). Anal. Calcd for $C_{18}H_{21}N_3O_5$: C, 60.16; H, 5.89; N, 11.69. Found: C, 60.26; H, 5.99; N, 11.30.

3.6. Demethylation of compounds 15, 17 and 19

General procedure. The dimethoxy derivative **15** or **17** or **19** (0.2 mmol) was heated with sodium iodide (0.1 g) in glacial acetic acid (3 ml) at 90 °C for 1 h. 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.

3.6.1. 5-(5′-Benzoyloxymethyl-isoxazolin-3′-yl)-uracil (16). This compound was obtained in 72% yield as a white solid, mp 253–257 °C; IR (Nujol): ν_{max} 3210, 3080, 3040, 1710, 1640 cm^{-1}; ^{1}H NMR ($CDCl_3$/DMSO-d_6): δ 3.35 (dd, J=17.8, 6.9 Hz, 1H, 4′-H), 3.52 (dd, J=17.8, 11.0 Hz, 1H, 4′-H), 4.33 (dd, J=12.3, 5.5 Hz, 1H, CH_2OCOPh), 4.42 (dd, J=12.3, 3.5 Hz, 1H, CH_2OCOPh), 4.96 (dddd, J=11.0, 6.9, 5.5, 3.5 Hz, 1H, 5′-H), 7.48 (t, J=7.7 Hz, 2H, Ph-H), 7.63 (t, J=7.7 Hz, 1H, Ph-H), 7.77 (s, 1H, 6-H), 7.96 (d, J=7.7 Hz, 2H, Ph-H), 10.12 (br s, 2H, NH); ^{13}C NMR ($CDCl_3$/DMSO-d_6): δ 36.5 (C-4′), 63.7 (*C*H_2OCOPh), 75.5 (C-5′), 101.1 (C-5), 126.7, 127.4, 127.7 and 131.4 (C-Ph), 139.6 (C-6), 148.9 (C-2), 150.4 (C=N), 160.1 (C-4), 163.4 (C=O); HRESIMS for $C_{15}H_{13}N_3O_5$ $(M+Na)^+$: calcd 338.0747, found 338.0748.

3.6.2. 5-(5′-Benzoyloxymethyl-isoxazol-3′-yl)-uracil (18). This compound was obtained in 67% yield as a white solid, mp 217–220 °C; IR (Nujol): ν_{max} 3210, 3080, 3050, 1715, 1590 cm^{-1}; ^{1}H NMR ($CDCl_3$/DMSO-d_6): δ 5.47 (s, 2H, CH_2OCOPh), 7.02 (s, 1H, 4′-H), 7.51 (t, J=7.4 Hz, 2H, Ph-H), 7.64 (t, J=7.4 Hz, 1H, Ph-H), 8.01–8.07 (overlapped d and s, 3H, Ph-H and 6-H), 11.34–11.52 (overlapped br s, 2H, NH); ^{13}C NMR ($CDCl_3$/DMSO-d_6): δ 55.1 (*C*H_2OCOPh), 100.0 (C-5), 102.7 (C-4′), 126.9, 127.7, 128.0 and 131.9 (C-Ph), 139.5 (C-6), 149.3, 155.1, 160.6 163.5 and 164.6 (C-2, C-4, C=N C-5′and C=O); HRESIMS for $C_{15}H_{11}N_3O_5$ $(M+Na)^+$: calcd 336.0591, found 336.0591.

3.6.3. (3′*RS*,5′*SR*)-5-(5′-Benzoyloxymethyl-isoxazolidin-3′-yl)-uracil (21). This compound was obtained in 76% yield as a white solid, mp 210–212 °C; IR (Nujol): ν_{max} 3190, 3150, 3060, 1710, 1660 cm^{-1}; ^{1}H NMR ($CDCl_3$/CD_3OD): δ 2.03 (dt, J=12.9, 6.1 Hz, 1H, 4′-H), 2.72 (s, 3H, *N*–CH_3), 2.98 (ddd, J=12.9, 9.2, 7.4 Hz, 1H, 4′-H), 3.85 (dd, J=7.4, 6.1 Hz, 1H, 3′-H), 4.33–4.42 (m, 2H, CH_2OCOPh), 4.61–4.70 (m, 1H, 5′-H), 7.42 (s, 1H, 6-H), 7.43 (t, J=7.4 Hz, 2H, Ph-H), 7.56 (t, J=7.4 Hz, 1H, Ph-H), 8.00 (d, J=7.4 Hz, 2H, Ph-H); ^{13}C NMR ($CDCl_3$/CD_3OD): δ 37.7 (C-4′), 43.9 (*N*–CH_3), 63.2 and 65.3 (C-3′ and *C*H_2OCOPh), 74.6 (C-5′), 113.0 (C-5), 128.3, 129.5 and 133.2 (C-Ph), 138.2 (C-6), 151.6 (C-2), 163.9 (C-4), 166.5 (C=O); MS: *m*/*z* (%) 331 (M^+, 10). Anal. Calcd for $C_{16}H_{17}N_3O_5$: C, 58.00; H, 5.17; N, 12.68. Found: C, 57.98; H, 5.01; N, 12.82.

