Synthesis of annelated analogues of 6-benzyl-1-(ethoxymethyl)-5-isopropyluracil (MKC-442) using 1,3-oxazine-2,4(3*H*)-diones as key intermediates

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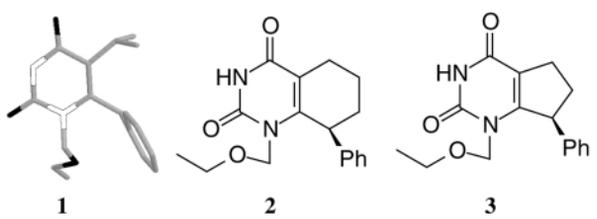
Condensation of ethyl 3-phenyl-2-oxocyclopentanecarboxylate **5** with 2-(*S*-methylthio)isourea followed by hydrolysis with HCl gave 6,7-dihydro-7-phenylcyclopenta[*e*][1,3]oxazine-2,4(3*H*,5*H*)-dione (**10a**). 7,8-Dihydro-8-phenyl-6*H*-cyclohexa[*e*][1,3]oxazine-2,4(3*H*,5*H*)-dione (**10b**) was synthesised by reacting 2-phenylcyclohexanone (**9b**) with *N*-(chlorocarbonyl) isocyanate. The oxazines **10a**,**b** were reacted with ammonia to obtain the corresponding uracil derivatives **12a**,**b** which after silylation were alkylated with diethoxymethane using trimethylsilyl triflate (TMS-triflate) as the catalyst or alkylated with chloromethyl ethyl ether to give annelated MKC-442 analogues **2**,**3** which are locked in a conformation close to the one of MKC-442. In spite of this, only moderate activities were found against HIV-1 for the annelated analogues of MKC-442.

Introduction

Since the synthesis of 1-[(2-hydroxyethoxy)methyl]-6-(phenylthio)thymine (HEPT) by Miyasaka *et al.*[1] in 1989, there has been a growing interest in nonnucleoside reverse transcriptase inhibitors. Although HEPT did not show very high activity against HIV-1 it was considered an interesting lead compound for the synthesis of new analogues, among them the 6-benzyl-1-(ethoxymethyl)-5-isopropyluracil (MKC-442) **1**.[2] This compound showed high activity against HIV-1 and was chosen as a candidate for clinical trials with AIDS patients.[3] MKC-442 inhibits reverse transcriptase (RT) of the HIV-1 virus allosterically, as it binds to the enzyme in a hydrophobic pocket outside the active site and thereby changes the conformation of the active site, making RT inactive. The inhibitor is mainly held in place in the pocket by hydrogen bonds and hydrophobic bonds to the nearby amino acids.

Structure–activity relationships (SAR) studies of HEPT-derivatives have shown, that an ethyl or isopropyl group in the C-5 position of the pyrimidine ring is important for antiviral activity.[4] This substituent forces Tyr 181 of the enzyme to make a 180° rotation and thereby making it favourable for interaction with the 6-benzyl group of the inhibitor. In this paper we investigate the effect of fixing the orientation of the phenyl group in MKC-442 by synthesising annelated compounds **2** and **3** with rigid structures to fix the position of the aromatic ring. The crystal structure of MKC-442 bound in the RT[5] (Fig. 1) makes it likely that the position of the aromatic ring and angle to the plan of the pyrimidine ring in MKC-442 and in the two annelated analogues are very similar. It was therefore interesting to find out whether fixing the orientation of the aromatic ring in an MKC-442 type structure, could improve the activity against HIV-1.



