130. Hetero-*Diels-Alder* Cycloadditions of α,β-Unsaturated Acyl Cyanides

Part 2[1])

Reactions with *N,N*-Dimethyluracils, a New Route to 5-Substituted Uracil Derivatives

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The [4 + 2] cycloadditions of 2-oxobut-3-enenitrile (**1a**), 2-oxopent-3-enenitrile (**1b**), and ethyl 4-cyano-4-oxobut-2-enoate (**1c**) with 1,3-dimethyluracil (**2**), 1,3,6-trimethyluracil (**9**), or 1,3,5-trimethyluracil (**16**) were investigated. The reactions of **1a** with **2** or with **9** lead to bicyclic adducts **3** and **10**, respectively. These hexahydro-*cis*-pyranopyrimidines undergo ring opening under acidic conditions, restoring in **4** and **11**, respectively, an uracil system comprising 2-hydroxybut-2-enenitrile as a side chain at C(5). The surprisingly stable enols tautomerize slowly to the corresponding acyl cyanides **6a** and **13a**, respectively. Reacting **1b** or **1c** with **2** and with **9** does not afford cycloadducts; instead the uracil derivatives **6b, c** and **13b, c**, respectively, show up, carrying at C(5) α-oxobutanenitrile side chains. Cleavage of the acyl cyanide functions in **6a–c** and **13a–c** with nucleophilic agents produces various acids, esters, or amides, *i.e.* derivatives **8a–c** and **15a–c**, respectively. The methyl esters **8a** (X = MeO, R = H) and **15a** (X = MeO, R = H) are also formed directly from the adducts **3** and **10**, respectively, with acid or base catalysis in presence of MeOH. The cycloadducts **17a** and **17c**, resulting from the reaction of **1a** and **1c** with **16**, respectively, have a Me group at the ring junction C(4a) and are stable. The structure of **17c** proves that this hetero-*Diels-Alder* addition of inverse electron demand follows the *endo*-mode.

Introduction. – Modified nucleic bases have been of interest as possible inhibitors of nucleic-acid biosynthesis in viral reproduction [1]. Among these figure alkylated uracils which were prepared [2] *a*) by metal-mediated coupling of halogenated derivatives with alkenes [3] or alkynes [4], and with photocoupling [5] [6] or *b*) by direct alkylations of uracil such as the hydroxymethylation [7], the *Mannich*-type (dimethylamino)-methylation [8], free-radical alkylations [9], and Pd-catalyzed oxidative coupling with olefins [10].

Though a certain enamine character of the 5,6-double bond of uracil was predicted on theoretical grounds [11], there is no experimental evidence of reactions typical for it. Related are some examples of additions with electrophiles [2], carbenes [12], or ylides [13], as well as the recently reported 1,3-dipolar addition to the 5,6-double bond of dimethyluracil of *in situ* generated nitrile oxides [14]; a *Diels-Alder*-type addition to this bond of uracil appears to be unknown.

In an earlier publication, it was shown that α,β-unsaturated acyl cyanides exhibit extraordinary reactivity towards enol ethers in a hetero-*Diels-Alder* cycloaddition of inverse electron demand [15]. This paper reports on successful reactions of such dienes with *N,N*-dimethyluracils as dienophiles. Cycloadducts were obtained in some cases, but

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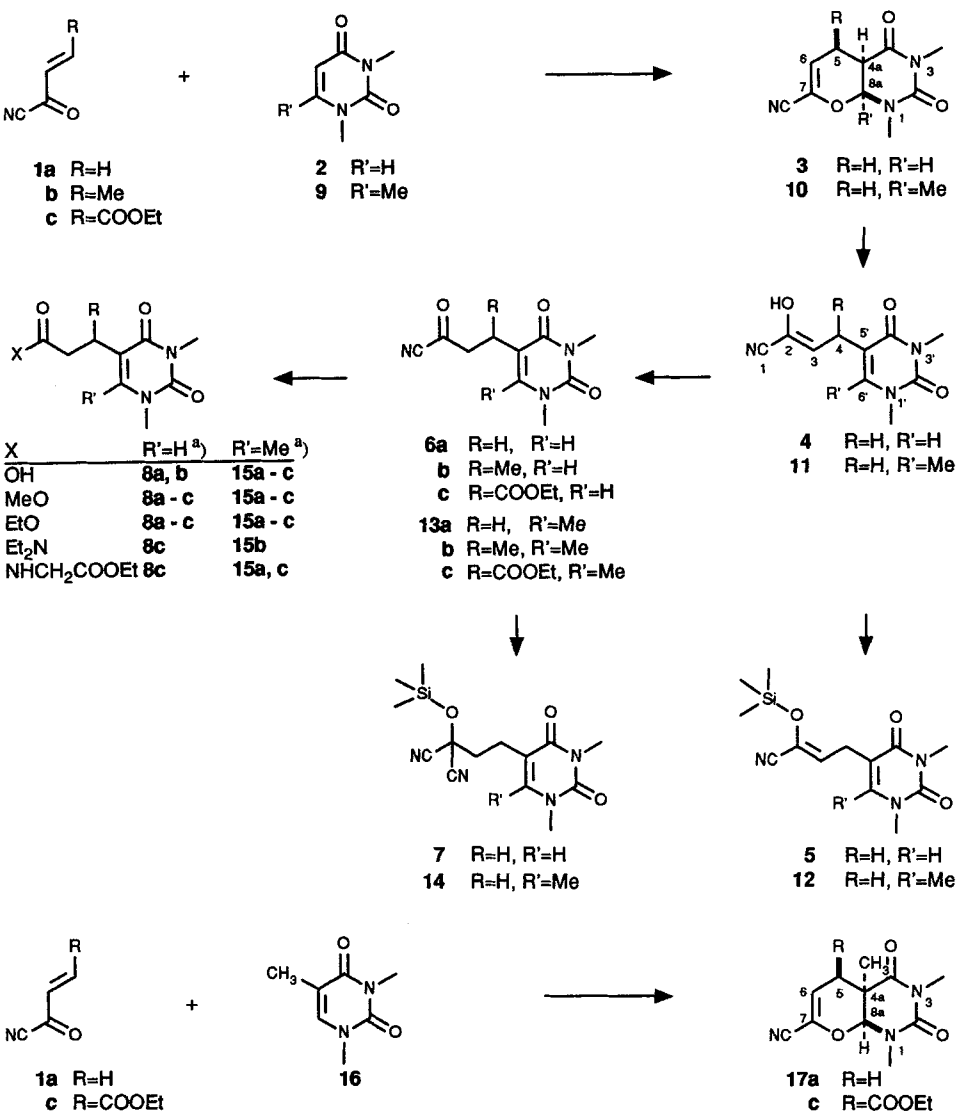
mostly uracil derivatives showed up carrying a side chain at C(5), an incident which has raised our interest.

Results. – 1. *Cycloadducts.* The reaction of the unsubstituted acryloyl cyanide **1a** with 1,3-dimethyluracil (**2**) in refluxing MeCN (81°) produces the bicyclic hexahydro-pyranopyrimidine **3**, isolated in 81% yield (*Scheme*). Its structure can be confirmed by MS and NMR spectroscopy.

Scheme



X	R'=H [a])	R'=Me [a])
OH	**8a, b**	**15a - c**
MeO	**8a - c**	**15a - c**
EtO	**8a - c**	**15a - c**
Et_2N	**8c**	**15b**
$NHCH_2COOEt$	**8c**	**15a, c**

[a]) For R (*i.e.* **a–c**), see **1a–c**.

The MS of **3** shows the molecular ion at *m/z* 221 and fragments of a *retro-Diels-Alder* reaction at *m/z* 140 (*N*,*N*-dimethyluracil; at *m/z* 83 and 55 are further fragments of it), and 81 (2-oxobut-3-enenitrile). A ^{1}H-NMR spectrum in CD_3COCD_3 presents all *m*'s well separated[2]). The angular protons H–C(4a) (δ 3.50) and H–C(8a) (δ 5.52), with a small coupling (J = 3.2 Hz) are *cis* as shown in NOE experiments by mutual enhancements (4–5%). Irradiation of H–C(4a) causes also enhancement (by 3.1%) of one of the geminal protons at C(5) (Hα–C(5)), the latter thus being *cis* to H–C(4a) and H–C(8a). The other proton at C(5), H$_\beta$–C(5), hence *trans* to H–C(4a) and H–C(8a), shows a weak ^4J coupling constant (< 0.5 Hz) with H–C(8a) (not visible in the spectrum in $CDCl_3$), usually only found for 1,3-protons in a *W*-conformation.

The cycloadduct **3**, when treated with a catalytic amount of HCl/Et_2O in MeCN, undergoes ring opening to form an enol **4**. Significant for the structure of enol **4** is its reaction with trimethylsilyl cyanide leading to trimethylsilyl ether **5**; the ^{1}H- and ^{13}C-NMR data of this compound correspond to those of known enol ethers of this type (which were prepared from acyl chlorides by treatment with trimethylsilyl cyanide or with trimethylsilyl chloride in presence of Et_3N [16a]).

Enol **4** exhibits in the ^{1}H-NMR spectrum ($CDCl_3$, 20°) a broad *s* at δ 9.58 of the enolic OH which disappears in presence of D_2O. There are 2 *t*'s of two olefinic protons at δ 7.17 (J = 0.7 (allylic), H–C(6')) and 5.38 (J = 8.6, H–C(3)), both being coupled to CH_2(4) at δ 3.09 (*dd*). The ^{13}C-NMR spectrum ($CDCl_3$) confirms that 4 C-atoms are involved in double bonds: those of the uracil moiety C(5')–C(6') (δ 141.3 (*d*), 109.7 (*s*)) and of the enol group in the side chain C(2)–C(3) (δ 130.0 (*s*), 116.8 (*d*)). The CN group (^{13}C-NMR: 116.2 ppm) is also supported by a band at 2230 cm^{-1} in the IR spectrum.

The solid enol **4**, pure according to NMR, melts within an interval (66–136°), indicating a transformation. At room temperature, **4** tautomerises slowly to ketone **6a**, an acyl cyanide, which is characterized by ^{1}H- and ^{13}C-NMR data; tautomerization also takes place in solution, it is faster in MeCN than in $CHCl_3$. The tautomer **6a** reacts as a ketone with trimethylsilyl cyanide to form an addition product, the expected dicyanide **7** [16]. Another reaction of **6a** involves nucleophilic addition of MeOH and loss of HCN which leads to the methyl ester **8a** (X = MeO, R = H). This ester **8a** is formed also directly from **3** on treatment with MeOH containing acid or a little pyridine; pyridine alone in $CHCl_3$ does not affect **3**.

A cycloadduct **10**, having a Me group at C(8a), results from the reaction of 1,3,6-trimethyluracil (**9**) with diene **1a**; it also undergoes ring cleavage upon acid treatment to form enol **11**, from which a trimethylsilyl ether **12** can be prepared. The enol **11**, similar but more stable than **4**, allows some additional physical studies. Due to a transformation it does not have a definite melting point (75–150°; only when inserted at 80°, the sample melts at once). The signal of the enolic proton in the ^{1}H-NMR spectrum of **11** at various temperatures sharpens on cooling, and its chemical shift increases linearly (from δ 9.66 at 20° to δ 9.98 at −60° by 0.04 ppm/10°)[3]). In the IR spectrum in $CHCl_3$, the position of the rather weak broad band near 3000 cm^{-1} does not change on dilution which may indicate intramolecular H-bonding. This is different in DMSO: in a more concentrated solution, the OH band is found at 3450 cm^{-1}, and in a diluted one at 3367 cm^{-1}. Enol **11** tautomerizes to **13a** under acidic conditions or on heating, and acyl cyanide **13a** under-

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[2]) In acetone, compared to $CDCl_3$, the protons H–C(4a), H–C(8a), H–C(6), and H$_z$–C(5) (δ 2.64) are deshielded by 0.35, 0.42, 0.19, and 0.13 ppm, respectively; shielding effects are noted for the *N*–Me groups (0.05 and 0.09 ppm), and for H$_\beta$–C(5) (δ 3.05; 0.13 ppm).

