Synthesis of 1-Substituted-6-methyluracils

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A series of 6-methyl-1*H*-pyrimidin-2,4-diones bearing different substituents in the 1-position of the uracil ring were prepared starting from substituted ureas and diketene.

Key words uracil; diketene; piperazine

One of the most important goals in organic and medicinal chemistry is the design and synthesis of molecules that have value as therapeutic agents. In this regard, heterocyclic compounds have proven to be versatile support structures that offer a high degree of structural diversity. Among these compounds uracils, together with purines and indoles, are probably the most representative examples of the so-called "privileged structures" due to their significative presence in natural structures.[1,2)]

The uracil nucleus is a fundamental constituent of a large number of natural products that have strategical biological functions. This observation could explain the wide range of biological actions shown by uracil derivatives. A significative number of reports describing the pharmacological actions of these compounds have been published, and this structure still continues to attract the attention of medicinal and organic chemists.[3,4)] As a result of the high degree of activity in this field, a large number of compounds containing the uracil moiety have been developed as drugs (Fig. 1). A range of biological actions have been reported for these compounds and some of the most representative examples are antineoplastic,[5)] antihypertensive,[6)] anti-inflammatory,[7)] antiviral,[8,9)] or reverse transcriptase inhibitors.[10—13)]

On the other hand, the importance of piperazines in the field of Medicinal Chemistry is also widely recognised. Particularly in recent years the piperazinone ring system has attracted a great deal of attention in the search for peptidomimetic conformationally constrained structures in biologically active molecules.[14,15)]

The piperazine function allows the step-by-step introduction of pharmacophoric moieties—a characteristic that represents one of the main advantages of this system in Medicinal Chemistry. Several drugs acting on the CNS (Fluanisone, Trazodone) or cardiovascular system (Urapidil, Prazosin) contain a piperazine subunit. In this regard Urapidil is an antihypertensive agent that incorporates both uracil and piperazine groups.

As part of our drug discovery program directed toward the synthesis of new uracil-based biologically active compounds, we have prepared several new 6-methyluracil derivatives bearing substituents at position 1. These compounds are attractive starting materials for the preparation of highly substituted and heterofused uracil derivatives.

1-Substituted-6-methyluracils **3** were prepared by following the general synthetic strategy shown in Chart 1.[15,16)] Regioselective condensation of monosubstituted ureas **1** with diketene was accomplished in pyridine at 0 °C to afford the corresponding 3-substituted 1-acetoacetylureas **2** in excellent yields. These compounds were isolated and characterised (see Experimental part).

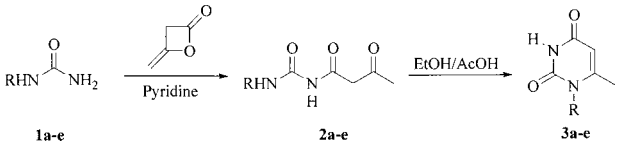

Chart 1

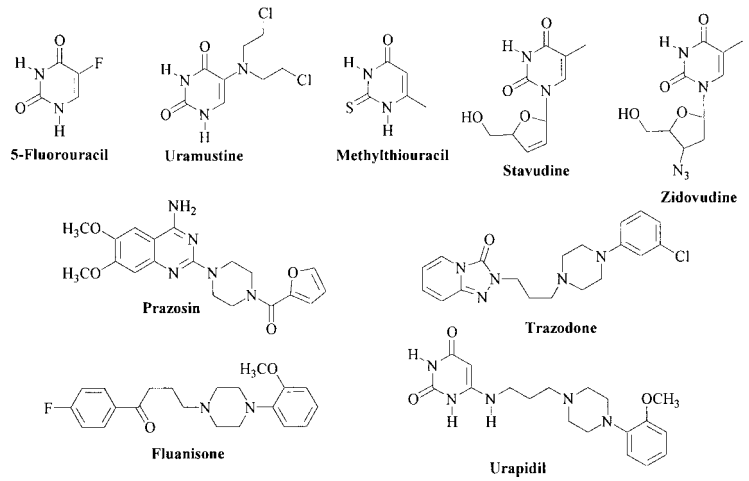

Fig. 1. Several Pharmacologically Useful Agents Containing Uracil and Piperazine Moieties