1 **2** **3**

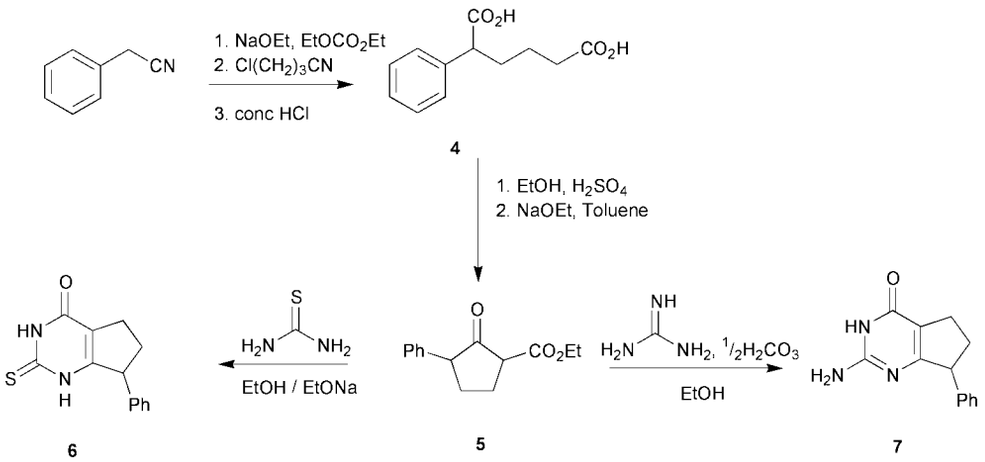
Fig. 1 **1** Crystal structure of MKC-442 when bound to RT. **2** Structure of cyclohexane-annelated MKC-442 analogue. **3** Structure of cyclopentane-annelated MKC-442 analogue.

Results and discussion

In order to synthesise the cyclopentane annelated compound **3**, a conventional route was chosen in which the β-keto ester **5** would be a key intermediate as in the synthesis of MKC-442 by Danel *et al.*[6] 2-Phenyladipic acid **4** was prepared in 64% yield according to the method of Baker and Jones[7] by reaction of phenylacetonitrile with diethyl carbonate under alkaline conditions, followed by addition of 4-chlorobutyronitrile and hydrolysis with conc. HCl. Compound **4** was reacted with EtOH and H_2SO_4 to give the corresponding diester which was then ring closed in a Dieckmann reaction to afford ethyl 3-phenyl-2-oxocyclopentanecarboxylate (**5**) using the same conditions as Clark and Howes[8] used in the synthesis of the corresponding *m*-methoxy derivative (Scheme 1).

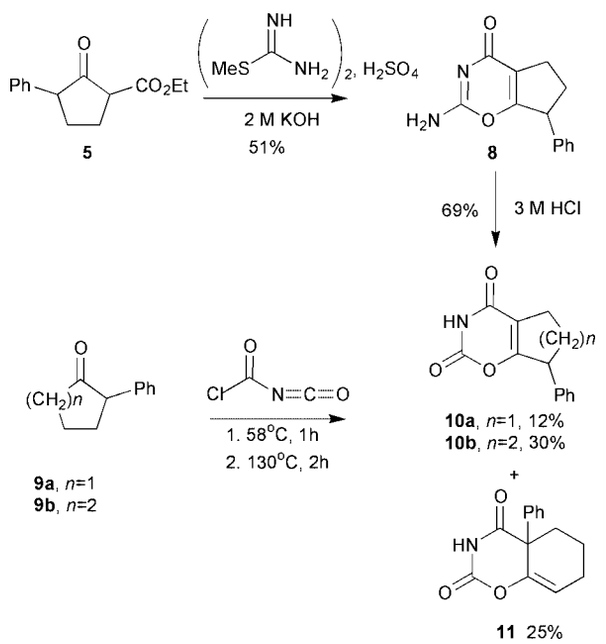
Compound **5** was reacted with thiourea and sodium in EtOH using the method of Danel *et al.*[6] to give the 2-thio analogue **6** in only 4% yield. In an attempt to obtain a better yield, the reaction was carried out in different solvents (MeOH and EtOH) and bases (NaH and tBuOK), but without any success. In an alternative route compound **5** was reacted with guanidine carbonate[9] in EtOH to give the 2-amino-7-phenyl-6,7-dihydro-5*H*-cyclopenta[*d*]pyrimidin-4(3*H*)-one **7**, but again in a poor yield (11%), indicating that the cyclic β-keto ester **5** was quite unreactive towards nucleophiles and therefore this strategy was abandoned without further optimisation.