[3]) Such a behaviour was reported for a few enols of 1,3-diketones, *e.g.* 4-hydroxybut-3-en-2-one [17]; the changes of chemical shift in these cases are more important.

goes, analogous to **6a**, addition of trimethylsilyl cyanide to produce **14**, and it reacts with MeOH in presence of acid or base to form the methyl ester **15a** (X = MeO, R = H).

2. *Uracils with a Side Chain at C(5).* The reaction of **2** or of **9** with the β-substituted acryloyl derivatives **1b** and **1c**, performed at a slightly higher temperature (100°), do not provide cycloadducts; instead the uracils **6b**, **c** or **13b**, **c**, respectively, show up, with an α-oxobutanenitrile side chain at C(5), as confirmed by MS and ^{1}H- and ^{13}C-NMR. The acyl cyanide group in these products is cleaved quantitatively by various nucleophiles with liberation of HCN to afford carboxylic-acid derivatives of general structures **8b**, **c** or **15b**, **c**, respectively: alcoholysis leads to the corresponding esters (X = MeO, EtO), hydrolysis to the acids (X = OH), and aminolysis to amides (X = Et_2N, $NHCH_2COOEt$) [16b].

3. *On the Stability of the Adducts.* We may suppose that the products **6b, c** and **13b, c** originate from initially formed but non-isolable cycloadducts by ring opening and tautomerization. This implies cleavage of the O–C bond C(8a) in the original bicyclic adduct and loss of the proton at the angular position C(4a), restoring the uracil system.

Ring opening would thus be feasible only if a proton was present at C(4a) but not when this position was blocked, *e.g.* by a Me group as in the adducts **17a** and **17c**. These compounds are prepared by the reaction of dienes **1a** and **1c** with 1,3,5-trimethyluracil (**16**), in exceptionally low yields, however. Both adducts **17a** and **17c** are stable under acidic or basic conditions of ring opening, and their structures are confirmed by spectral analyses.

NOE Experiments with **17a** in $CDCl_3$ show the proximity of Me–C(4a) (δ 1.34) to both the neighboring H_α–C(5) (δ 2.10; NOE 6.5%) and H–C(8a) (δ 4.83; NOE 7.6%), confirming by analogy the previous assignments in **3**; no effect is observed on H_β–C(5) (δ 3.23). Most relevant is the structure of **17c** where the COOEt group at C(5) and the dihydrouracil ring are *cis*; an NOE experiment shows the proximity of Me–C(4a) (δ 1.33) to H–C(8a) (δ 5.47; NOE 8%) and to H_α–C(5) (δ 4.07 (NOE 6.6%)). A weak coupling between H_β–C(5) and H–C(8a) in acetone, as found for **3**, is not observed, neither in **17a** nor in **17c**.

Discussion. – Uracil derivatives with a propanoate side chain at C(5) are of particular biological interest. Such compounds were prepared by the conventional methods on a multistep pathway, as cited. Our procedure using 1,3-dimethyluracil as starting material presents a simple short route to a new type of uracil derivatives.

The ease of this [4 + 2] cycloaddition of the α,β-unsaturated acyl cyanides to the 5,6-double bond of 1,3-dimethyluracil is remarkable. The reaction proceeds in agreement with theoretical requirements of a *Diels-Alder* addition of inverse electron demand concerted *via* the *endo* transition state leading stereospecifically to a *cis*-adduct, as proven in the case of **17c**; this we have shown earlier to occur with ethyl vinyl ether as dienophile [15]. The mechanism of this type of [4 + 2] additions is, however, still under discussion: alternatively, a two-step pathway was suggested, the initial step, a *Michael*-type addition, would lead to a zwitterionic intermediate cyclizing in the second step [18]. A zwitterionic, relatively stable intermediate was hitherto demonstrated unequivocally in the special case of the reaction of tetrazine with a N,N-ketene acetal [19]. Such a mechanism could explain, in our case, the formation of the products with side chains **6b**, **c** and **13b**, **c**, but not that of the *cis*-cycloadducts **3** and **10**. We suggest that the *Diels-Alder* adducts are formed as the first products of concerted additions of α,β-unsaturated acyl cyanides with the 1,3-dimethyluracils; in the strained species, ring opening would occur at the elevated temperatures to restore the more stable uracil system.

The kinetic stability of the enols **4** or **11** formed upon acid-catalyzed ring opening is surprising. Stabilized enols were encountered only when substituted by fluorinated aliphatic groups or bulky aromatic rings [20]; the case of 2-hydroxy-3-methoxybut-2-enenitrile [21] appears to be exceptional and has not been fully explained. It is possible that intramolecular H-bonding of the enolic proton to the carbonyl group on C(4) contributes to the stability of the derivatives **4** and **11**; further studies on this type of structure will be presented in a forthcoming paper.

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Experimental Part

General. Starting materials were purchased from *Fluka AG*. The α,β-unsaturated acyl cyanides **1a–c** were prepared by reacting acyl chlorides for 0.5 h with CuCN and NaI as mentioned in [15]. The unstable **1a** was prepared as a *ca.* 0.3M soln. in MeCN, obtained by distillation of the solvent and the product from the reaction mixture of acryloyl chloride (18.1 g, 200 mmol), NaI (57.5 g, 375 mmol), CuCN (18 g, 200 mmol), and MeCN (400 ml); this soln. was stored at −20°. The *N,N*-dimethyluracils **2**, **9**, and **16** were prepared from uracil, 6-, and 5-methyluracil, respectively, by treatment with Me_2SO_4 and aq. NaOH soln. following [22]. Column chromatography: silica gel *60* (200–400 mesh ASTM, *Merck 9385*); FC = flash chromatography. Prep. TLC: precoated plates (2 mm), silica gel *60* F_{254} (*Merck 5717*). M.p.: observed under the microscope using a *Mettler-FP-52* instrument. UV Spectra: λ_{max} (E) in nm; *Hewlett-Packard-8450* diode array spectrophotometer. IR Spectra: in cm^{-1}; *Perkin-Elmer-1420* spectrometer: NMR Spectra: chemical shifts δ in ppm rel. to tetramethylsilane (= 0 ppm) as an internal standard J in Hz; *Bruker-WH-250* and *-WH-360* spectrometers. NOE: indication of irradiated H→affected (H's) (%). MS: EI = electron impact; CI = chemical ionization, in NH_3, m/z (intensities in % of base peak); *Nermag-R-10-10C* spectrometer.

*1,3,4,4a,5,8a-Hexahydro-1,3-dimethyl-2,4-dioxo-2*H*-pyrano[2,3-*d*]pyrimidine-7-carbonitrile* (**3**). For 24 h **1a** (20 ml of a MeCN soln.; *ca.* 6 mmol) and **2** (0.70 g, 5 mmol) were heated under reflux. The solvent was evaporated and the residue flash chromatographed (AcOEt): **3** (0.90 g, 81%). Recrystallization from Et_2O/hexane 1:1. M.p. 132.8–133.5°. R_f 0.51. IR (KBr): 3080*m*, 2230*s*, 1719v*s*, 1675v*s*, 1647v*s*, 1480v*s*, 1430v*s*, 1383*s*, 1361*s*, 1317*s*, 1282v*s*, 1265*s*, 1213v*s*, 1109v*s*, 1012v*s*, 970*m*, 949*m*, 927v*s*, 860*s*, 790v*s*, 760v*s*. ^{1}H-NMR ($CDCl_3$): 5.74 (*ddd*, J = 5.0, 2.9, 1.0, H–C(6)); 5.10 (*d*, J = 3.2, H_α–C(8)); 3.23 (*s*, Me–N(1)); 3.21 (*s*, Me–N(3)); 3.18 (*ddd*, J = 19.8, 5.0, 0.8, H_β–C(5)); 3.15 (*dddd*, J = 7.8, 3.2, 1.0, 0.8, H_α–C(4a)); 2.51 (*ddd*, J = 19.8, 7.8, 2.9, H_α–C(5)). ^{1}H-NMR (CD_3COCD_3): 5.93 (*ddd*, J = 5.3, 2.9, 0.8, H–C(6)); 5.52 (*dd*, J = 3.2, < 0.5, H_α–C(8a)); 3.50 (*dddd*, J = 7.3, 3.2, 1.1, 0.8, H_α–C(4a)); 3.18 (*s*, Me–N(1)); 3.12 (*s*, Me–N(3)); 3.05 (*dddd*, J = 19.6, 5.3, 1.1, 0.3, H_β–C(5)); 2.64 (*ddd*, J = 19.6, 7.3, 2.9, H_α–C(5)). NOE (CD_3COCD_3): H_α–C(4a)→H_α–C(8a) (4.0%), H_α–C(5) (3.1%) H_β–C(5) 0.6%; H_α–C(8a)→H_α–C(4a) (5.0%), H_α–C(5) (1.4%), H_β–C(5) (0.3%), Me–N(1) (1.2%). ^{13}C-NMR ($CDCl_3$): 167.3 (C(4)); 152.5 (C(2)); 127.5 (C(7)); 115.5 (CH(6)); 113.2 (CN); 83.4 (CH(8a)); 38.0 (CH(4a)); 35.2 (Me–N(3)); 28.0 (Me–N(1)); 21.0 (CH_2(5)). EI-MS: 222 (4, $[M + H]^+$), 221 (19, M^+), 194 (4), 193 (7), 192 (3), 167 (15), 166 (26), 165 (8), 141 (7), 140 (83), 112 (4), 96 (4), 84 (7), 83 (100), 82 (11), 81 (5), 56 (11), 55 (44).

2-Hydroxy-4-(1,2,3,4-tetrahydro-1,3-dimethyl-2,4-dioxopyrimidin-5-yl)but-2-enenitrile (**4**). To a soln. of **3** (0.235 g) in MeCN (10 ml), 0.3N HCl/Et_2O (5 drops) was added. After 4.5 h at r.t., the solvent was evaporated, the product **4**/**6a** (77:23) triturated with Et_2O which dissolved **6a**, and the solid residue of **4** washed again with Et_2O (0.155 g, 66%). M.p. 66°–136° (due to a transformation). UV (MeCN): 270 (6750). IR (KBr): 3600–2500 (br.), 2230*m*, 1710v*s*, 1655v*s*, 1640v*s*, 1595v*s*, 1485v*s*, 1460*s*, 1395*m*, 1370*m*, 1340*s*, 1230*m*, 1130*s*, 1080*m*, 955*m*, 925*m*, 835*s*, 780*s*, 752*s*. ^{1}H-NMR ($CDCl_3$): 9.58 (br. *s*, OH); 7.17 (*t*, J = 0.7, H–C(6′)); 5.38 (*t*, J = 8.6, H–C(3)); 3.45 (*s*, Me–N(1′)); 3.41 (*s*, Me–N(3′)); 3.09 (*dd*, J = 8.6, 0.7, CH_2(4)); temp. dependence of δ(OH) in $CDCl_3$: 9.58 (20°); 9.54 (30°); 9.49 (40°); 9.43 (50°). ^{13}C-NMR ($CDCl_3$): 166.2 (C(4′)); 150.8 (C(2′)=O); 141.3 (CH(6′)); 130.0 (C(2)); 116.8 (CH(3)); 116.2 (CN); 109.7 (C(5′)); 37.2 (Me–N(3′)); 28.5 (Me–N(1′)); 23.5 (CH_2(4)). EI-MS: 222 (6, $[M + H]^+$), 221 (37, M^+), 195 (3), 166 (5), 153 (10), 110 (22), 96 (100), 81 (26), 69 (21), 68 (15), 67 (11), 66 (11), 56 (10), 55 (51), 54 (12). CI-MS: 222 (33, $[M + H]^+$), 221 (55, M^+), 213 (37), 212 (38), 195 (34), 194 (11), 167 (16), 166 (62), 153 (43), 140 (6), 110 (22), 96 (100), 81 (45).

