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The synthesis of a polycyclic heterocyclic ring system compound, ethyl 7-hydroxy-4-oxo-2-phenyl-4,5-dihydro-3*H*-benzo[6,7]cyclohepta[1,2-*d*]pyrimidine-6-carboxylate was carried out by condensation of benzamidine on diethyl 5,9-dihydroxy-7*H*-benzo[*a*]cycloheptene-6,8-dicarboxylate, after opening and then closure of the seven membered ring.

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A large number of benzocycloheptene derivatives containing additional heterocycles were reported to possess interesting biological properties such as antitumour [1], antihypertensive, antithrombotic [2-3] or anticytokine activity [4]. On the other hand, pyrimidine base derivatives have been investigated due to their potential for medicinal activity [5-6]. Benzocycloheptene derivatives containing pyrimidine bases are also compounds of pharmacological interest [3,7]. In connection with our investigations for novel benzocycloheptene derivatives [8-10], we have been interested in the reaction of benzamidine hydrochloride with β -keto ester-benzocycloheptene **2** (Scheme 1) and we describe in this paper the synthesis of a novel family of pyrimidinones after an original ring opening of a seven membered cycle by retro-Claisen condensation.

Starting from commercially available diethyl phthalate **1** (Scheme 1), β -keto ester **2** is obtained by Dieckmann method [11] after reaction of compound **1** with diethyl glutarate in the presence of sodium ethoxide. The infrared spectrum of the bicyclic compound **2** shows C=O ester bands at 1610-1640 cm^{-1} . We already assume that the presence of strong hydrogen bonding, between the hydroxyl group at the 5 and 9-position and the ester group at the 6 and 8-position, favour the enol form of this compound. The ^1H nmr as well the ^{13}C nmr spectra strongly supports this enol form (δ 12.6 ppm s OH; δ 166.5 ppm C-enol) and the symmetry of the molecule **2**.

The attempted condensation of **2** with benzamidine does not allow isolation of the expected benzocycloheptenopyrimidine **3** but rather gives predominantly the pyrimidinone **4** in 56% yield. The structure of the pyrimidinone **4** can be