The difficulties in the above mentioned reactions made us look for an alternative synthetic route. Ross *et al.*[10] have shown that reasonable yields of 2-amino-1,3-oxazine-4(3*H*)-ones were obtained by reaction of 2-(*S*-methylthio)isourea with non-



Scheme 1

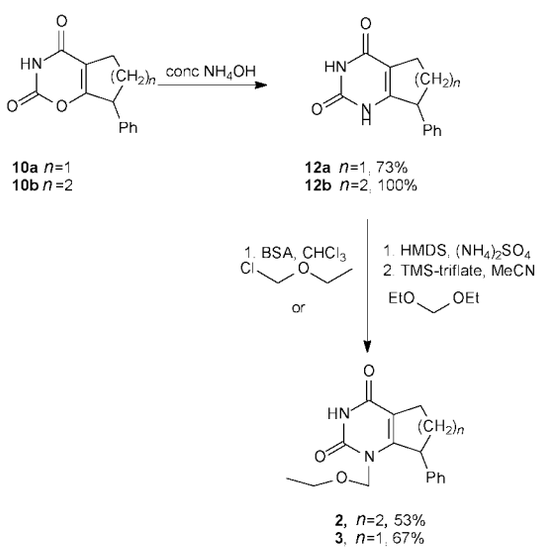
cyclic β-keto esters in aqueous KOH. The reaction of **5** under the same conditions gave 51% yield of 2-amino-7-phenyl-6,7-dihydrocyclopenta[*e*][1,3]oxazin-4(5*H*)-one **8** which was easily converted to the corresponding 7-phenyl-6,7-dihydrocyclopenta[*e*][1,3]oxazine-2,4(3*H*,5*H*)-dione **10a** by treatment with 3 M HCl under reflux (Scheme 2).



Scheme 2

The cyclohexyl annelated compound **2** was synthesised *via* the 1,3-oxazine-2,4(3*H*)-dione **10b** as intermediate but using another synthetic pathway for the intermediate. The commercially available **9b** was reacted with *N*-(chlorocarbonyl) isocyanate[11] to give a mixture of products **10b** and **11** in 30% and 25% yield, respectively. 2-Phenylcyclopentanone **9a** could likewise be used for the synthesis of **10a** and was easily obtained by reacting cyclopentanone with phenylmagnesium bromide followed by treatment with sulfuric acid to give 1-phenylcyclopentene,[12] which was oxidized using formic acid and hydrogen peroxide.[13] Unfortunately, the reaction of **9a** with *N*-(chlorocarbonyl)isocyanate gave **10a** in 12% yield, only.

In order to synthesise the *N*-1 substituted uracils **2** and **3**, the oxazines **10a,b** were reacted with concentrated aqueous ammonia to give **12a,b** in 73% and 100% yield, respectively.[14] Compound **12a** was then silylated with 1,1,1,3,3,3-hexamethyldisilazane (HMDS) in the presence of $(NH_4)_2SO_4$ and reacted with diethoxymethane under standard Vorbrüggen conditions,[15] using trimethylsilyl trifluoromethanesulfonate (TMS-triflate) as a Lewis acid catalyst. This gave **3** in 67% yield (Scheme 3).



Scheme 3

Compound **12b** was silylated using *N*,*O*-bis(trimethylsilyl) acetamide (BSA) in $CHCl_3$ followed by coupling with chloromethyl ethyl ether[6] to give **2** in 53% yield.

Biological activity

The compounds **2**,**3**,**6**–**8**,**10**–**12** were tested for their activity against HIV-1 in MT-4 cells using HIV antigen detection ELISA for quantifying expression of HIV in culture medium. Only compound **2** (ED_{50} = 29 μM, CD_{50} > 100 μM) and **3** (ED_{50} = 36 μM, CD_{50} > 100 μM) showed activity against HIV-1, but at considerably higher concentrations than the reference compound MKC-442 (ED_{50} = 0.005 μM).

Conclusion

We have developed new routes for the synthesis of the target compounds **2** and **3** as the already known procedures gave very low yields. The target compounds were synthesised from the corresponding 1,3-oxazine-2,4(3*H*)-diones which were synthesised using two new strategies. Unfortunately the annelated compounds did not show antiviral activities in the nanomolar range as does MKC-442 and therefore we conclude that these compounds are not able to induce the Tyr 181 switch.

Experimental

^{1}H NMR spectra were recorded on a Varian Gemini 2000 NMR spectrometer at 300 MHz for ^{1}H and 62.9 MHz for ^{13}C with TMS as an internal standard. EI mass spectra were recorded on a Finnigan MAT SSQ 710. FAB mass spectra were recorded on a Kratos MS 50 RF. Thin-layer chromatography (TLC) analyses were carried out on TLC plates 60 F_{254} and for preparative TLC silica gel 60 $PF_{254/366}$ were used, both purchased form Merck and were visualized with UV-light. The silica gel (0.040–0.063 mm) used for column chromatography was purchased from Merck. Microanalyses were carried out at the H. C. Ørsted Institute, Copenhagen. Preparative HPLC was performed on a Waters Delta Pak 300 A, 10 μm 305 × 7 mm semi-prep HPLC column.