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Table 1. 1-Substituted-6-methyluracils **3a**—**e**

Entry	R	Yield (%)	mp (°C)
3a	$MeOCH_2CH_2$	93	121—122
3b	$MeOCH_2CH_2CH_2$	97	125—126
3c	$PhCH_2CH_2$	93	205—206
3d	2-Furfuryl	91	146—147
3e	$NH(CH_2CH_2)_2NCH_2CH_2$	85	117—119 (dec)

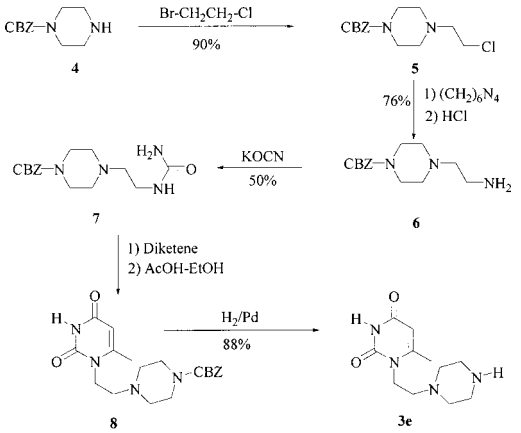

Chart 2

Although most of the studies that describe a similar process usually involve direct ring closure without isolation of **2**, we decided to isolate these compounds since they are versatile synthons in their own right and can be used as starting materials in the synthesis of other heterocyclic systems.

In a subsequent cyclization step the 6-methyl-1-substituted uracils **3a**—**e** were obtained as crystalline solids (after recrystallization from ethanol) in nearly quantitative yields (Table 1) by treatment of the 3-substituted 1-acetoacetylureas **2** with a mixture of ethanol/acetic acid (3 : 1) and heating under reflux.

Two synthetic strategies were developed for the preparation of the 1-(1′-piperazinyl-2-ethyl)uracil **3e** (Chart 2, 3). The regioselective nucleophilic substitution of 1-bromo-2-chloroethane with 1-(benzyloxycarbonyl)piperazine **4** in acetonitrile afforded the 1-(*β*-chloroethyl)-4-(benzyloxycarbonyl)piperazine **5** in high yield (Chart 2).

Transformation of **5** into the 1-(*β*-aminoethyl)-4-(benzyloxycarbonyl)piperazine **6** was successfully achieved using the classical conditions described for the Delepine reaction.[17,18] Thus, treatment of **5** with hexamethylenetetramine, followed by acid hydrolysis of the resulting complex, gave the corresponding amine hydrochloride, which, after neutralization, afforded amine **6** (Chart 2). In the next step, **6** was transformed into urea **7** by reaction with potassium isocyanate.[19] Acetoacetylation and subsequent dehydration of **7** were performed following the general route shown in Chart 1. Finally, the 1-[(1′-piperazinyl)-2-ethyl]-uracil **3e** was obtained by removing the benzyloxycarbonyl group in **8** by catalytic hydrogenation.

Our second approach to prepare (**3e**) employed as a starting material the readily obtainable 1-methoxyethyl-6-methyl-1*H*-pyrimidin-2,4-dione (**3a**) (Chart 3). Hydrolysis of the ether group on **3a** and subsequent bromination of the intermediate alcohol was accomplished in a high yielding one-pot

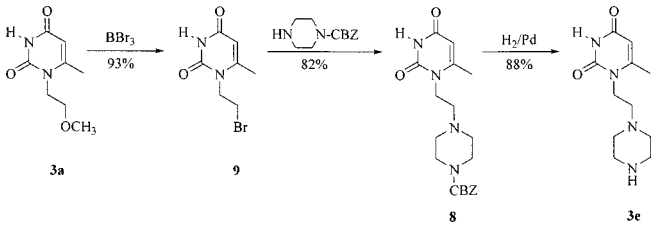

Chart 3

procedure using boron tribromide. Replacement of the halogen on this compound by treatment with 1-(benzyloxycarbonyl)piperazine and removal of the protecting group by hydrogenolysis gave compound **3e**.