4-(1,2,3,4-Tetrahydro-1,3-dimethyl-2,4-dioxopyrimidin-5-yl)-2-(trimethylsiloxy)but-2-enenitrile (**5**). Trimethylsilyl cyanide (0.1 ml, 0.8 mmol) was added to a soln. of **4** (0.110 g, 0.5 mmol) in $CHCl_3$ (5 ml) and the mixture left at r.t. overnight and then evaporated: **5**. Oil. ^{1}H-NMR ($CDCl_3$): 6.93 (*t*, J = 1.0, H–C(6′)); 5.62 (*t*, J = 7.4, H–C(3)); 3.38 (*s*, Me–N(1′)); 3.33 (*s*, Me–N(3′)); 3.17 (*dd*, J = 7.4, 1.0, CH_2(4)); 0.31 (*s*, Me_3Si). ^{13}C-NMR

($CDCl_3$): 163.1 (C(4')); 151.5 (C(2')); 139.5 (CH(6')); 125.0 (C(2)); 123.9 (CH(3)); 116.2 (CN); 109.9 (C(5')); 36.8 (Me–N(3')); 27.9 (Me–N(1')); 23.1 (CH_2(4)); –0.07 (Me_3Si).

2-Oxo-4-(1,2,3,4-tetrahydro-1,3-dimethyl-2,4-dioxopyrimidin-5-yl)butanenitrile (**6a**). A mixture of **3** (0.235 g, 1 mmol) in MeCN (10 ml)[4]) and 0.3N HCl/Et_2O (4 drops) was left at r.t. for 20 h and then evaporated: **6a** (0.235 g) Oil. UV (MeCN): 270 (8030). IR (KBr): 3070*m*, 2222*s*, 1705*vs*, 1660*vs*, 1640*vs*, 1480*vs*, 1455*vs*, 1435*vs*, 1395*vs*, 1380*s*, 1340*vs* 1165*vs*, 1075*vs*, 950*s*, 930*s*, 775*vs*, 752*vs*. ^{1}H-NMR ($CDCl_3$): 7.14 (*t*, *J* = 0.6, H–C(6')); 3.40 (*s*, Me–N(1')); 3.35 (*s*, Me–N(3')); 3.11 (*t*, *J* = 6.5, CH_2(3)); 2.71 (*td*, *J* = 6.5, 0.6, CH_2(4)). ^{13}C-NMR ($CDCl_3$): 176.1 (C(2)); 163.1 (C(4')); 151.2 (C(2')); 141.0 (CH(6')); 113.0 (CN); 109.3 (C(5')); 43.3 (CH_2(3)); 36.6 (Me–N(3')); 27.6 (Me–N(1')); 21.2 (CH_2(4)). EI-MS: 236 (1, $[M + H]^+$), 235 (2, M^+), 209 (7), 207 (11), 182 (6), 181 (22), 167 (39), 124 (6), 110 (32), 56 (100). CI-MS: 255 (11), 254 (10), 235 (10, M^+), 227 (53, $[M - CN + NH_4]^+$), 226 (100, $[M - CN + NH_3]^+$), 182 (24), 181 (74), 167 (41), 154 (159), 125 (6), 110 (20), 96 (6), 95 (6), 94 (13), 82 (17).

2-Oxo-4-(1,2,3,4-tetrahydro-1,3-dimethyl-2,4-dioxopyrimidin-5-yl)pentanenitrile (**6b**). A mixture of 2-oxo-pent-3-enenitrile (**1b**; 0.760 g, 8 mmol) and **2** (0.700 g, 5 mmol) was heated at 100° for 36 h. The mixture was then cooled and triturated with hexane and the solid obtained filtered, washed with hexane, and dried under vacuum: **6b** (1.150 g, 98%). IR (neat): 3070*m*, 2218*s*, 1700*vs*, 1655*vs*, 1640*vs*, 1480*vs*, 1455*vs*, 1370*vs*, 1345*vs*, 1015*s*, 970*m*, 915*s*, 780*vs*, 753*vs*, 740*s*. ^{13}C-NMR ($CDCl_3$): 175.7 (C(2)); 162.6 (C(4')); 151.1 (C(2')); 139.9 (CH(6')); 113.9 (C(5')); 113.1 (CN); 49.7 (CH_2(3)); 36.7 (Me–N(3')); 28.4 (CH(4)); 27.6 (Me–N(1')); 18.2 (Me–C(4)). EI-MS: 235 (5, M^+), 220 (1), 209 (8), 180 (51), 167 (44), 165 (31), 140 (53), 124 (6), 110 (39), 97 (12), 96 (12), 95 (23), 94 (34), 84 (24), 83 (85), 82 (55), 81 (34), 69 (56), 68 (23), 67 (27), 57 (26), 56 (27), 55 (100), 54 (25).

4-(Ethoxycarbonyl)-2-oxo-4-(1,2,3,4-tetrahydro-1,3-dimethyl-2,4-dioxopyrimidin-5-yl)butanenitrile (= *Ethyl 4-Cyano-4-oxo-2-(1,2,3,4-tetrahydro-1,3-dimethyl-2,4-dioxopyrimidin-5-yl)butanoate*; **6c**). A mixture of **1c** (0.842 g, 5.5 mmol) and **2** (0.700 g, 5 mmol) was heated at 100° for 6 h. Excess **1c** was removed by distillation (70°/0.01 Torr), leaving pure **6c**. Oil. IR (neat): 3070*m*, 2220*s*, 1725*vs*, 1705*vs*, 1660*vs*, 1640*vs*, 1515*s*, 1480*vs*, 1460*vs*, 1375*vs*, 1345*vs*, 1305*s*, 1270*s*, 1230*s*,1215*s*, 1190*s*, 1090*vs*, 1015*s*, 925*m*, 855*s*, 795*vs*, 780*vs*, 755*vs*. ^{1}H-NMR ($CDCl_3$): 7.22 (*s*, H–C(6')); 4.19 (*q*, *J* = 7.0, MeCH_2O); 3.94 (*dd*, *J* = 7.0, 6.0, H–C(4)); 3.65 (*dd*, *J* = 18.9, 7.0, 1 H–C(3)); 3.42 (*s*, Me–N(1')); 3.33 (*s*, Me–N(3')); 3.14 (*dd*, *J* = 18.9, 6.0, 1 H–C(3)); 1.24 (*t*, *J* = 7.0, *Me*CH_2O). ^{13}C-NMR ($CDCl_3$): 174.8 (C(2)); 170.2 (*C*OO); 161.9 (C(4')); 150.8 (C(2')); 142.0 (CH(6')); 112.7 (CN); 108.5 (C(5')); 61.5 (Me*C*H_2O); 44.8 (CH_2(3)); 39.1 (CH(4)); 36.5 (Me–N(3')); 27.3 (Me–N(1')); 13.4 (*Me*CH_2O). CI-MS: 311 (16, $[M + NH_4]^+$), 310 (9), 295 (16), 294 (100, $[M + H]^+$), 293 (42, M^+), 269 (3), 267 (3), 247 (4), 220 (3), 193 (3), 158 (3), 141 (10), 140 (1).

2-[2-(1,2,3,4-Tetrahydro-1,3-dimethyl-2,4-dioxopyrimidin-5-yl)ethyl]-2-(trimethylsiloxy)propanedinitrile (**7**). Trimethylsilyl cyanide (0.1 ml) was added to a soln. of **6a** (0.100 g) in MeCN (5 ml). After 24 h, the mixture was evaporated. The oily residue was triturated with Et_2O and the Et_2O layer decanted: pure **7** (0.125 g, 96%). IR (KBr): 3060*m*, 2240*w*, 1703*vs*, 1660*vs*, 1640*vs*, 1480*vs*, 1455*vs*, 1375*s*, 1342*vs*, 1253*vs*, 1215*s*, 1134*vs*, 857*vs*, 842*vs*, 755*vs*. ^{1}H-NMR ($CDCl_3$): 7.10 (*s*, H–C(6')); 3.41 (*s*, Me–N(1')); 3.37 (*s*, Me–N(3')); 2.65 (*m*, CH_2); 2.45 (*m*, CH_2); 0.37 (*s*, Me_3Si). ^{13}C-NMR ($CDCl_3$): 163.0 (C(4')); 151.4 (C(4')); 140.4 (CH(6')); 114.7 (2 CN); 109.7 (C(5')); 62.4 (C(2)); 40.2 (CH_2(1')); 36.7 (Me–N(3')); 27.7 (Me–N(1')); 22.6 (CH_2(2')); 0.15 (Me_3Si). CI-MS: 321 (45, $[M + H]^+$), 320 (30, M^+), 305 (63), 294 (7), 293 (11), 285 (31), 284 (22), 270 (17), 269 (70), 239 (11), 222 (31), 221 (64), 209 (10), 195 (24), 167 (50), 154 (12), 153 (32), 110 (39), 96 (100), 84 (37), 81 (47), 80 (23), 75 (97), 74 (33), 73 (98).

*1,3,4,4a,5,8a-Hexahydro-1,3,8a-trimethyl-2,4-dioxo-2*H*-pyrano[2,3-*d*]pyrimidine-7-carbonitrile* (**10**). A mixture of **1a** (40 ml of MeCN soln.; *ca.* 12 mmol) and 1,3,6-trimethyluracil (**9**; 0.77 g, 5 mmol) was kept at r.t. for 48 h. The product **10**, crystallizing from the mixture, was filtered off and washed with anh. Et_2O (1.15 g, 98%). M.p. 127–127.5°. IR (KBr): 3070*s*, 2232*s*, 1710*vs*, 1670*vs*, 1640*vs*, 1470*vs*, 1440*vs*, 1420*vs*, 1385*vs*, 1360*vs*, 1340*vs*, 1320*vs*, 1260*s*, 1165*vs*, 1140*vs*, 1095*vs*, 1047*s*, 987*vs*, 940*s*, 835*s*, 820*s*, 778*s*, 762*vs*, 700*s*. ^{1}H-NMR ($CDCl_3$): 5.73 (*ddd*, *J* = 5.0, 3.2, 0.8, H–C(6)); 3.23 (*s*, Me–N(1)); 3.18 (*s*, Me–N(3)); 3.14 (*ddd*, *J* = 19.5, 5.0, 2.9, H_β–C(5)); 2.90 (*dd*, broadened since probably coupled to H–C(6), *J* = 7.0, 2.9, H_α–C(4a)); 2.49 (*ddd*, *J* = 19.5, 7.0, 3.2, H_α–C(5)); 1.68 (*s*, Me_α–C(8a)). NOE ($CDCl_3$): H_α–C(4a)→H_α–C(5) (2.9%), Me_α–C(8a) (0.4%), Me–N(1') (1.2%); Me_α–C(8a)→H_α–C(4a) (5.4%), H_α–C(5) (2.6%), Me–N(1) (2.6%). ^{13}C-NMR ($CDCl_3$): 167.4 (C(4)); 152.8 (C(2)); 127.4 (C(7)); 114.3 (CH(6)); 113.5 (CN); 84.5 (C(8a)); 42.3 (CH(4a)); 29.4 (Me–N(3)); 28.5 (Me–N(1)); 21.6 (C(4a)); 21.5 (CH_2(5)). EI-MS: 235 (11, M^+), 180 (5), 179 (5), 154 (60), 126 (7), 125 (7), 110 (3), 106 (3), 97 (57), 82 (51), 69 (13), 68 (7), 56 (100), 55 (11). CI-MS: 236 (34, $[M + H]^+$), 235 (97, M^+), 220 (10), 209 (15), 208 (5), 181 (8), 180 (7), 179 (6), 154 (100), 126 (5), 125 (7), 97 (32), 82 (41).

2-Hydroxy-4-(1,2,3,4-tetrahydro-1,3,6-trimethyl-2,4-dioxopyrimidin-5-yl)but-2-enenitrile (**11**) *and 2-Oxo-4-(1,2,3,4-tetrahydro-1,3,6-trimethyl-2,4-dioxopyrimidin-5-yl)butanenitrile* (**13a**). *Method A*: 0.3N HCl/Et_2O (2

[4]) The isomerization of **4** → **6a** was slower in $CHCl_3$ as solvent.

drops) was added to a soln. of **10** (0.120 g) in MeCN (10 ml). The mixture was left at r.t. for 15 min. Evaporation gave **11** containing 2% of **13a**.

Method B: A mixture of **9** (0.77 g, 5 mmol), **1a** (12 mmol) in MeCN (40 ml), and 0.3N HCl/Et_2O (4 drops) was left at r.t. for 48 h. Removal of the solvent gave **11**/**13a** 3:1. More 0.3N HCl/Et_2O (5 drops) was added and the mixture left for another 24 h. After evaporation, the residue was triturated with Et_2O and the remaining solid filtered off and washed with Et_2O: **13a** (0.94 g, 80%). M.p. 146–148°.