Scheme 1

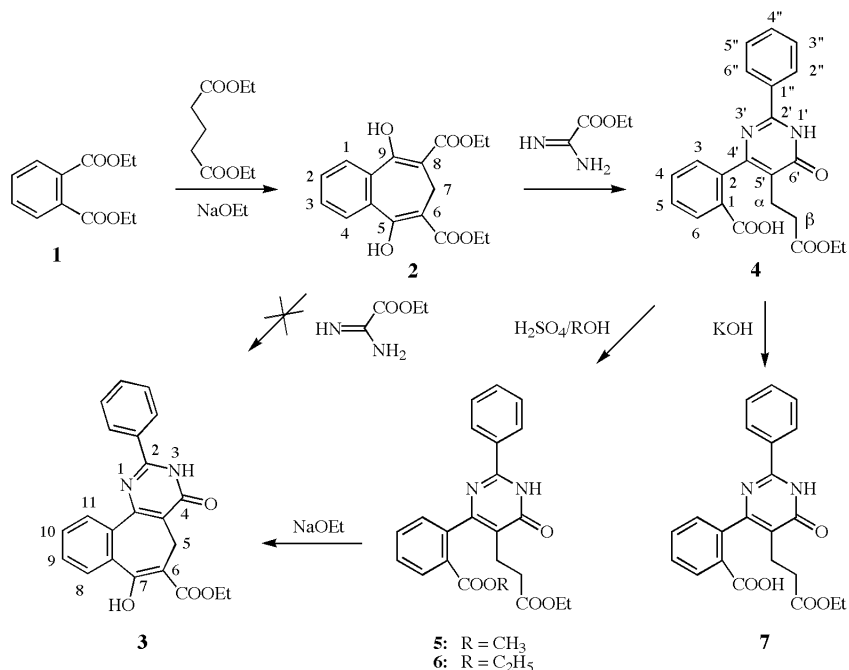


Table 1
Yield, Melting Points and Elemental Analyses of Compounds 2-7

Compound No	Yield (%)	Mp °C	Formula	Calcd. %			Found. %		
				C	H	N	C	H	N
2	55	87	C ₁₅ H ₁₈ O ₆	64.15	5.66	-----	63.99	5.73	-----
3	31	238	C ₂₂ H ₁₈ O ₄ N ₂ , H ₂ O	67.33	5.14	7.14	67.86	5.48	7.47
4	56	220	C ₂₂ H ₂₀ O ₅ N ₂	67.33	5.14	7.14	67.37	5.46	7.37
5	73	175	C ₂₄ H ₂₂ O ₅ N ₂	67.96	5.46	6.89	67.72	5.35	7.10
6	92	140	C ₂₄ H ₂₄ O ₅ N ₂ , H ₂ O	65.74	5.98	6.39	66.06	5.50	6.43
7	80	262	C ₂₀ H ₁₆ O ₅ N ₂	65.93	4.43	7.69	65.85	4.55	7.57

established from its elemental (Table 1) and spectral analyses. Thus the IR of **4** shows a major absorption at 3350-3150 cm⁻¹ that can be attributed to NH and OH groups. The strong band that appears at 1625 cm⁻¹ corresponds to the pyrimidine carbonyl. The assignment of its ¹H and ¹³C nmr spectra was also accomplished by utilising two dimensional nmr methods: ¹H-¹³C HMQC (Heteronuclear Multiple Quantum Coherence), and ¹H-¹H COSY. In the ¹H nmr spectrum of **4** in DMSO-*d*₆, a four protons multiplet centered at δ 2.49 ppm was observed. (The HMQC correlation proton-carbon allows us to establish the presence of two neighbouring methylene groups -δ 22.4-31.4 ppm- in the same multiplet at δ 2.49 ppm). This result demonstrates that the seven membered ring has been converted to an other compound which contains not one, but two methylene groups. On the other hand the ¹H nmr reveals a broad signal at δ 11.0-10.5 ppm (NH+OH) which disappears upon deuteration. The spectrum shows multiplets in the region of δ 8.07-7.20 ppm that can be ascribed to the aromatic protons. We propose a reaction pathway for the formation of this ring showed in Scheme 2. Initially, the condensation of free benzamidine with compound **2** leads to the formation of the pyrimidinone [12] resulting from addition of the NH₂ group to the ketone group followed by a cyclisation of the

intermediate addition product. However, simultaneously, the strongly basic environment leads to a retro-Claisen condensation on the seven membered ring.

Treatment of **4** with sulfuric acid in methanol or ethanol give the diesters **5** and **6** respectively. The ¹H nmr spectrum of **5** shows clearly the two different ester functions. For the compounds **5** and **6** the ¹H nmr shows also the two CH₂ as two distinct multiplets. Saponification of **4** with potassium hydroxide in methanol gives the diacid **7**.

Reaction of **5** and **6** with sodium ethoxide in dry toluene affords the benzocycloheptenopyrimidinone **3**. The structure of **3** is assigned by chemical (Table 1) and spectral analyses. The infrared spectrum shows the stretching frequencies which are characteristic of the NH (3400-3200 cm⁻¹), C=O (1630 cm⁻¹) and C=N (1600 cm⁻¹) groups of the pyrimidine nucleus. The ¹H and ¹³C nmr show the methylene group of the seven membered ring at δ 3.32 ppm (as a singlet) and δ 17.2 ppm respectively (Scheme 2).

It is interesting to observe over all the compounds **3-6**, the tautomeric properties of the phenyl-pyrimidinone. The infrared and nmr spectra of these compounds show both the NH and the C=O bands and therefore the predominant tautomeric form of this phenylpyrimidinone should be the lactam pyrimidine which is the usual form in pyrimidinones.