Although these two synthetic routes do successfully lead to compound **3e**, the second pathway is a more general strategy since it allows the efficient and quick synthesis of new compounds by nucleophilic substitution of other piperazine derivatives onto the 1-(2-bromoethyl)-6-methyl-1*H*-pyrimidine-2,4-dione (**9**). The real value of the route shown in Chart 2 is exemplified by the fact that these transformations represent a model system that has been used during our current research project aimed at the solid-phase synthesis of 4-aminoalkyl-piperazines.[20]

The structure of all compounds described here were confirmed by analytical and spectroscopic data. Work is currently in progress in our Laboratory to prepare several new pharmacologically useful derivatives starting from uracils **3**.

Experimental

Melting points were determined on a Gallenkamp melting point apparatus and are uncorrected. IR spectra were obtained using a Perkin-Elmer 1640 FTIR spectrophotometer with samples as potassium bromide pellets. The NMR spectra were recorded on Bruker AM300 and XM500 spectrometers. Chemical shifts are given as δ values against tetramethylsilane as internal standard and J values are given in Hz. Mass spectra were obtained on a Varian MAT-711 instrument. The high resolution mass spectra were obtained on an Autospec Micromass instrument. Elemental analyses were performed on a Perkin-Elmer 240B apparatus at the Microanalysis Service of the University of Santiago de Compostela. The reactions were monitored by TLC with 2.5 mm Merck silica gel GF 254 strips, and the purified compounds each showed a single spot; unless stated otherwise, iodine vapour and/or UV light were used for detection of compounds. Commercially available starting materials and reagents were purchased from commercial sources and were used without further purification.

1-Substituted-3-acetoacetylureas 2a—e. General Procedure Diketene (2.10 ml, 27.7 mmol) was added slowly to a solution of the corresponding urea **1a**—**e** (27.7 mmol) in dry pyridine (15 ml) at 0 °C. The reaction mixture was stirred under these conditions during 2 h, for a further 2 h at room temperature and then heated at 60 °C (oil bath) during 4 h. The reaction mixture was cooled and concentrated to dryness under reduced pressure. Ice was added to the oily residue and the resulting solid was collected by filtration, washed with water and recrystallized from ethanol.

1-(2-Methoxyethyl)-3-acetoacetylurea (2a) This compound was prepared by following the procedure described above. Yield 95%. mp 111—112 °C (EtOH). IR (cm^{-1}, KBr): 1665, 1582. ^{1}H-NMR ($CDCl_3$/TMS) δ (ppm), J (Hz): 10.20 (bs, 1H, NH), 8.43 (bs, 1H, NH), 3.52—3.40 (m, 6H, 3×CH_2), 3.37 (s, 3H, OCH_3), 2.20 (s, 3H, CH_3). MS (70 eV) m/z (%): 202 (M^+, 44), 184 (100). High resolution (HR)-MS, m/z: Calcd for $C_8H_{14}N_2O_4$ (M^+): 202.2078, Found 202.2086.

1-(3-Methoxypropyl)-3-acetoacetylurea (2b) This compound was prepared by following the procedure described above. Yield 95%. mp 120—122 °C (EtOH). IR (cm^{-1}, KBr): 3500—3000, 1685. ^{1}H-NMR ($CDCl_3$/TMS) δ (ppm), J (Hz): 10.25 (bs, 1H, NH), 8.52 (bs, 1H, NH), 3.54—3.35 (m, 9H, 3×CH_2, OCH_3), 2.27 (s, 3H, CH_3), 1.89 (m, 2H, CH_2). MS (70 eV) m/z (%): 216 (M^+, 100), 198 (30). *Anal.* Calcd for $C_9H_{16}N_2O_4$: C, 49.99; H, 7.46; N, 12.96. Found: C, 50.21; H, 7.50; N, 13.09.

1-(2-Phenylethyl)-3-acetoacetylurea (2c) This compound was prepared

by following the procedure described above. Yield 93%. mp 114—115 °C (EtOH). IR (cm^{-1}, KBr): 3000, 1770, 1680. ^{1}H-NMR ($CDCl_3$/TMS) δ (ppm), *J* (Hz): 10.08 (bs, 1H, NH), 8.73 (bs, 1H, NH), 7.04—7.19 (m, 5H, Ph), 2.79—3.41 (m, 6H, 3×CH_2), 2.18 (s, 3H, CH_3). MS (70 eV) *m/z* (%): 248 (M^+, 22), 230 (100). HR-MS, *m/z*: Calcd for $C_{13}H_{16}N_2O_3$ (M^+): 248.1161, Found 248.1180.