Data of **11**: M.p. 75°–150° (due to transformation); when the sample was inserted at 80°, it melted at once. UV (MeCN): 271 (8660). IR (neat): 3500–2500 (br.), 2221*s*, 1690*vs*, 1640*vs*, 1625*vs*, 1590*vs*, 1485*vs*, 1460*vs*, 1428*vs*, 1355*vs*, 1340*vs*, 1250*s*, 1215*s*, 1142*s*, 1160*s*, 1040*s*, 973*s*, 895*s*, 820*s*, 788*s*, 755*s*. IR ($CHCl_3$): 3029 and 3012*m*, (unchanged in more dil. soln.), 1698*s*, 1638*s*, 1605*m*, 1488*m*, 1434*m*. IR (DMSO): 3432 (br., in a more dil. soln. at 3367*s*), 2225*w*, 1718*w*, 1692*m*, 1643*s*, 1482*w*, 1359*w*. ^{1}H-NMR ($CDCl_3$): 9.66 (br. *s*, OH); 5.40 (*t*, *J* = 9.0, H–C(3)); 3.50 (*s*, Me–N(1′)); 3.41 (*s*, Me–N(3′)); 3.21 (*d*, *J* = 9.0, CH_2(4)); 2.36 (*s*, Me–C(6′)); temp. dependence of δ(OH) in $CDCl_3$: 9.66 (20°); 9.70 (10°); 9.75 (0°); 9.79 (−10°); 9.83 (−20°); 9.87 (−30°); 9.87 (−30°); 9.91 (−40°); 9.95 (−50°); 9.98 (−60°). ^{13}C-NMR ($CDCl_3$): 165.5 (C(4′)); 150.9 (C(2′)); 149.8 (C(6′)); 129.6 (C(2)); 116.1 (CH(3)); 115.6 (CN); 107.9 (C(5′)); 32.4 (Me–N(3′)); 28.7 (Me–N(1′)); 22.2 (CH_2(4)); 16.6 (*Me*–C(6′)).

Data of **13a**: UV (MeCN): 271 (8430). IR (KBr): 2220*s*, 1720*vs*, 1693*vs*, 1645*vs*, 1620*vs*, 1475*vs*, 1428*vs*, 1368*vs*, 1350*vs*, 1090*s*, 1060*s*, 1000*s*, 930*s*, 850*s*, 774*s*, 752*s*. ^{1}H-NMR ($CDCl_3$): 3.46 (*s*, Me–N(1′)); 3.35 (*s*, Me–N(3′)); 3.04 (*t*, *J* = 6.9, CH_2(2)); 2.83 (*t*, *J* = 6.9, CH_2(3)); 2.33 (*s*, Me–C(6′)). ^{13}C-NMR ($CDCl_3$): 176.2 (*C*OCN); 162.4 (C(4′)); 151.5 (C(2′)); 148.4 (C(6′)); 113.1 (CN); 107.6 (C(5′)); 43.8 (CH_2(2)); 32.1 (Me–N(3′)); 28.0 (Me–N(1′)); 20.2 (CH_2(3)); 16.4 (*Me*–C(6′)). CI-MS: 236 (4, $[M + H]^+$), 235 (10, M^+), 227 (53, $[M - CN + NH_3]^+$), 226 (100, $[M - CN + NH_2]^+$), 209 (43), 208 (21), 180 (74), 167 (41), 154 (15), 125 (6), 110 (20), 94 (13), 82 (17), 81 (6).

4-(1,2,3,4-Tetrahydro-1,3,6-trimethyl-2,4-dioxopyrimidin-5-yl)-2-(trimethylsiloxy)but-2-enenitrile (**12**). Trimethylsilyl cyanide (0.1 ml) was added to a soln. of **11** (0.117 g, 0.5 mmol) in $CHCl_3$ (5 ml) and left at r.t. overnight to give **12**. IR (neat): 3050*m*, 2218*s*, 1693*vs*, 1640*vs*, 1475*vs*, 1455*vs*, 1430*vs*, 1352*vs*, 1252*vs*, 1152*vs*, 1107*s*, 1040*s*, 989*s*, 848*vs*, 755*s*. ^{1}H-NMR ($CDCl_3$): 5.51 (*t*, *J* = 7.5, H–C(3)); 3.43 (*s*, Me–N(1′)); 3.36 (*s*, Me–N(3′)); 3.32 (*d*, *J* = 7.5, CH_2(4)); 2.23 (*s*, Me–C(6′)); 0.33 (*s*, Me_3Si). ^{13}C-NMR ($CDCl_3$): 162.2 (C(4′)); 151.6 (C(2′)); 148.4 (C(6′)); 125.3 (CH_3); 123.3 (C(2)); 116.1 (2 CN); 107.8 (C(5′)); 31.9 (Me–N(3′)); 28.1 (Me–N(1′)); 22.3 (CH_2(4)); 16.3 (*Me*–C(6)). EI-MS: 308 (20, $[M + H]^+$), 307 (41, M^+), 253 (13), 251 (8), 233 (10), 232 (10), 224 (17), 214 (13), 207 (17), 204 (13), 196 (15), 190 (12), 180 (58), 179 (100), 177 (17), 170 (15), 167 (28), 164 (17), 154 (9), 135 (28), 127 (19), 110 (46), 94 (33), 75 (23), 73 (14), 59 (18), 58 (19), 56 (81).

2-Oxo-4-(1,2,3,4-tetrahydro-1,3,6-trimethyl-2,4-dioxopyrimidin-5-yl)pentanenitrile (**13b**). A mixture of **1b** (0.76 g, 8 mmol) and **9** (0.77 g, 5 mmol) was heated at 100° for 15 h. The product was cooled and washed with hexane: **13b** (1.24 g, quant.), solid residue. IR (KBr): 2220*s*, 1723*vs*, 1690*vs*, 1640*vs*, 1465*vs*, 1448*vs*, 1420*vs*, 1390*vs*, 1350*vs*, 1278*s*, 1250*s*, 1137*s*, 1105*s*, 1055*vs*, 1002*vs*, 925*s*, 885*s*, 850*s*, 808*s*, 780*vs*, 752*vs*. ^{1}H-NMR ($CDCl_3$): 3.79 (*dd*, *J* = 18.9, 8.5, 1 H–C(3)); 3.48 (*s*, Me–N(1′)); 3.38 (*m*, H–C(4)); 3.33 (*s*, Me–N(3′)); 3.10 (*dd*, *J* = 18.9, 5.0, 1 H–C(3)); 2.38 (*s*, Me–C(6′)); 1.32 (*d*, *J* = 7.0, Me–C(4)). ^{13}C-NMR ($CDCl_3$): 176.7 (*C*OCN); 161.7 (C(4′)); 151.7 (C(2′)); 148.4 (C(6′)); 113.2 (CN); 111.5 (C(5′)); 49.5 (CH_2(3)); 32.4 (Me–N(3′)); 28.7 (CH(4)); 27.8 (Me–N(1′)); 18.7 (*Me*–C(4)); 16.4 (*Me*–C(6′)). EI-MS: 250 (2, $[M + H]^+$), 249 (7, M^+), 234 (1), 207 (8), 195 (9), 194 (7), 181 (36), 179 (19), 124 (11), 94 (5), 82 (5), 69 (3), 66 (5), 57 (5), 56 (100), 55 (6).

4-(Ethoxycarbonyl)-2-oxo-4-(1,2,3,4-tetrahydro-1,3,6-trimethyl-2,4-dioxopyrimidin-5-yl)butanenitrile (= *Ethyl 4-Cyano-4-oxo-2-(1,2,3,4-tetrahydro-1,3,6-trimethyl-2,4-dioxopyrimidin-5-yl)butanoate;* **13c**). A mixture of **1c** (0.765 g, 5 mmol) and **9** (0.770 g, 5 mmol) was heated at 100° for 10 h. ^{1}H-NMR: no starting material left, **13c** as only product. This material was used for transformations to derivatives of type **15c**. IR (neat): 2220*s*, 1725*vs*, 1695*vs*, 1640*vs*, 1490–1420 (br.), 1390*m*, 1360*vs*, 1320–1150 (br.), 1095*s*, 1015*s*, 975*m*, 860*m*, 785*s*, 755*vs*. ^{1}H-NMR ($CDCl_3$): 4.18 (*q*, *J* = 7.0, MeCH_2O); 4.15 (*dd*, *J* = 7.1, 6.2, H–C(4)); 3.87 (*dd*, *J* = 18.8, 7.1, 1 H–C(3)); 3.50 (*s*, Me–N(1′)); 3.33 (*s*, Me–N(3′)); 3.08 (*dd*, *J* = 18.8, 6.2, 1 H–C(3)); 2.37 (*s*, Me–C(6′)); 1.23 (*t*, *J* = 7.0, *Me*CH_2O). ^{13}C-NMR ($CDCl_3$): 175.2 (*C*OCN); 170.6 (*C*OO); 161.4 (C4′)); 151.3 (C(2′)); 149.7 (C(6′)); 112.9 (CN); 108.0 (C(5′)); 61.6 (Me*C*H_2O); 44.9 (CH_2(3)); 38.9 (CH(4)); 32.2 (Me–N(3′)); 27.8 (Me–N(1′)); 16.6 (*Me*–C(6′)); 13.7 (*Me*CH_2O). CI-MS: 325 (10, $[M + NH_4]^+$), 309 (18), 308 (100, $[M + H]^+$), 307 (8, M^+), 283 (8), 281 (8), 255 (48), 241 (10), 234 (8), 225 (6), 207 (32), 181 (22), 179 (8), 155 (18), 154 (4), 124 (2), 95 (2), 94 (4), 82 (2).

2-[2-(1,2,3,4-Tetrahydro-1,3,6-trimethyl-2,4-dioxopyrimidin-5-yl)ethyl]-2-(trimethylsiloxy)propanedinitrile (**14**). The mixture of trimethylsilyl cyanide (0.1 ml) and a soln. of **13a** (0.120 g) in MeCN (5 ml) was left at r.t. for 24 h. Evaporation gave **14**. IR (neat): 2240*m*, 1694*vs*, 1640*vs*, 1475*vs*, 1455*vs*, 1428*vs*, 1355*vs*, 1253*vs*, 1210*s*, 1134*vs*, 850*vs*, 755*s*. ^{1}H-NMR ($CDCl_3$): 3.46 (*s*, Me–N(1′)); 3.36 (*s*, Me–N(3′)); 2.77 (*m*, CH_2(3)); 2.31 (*s*, Me–C(6′)); 2.30 (*m*, CH_2(4)); 0.38 (*s*, Me_3Si). ^{13}C-NMR ($CDCl_3$): 162.3 (C(4′)); 151.6 (C(2′)); 148.1 (C(6′)); 114.7 (2 CN); 107.9

(C(5')); 62.3 (C(2)); 40.6 (CH_2); 32.1 (Me–N(3')); 28.0 (Me–N(1')); 20.8 (CH_2); 16.2 (*Me*–C(6')); 0.11 (Me_3Si). CI-MS: 335 (16, $[M + H]^+$), 334 (13, M^+), 319 (18), 308 (30), 307 (35), 299 (9), 298 (9), 292 (17), 283 (17), 265 (7), 241 (9), 240 (10), 236 (16), 235 (26), 209 (28), 208 (17), 207 (11), 181 (26), 180 (44), 179 (20), 167 (24), 154 (14), 124 (7), 110 (48), 95 (13), 94 (16), 84 (25), 81 (16), 75 (100), 74 (28), 73 (90).