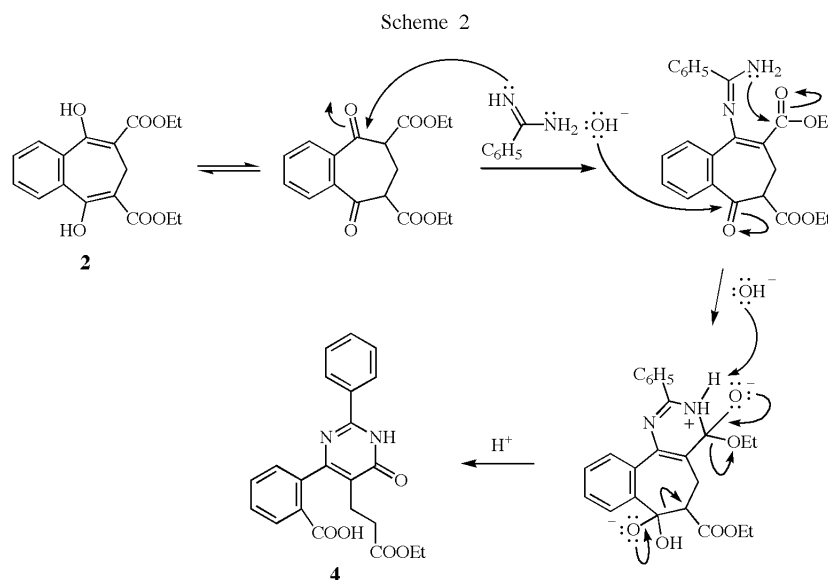


Table 2

Single Crystal X-Ray Crystallographic Analysis of 5

A) Crystal Parameters	
formula	C ₂₃ H ₂₂ N ₂ O ₅ (406.4)
crystallization medium	méthanol
Crystal Size (mm)	0.2 X 0.2 X 0.15
Crystal System and Space Group	triclinic P -1
Cell Dimensions : (Å and °)	a: 8.037(2) alpha: 98.31(2) b: 10.362(2) beta: 101.97(2) c: 13.146(2) gamma: 99.81(2)
Cell Volume (Å ³)	1036.8(4)
Z (formula units/cell)	2
Density (calculated) (g/ml)	1.302
Absorption Coefficient μ(mm-1)	0.093
Diffractometer	P3
Radiation Source and Wavelength (Å)	MoKα = 0.7107
Data Collection Temperature (K)	293(2)
Two-theta range (°)	4.06 to 60.00

Table 2 (continued)

B) Refinement Parameters	
Index ranges	-11<h<1; -14<k<14; -18<l<18
Collected Reflections	6026
Observed Reflections	3073
Absorption Correction Method	psi-scan
Structure Solution Program	SHELXS-97 (Sheldrick, 1997)
Structure Refinement Program	SHELXL-97 (Sheldrick, 1997)
Extinction Coefficient	0.009(3)
Number of l.s. Parameters	361
Residuals (observed data)	R1 = 0.0642; wR2 = 0.1358
Residuals (all data)	R1 = 0.1403; wR2 = 0.1698
Goodness-of-fit (all data)	S = 1.0120
Largest e-Density Peak and Hole (e.Å ⁻³)	0.303; -0.218