1-(Furfuryl)-3-acetoacetylurea (2d) This compound was prepared by following the procedure described above. Yield 94%. mp 168—169 °C (EtOH). IR (cm^{-1}, KBr): 3500—3000, 1772, 1683. ^{1}H-NMR (DMSO-d_6/TMS) δ (ppm), *J* (Hz): 10.43 (bs, 1H, NH), 8.50 (bs, 1H, NH), 7.58 (s, 1H, CH), 6.39 (m, 1H, CH), 6.27 (m, 1H, CH), 4.37 (d, *J*=2.6 Hz, 2H, NCH_2), 3.58 (s, 2H, CH_2), 2.15 (s, 3H, CH_3). MS (70 eV) *m/z* (%): 224 (M^+, 45), 140 (18). HR-MS, *m/z*: Calcd for $C_{10}H_{12}N_2O_4$ (M^+): 224.2134, Found 224.2139.

1-[2-(1-Benzyloxycarbonylpiperazinyl)-1-ethyl]-3-acetoacetylurea (2e) This compound was prepared by following the procedure described above. Yield 88%. mp 196—197 °C (EtOH). IR (cm^{-1}, KBr): 3000, 1760, 1680. ^{1}H-NMR ($CDCl_3$/TMS) δ (ppm), *J* (Hz): 10.08 (bs, 1H, NH), 7.72 (bs, 1H, NH), 7.35 (s, 5H, Ph), 5.13 (s, 2H, CH_2), 3.54—3.47 (m, 6H, 3×CH_2), 2.79—2.73 (m, 4H, 2×CH_2), 2.44 (m, 4H, 2×CH_2), 2.23 (s, 3H, CH_3). MS (70 eV) *m/z* (%): 390 (M^+, 56), 372 (89). HR-MS, *m/z*: Calcd for $C_{19}H_{26}N_4O_5$ (M^+): 390.4337, Found 390.4368.

1-Substituted-6-methyl-1*H*-pyrimidin-2,4-diones 3a—e. General Procedure A solution of the 1-substituted-3-acetoacetylureas **2a—e** (2.6 mmol) in a mixture of ethanol/acetic acid (3 : 1) was stirred and heated under reflux (oil bath 85 °C) under argon until the starting material had been consumed (2—4 h, TLC monitoring). The reaction mixture was allowed to cool and concentrated to dryness under reduced pressure. The resulting solid was purified by recrystallization (*i*-PrOH). Yield 85—97%.

1-(2-Methoxyethyl)-6-methyl-1*H*-pyrimidin-2,4-dione (3a) This compound was prepared by following the procedure described above. Yield 93%. mp 121—122 °C (*i*-PrOH). IR (cm^{-1}, KBr): 3500—3000, 1684. ^{1}H-NMR ($CDCl_3$/TMS) δ (ppm), *J* (Hz): 9.89 (bs, 1H, NH), 5.51 (s, 1H, CH), 3.96 (t, *J*=5.0 Hz, 2H, CH_2), 3.56 (t, *J*=5.0 Hz, 2H, CH_2), 3.28 (s, 3H, CH_3), 2.27 (s, 3H, CH_3). MS (70 eV) *m/z* (%): 184 (M^+, 68). *Anal.* Calcd for $C_8H_{12}N_2O_3$: C, 52.17; H, 6.57; N, 15.21. Found: C, 52.21; H, 6.55; N, 15.29.