3.7. Hydrolysis of compounds 9

General procedure. An aqueous solution (1 ml) of KOH (10%) was added to a methanolic solution (5 ml) of the compound **9a** or **9b** (0.1 mmol) and the reaction mixture was stirred at room temperature for 24 h. After that the methanol was evaporated, water was added, neutralized with ammonium chloride and the mixture was extracted with methylene chloride. The organic layer was dried over sodium sulfate and after evaporation of the solvent compounds **22** were obtained quantitatively as oils. For analytical purposes, they were further purified by column chromatography on a silica gel column with ethyl acetate as the eluent.

3.7.1. (3′*RS*,5′*SR*)-5-(5′-Hydroxymethyl-isoxazolidin-3′-yl)-1-octyluracil (22a). This compound was obtained in 100% yield as an oil; IR (liquid film): ν_{max} 3400, 3180, 3050, 1690–1640 cm^{-1}; ^{1}H NMR: δ 0.87 (t, J=6.6 Hz, 3H, CH_3), 1.19–1.40 (m, 10H, $CH_2CH_2(CH_2)_5CH_3$), 1.59–1.73 (m, 2H, $CH_2CH_2(CH_2)_5CH_3$), 2.01 (dt, J=12.9, 5.9 Hz, 1H, 4′-H), 2.50 (br s, 1H, OH), 2.69 (s, 3H, *N*–CH_3), 2.91 (dt, J=12.9, 7.9 Hz, 1H, 4′-H), 3.59 (dd, J=12.8, 5.3 Hz, 1H, CH_2OH), 3.64–3.79 (m, 3H, $CH_2CH_2(CH_2)_5CH_3$ and CH_2OH), 3.90 (dd, J=7.9, 5.9 Hz, 1H, 3′-H), 4.36–4.46 (m, 1H, 5′-H), 7.48 (s, 1H, 6-H), 9.62 (br s, 1H, NH); ^{13}C NMR: δ 14.0 (CH_3), 22.5, 26.4, 29.1, 29.7 and 31.6 ($CH_2(CH_2)_6CH_3$), 37.7 (C-4′), 44.0 and 49.1 ($CH_2(CH_2)_6CH_3$ and *N*–CH_3), 63.6 and 64.5 (C-3′ and *C*H_2OH), 76.6 (C-5′), 112.9 (C-5), 141.7 (C-6), 150.5 (C-2), 163.5 (C-4); MS (EI): *m*/*z* (%) 339 (M^+, 8). Anal. Calcd for $C_{17}H_{29}N_3O_4$: C, 60.15; H, 8.61; N,12.38. Found: C, 60.01; H, 8.90; N, 12.14.

3.7.2. (3′*RS*,5′*SR*)-5-(5′-Hydroxymethyl-isoxazolidin-3′-yl)-1,3-dioctyluracil (22b). This compound was obtained in 100% yield as an oil; IR (liquid film): ν_{max} 3400, 3060, 1690, 1660–1630 cm^{-1}; ^{1}H NMR: δ 0.85–0.92 (m, 6H, CH_3), 1.14–1.41 (m, 20H, $CH_2CH_2(CH_2)_5CH_3$), 1.50–1.75 (m, 4H, $CH_2CH_2(CH_2)_5CH_3$), 1.97 (dt, J=12.6, 6.4 Hz, 1H, 4′-H), 2.30 (br s, 1H, OH), 2.68 (s, 3H, *N*–CH_3), 2.87 (dt, J=12.6, 8.3 Hz, 1H, 4′-H), 3.59 (dd, J=11.9, 5.2 Hz, 1H, CH_2OH), 3.69–3.80 (m, 3H, $CH_2CH_2(CH_2)_5CH_3$ and CH_2OH), 3.85–3.96 (m, 3H, $CH_2CH_2(CH_2)_5CH_3$ and 3′-H), 4.34–4.43 (m, 1H, 5′-H), 7.35 (s, 1H, 6-H); ^{13}C NMR: δ 14.0 (CH_3), 22.6, 26.5, 27.0, 27.5, 29.1, 29.2, 29.7, 31.7 and 31.8 ($CH_2(CH_2)_6CH_3$), 38.0 (C-4′), 41.6, 44.0 and 50.0 ($CH_2(CH_2)_6CH_3$ and N–CH_3), 64.1 and 64.9 (C-3′ and *C*H_2OH), 76.9 (C-5′), 112.1 (C-5), 139.2 (C-6), 150.8 (C-2), 162.7 (C-4); MS (EI): *m*/*z* (%) 451 (M^+, 9). Anal. Calcd for $C_{25}H_{45}N_3O_4$: C, 66.48; H, 10.04; N, 9.30. Found: C, 66.26; H, 10.21; N, 9.25.

References and notes

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