Table 3

Bond Lengths (Å), Bond Angles (°) and Symmetry

N(1)-C(2)	1.306(2)	C(15)-C(16)	1.308(3)	
N(1)-C(6)	1.379(2)	C(16)-O(16)	1.458(3)	
N(3)-C(2)	1.364(2)	C(16)-C(17)#	1.483(4)	#1: x+1,y,z
N(3)-C(4)	1.383(3)	C(6)-C(18)	1.497(3)	
C(4)-O(4)	1.243(2)	C(18)-C(19)	1.404(3)	
C(4)-C(5)	1.431(3)	C(18)-C(23)	1.393(3)	
C(5)-C(6)	1.368(3)	C(19)-C(20)	1.398(3)	
C(2)-C(7)	1.488(3)	C(20)-C(21)#	1.375(3)	#1: x+1,y,z
C(7)-C(8)	1.389(3)	C(21)-C(22)#	1.374(4)	#1: x-1,y,z
C(7)-C(12)	1.392(3)	C(22)-C(23)	1.385(3)	
C(8)-C(9)	1.389(3)	C(19)-C(24)	1.494(3)	
C(9)-C(10)	1.374(4)	C(24)-O(24)#	1.199(2)	#1: x,y+1,z
C(10)-C(11)	1.374(4)	C(24)-O(25)	1.340(3)	
C(11)-C(12)	1.384(3)	O(25)-C(25)	1.441(3)	
C(5)-C(13)	1.507(3)	C(21)-C(20)#	1.375(3)	#1: x-1,y,z
C(13)-C(14)	1.526(4)	C(22)-C21#	1.374(4)	#1: x+1,y,z
C(14)-C(15)	1.503(4)	C(17)-C(16)#	1.483(4)	#1: x-1,y,z
C(15)-O(15)	1.189(3)	O(24)-C(24)#	1.199(2)	#1: x,y-1,z
C(6)-N(1)-C(2)	117.4(2)	N(3)-C(4)-C(5)	115.3(2)	
C(2)-N(3)-C(4)	123.3(2)	C(7)-C(8)-C(9)	120.2(2)	
C(18)-C(23)-C(19)	118.9(2)	C(21)-C(20)#1-C(19)	121.1(2)	#1: x+1,y,z
C(23)-C(18)-C(6)	117.0(2)	C(5)-C(13)-C(14)	112.0(2)	
C(19)-C(18)-C(6)	124.1(2)	C(16)-C(11)-C(3)	120.7(2)	
C(5)-C(6)-N(1)	124.1(2)	O(24)-C(24)-O(25)#1	123.3(2)	#1: x,y+1,z
C(18)-C(6)-C(5)	121.4(2)	O(24)-C(24)-C(19)	125.3(2)	
N(1)-C(6)-C(18)	114.4(2)	O(25)-C(24)#1-C(19)	111.4(2)	# 1: x,y+1,z
C(12)-C(7)-C(8)	118.7(2)	C(22)-C(23)-C(18)	121.1(2)	
C(8)-C(7)-C(2)	122.7(2)	C(20)-C(21)#1-C(22)#1	120.2(2)	#1: x-1,y,z
C(12)-C(7)-C(2)	118.6(2)	C(9)-C(10)-C(11)	120.1(2)	
C(18)-C(19)-C(20)	119.0(2)	C(10)-C(11)-C(12)	119.9(2)	
C(20)-C(19)-C(24)	120.3(2)	C(10)-C(9)-C(8)	120.3(2)	
C(24)-C(19)-C(18)	120.8(2)	C(21)-C(22)#1-C(23)	119.8(2)	#1: x+1,y,z
N(1)-C(2)-N(3)	122.0(2)	O(15)-C(15)-O(16)	122.6(3)	
N(1)-C(2)-C(7)	119.2(2)	O(15)-C(15)-C(14)	124.2(3)	
N(3)-C(2)-C(7)	118.8(2)	O(16)-C(15)-C(14)	113.1(3)	
C(4)-C(5)-C(6)	118.0(2)	O(16)-C(16)-C(17)#1	107.1(3)	#1: x+1,y,z
C(6)-C(5)-C(13)	124.3(2)	C(15)-C(14)-C(13)	111.4(3)	
C(4)-C(5)-C(13)	117.7(2)	C(24)-O(25)#1-C(25)	117.1(2)	#1: x,y-1,z
O(4)-C(4)-N(3)	120.2(2)	C(16)-O(16)-C(15)	118.7(2)	
O(4)-C(4)-C(5)	124.5(2)			

Estimated standard deviations are given in parenthesis.