1-(3-Methoxypropyl)-6-methyl-1*H*-pyrimidin-2,4-dione (3b) This compound was prepared by following the procedure described above. Yield 97%. mp 125—126 °C (*i*-PrOH). IR (cm^{-1}, KBr): 3000, 1655. ^{1}H-NMR ($CDCl_3$/TMS) δ (ppm), *J* (Hz): 10.07 (bs, 1H, NH), 5.56 (s, 1H, CH) 3.92 (t, *J*=7.3 Hz, 2H, CH_2O), 3.40 (m, 2H, CH_2N), 3.33 (s, 3H, OCH_3), 2.28 (s, 3H, CH_3), 1.94 (m, 2H, CH_2). MS (70 eV) *m/z* (%): 198 (M^+, 78). *Anal.* Calcd for $C_9H_{14}N_2O_3$: C, 54.53; H, 7.12; N, 14.13. Found: C, 54.72; H, 7.09; N, 14.21.

1-(2-Phenylethyl)-6-methyl-1*H*-pyrimidin-2,4-dione (3c) This compound was prepared by following the procedure described above. Yield 93%. mp 205—206 °C (*i*-PrOH). IR (cm^{-1}, KBr): 1673, 1482. ^{1}H-NMR ($CDCl_3$/TMS) δ (ppm), *J* (Hz): 9.90 (bs, 1H, NH), 7.36—7.29 (m, 3H, Ph), 7.23—7.14 (m, 2H, Ph), 5.48 (s, 1H, CH), 4.00 (t, *J*=7.1 Hz, 2H, CH_2), 2.98 (t, *J*=7.1 Hz, 2H, CH_2), 2.16 (s, 3H, CH_3). MS (70 eV) *m/z* (%): 230 (M^+, 33), 104 (100). *Anal.* Calcd for $C_{13}H_{14}N_2O_2$: C, 67.81; H, 6.13; N, 12.17. Found: C, 67.98; H, 6.09; N, 12.18.

1-(Furfuryl)-6-methyl-1*H*-pyrimidin-2,4-dione (3d) This compound was prepared by following the procedure described above. Yield 91%. mp 146—147 °C (*i*-PrOH). IR (cm^{-1}, KBr): 1684, 1560, 1499. ^{1}H-NMR ($CDCl_3$/TMS) δ (ppm), *J* (Hz): 9.41 (bs, 1H, NH), 7.36 (s, 1H, CH), 6.39 (m, 1H, CH), 6.34 (m, 1H, CH), 5.57 (s, 1H, CH), 5.01 (s, 2H, CH_2), 2.40 (s, 3H, CH_3). MS (70 eV) *m/z* (%): 206 (M^+, 20), 81 (100). HR-MS, *m/z*: Calcd for $C_{10}H_{10}N_2O_3$ (M^+): 206.1981, Found 206.1998.

1-[2-(1-Benzyloxycarbonylpiperazinyl)-4-ethyl]-6-methyl-1*H*-pyrimidin-2,4-dione (8). Method A This compound was prepared by following the procedure described above. Yield 89%. mp 231—233 °C (acetonitrile). IR (cm^{-1}, KBr): 3500—3000, 1765, 1680. ^{1}H-NMR ($CDCl_3$/TMS) δ (ppm), *J* (Hz): 9.72 (bs, 1H, NH), 7.33 (s, 5H, Ph), 5.52 (s, 1H, CH), 5.11 (s, 2H, OCH_2), 3.90 (t, *J*=6.4 Hz, 2H, NCH_2), 3.49 (m, 4H, 2×NCH_2), 2.61 (t, *J*=6.4 Hz, 2H, NCH_2), 2.49 (m, 4H, 2×CH_2), 2.27 (s, 3H, CH_3). MS (70 eV) *m/z* (%): 372 (M^+, 15), 233 (70).

6-Methyl-1-[2-(1-piperazinyl)-4-ethyl]-1*H*,3*H*-pyrimidin-2,4-dione (3e) To a solution of **8** (0.26 g, 0.64 mmol) in dry methylene chloride (15 ml) was added a catalytic amount of palladium on charcoal. The mixture was stirred at room temperature under a hydrogen atmosphere until the starting material had disappeared (24 h, TLC monitoring). The reaction mixture was filtered through celite and evaporation of the solvent under reduced pressure gave a solid residue, which was purified by recrystallization. Yield 85%. mp 117—119 °C (dec) (*i*-PrOH). IR (cm^{-1}, KBr): 3500—3000, 1684. ^{1}H-NMR ($CDCl_3$/TMS) δ (ppm), *J* (Hz): 9.31 (bs, 1H, NH), 6.47 (bs, 1H, NH), 5.53 (s, 1H, CH), 3.91 (m, 2H, CH_2), 2.96 (m, 4H, 2×CH_2), 2.63—2.58 (m, 6H, 3×CH_2), 2.21 (s, 3H, CH_3). MS (70 eV) *m/z* (%): 238 (M^+, 10), 153 (25). *Anal.* Calcd for $C_{11}H_{18}N_4O_2$: C, 55.44; H, 7.61; N, 23.51. Found: C, 55.47; H, 7.64; N, 23.49.