*1,3,4,4a,5,8a-Hexahydro-1,3,4a-trimethyl-2,4-dioxo-2*H*-pyrano[2,3-*d*]pyrimidine-7-carbonitrile* (**17a**). To a soln. of **1a** (60 ml of MeCN soln.; *ca.* 18 mmol) was added 1,3,5-trimethyluracil (**16**, 1.54 g, 10 mmol). After refluxing for 48 h, the solvent was evaporated and the residue flash chromatographed (AcOEt/hexane 1:1): crystalline **17a** (0.7 g, 30%) and **16** (1.06 g). **17a**: R_f 0.28. M.p. 130–130.5°. IR (KBr): 3070*s*, 2226*s*, 1720*vs*, 1685*vs*, 1645*vs*, 1468*vs*, 1428*vs*, 1385*s*, 1370*vs*, 1349*vs*, 1293*vs*, 1277*vs*, 1190*vs*, 1150*vs*, 1063*vs*, 1043*vs*, 990*vs*, 940*s*, 918*vs*, 810*vs*, 760*s*. ^{1}H-NMR ($CDCl_3$): 5.69 (*dd*, J = 5.4, 2.8, H–C(6)); 4.83 (*s*, H_α–C(8a)); 3.23 (*dd*, J = 19.4, 5.4 H_β–C(5)); 3.22 (*s*, 2 Me–N); 2.10 (*dd*, J = 19.4, 2.8, H_α–C(5)); 1.34 (*s*, Me_α–C(4a)). NOE ($CDCl_3$): Me–C(4a)→H_α–C(8a) (7.6%), H_α–C(5) (6.5%); H_α–C(8a)→Me_α–C(4a) (0.3%), H_α–C(5) (1.8%). ^{13}C-NMR ($CDCl_3$): 171.0 (C(4)); 152.5 (C(2)); 127.5 (C(7)); 115.5 (CH(6)); 113.2 (CN); 89.0 (CH(8a)); 40.7 (C(4a)); 35.6 (Me–N(3)); 29.3 (CH_2(5)); 28.2 (Me–N(1)); 23.5 (C(4a)). EI-MS: 235 (2, M^+), 155 (9), 154 (100), 120 (2), 98 (3), 97 (33), 96 (6), 70 (6), 69 (83), 68 (55), 56 (15), 55 (16). CI-MS: 253 (5, $[M + NH_4]^+$), 236 (24, $[+ H]^+$), 235 (2, M^+), 209 (1), 155 (18), 154 (100), 97 (9), 81 (1).

*Ethyl 7-Cyano-1,3,4,4a,5,8a-hexahydro-1,3,4a-trimethyl-2,4-dioxo-2*H*-pyrano[2,3-*d*]pyrimidine-5-carboxylate* (**17c**). A mixture of **1c** (2.30 g, 15 mmol) and **16** (0.77 g, 5 mmol) was heated at 115° for 7 h. The mixture was triturated with Et_2O, solid **16** filtered off and washed with Et_2O, and the concentrated filtrate purified by prep. TLC (AcOEt): **17c** (0.18 g, 12%). R_f 0.40. ^{1}H-NMR ($CDCl_3$): 5.64 (*d*, J = 5.8, H–C(6)); 5.47 (*s*, H_α–C(8a)); 4.24 (*q*, J = 7.0, MeCH_2O); 4.07 (*d*, J = 5.8, H_α–C(5)); 3.25 (*s*, Me–N(1)); 3.21 (*s*, Me–N(3)); 1.33 (*s*, Me_α–C(4a)); 1.32 (*t*, J = 7.0, *Me*CH_2O). NOE ($CDCl_3$): Me_α–C(4a)→H_α–C(8a) (8.5%), H_α–C(5) (6.6%); H_α–C(8a)→Me_α–C(4a) (0.4%), H_α–C(5) (0.8%). ^{13}C-NMR ($CDCl_3$): 170.1 (*C*OO); 170.0 (C(4)); 152.1 (C(2)); 129.4 (C(7)); 111.3 (CH(6)); 112.9 (CN); 86.7 (CH(8a)); 62.3 (Me*C*H_2O); 43.0 (CH(5)); 41.8 (C(4a)); 35.8 (Me–N(3)); 28.5 (Me–N(1)); 19.9 (*Me*–C(4a)); 14.1 (*Me*CH_2O). EI-MS: 307 (2, M^+), 262 (2), 235 (1), 234 (3), 165 (2), 155 (22), 154 (100), 120 (5), 97 (9), 94 (4), 85 (8), 69 (24), 68 (19), 65 (5). CI-MS: 325 (8, $[M + NH_4]^+$), 308 (37, $[M + H]^+$), 307 (3, M^+), 155 (44), 154 (100), 97 (8).

3-(1,2,3,4-Tetrahydro-1,3-dimethyl-2,4-dioxopyrimidin-5-yl)propanoic-Acid Derivatives **8a** (varying X) *and 3-(1,2,3,4-Tetrahydro-1,3,6-trimethyl-2,4-dioxopyrimidin-5-yl)propanoic-Acid Derivatives* **15a–c** (varying X). *General Procedure for Acids* (X = OH). H_2O/Acetone 1:3 (5 ml) was added to a soln. of cyanide **6a–b** or **13a–c** (1 mmol) in acetone (5 ml). The mixture was left at r.t. for 30 min and evaporated. The residue was purified by prep. TLC (AcOEt) to give the corresponding acid.

General Procedure for Esters (X = Alkoxy). Alkanol (1 ml) was added to a soln. of cyanide **6a–c** or **13a–c** (1 mmol) in $CHCl_3$ (5 ml). The mixture was left at r.t. for 5 h. The solvent was evaporated and in most cases, the residue was pure ester. If necessary, the product was purified by prep. TLC (AcOEt).

General Procedure for N,N-*Diethylamides* (X = Et_2N). Et_2NH (1.3 mmol) was added to a soln. of cyanide **6c** or **13b** (1 mmol) in $CHCl_3$ (5 ml). The mixture was left at r.t. for 2 h, the solvent evaporated, and the residue purified by prep. TLC (AcOEt) to give the corresponding amide.

General Procedure for N-*[(Ethoxycarbonyl)methyl]amides* (X = $NHCH_2COOEt$). Glycine ethyl ester hydrochloride (0.170 g, 1.2 mmol) and Et_3N (0.150 g, 1.5 mmol) were added to a soln. of the cyanide **6c**, **13a**, or **13c** (1 mmol) in $CHCl_3$ (5 ml). The mixture was left at r.t. for 2 h, the precipitate filtered and washed with $CHCl_3$, the filtrate evaporated, and the residue purified by prep. TLC (AcOEt).

3-(1,2,3,4-Tetrahydro-1,3-dimethyl-2,4-dioxopyrimidin-5-yl)propanoic Acid (**8a**, X = OH, R = H). Yield 98%. M.p. 143–144°. IR (KBr): 3300–2500 (br.), 3070*m*, 1735*vs*, 1705*vs*, 1690*vs*, 1660*vs*, 1628*vs*, 1375*s*, 1340*vs*, 1212*vs*, 1163*vs*, 1090*s*, 1040*s*, 935*vs*, 840*s*, 755*vs*. ^{1}H-NMR ($CDCl_3$): 10.49 (br., OH); 7.12 (*s*, H–C(6')); 3.39 (*s*, Me–N(1')); 3.36 (*s*, Me–N(3')); 2.65 (*m*, CH_2CH_2). ^{13}C-NMR ($CDCl_3$): 177.8 (COOH); 163.5 (C(4')); 151.7 (C(2')); 140.6 (CH(6')); 111.3 (C(5')); 36.9 (Me–N(3')); 32.3 (CH_2(2)); 27.9 (Me–N(1')); 22.8 (CH_2(3)).

Methyl 3-(1,2,3,4-Tetrahydro-1,3-dimethyl-2,4-dioxopyrimidin-5-yl)propanoate (**8a**, X = MeO, R = H). This compound was also prepared by adding pyridine (10 drops) to a soln. of **3** (0.110 g) in MeOH (3 ml). The mixture was left at r.t. for 24 h, and then evaporated. The residue was purified by FC and recrystallized from EtOH: **8a** (0.110 g, 97%). M.p. 77.2–78.0°. IR (KBr): 3070*w*, 1731*vs*, 1703*vs*, 1665*vs*, 1635*vs*, 1460 (br.), 1383*m*, 1365*m*, 1345*s*, 1195*vs*, 1085*m*, 983*m*, 920*m*, 885*m*, 755*vs*. ^{1}H-NMR ($CDCl_3$): 7.14 (*s*, H–C(6')); 3.68 (*s*, MeO); 3.39 (*s*, Me–N(3')); 3.36 (*s*, Me–N(1')); 2.64 (*t*, CH_2CH_2). ^{13}C-NMR ($CDCl_3$): 173.3 (*C*OO); 163.3 (C(4')); 151.6 (C(2')); 140.5 (CH(6')); 114.4 (C(5')); 51.5 (MeO); 36.8 (Me–N(3')); 32.2 (CH_2(2)); 27.8 (Me–N(3')); 22.9 (CH_2(3)). EI-MS: 227 (5, $[M + H]^+$), 226 (19, M^+), 196 (3), 195 (23), 194 (13), 167 (21), 166 (100), 153 (36), 138 (5), 110 (29), 97 (7), 96 (97), 81 (65), 69 (27), 55 (42).

Ethyl 3-(1,2,3,4-Tetrahydro-1,3-dimethyl-2,4-dioxopyrimidin-5-yl)propanoate (**8a**, X = EtO, R = H). Purification by FC: crystals. M.p. 83.9–84.2°. IR (KBr): 3075*s*, 1728*vs*, 1690*vs*, 1660*vs*, 1640*vs*, 1625*vs*, 1370*vs*, 1340*vs*, 1300*vs*, 1242*vs*, 1185*vs*, 1165*vs*, 1082*vs*, 1020*vs*, 970*s*, 920*vs*, 860*s*, 758*vs*. ^{1}H-NMR ($CDCl_3$): 7.13 (*t*, *J* = 0.6, H–C(6′)); 4.12 (*q*, *J* = 7.1, MeCH_2O); 3.38 (*s*, Me–N(1′)); 3.35 (*s*, Me–N(3′)); 2.62 (*m*, CH_2CH_2); 1.24 (*t*, *J* = 7.1, *Me*CH_2O). ^{13}C-NMR ($CDCl_3$): 172.6 (*C*OOEt); 163.1 (C(4′)); 151.4 (C(2′)); 140.3 (CH(6′)); 111.2 (C(5′)); 60.1 (Me*C*H_2O); 36.5 (Me–N(3′)); 32.3 (CH_2(2)); 27.5 (Me–N(1′)); 22.7 (CH_2(3)); 13.9 (*Me*CH_2O). EI-MS: 240 (18, M^+), 195 (28), 194 (20), 167 (25), 166 (100), 153 (31), 138 (6), 110 (20), 96 (37), 81 (32), 69 (18), 68 (12), 67 (7), 66 (6), 57 (10), 56 (11), 55 (24), 54 (11).

3-(1,2,3,4-Tetrahydro-1,3-dimethyl-2,4-dioxopyrimidin-5-yl)butanoic Acid (**8b**, X = OH, R = Me). Not crystalline. ^{1}H-NMR ($CDCl_3$): 10.50 (br., COOH); 7.00 (*s*, H–C(6′)); 3.39 (*s*, Me–N(1′)); 3.34 (*s*, Me–N(3′)); 3.17 (*sext.*, *J* = 7.0, H–C(3)); 2.83 (*dd*, *J* = 16.0, 7.0, 1 H–C(2)); 2.53 (*dd*, *J* = 16.0, 7.0, 1 H–C(2)); 1.28 (*d*, *J* = 7.0, *Me*–C(3)). ^{13}C-NMR ($CDCl_3$): 176.6 (COOH); 162.9 (C(4′)); 151.5 (C(2′)); 139.3 (CH(6′)); 115.9 (C(5′)); 39.1 (CH_2(2)); 36.8 (Me–N(3′)); 29.4 (CH(3)); 27.8 (Me–N(1′)); 18.7 (*Me*–C(3)). EI-MS: 227 (11, $[M + H]^+$), 226 (11, M^+), 210 (9), 209 (11), 182 (9), 181 (56), 180 (62), 168 (17), 167 (44), 140 (56), 111 (10), 110 (60), 80 (13), 69 (43), 68 (14), 56 (25), 55 (100), 54 (23).