Table 4
Atomic Coordinates ($\times 10^4$) and Equivalent Isotropic Displacement
Parameters ($\text{\AA}^2 \times 10^3$)

	x	y	z	U(eq)
N(1)	4192(2)	6253(2)	2763(1)	39(1)
N(3)	1794(2)	5391(2)	1338(1)	40(1)
C(18)	6727(2)	7764(2)	2596(2)	36(1)
C(6)	4921(2)	6978(2)	2106(2)	36(1)
C(7)	1790(3)	4729(2)	3058(2)	37(1)
C(19)	7112(2)	9029(2)	3246(2)	35(1)
C(2)	2653(3)	5491(2)	2366(2)	35(1)
C(5)	4135(3)	6941(2)	1072(2)	38(1)
C(4)	2468(3)	6076(2)	637(2)	40(1)
C(8)	13(3)	4212(2)	2809(2)	46(1)
C(20)	8852(3)	9657(2)	3675(2)	44(1)
C(13)	4920(3)	7736(2)	351(2)	45(1)
C(12)	2802(3)	4554(2)	4004(2)	49(1)
C(24)	5692(3)	9713(2)	3455(2)	40(1)
C(23)	8092(3)	7185(2)	2387(2)	50(1)
C(21)	177(3)	9063(3)	3461(2)	51(1)
C(10)	284(4)	3392(2)	4436(2)	54(1)
C(11)	2051(4)	3885(2)	4688(2)	56(1)
C(9)	-731(4)	3546(3)	3501(2)	53(1)
C(22)	9806(3)	7833(3)	2814(2)	54(1)
C(15)	6306(4)	7655(3)	-1189(2)	71(1)
C(16)	8783(4)	8791(3)	-1664(2)	62(1)
C(25)	5098(4)	1670(3)	4364(3)	60(1)
C(14)	5678(4)	6883(3)	-409(2)	65(1)
C(17)	688(4)	9101(4)	-1217(3)	72(1)
O(4)	1641(2)	5915(2)	-297(1)	57(1)
O(24)	4167(2)	9285(2)	3089(1)	60(1)
O(25)	6329(2)	878(2)	4129(1)	55(1)
O(16)	8001(2)	7984(2)	-997(1)	63(1)
O(15)	5376(3)	7980(4)	-1891(2)	162(2)

U(eq) is defined as 1/3 of the trace of the orthogonalized Uij tensor.

In order to prove the structure of this heterocycle in solid state, a X-ray structural determination of compound **5** was performed on a single crystal grown from methanol (mp 175 °C). The structure has been solved by direct methods using ShelXs-97 [13] and refined with ShelXl-97 [14] under the experimental conditions gathered on Table 2. All atoms, including hydrogen atoms have been localised and refined with isotropic thermal vibration factors. Then, anisotropy of the thermal vibrations has been introduced for all atoms except H. The refinement converges to satisfying R values ($R_1 = 0.064$ $wR_2 = 0.136$ for all observed data) after introduction of an extinction correction and of a weighting scheme. A last Fourier-difference calculation does not show any significant residual electronic density. The atomic coordinates are reported in Table 4 and the main interatomic distances and angles in Table 3. Figure 1 presents the molecular structure of the pyrimidinone **5**. The most salient feature of the structure of the heterocycle is that the C(5) - C(13), C(13) - C(14) and C(14) - C(15) bond lengths of 1.507(3)Å, 1.526(4)Å and 1.503(4)Å respec-