4-(2-Chloroethyl)piperazine-1-carboxylic Acid Benzyl Ester (5) To a suspension of piperazine-1-carboxylic acid benzyl ester 4 (5.38 g, 24 mmol) and K_2CO_3 (5.0 g, 40 mmol) in acetonitrile (55 ml) was added 1-bromo-2-chloroethane (12 ml, 146.4 mmol). The mixture was flushed with argon for 5 min and then stirred at room temperature until the starting material had been consumed (96 h, TLC monitoring). The solid was filtered off and the filtrate was concentrated to dryness under reduced pressure to give an oil, which was identified as **5**. Yield 90%. ^{1}H-NMR ($CDCl_3$/TMS) δ (ppm), *J* (Hz): 7.32 (s, 5H, Ph), 5.11 (s, 2H, OCH_2), 3.56—3.48 (m, 6H, 3×CH_2), 2.68 (t, *J*=6.8 Hz, 2H, CH_2), 2.47 (m, 4H, 2×CH_2). MS (70 eV) *m/z* (%): 282 (M^+, 12), 233 (40). HR-MS, *m/z*: Calcd for $C_{14}H_{19}N_2O_2Cl$ (M^+): 282.7656, Found 282.7670.

4-(2-Aminoethyl)piperazine-1-carboxylic Acid Benzyl Ester (6) A mixture of 4-(2-chloroethyl)piperazine-1-carboxylic acid benzyl ester (**5**) (6.6 g, 23.3 mmol), KI (3.8 g, 23.3 mmol) and hexamethylenetetramine (3.2 g, 23.3 mmol) in ethanol (120 ml) was flushed with argon for 5 min and then stirred at room temperature until the starting material had been consumed (113 h, TLC monitoring). The resulting precipitate was was filtered off, dissolved in ethanol (420 ml) and the solution treated with concentrated hydrochloric acid (37%) (30 ml). The reaction mixture was stirred at room temperature until reaction was complete (36 h, TLC monitoring) and concentrated to dryness under reduced pressure. The residue was dissolved in the minimum amount of water (120 ml) and the solution treated with 10% NaOH until a pH of 7 was achieved. The mixture was then extracted with diethyl ether (3×30 ml), the organic phase was dried (Na_2SO_4) and concentrated to dryness under reduced pressure to give amine **6** as a white solid, which was crystallized from *i*-PrOH. Yield 73%. mp 163—164 °C (*i*-PrOH). IR (cm^{-1}, KBr): 3500—3000, 1770. ^{1}H-NMR ($CDCl_3$/TMS) δ (ppm), *J* (Hz): 7.35 (s, 5H, Ph), 5.13 (s, 2H, OCH_2), 3.51 (m, 4H, 2×CH_2), 2.78 (m, 2H, CH_2), 2.43 (m, 6H, 3×CH_2), 1.67 (s, 2H, NH_2). MS (70 eV) *m/z* (%): 263 (25). *Anal.* Calcd for $C_{14}H_{21}N_3O_2$: C, 63.85; H, 8.04; N, 15.96. Found: C, 63.88; H, 8.10; N, 15.99.