Methyl 3-(1,2,3,4-Tetrahydro-1,3-dimethyl-2,4-dioxopyrimidin-5-yl)butanoate (**8b**, X = MeO, R = Me). Not crystalline. IR (neat): 3070*w*, 1735*vs*, 1700*vs*, 1655*vs*, 1635*vs*, 1480*s*, 1455*vs*, 1435*vs*, 1365*m*, 1345*vs*, 1285*m*, 1190*s*, 1165*s*, 1020*s*, 780*s*, 755*s*. ^{1}H-NMR ($CDCl_3$): 7.00 (*s*, H–C(6′)); 3.65 (*s*, MeO); 3.39 (*s*, Me–N(1′)); 3.36 (*s*, Me–N(3′)); 3.16 (*m*, H–C(3)); 2.78 (*dd*, *J* = 15.8, 7.0, 1 H–C(2)); 2.48 (*dd*, *J* = 15.8, 6.8, 1 H–C(2)); 1.27 (*d*, *J* = 7.0, Me–C(3)). ^{13}C-NMR ($CDCl_3$): 171.8 (COO); 162.1 (C(4′)); 150.7 (C(2′)); 138.9 (CH(6′)); 115.0 (C(5′)); 50.6 (MeO); 38.5 (CH_2(2)); 36.0 (Me–N(3′)); 28.7 (CH(3)); 26.9 (Me–N(1′)); 18.0 (*Me*–C(3)). EI-MS: 241 (3, $[M + H]^+$), 240 (15, M^+), 209 (17), 208 (11), 193 (12), 180 (100), 179 (12), 167 (59), 110 (70), 95 (17), 94 (17), 83 (15), 82 (14), 81 (27), 69 (38), 59 (7), 55 (12).

Ethyl 3-(1,2,3,4-Tetrahydro-1,3-dimethyl-2,4-dioxopyrimidin-5-yl)butanote (**8b**, X = EtO, R = Me). Not crystalline. IR (neat): 3075*w*, 1728*vs*, 1700*vs*, 1655*vs*, 1638*vs*, 1452*vs*, 1368*s*, 1343*s*, 1176*vs*, 1026*s*, 970*m*, 915*m*, 847*m*, 782*vs*, 756*vs*, 730*m*. ^{1}H-NMR ($CDCl_3$): 6.96 (*s*, H–C(6′)); 4.02 (*q*, *J* = 7.0, MeCH_2O); 3.32 (*s*, Me–N(1′)); 3.26 (*s*, Me–N(3′)); 3.09 (*sext.*, *J* = 7.0, H–C(3)); 2.66 (*dd*, *J* = 16.0, 7.0, 1 H–C(2)); 2.38 (*dd*, *J* = 16.0, 7.0, 1 H–C(2)); 1.18 (*d*, *J* = 7.0, Me–C(3)); 1.15 (*t*, *J* = 7.0, *Me*CH_2O). ^{13}C-NMR ($CDCl_3$): 171.5 (COO); 162.3 (C(4′)); 150.9 (C(2′)); 138.8 (CH(6′)); 115.4 (C(5′)); 59.5 (Me*C*H_2O); 39.0 (CH_2(2)); 36.2 (Me–N(3′)); 29.1 (CH(3)); 27.1 (Me–N(1′)); 18.3 (Me–C(3)); 13.6 (*Me*CH_2O). EI-MS: 255 (4, $[M + H]^+$), 254 (11, M^+), 209 (25), 208 (13), 181 (18), 180 (100), 179 (16), 167 (48), 166 (7), 165 (12), 124 (13), 110 (82), 95 (15), 94 (17), 91 (28), 80 (20), 69 (47), 68 (19), 56 (10), 55 (19).

Methyl 3-(Ethoxycarbonyl)-3-(1,2,3,4-tetrahydro-1,3-dimethyl-2,4-dioxopyrimidin-5-yl)propanoate (= *1-Ethyl 4-Methyl 2-(1,2,3,4-Tetrahydro-1,3-dimethyl-2,4-dioxopyrimidin-5-yl)butanedioate*; **8c**, X = MeO, R = COOEt). Not crystalline. IR (neat): 3070*m*, 1730*vs*, 1660*vs*, 1640*vs*, 1480*vs*, 1457*vs*, 1440*vs*, 1370*s*, 1345*vs*, 1270*vs*, 1195*vs*, 1155*vs*, 1095*s*, 1022*s*, 780*s*, 755. ^{1}H-NMR ($CDCl_3$): 7.23 (*s*, H–C(6′)); 4.14 (*q*, *J* = 7.2, MeCH_2O); 3.88 (*dd*, *J* = 7.2, 6.4, H–C(3)); 3.64 (*s*, MeO); 3.39 (*s*, Me–N(1′)); 3.30 (*s*, Me–N(3′)); 3.05 (*dd*, *J* = 17.4, 6.4, 1 H–C(2)); 2.75 (*dd*, *J* = 17.4, 7.2, 1 H–C(2)); 1.21 (*t*, *J* = 7.2, *Me*CH_2O). ^{13}C-NMR ($CDCl_3$): 171.9 (COO); 171.5 (COO); 162.2 (C(4′)); 151.2 (C(2′)); 141.6 (CH(6′)); 110.1 (C(5′)); 61.2 (Me*C*H_2); 51.6 (MeO); 39.9 (CH(3)); 36.9 (Me–N(3′)); 34.8 (CH_2(2)); 27.7 (Me–N(1′)); 13.8 (*Me*CH_2O). EI-MS: 299 (1, $[M + H]^+$), 298 (6, M^+), 267 (3), 266 (4), 253 (7), 252 (22), 239 (3), 238 (8), 237 (3), 224 (33), 194 (12), 193 (100), 167 (3), 166 (13), 165 (15), 110 (5), 81 (23), 80 (15), 56 (5).

Ethyl 3-(Ethoxycarbonyl)-3-(1,2,3,4-tetrahydro-1,3-dimethyl-2,4-dioxopyrimidin-5-yl)propanoate (= *Diethyl 2-(1,2,3,4-Tetrahydro-1,3-dimethyl-2,4-dioxopyrimidin-5-yl)butanedioate*; **8c**, X = EtO, R = COOEt). Not crystalline. IR (neat): 3070*w*, 1730*vs*, 1660*vs*, 1643*vs*, 1480*vs*, 1457*vs*, 1370*s*, 1343*s*, 1256 (br.), 1190 (br.), 1155 (br.), 1093*s*, 1027*s*, 857*s*, 780*s*, 755. ^{1}H-NMR ($CDCl_3$): 7.23 (*s*, H–C(6′)); 4.17 (*q*, *J* = 7.0, MeCH_2O); 4.11 (*q*, *J* = 7.0, MeCH_2O); 3.91 (*dd*, *J* = 7.2, 6.9, H–C(3)); 3.39 (*s*, Me–N(1′)); 3.32 (*s*, Me–N(3′)); 3.05 (*dd*, *J* = 17.3, 6.9, 1 H–C(2)); 2.75 (*dd*, *J* = 17.3, 7.2, 1 H–C(2)); 1.22 (*t*, *J* = 7.0, *Me*CH_2O). ^{13}C-NMR ($CDCl_3$): 171.3 (COO); 171.1 (COO); 161.1 (C(4′)); 151.0 (C(2′)); 141.4 (CH(6′)); 109.9 (C(5′)); 60.9 (Me*C*H_2O); 60.2 (Me*C*H_2O); 39.6 (CH(3)); 36.6 (Me–N(3′)); 34.9 (CH_2(2)); 27.4 (Me–N(1′)); 13.7 (*Me*CH_2O); 13.6 (*Me*CH_2O). EI-MS: 313 (1, $[M + H]^+$), 312 (6, M^+), 267 (19), 266 (32), 239 (9), 238 (43), 237 (12), 194 (12), 193 (100), 169 (5), 167 (11), 166 (19), 165 (17), 110 (11), 81 (12).

*3-(Ethoxycarbonyl)-*N*-[(ethoxycarbonyl)methyl]-3-(1,2,3,4-tetrahydro-1,3-dimethyl-2,4-dioxopyrimidin-5-yl)propanamide* (= *Ethyl 3-{[(Ethoxycarbonyl)methyl]carbamoyl}-2-(1,2,3,4-tetrahydro-1,3-dimethyl-2,4-dioxopyrimidin-5-yl)propanoate*; **8c**, X = $NHCH_2COOEt$, R = COOEt). Yield 94%. Not crystalline. IR (neat): 3340 (br.), 3075*m*, 1735*vs*, 1700*vs*, 1660*vs*, 1640*vs*, 1550*vs*, 1535*vs*, 1480*vs*, 1460*vs*, 1375*vs*, 1345*vs*, 1200*vs*, 1160*vs*,

1093*vs*, 1020*vs*, 970*m*, 920*s*, 860*s*, 780*s*, 758*s*, 730*s*. ^{1}H-NMR ($CDCl_3$): 7.26 (*s*, H–C(6′)); 6.20 (*dd*, *J* = 5.7, 5.0, N*H*CH_2); 4.18 (*q*, *J* = 7.4, MeC*H*$_2$O); 4.14 (*q*, *J* = 7.1, MeC*H*$_2$O); 4.04 (*dd*, *J* = 18.4, 5.7, 1 H, NHC*H*$_2$); 3.89 (*dd*, *J* = 8.3, 5.5, H–C(3)); 3.89 (*dd*, *J* = 18.4, 5.0, 1 H, NHC*H*$_2$); 3.39 (*s*, Me–N(1′)); 3.33 (*s*, Me–N(3′)); 3.05 (*dd*, *J* = 15.5, 5.5, 1 H–C(2)); 2.77 (*dd*, *J* = 15.5, 8.3, 1 H–C(2)); 1.27 (*t*, *J* = 7.1, *Me*CH_2O); 1.22 (*t*, *J* = 7.4, *Me*CH_2O). ^{13}C-NMR ($CDCl_3$): 171.6 (COO); 170.9 (COO); 169.2 (CONH); 162.1 (C(4′)); 151.0 (C(2′)); 144.2 (CH(6′)); 109.4 (C(5′)); 60.6 (MeC*H*$_2$O); 60.5 (Me*C*H_2O); 40.6 (NHC*H*$_2$); 40.4 (CH(3)); 36.3 (Me–N(3)); 35.7 (CH_2(2)); 27.1 (Me–N(1′)); 13.5 (*Me*CH_2O); 13.4 (*Me*CH_2O). EI-MS: 369 (10, M^+), 323 (35), 267 (12), 266 (15), 249 (17), 238 (37), 220 (11), 193 (100), 167 (37), 166 (30), 165 (39), 110 (22), 108 (9), 99 (6), 97 (6), 95 (10), 82 (9), 81 (50), 74 (13), 71 (7), 69 (4), 68 (28), 58 (8), 57 (7), 55 (48).

N,N-*Diethyl-3-(ethoxycarbonyl)-3-(1,2,3,4-tetrahydro-1,3-dimethyl-2,4-dioxopyrimidin-5-yl)propanamide* (= *Ethyl 3-(Diethylcarbamoyl)-2-(1,2,3,4-tetrahydro-1,3-dimethyl-2,4-dioxopyrimidin-5-yl)propanoate*; **8c**, X = Et_2N, R = COOEt). Yield 95%. Not crystalline. IR (neat): 3070*m*, 1730*vs*, 1700*vs*, 1660*vs*, 1640*vs*, 1480*s*, 1455*vs*, 1435*vs*, 1372*vs*, 1340*s*, 1270*s*, 1235*s*, 1215*s*, 1180*s*, 1140*s*, 1095*s*, 1020*s*, 780*s*, 755*s*. ^{1}H-NMR ($CDCl_3$): 7.37 (*s*, H–C(6′)); 4.18 (*q*, *J* = 7.0, MeC*H*$_2$O); 4.03 (*dd*, *J* = 7.2, 5.6, H–C(3)); 3.43 (*s*, Me–N(1′)); 3.36 (*s*, Me–N(3)); 3.34 (*t*, *J* = 7.1, 1 MeC*H*$_2$N); 3.28 (*t*, *J* = 7.1, 1 MeC*H*N); 3.09 (*dd*, *J* = 16.6, 5.6, 1 H–C(2)); 2.85 (*dd*, *J* = 16.6, 7.2, 1 H–C(2)); 1.24 (*t*, *J* = 7.0, *Me*CH_2O); 1.17 (*t*, *J* = 7.1, 1 *Me*CH_2N); 1.10 (*t*, *J* = 7.1, 1 *Me*CH_2N). ^{13}C-NMR ($CDCl_3$): 172.3 (COO); 169.9 (*C*ON(Et)$_2$); 162.6 (C(4′)); 151.4 (C(2′)); 142.4 (CH(6)); 110.8 (C(5)); 61.1 (Me-*C*H_2O); 41.7 (MeC*H*$_2$N); 40.6 (CH(3)); 40.2 (MeC*H*$_2$N); 36.9 (Me–N(3)); 33.7 (CH_2(2)); 27.8 (Me–N(1′)); 14.0 (2 *Me*CH_2N); 12.9 (*Me*CH_2O). EI-MS: 340 (10, $[M + H]^+$), 339 (20, M^+), 295 (4), 294 (15), 293 (23), 267 (3), 266 (8), 264 (9), 239 (10), 238 (30), 237 (7), 194 (14), 193 (100), 167 (7), 166 (18), 165 (19), 100 (27), 81 (27), 80 (12), 74 (8), 72 (64), 69 (6), 68 (9), 58 (14), 56 (7), 55 (6).