Ethyl 3-phenyl-2-oxo-cyclopentanecarboxylate 5

Na (3.79 g, 0.165 mol) Na was dissolved in 100 mL absolute EtOH and the excess EtOH was removed *in vacuo*, 200 mL dry toluene and 23.0 g (0.099 mol) diethyl 2-phenyladipate were added under N_2. The mixture was refluxed for 1 week and after cooling to room temp. the mixture was acidified with acetic acid to pH 5. The organic fraction was washed with H_2O and $NaHCO_3$ and dried over Na_2SO_4. The product was an orange oil (12.8 g, 67%); ^{1}H NMR ($CDCl_3$): δ = 1.31 (3H, m, CH_3), 2.30 (4H, m, 2 × CH_2), 3.41 (2H, m, 2 × CH), 4.23 (2H, m, CH_2), 7.18–7.38 (5H, m, Ph). ^{13}C NMR ($CDCl_3$): δ = 13.95 (CH_3), 24.83 (CH_2), 29.06 (CH_2), 53.80 (CH), 55.02 (CH), 61.32 (CH_2O), 127.13, 128.10, 128.61, 138.14 (Ph), 169.33 (*C*OOEt), 210.15 (C=O); MS (EI) *m*/*z* 232 (M^+).

1,2,6,7-Tetrahydro-7-phenyl-2-thioxo-5*H*-cyclopenta[*d*]-pyrimidin-4(3*H*)-one 6

Na (0.5 g, 21.6 mmol) Na was dissolved in 30 mL 99.9% EtOH. Ethyl 3-phenyl-2-oxocyclopentanecarboxylate **5** (1.00 g, 4.30 mmol) was added together with 1.31 g (17.2 mmol) thiourea and the mixture was refluxed for 22 h. EtOH was removed *in vacuo* and the remaining solid was dissolved in 20 mL H_2O. The solution was acidified with conc. HCl and extracted with Et_2O (3 × 10 mL), dried (Na_2SO_4) and evaporated *in vacuo*. The resulting oil was purified by column chromatography (10% ethyl acetate in petroleum ether→ethyl acetate) and followed by preparative TLC (50% ethyl acetate in petroleum ether) which gave an orange oil (0.047 g, 4%); ^{1}H NMR (DMSO): δ = 1.46 (2H, m, H-5), 2.58 (2H, m, H-6), 4.07 (1H, m, H-7), 7.14–7.40 (5H, m, Ph). ^{13}C NMR (DMSO): δ = 25.22 (C-5), 31.49 (C-6), 49.36 (C-7), 115.24 (C-4a), 126.35, 127.26, 128.51, 142.44 (Ph), 160.19 (C-7a), 160.75 (C-4), 176.51 (C-2); MS (EI) *m*/*z* 244 (M^+).

2-Amino-7-phenyl-6,7-dihydro-5*H*-cyclopenta[*d*]pyrimidin-4(3*H*)-one 7

Ethyl 3-phenyl-2-oxocyclopentanecarboxylate **5** (2.20 g, 9.47 mmol) and 1.71 g (9.49 mmol) guanidine carbonate were dissolved in 10 mL 99.9% EtOH and refluxed for 18 h. EtOH was evaporated *in vacuo*. The resulting brown oil was dissolved in 10 mL H_2O and the solution was neutralised with ice cold acetic acid. An orange solid precipitated and was further purified by recrystallisation from EtOH (0.23 g, 11%); mp >240 °C (decomp.); ^{1}H NMR (DMSO): δ = 1.80 (1H, m, H_a-6), 2.52 (3H, m, H_b-6, H-5), 3.97 (1H, t, *J* = 7.47 Hz, H-7), 6.40 (2H, s, NH_2), 7.10–7.28 (5H, m, Ph), 10.64 (1H, s, NH). ^{13}C NMR (DMSO): δ = 25.43 (C-5), 32.01 (C-6), 52.08 (C-7), 111.53 (C-4a), 126.26, 128.11, 128.40, 144.17 (Ph), 156.59 (C-2), 160.96 (C-7a), 172.24 (C-4); $C_{13}H_{13}N_3O{\cdot}0.2H_2O$ (230.87): Calc. C, 67.63; H, 5.85; N, 18.20. Found: C, 67.85; H, 5.73; N, 17.85%; MS (EI) *m*/*z* 227 (M^+).