4-(2-Ureidoethyl)piperazine-1-carboxylic Acid Benzyl Ester (7) To a suspension of 4-(2-aminoethyl)piperazine-1-carboxylic acid benzyl ester (**6**) (0.70 g, 2.6 mmol) in water (70 ml) at 55 °C was added potassium isocyanate (0.8 g, 10.6 mmol) in small portions. The reaction mixture was stirred and heated (oil bath 100 °C) under argon until the starting material had been consumed (4 h, TLC monitoring). The mixture was cooled to room temperature, extracted with methylene chloride (3×30 ml) and the combined organic phases organic phase were dried (Na_2SO_4). The solution was concentrated to dryness under reduced pressure to give 0.41 g of the urea **7**. Yield 50%. mp 132—134 °C (*i*-PrOH). IR (cm^{-1}, KBr): 3500—3000, 1685, 1653, 1575. ^{1}H-NMR ($CDCl_3$/TMS) δ (ppm), *J* (Hz): 7.35 (m, 5H, Ph), 5.13 (m, 3H, OCH_2, NH), 4.65 (bs, 2H, NH_2), 3.50 (m, 4H, 2×CH_2), 3.24 (m, 2H, CH_2), 2.48 (m, 2H, CH_2), 2.42 (m, 4H, 2×CH_2). MS (70 eV) *m/z* (%): 307 (M+1, 10), 233 (100). *Anal.* Calcd for $C_{15}H_{22}N_4O_3$: C, 58.81; H, 7.24; N, 18.29. Found: C, 58.93; H, 7.19; N, 18.28.

1-[2-(1-Benzyloxycarbonylpiperazinyl)-1-ethyl]-6-methyl-1*H*-pyrimidin-2,4-dione (8). Method B To a suspension of the piperazine-1-carboxylic acid benzyl ester (0.15 g, 0.81 mmol) and K_2CO_3 (0.11 g, 0.81 mmol) in acetonitrile, was slowly added a solution of 1-(2-bromoethyl)-6-methyl-1*H*-pyrimidine-2,4-dione (0.20 g, 0.81 mmol) in acetonitrile (3 ml). The reaction mixture was flushed with argon for 5 min and then stirred at room temperature under argon until the starting material had been consumed (48 h, TLC monitoring). The solvent was evaporated under reduced pressure to give a solid residue, which was purified by column chromatography on silica gel. Yield 82%. mp 208—210 °C (*i*-PrOH). IR (cm^{-1}, KBr): 1696, 1669. ^{1}H-NMR ($CDCl_3$/TMS) δ (ppm), *J* (Hz): 9.30 (bs, 1H, NH), 7.30—7.35 (m, 5H, Ph), 5.45 (s, 1H, CH), 5.11 (s, 2H, CH_2), 3.80 (t, *J*=6.6 Hz, 2H, CH_2), 3.26 (m, 4H, 2×NCH_2), 2.46 (t, *J*=6.6 Hz, 2H, NCH_2), 2.32 (m, 4H, 2×CH_2), 2.16 (s, 3H, CH_3). MS (70 eV) *m/z* (%): 353 (M+1, 25). *Anal.* Calcd for $C_{17}H_{28}N_4O_4$: C, 57.94; H, 8.01; N, 15.90. Found: C, 58.02; H, 8.12; N, 15.87.

1-(2-Bromoethyl)-6-methyl-1*H*-pyrimidine-2,4-dione (9) To a solution of 1-methoxyethyl-6-methyluracil (0.30 g, 1.51 mmol) in dry methylene chloride (20 ml) at 0 °C was slowly added a solution of boron tribromide (3.02 ml, 3.03 mmol). The reaction mixture was stirred under argon during 2 h and then at room temperature until the starting material had been con-

sumed (TLC monitoring). The reaction mixture was treated with ammonium acetate (0.23 g, 3.03 mmol) and the solvent was evaporated under reduced pressure. The resulting residue was purified by column chromatography on silica gel. Yield 93%. mp 235—236 °C (*i*-PrOH). IR (cm^{-1}, KBr): 1693, 1662. ^{1}H-NMR ($CDCl_3$/TMS) δ (ppm), J (Hz): 9.85 (bs, 1H, NH), 5.60 (s, 1H, CH), 4.17 (t, J=6.63 Hz, 2H, CH_2), 3.61 (t, J=6.63 Hz, 2H, CH_2), 2.30 (s, 3H, CH_3). MS (70 eV) *m*/*z* (%): 246 (M^+, 12), 167 (30), 140 (70). *Anal.* Calcd for $C_7H_9BrN_2O_2$: C, 36.07; H, 3.89; Br, 34.28; N, 12.02. Found: C, 36.09; H, 3.94; Br, 34.31; N, 12.01.

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