3-(1,2,3,4-Tetrahydro-1,3,6-trimethyl-2,4-dioxopyrimidin-5-yl)propanoic Acid (**15a**, X = OH, R = H). Recrystallized from EtOH. M.p. 178.0–178.5°. IR (KBr): 3200–2500 (br.), 1735*vs*, 1690*vs*, 1660*vs*, 1640*vs*, 1485*vs*, 1465*vs*, 1420*vs*, 1340*s*, 1315*s*, 1240*s*, 1210*s*, 1180*s*, 1165*vs*, 1090*vs*, 1040*s*, 938*vs*, 840*s*, 782*vs*, 755*vs*. ^{1}H-NMR ($CDCl_3$): 10.50 (br., COOH); 7.12 (*s*, H–C(6′)); 3.39 (*s*, Me–N(1′)); 3.36 (*s*, Me–N(3′)); 2.66 (*m*, CH_2CH_2). ^{13}C-NMR ($CDCl_3$): 177.8 (COOH); 163.5 (C(4′)); 151.7 (C(2′)); 140.6 (CH(6′)); 111.3 (C(5′)); 36.9 (Me–N(3′)); 32.3 (CH_2(2)); 27.9 (Me–N(1′)); 22.8 (CH_2(3)).

Methyl 3-(1,2,3,4-Tetrahydro-1,3,6-trimethyl-2,4-dioxopyrimidin-5-yl)propanoate (**15a**, X = MeO, R = H). This compound was obtained by adding MeOH (2 ml) to the following preparations: *a*) **13a** (see *General Method*), *b*) **10** in presence of pyridine (see also **8a** X = MeO, R = H), *c*) **10** in presence of HCl/Et_2O (see above **11**/**13a** by *Method A*), and *d*) **11** prepared by *Method B* (yield 1.17 g, 98%). Crystals after FC. M.p. 101.5–102.0°. IR (KBr): 1730*vs*, 1694*vs*, 1645*vs*, 1623*vs*, 1460*vs*, 1435*vs*, 1355*vs*, 1300*vs*, 1192*s*, 1170*s*, 1050*vs*, 980*s*, 918*m*, 878*m*, 785*s*, 775*s*, 758*s*. ^{1}H-NMR ($CDCl_3$): 3.77 (*s*, MeO); 3.45 (*s*, Me–N(1′)); 3.36 (*s*, Me–N(3′)); 2.78 (*t*, *J* = 7.5, 2 H–C(2)); 2.55 (*t*, *J* = 7.5, 2 H–C(3)); 2.32 (*s*, Me–C(6)). ^{13}C-NMR ($CDCl_3$): 173.2 (COO); 162.4 (C(4′)); 151.7 (C(2′)); 147.8 (C(6′)); 109.4 (C(5′)); 51.3 (MeO); 32.5 (CH_2(2)); 32.0 (Me–N(3′)); 27.9 (Me–N(1′)); 21.9 (CH_2(3)); 16.3 (Me–C(6′)). CI-MS: 241 (13, $[M + H]^+$), 240 (64, M^+), 209 (45), 208 (5), 180 (100), 167 (43), 154 (12), 124 (6), 97 (4), 94 (11), 81 (9).

Ethyl 3-(1,2,3,4-Tetrahydro-1,3,6-trimethyl-2,4-dioxopyrimidin-5-yl)propanoate (**15a**, X = EtO, R = H). Crystals after FC. M.p. 75.0–75.5°. IR (KBr): 1735*vs*, 1700*vs*, 1690*vs*, 1660*vs*, 1630*vs*, 1480*vs*, 1455*vs*, 1370*s*, 1340*vs*, 1250*vs*, 1215*s*, 1180*vs*, 1160*vs*, 1134*vs*, 1085*s*, 925*s*, 860*vs*, 840*vs*, 753*vs*. ^{1}H-NMR ($CDCl_3$): 4.11 (*q*, *J* = 7.2, MeC*H*$_2$O); 3.44 (*s*, Me–N(1′)); 3.35 (*s*, Me–N(3′)); 2.76 (*t*, *J* = 7.5, CH_2(2)); 2.51 (*t*, *J* = 7.5, CH_2(3)); 2.32 (*s*, Me–C(6′)); 1.24 (*t*, *J* = 7.2, *Me*CH_2O). ^{13}C-NMR ($CDCl_3$): 172.1 (COO); 161.8 (C(4′)); 151.2 (C(2′)); 147.5 (C(6′)); 108.8 (C(5′)); 59.6 (MeC*H*$_2$O); 32.4 (CH_2(2)); 31.4 (Me–N(3′)); 27.3 (Me–N(1′)); 21.5 (CH_2(3)); 15.8 (Me–C(6′)); 13.5 (*Me*CH_2O). EI-MS: 255 (4, $[M + H]^+$), 254 (23, M^+), 209 (15), 208 (5), 180 (5), 110 (20), 95 (9), 94 (10), 69 (9), 68 (5), 67 (8), 58 (8), 57 (15), 56 (100), 55 (14). CI-MS: 255 (71, $[M + H]^+$), 254 (79, M^+), 209 (100), 208 (36), 181 (17), 180 (62), 167 (22), 154 (7), 110 (51), 95 (18), 94 (22), 82 (15), 81 (14), 80 (13).

N-*[(Ethoxycarbonyl)methyl]-3-(1,2,3,4-tetrahydro-1,3,6-trimethyl-2,4-dioxopyrimidin-5-yl)propanamide* (= *Ethyl 2-[3-(1,2,3,4-Tetrahydro-1,3,6-trimethyl-2,4-dioxopyrimidin-5-yl)propanamido]acetate*; **15a**, X = NHCH_2COOEt, R = H). Crystals after FC and recrystallization from EtOH. M.p. 158.2–159.1°. IR (KBr): 3330*s*, 3295*s*, 3070*m*, 1750*s*, 1735*s*, 1690*vs*, 1637*vs*, 1630*vs*, 1550*s*, 1375*m*, 1353*s*, 1200*vs*, 1035*s*, 1023*s*, 780*s*, 756*s*. ^{1}H-NMR ($CDCl_3$): 6.28 (*t*, *J* = 5.2, NH); 4.19 (*q*, *J* = 7.1, MeC*H*$_2$O); 3.99 (*d*, *J* = 5.2, NHC*H*$_2$); 3.44 (*s*, Me–N(1′)); 3.36 (*s*, Me–N(3′)); 2.81 (*t*, *J* = 7.0, 2 H–C(2)); 2.48 (*t*, *J* = 7.0, 2 H–C(3)); 2.31 (*s*, Me–C(6′)); 1.28 (*t*, *J* = 7.1, *Me*CH_2O). ^{13}C-NMR ($CDCl_3$): 172.4 (*C*OO); 169.6 (CONH); 162.8 (C(4′)); 151.7 (C(2′)); 148.4 (C(6′)); 109.5 (C(5′)); 61.0 (MeC*H*$_2$O); 41.0 (NHCH_2); 34.7 (CH_2(2)); 32.0 (Me–N(3′)); 27.9 (Me–N(1′)); 22.5 (CH_2(3)); 16.4 (Me–C(6′)); 13.9 (*Me*CH_2O). CI-MS: 312 (100, $[M + H]^+$), 311 (34, M^+), 266 (4), 209 (11), 208 (11), 180 (12), 167 (3), 110 (3), 95 (2), 94 (3), 82 (2).

3-(1,2,3,4-Tetrahydro-1,3,6-trimethyl-2,4-dioxopyrimidin-5-yl)butanoic Acid (**15b**, X = OH, R = Me). Recrystallized from EtOH. M.p. 149.5–150.5°. IR (KBr): 3200–2500 (br.), 1710*vs*, 1690*vs*, 1640*vs*, 1610*vs*, 1475*vs*, 1465*vs*, 1450*vs*, 1430*vs*, 1365*s*, 1355*s*, 1300*s*, 1230*s*, 1195*s*, 1105*s*, 1005*vs*, 940*vs*, 850*vs*, 782*vs*, 755*vs*, 700*s*. ^{1}H-NMR ($CDCl_3$): 10.51 (br., COOH); 3.44 (*s*, Me–N(1′)); 3.31 (*s*, Me–N(3′)); 3.27 (*m*, H–C(3)); 3.11 (*dd*, J = 16.7, 8.7, 1 H–C(2)); 2.69 (*dd*, J = 16.7, 5.7, 1 H–C(2)); 2.32 (*s*, Me–C(6′)); 1.29 (*d*, J = 7.0, Me–C(3)). ^{13}C-NMR ($CDCl_3$): 180.0 (COOH); 161.7 (C(4′)); 151.9 (C(2′)); 147.9 (C(6′)); 113.1 (C(5′)); 38.3 (CH_2(2)); 32.3 (Me–N(3′)); 30.1 (CH(3)); 27.8 (Me–N(1′)); 18.6 (Me–C(3)); 16.2 (Me–C(6′)). EI-MS: 241 (3, $[M + H]^+$), 240 (22, M^+), 224 (13), 210 (18), 195 (14), 194 (12), 181 (45), 180 (8), 179 (20), 178 (12), 165 (28), 164 (10), 154 (5), 124 (11), 96 (7), 82 (18), 69 (12), 57 (12), 56 (100), 55 (18).

Methyl 3-(1,2,3,4-Tetrahydro-1,3,6-trimethyl-2,4-dioxopyrimidin-5-yl)butanoate (**15b**, X = MeO, R = Me). Purified by FC. Not crystalline. IR (neat): 1732*vs*, 1690*vs*, 1640*vs*, 1480–1420 (br.), 1365*vs*, 1285*s*, 1255*s*, 1190*s*, 1170*vs*, 1012*vs*, 850*m*, 782*vs*, 755*vs*. ^{1}H-NMR ($CDCl_3$): 3.63 (*s*, MeO); 3.47 (*s*, Me–N(1′)); 3.33 (*s*, Me–N(3′)); 3.31 (*m*, H–C(3)); 3.12 (*dd*, J = 16.5, 9.0, 1 H–C(2)); 2.64 (*dd*, J = 16.5, 5.5, 1 H–C(2)); 2.37 (*s*, Me–C(6′)); 1.32 (*d*, J = 7.0, Me–C(3)). ^{13}C-NMR ($CDCl_3$): 173.2 (COO); 161.3 (C(4′)); 151.5 (C(2′)); 147.5 (C(6′)); 112.6 (C(5′)); 50.8 (MeO); 37.8 (CH_2(2)); 31.9 (Me–N(3′)); 29.9 (CH(3)); 27.3 (Me–N(1′)); 18.3 (*Me*–C(3)); 15.9 (*Me*–C(6′)). EI-MS: 255 (4, $[M + H]^+$), 254 (14, M^+), 223 (9), 207 (13), 195 (24), 194 (14), 181 (47), 179 (11), 124 (12), 94 (7), 69 (2), 56 (100), 55 (5).