2-Amino-7-phenyl-6,7-dihydrocyclopenta[*e*][1,3]oxazin-4(5*H*)-one 8

2-(*S*-Methylthio)isourea (1.36 g, 9.77 mmol) was dissolved in 10 mL H_2O and 1.15 g (20.5 mmol) KOH was added. Under stirring 2.03 g (9.74 mmol) ethyl 3-phenyl-2-oxocyclopentanecarboxylate **5** was added and the inhomogenous mixture was stirred for 18 h at room temp. The mixture was filtered and the solid was washed with H_2O and Et_2O. White crystals (0.99 g, 51%); mp 208–210 °C; ^{1}H NMR (DMSO): δ = 1.87 (1H, m, H_a-6), 2.59 (3H, m, H_b-6, H-5), 3.17 (1H, s, H-7), 4.30 (2H, m, NH_2), 7.22–7.69 (5H, m, Ph). ^{13}C NMR (DMSO): δ = 24.70 (C-5), 30.11 (C-6), 48.33 (C-7), 116.08 (C-4a), 127.07, 127.50, 128.83, 141.24 (Ph), 160.33 (C-2), 164.52 (C-7a), 167.24 (C-4); MS (EI) *m*/*z* 228 (M^+).

7-Phenyl-6,7-dihydrocyclopenta[*e*][1,3]oxazine-2,4(3*H*,5*H*)-dione 10a

2-Amino-7-phenyl-6,7-dihydrocyclopenta[*e*][1,3]oxazin-4(5*H*)-one **8** (0.27 g, 12.1 mmol) was dissolved in 8 mL 3 M HCl under stirring. The heterogeneous mixture was heated to reflux for 1 h, then cooled and filtered. The solid was washed well with H_2O (0.19 g, 69%); mp >240 °C; ^{1}H NMR (DMSO): δ = 1.89 (1H, m, H_a-6), 2.54 (3H, m, H_b-6, H-5), 4.26 (1H, m, H-7), 7.23–7.36 (5H, m, Ph), 11.76 (1H, s, NH). ^{13}C NMR (DMSO): δ = 23.73 (C-5), 30.52 (C-6), 48.52 (C-7), 112.62 (C-4a), 127.39, 127.86, 128.95, 140.61 (Ph), 149.40 (C=O), 161.05 (C=O), 168.24 (C-7a); $C_{13}H_{11}NO_3$ (229.24): Calc. C, 68.11; H, 4.84; N, 6.11. Found: C, 67.89; H, 4.90; N, 5.78%; MS (EI) *m*/*z*: 229 (M^+).

General procedure for preparation of annelated-1,3-oxazine-2,4(3*H*)-diones 10a and 10b

The appropriate ketone (10 mmol) was mixed with 12 mmol of *N*-(chlorocarbonyl) isocyanate in a 100 ml 3-necked flask fitted with a septum, a condenser and the mixture was heated at 58 °C for 1 h under a nitrogen atmosphere. After additional heating at 130 °C for 2 h and cooling to room temperature, the mixture was taken up in 100 ml EtOAc and the organic phase was washed with sat. aq. $NaHCO_3$, (2 × 50 ml to remove traces of HCl) followed by washing with 2 × 50 ml H_2O. The organic phase was dried (Na_2SO_4) and evaporated *in vacuo* to an oily product which was purified by silica gel column chromatography with EtOAc–petroleum ether (60–80 °C) 1 : 1 to give the products **10** and **11**.

7-Phenyl-6,7-dihydrocyclopenta[*e*][1,3]oxazine-2,4(3*H*,5*H*)-dione 10a. (0.22g, 12%) Spectral data and melting point were the same as above where **10a** was prepared from **8**.

7,8-Dihydro-8-phenyl-6*H*-cyclohexa[*e*][1,3]oxazine-2,4(3*H*,5*H*)-dione 10b. White solid (1.22 g, 30%); mp 181–183 °C; ^{1}H NMR ($CDCl_3$): δ = 1.70 (2H, m, 2 × H-6), 1.85 (2H, m, 2 × H-5), 2.50 (2H, m, 2 × H-7), 3.80 (1H, m, H-8), 7.20–7.47 (5H, m, Ph), 9.54 (1H, br s, NH). ^{13}C NMR ($CDCl_3$): δ = 18.03 (C-6), 20.63 (C-7), 31.71 (C-5), 43.03 (C-8), 111.32 (C-4a), 128.21, 129.33, 130.51, 140.17 (Ph), 147.81 (C-2), 163.15 (C-8a), 163.88 (C-4); MS (EI) *m*/*z* 243 (M^+); $C_{14}H_{13}NO_3$ (243.26): Calc. C, 69.12; H, 5.39; N, 5.76. Found: C, 69.21; H, 5.42; N, 5.59%.

6,7-Dihydro-4a-phenyl-5*H*-cyclohexa[*e*][1,3]oxazine-2,4(3*H*,4a*H*)-dione 11. White solid (1.09 g, 25%); mp 134–137 °C; ^{1}H NMR ($CDCl_3$): δ = 1.28 (2H, m, CH_2), 1.53 (2H, m, CH_2), 2.20–2.45 (2H, m, CH_2), 6.01 (1H, t, *J* 2.0 Hz, CH=), 7.33–7.47 (5H, m, Ph), 8.62 (1H, br s, NH). ^{13}C NMR ($CDCl_3$): δ = 16.82 (C-6), 23.13 (C-7), 33.58 (C-5), 49.33 (C-4a), 115.81 (C-8), 127.76, 128.22, 129.12, 137.39 (Ph), 143.93 (C-2), 147.58 (C-8a), 171.04 (C-4); MS (EI) *m*/*z* 243 (M^+).

7-Phenyl-6,7-dihydro-5*H*-cyclopenta[*d*]pyrimidine-2,4(1*H*, 3*H*)-dione 12a. 7-Phenyl-6,7-dihydrocyclopenta[*e*][1,3]oxazine-2,4(3*H*,5*H*)-dione **10a** was dissolved in 4.5 mL 12 M NH_4OH. The mixture was refluxed for 18 h, cooled and filtered and the solid was washed well with H_2O (71 mg, 73%); mp >250 °C; ^{1}H NMR (DMSO): δ = 1.85 (1H, m, H_a-6), 2.55 (3H, m, H_b-6, H-5), 4.14 (1H, d, *J* 7.3 Hz, H-7), 7.17–7.37 (5H, m, Ph), 10.88 (1H, s, NH), 10.96 (1H, s, NH). ^{13}C NMR (DMSO): δ = 25.46 (C-5), 32.24 (C-6), 49.18 (C-7), 110.92 (C-4a), 127.03, 127.53, 128.81, 142.10 (Ph), 152.71 (C-7a), 156.86 (C-2), 162.44 (C-4); $C_{13}H_{12}N_2O_2 \cdot 0.2H_2O$ (231.85): Calc. C, 67.35; H, 5.39; N, 12.08. Found: C, 67.63; H, 5.18; N, 11.97%; MS (EI) *m*/*z* 228 (M^+).

5,6,7,8-Tetrahydro-8-phenylcyclohexa[*d*]pyrimidine-2,4(1*H*, 3*H*)-dione 12b. 5,6,7,8-Tetrahydro-8-phenyl-2*H*-cyclohexa[*e*]-[1,3]oxazine-2,4(3*H*)-dione **10b** (1.20 g, 4.9 mmol) was suspended in 50 ml of conc. NH_4OH and the mixture was refluxed overnight. Evaporation of the solvent *in vacuo* and subsequent washing with Et_2O (50 ml) gave **12b** in 100% yield; mp 191–193 °C; ^{1}H NMR (DMSO*d*-$_6$): δ = 1.25–2.50 (6H, m, H-5, H-6, H-7), 3.75 (1H, m, CHPh), 7.25 –7.41 (5H, m, Ph), 10.20 (1H, s, NH), 10.95 (1H, s, NH). ^{13}C NMR (DMSO-d_6): 16.38 (C-6), 20.62 (C-7), 30.67 (C-5), 41.68 (C-8), 108.06 (C-4a), 126.61, 128.10, 142.42 (Ph), 148.70 (C-8a), 151.15 (C-2), 164.65 (C-4); MS (EI) *m*/*z* 242 (M^+).