Ethyl 3-(1,2,3,4-Tetrahydro-1,3,6-trimethyl-2,4-dioxopyrimidin-5-yl)propanoate (**15b**, X = EtO, R = Me). Purified by chromatography. Not crystalline. IR (neat): 1730*vs*, 1693*vs*, 1640*vs*, 1480–1420 (br.), 1365*s*, 1355*s*, 1255*s*, 1175*s*, 1028*s*, 1008*s*, 782*s*, 755*s*. ^{1}H-NMR ($CDCl_3$): 4.07 (*q*, J = 7.1, MeCH_2O); 3.46 (*s*, Me–N(1′)); 3.33 (*s*, Me–N(3′)); 3.30 (*m*, H–C(3)); 3.09 (*dd*, J = 16.5, 9.0, 1 H–C(2)); 2.63 (*dd*, J = 16.5, 5.5, 1 H–C(2)); 2.35 (*s*, Me–C(6′)); 1.31 (*d*, J = 7.0, Me–C(3)); 1.20 (*t*, J = 7.1, *Me*CH_2O). ^{13}C-NMR ($CDCl_3$): 173.2 (COO); 161.7 (C(4′)); 151.9 (C(2′)); 147.6 (C(6′)); 113.3 (C(5′)); 60.0 (MeCH_2O); 38.5 (CH_2(2)); 32.3 (Me–N(3′)); 30.3 (CH(3)); 27.7 (Me–N(1′)); 18.7 (*Me*–C(3)); 16.3 (*Me*–C(6′)); 14.0 (*Me*CH_2O). EI-MS: 269 (4, $[M + H]^+$), 268 (15, M^+), 223 (17), 207 (14), 195 (30), 194 (21), 181 (59), 179 (14), 124 (11), 94 (8), 69 (3), 57 (4), 56 (100), 55 (5).

N,N-*Diethyl 3-(1,2,3,4-Tetrahydro-1,3,6-trimethyl-2,4-dioxopyrimidin-5-yl)butanamide* (**15b**, X = Et_2N, R = Me). Not crystalline. IR (neat): 1690*vs*, 1640*vs*, 1470*vs*, 1450*vs*, 1425*vs*, 1385*s*, 1355*vs*, 1280*s*, 1250*s*, 1220*s*, 1150*s*, 1095*s*, 1005*s*, 783*s*, 755*s*. ^{1}H-NMR ($CDCl_3$): 3.44 (*s*, Me–N(1′)); 3.37 (*q*, J = 7.0, MeCH_2N); 3.32 (*s*, Me–N(3′)); 3.31 (*m*, H–C(3)); 3.30 (*q*, J = 7.0, MeCH_2N); 3.19 (*dd*, J = 15.5, 8.9, 1 H–C(2)); 2.56 (*dd*, J = 15.5, 5.5, 8.9, 1 H–C(2)); 2.41 (*s*, Me–C(6′)); 1.30 (*d*, J = 7.0, Me–C(3)); 1.13 (*t*, J = 7.0, *Me*CH_2N); 1.04 (*t*, J = 7.0, *Me*CH_2N). ^{13}C-NMR ($CDCl_3$): 171.5 (CON); 162.0 (C(4′)); 152.0 (C(2′)); 148.0 (C(6′)); 113.7 (C(5′)); 41.8 (MeCH_2N); 40.0 (MeCH_2N); 36.8 (CH_2(2)); 32.3 (Me–N(3′)); 30.6 (CH(3)); 27.6 (Me–N(1′)); 18.7 (*Me*–C(3)); 16.3 (*Me*–C(6′)); 14.1 (*Me*CH_2N); 12.9 (*Me*CH_2N). EI-MS: 296 (9, $[M + H]^+$), 295 (14, M^+), 224 (7), 223 (13), 222 (8), 208 (7), 207 (10), 196 (59), 195 (100), 194 (43), 182 (18), 181 (38), 154 (1), 138 (2), 124 (5), 115 (4), 100 (6), 72 (34), 56 (81).

3-(Ethoxycarbonyl)-3-(1,2,3,4-tetrahydro-1,3,6-trimethyl-2,4-dioxopyrimidin-5-yl)propanoic Acid (= *1-Ethyl Hydrogen 2-(1,2,3,4-Tetrahydro-1,3,6-trimethyl-2,4-dioxopyrimidin-5-yl)butanedioate*; **15c**, X = OH, R = COOEt). Not crystalline. Yield 93%. IR (neat): 3500–2500 (br.), 1730*vs*, 1710*vs*, 1690*vs*, 1640*vs*, 1360*vs*, 1270*vs*, 1210*vs*, 1160*vs*, 1020*vs*, 980*s*, 860*s*, 780*s*, 758*s*. ^{1}H-NMR ($CDCl_3$): 10.5 (br., COOH); 4.18 (*dq*, J = 11.0, 7.1, MeCH_2O); 4.14 (*dq*, J = 11.0, 7.1, MeCH_2O); 4.04 (*dd*, J = 7.5, 6.0, H–C(3)); 3.47 (*s*, Me–N(1′)); 3.37 (*dd*, J = 17.5, 6.0, 1 H–C(2)); 3.33 (*s*, Me–N(3′)); 2.73 (*dd*, J = 17.5, 7.5, 1 H–C(2)); 2.46 (*s*, Me–C(6′)); 1.21 (*t*, J = 7.1, *Me*CH_2O). ^{13}C-NMR ($CDCl_3$): 174.7 (COOH); 171.3 (*C*OOEt); 161.2 (C(4′)); 151.2 (C(2′)); 149.5 (C(6′)); 109.1 (C(5′)); 60.6 (MeCH_2O); 39.4 (CH(3)); 33.8 (CH_2(2)); 31.9 (Me–N(3′)); 27.4 (Me–N(1′)); 16.2 (Me–C(6′)); 13.3 *Me*CH_2O).

Methyl 3-(Ethoxycarbonyl)-3-(1,2,3,4-tetrahydro-1,3,6-trimethyl-2,4-dioxopyrimidin-5-yl)propanoate (= *1-Ethyl 4-Methyl 2-(1,2,3,4-Tetrahydro-1,3,6-trimethyl-2,4-dioxopyrimidin-5-yl)butanedioate*; **15c**, X = MeO, R = COOEt). Crystals after chromatography. M.p. 106.5 –107.0°. IR (KBr): 1732*vs*, 1692*vs*, 1640*vs*, 1475*vs*, 1455*s*, 1427*vs*, 1385*w*, 1358*vs*, 1275*vs*, 1253*s*, 1200*vs*, 1155*vs*, 1023*s*, 985*s*, 975*s*, 755*s*. ^{1}H-NMR ($CDCl_3$): 4.16 (*q*, J = 7.1, MeCH_2O); 4.06 (*dd*, J = 6.9, 5.8, H–C(3)); 3.68 (*s*, MeO); 3.50 (*s*, Me–N(1′)); 3.34 (*dd*, J = 17.1, 5.8, 1 H–C(2)); 3.33 (*s*, Me–N(3′)); 2.72 (*dd*, J = 17.1, 6.9, 1 H–C(2)); 2.40 (*s*, Me–C(6′)); 1.23 (*t*, J = 7.1, *Me*CH_2O). ^{13}C-NMR ($CDCl_3$): 172.8 (COO); 171.6 (COO); 161.6 (C(4′)); 151.8 (C(2′)); 149.2 (C(6′)); 109.9 (C(5′)); 61.2 (MeCH_2O); 51.6 (MeO); 40.2 (CH(3)); 34.4 (CH_2(2)); 32.4 (Me–N(3′)); 28.0 (Me–N(1′)); 16.8 (*Me*–C(6′)); 14.0 (*Me*CH_2O). EI-MS: 313 (2, $[M + H]^+$), 312 (8, M^+), 282 (1), 281 (4), 267 (7), 266 (14), 234 (7), 208 (15), 207 (100), 180 (7), 179 (24), 95 (6), 57 (7), 56 (76), 55 (7).

Ethyl 3-(Ethoxycarbonyl)-3-(1,2,3,4-tetrahydro-1,3,6-trimethyl-2,4-dioxopyrimidin-5-yl)propanoate (= *Diethyl 2-(1,2,3,4-Tetrahydro-1,3,6-trimethyl-2,4-dioxopyrimidin-5-yl)butanedioate*; **15c**, X = EtO, R = COOEt).

Crystals after chromatography. M.p. 86.2–87.0°. IR (KBr): 1740*vs*, 1730*vs*, 1700*vs*, 1633*vs*, 1485*s*, 1445*s*, 1425*s*, 1368*s*, 1353*s*, 1320*s*, 1275*vs*, 1235*s*, 1208*vs*, 1160*vs*, 1095*s*, 1025*vs*, 855*s*, 782*s*, 753*s*. ^{1}H-NMR ($CDCl_3$): 4.17 (*q*, J = 7.0, MeCH_2O); 4.12 (*q*, J = 7.0, MeCH_2O); 4.07 (*dd*, J = 7.8, 6.0, H–C(3)); 3.47 (*s*, Me–N(1′)); 3.33 (*s*, Me–N(3′)); 3.31 (*dd*, J = 17.0, 6.0, 1 H–C(2)); 2.71 (*dd*, J = 17.0, 7.8, 1 H–C(2)); 2.38 (*s*, Me–C(6′)); 1.25 (*t*, J = 7.0, *Me*CH_2O); 1.21 (*t*, J = 7.0, *Me*CH_2O). ^{13}C-NMR ($CDCl_3$): 172.4 (COO); 171.8 (COO); 161.7 (C(4′)); 151.9 (C(2′)); 149.2 (C(6′)); 110.1 (C(5′)); 61.3 (MeCH_2O); 60.6 (MeCH_2O); 40.2 (CH(3)); 34.8 (CH_2(2)); 32.4 (Me–N(3′)); 28.1 (Me–N(1′)); 16.8 (*Me*–C(6′)); 14.1 (*Me*CH_2O); 14.0 (*Me*CH_2O). EI-MS: 327 (3, $[M + H]^+$), 326 (8, M^+), 282 (3), 281 (13), 280 (15), 234 (8), 208 (16), 207 (100), 180 (9), 179 (22), 154 (3), 95 (7), 94 (12), 57 (8), 56 (74), 55 (8).

*3-(Ethoxycarbonyl)-*N*-[(ethoxycarbonyl)methyl]-3-(1,2,3,4-tetrahydro-1,3,6-trimethyl-2,4-dioxopyrimidin-5-yl)propanamide* (= *Ethyl 3-*{*[(Ethoxycarbonyl)methyl]carbamoyl*}*-2-(1,2,3,4-tetrahydro-1,3,6-trimethyl-2,4-dioxopyrimidin-5-yl)propanoate*; **15c**, X = $NHCH_2COOEt$, R = COOEt). Yield 91%. Not crystalline. IR (neat): 3340 (br.), 3080*m*, 1735*vs*, 1690*vs*, 1640*vs*, 1550*vs*, 1535*vs*, 1480*vs*, 1430*vs*, 1360*vs*, 1200*vs*, 1160*vs*, 1030*vs*, 975*s*, 860*s*, 782*s*, 758*s*, 730*s*. ^{1}H-NMR ($CDCl_3$): 6.18 (*dd*, J = 5.8, 5.0, NH); 4.18 (*q*, J = 7.1, MeCH_2O); 4.14 (*q*, J = 7.1, MeCH_2O); 4.10 (*dd*, J = 8.1, 5.7, H–C(3)); 4.05 (*dd*, J = 18.2, 5.8, 1 H, NHCH_2); 3.87 (*dd*, J = 18.2, 5.0, 1 H, NHCH_2); 3.47 (*s*, Me–N(1′)); 3.31 (*s*, Me–N(3′)); 3.22 (*dd*, J = 15.2, 5.7, 1 H–C(2)); 2.68 (*dd*, J = 15.2, 8.1, 1 H–C(2)); 2.36 (*s*, Me–C(6′)); 1.27 (*t*, J = 7.1, *Me*CH_2O); 1.20 (*t*, J = 7.1, *Me*CH_2O). ^{13}C-NMR ($CDCl_3$): 171.7 (*C*OOEt); 171.3 (*C*OOEt); 169.2 (CONH); 161.2 (C(4′)); 151.2 (C(2′)); 149.7 (C(6′)); 109.0 (C(5′)); 60.3 (2 Me*C*H_2O); 40.5 ($NHCH_2$); 39.9 (CH(3)); 35.5 (CH_2(2)); 31.8 (Me–N(3′)); 27.2 (Me–N(1′)); 16.3 (*Me*–C(6′)); 13.4 (2 *Me*CH_2O). EI-MS: 383 (9, M^+), 337 (13), 281 (4), 264 (3), 253 (3), 234 (9), 207 (87), 181 (15), 180 (13), 179 (31), 94 (16), 82 (16), 74 (5), 69 (6), 66 (8), 56 (100).

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