1-Ethoxymethyl-8-phenyl-5,6,7,8-tetrahydrocyclohexa[*d*]-pyrimidine-2,4(1*H*,3*H*)-dione 2. To a suspension of **12b** (0.55 g, 2.27 mmol) in dry $CHCl_3$ was added *N*,*O*-bis(trimethylsilyl)-acetamide (BSA) (0.56 ml, 4.54 mmol) and the stirring was continued until all the starting material had dissolved. Then (chloromethyl) ethyl ether (0.21 ml, 2.27 mmol) was added and the reaction mixture was stirred until TLC showed no change in amount of starting material. After evaporation of the solvent *in vacuo* the product was chromatographed on a silica gel column to obtain the pure *N*-1 alkylated product **2** as a yellow solid (0.36 g, 53%); mp 201–206 °C; $C_{17}H_{20}N_2O_3$ (300.36): Calc. C, 67.98; H, 6.71; N, 9.33. Found: C, 67.70; H, 6.87; N, 9.21%; ^{1}H NMR ($CDCl_3$): δ = 1.16 (3H, t, *J* 7 Hz, CH_3), 1.52 (2H, m, 2 × H-6), 2.01 (2H, m, 2 × H-5), 2.46 (1H, m, H-7), 2.70 (1H, m, H-7), 3.56 (2H, m, CH_2O), 4.33 (1H, m, H-8), 4.50 (1H, d, *J* 11 Hz, NCH_2), 5.43 (1H, d, *J* 11 Hz, NCH_2), 7.10–7. 36 (5H, m, Ph), 9.28 (1H, s, NH); ^{13}C NMR ($CDCl_3$): δ = 14.95 (CH_3), 15.23 (C-6), 21.55 (C-5), 31.11 (C-7), 39.69 (C-8), 64.97 (OCH_2), 71.78 (NCH_2), 112.37 (C-4a), 127.35, 127.84, 129.09, 141.36 (Ph), 149.96 (C-8a), 152.02 (C-2), 163.50 (C-4); MS (EI) *m*/*z* 300 (M^+).

1-Ethoxymethyl-7-phenyl-6,7-dihydro-5*H*-cyclopenta[*d*]-pyrimidine-2,4(1*H*,3*H*)-dione 3. A mixture of 7-phenyl-6,7-dihydro-5*H*-cyclopenta[*d*]pyrimidine-2,4(1*H*,3*H*)-dione **12a** (1.33 mmol), 5 mL HMDS and 5 mg $(NH_4)_2SO_4$ was heated under reflux for 2 h. The mixture was allowed to cool to room temp. and the excess HMDS was removed *in vacuo*. The resulting oil was dissolved in 5 mL dry acetonitrile and the mixture was stirred at −35 °C. TMS-triflate (0.22 mL, 1.22 mmol) was added to the solution, followed by dropwise addition of diethoxymethane (13.2 mmol). The mixture was stirred for 3 h and 5 mL ice cold saturated aqueous $NaHCO_3$ was added. The solution was coevaporated with 2 × 25 mL EtOH to almost dryness. The resulting solid was dissolved in 100 mL dry Et_2O and stirred for 1 h. The solution was filtered and the organic phase was dried (Na_2SO_4) and purified either by silica column chromatography (2% MeOH in CH_2Cl_2); White solid (0.26 g, 67%); mp 140–143 °C; ^{1}H NMR (DMSO): δ = 1.06 (3H, t, *J* 7.1 Hz, CH_3), 1.80 (1H, m, H_a-6), 2.58 (3H, m, H_b-6, H-5), 3.38 (2H, m, CH_2), 4.36 (1H, d, *J* 10.5 Hz, NCH_2), 4.47 (1H, d, *J* 7.2 Hz, H-7), 5.12 (1H, d, *J* 10.3 Hz, NCH_2), 7.17–7.37 (5H, m, Ph), 11.33 (1H, s, NH). ^{13}C NMR (DMSO): δ = 14.48 (CH_3), 25.28 (C-5), 32.69 (C-6), 49.12 (C-7), 63.50 (CH_2), 72.04 (CH_2), 114.24 (C-4a), 126.85, 127.06, 128.18, 141.68 (Ph), 152.62 (C-2), 156.26 (C-7a), 161.30 (C-4); MS (EI) *m*/*z*: 286 (M^+).

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