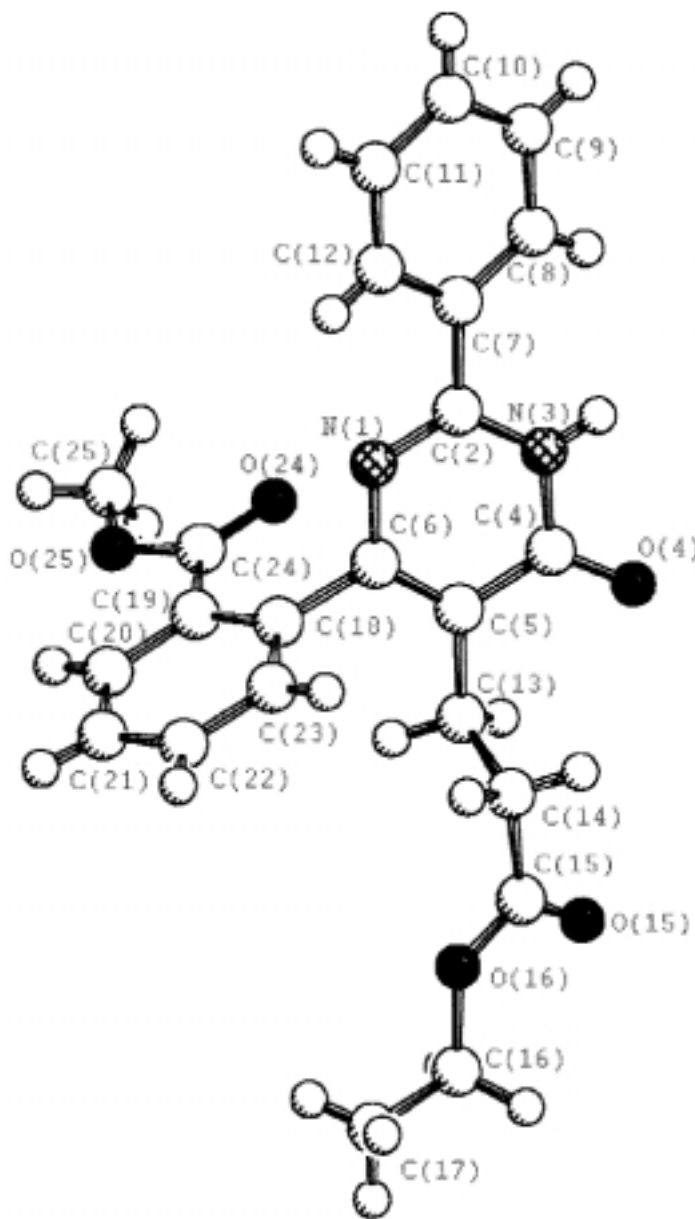


Figure 1. X-Ray crystallographic structure of **5**.

tively correspond to an aliphatic chain with two neighbouring methylene groups. The second feature to note is that the C(4) - O(4) and N(1) - C(2) bond lengths are short [1.243(2) and 1.306(2) Å] and correspond to C=O and N=C respectively. In addition, N(3) - C(2) and N(3) - C(4) bond lengths are longer at 1.364(2)Å and 1.383(3)Å respectively, corresponding to single bonds. X-ray diffraction shows that in the crystalline state, compound **5** exists in the lactam form.

Molecular ion peaks are observed in the mass spectra of all these compounds.

EXPERIMENTAL

General Methods.

All melting points were determined on an Electrothermal IA9000 apparatus in glass capillary tubes or a Kofler hot-stage and are uncorrected. Infrared spectra were recorded on a Perkin Elmer 1000 FTIR instrument and the frequencies are expressed in cm^{-1} . The ^1H and ^{13}C nmr spectra were acquired using a Brücker spectrometer operating at 400 MHz for ^1H and 100 MHz for ^{13}C . Chemical shifts are given in ppm (δ) and J in Hz and the signals are designated as follows; s singlet, d doublet, t triplet, m multiplet. The IC-mass on a R10-10 Nermag apparatus and microanalyses are realised at the University Pierre et Marie Curie, Paris VI.

Diethyl 5,9-dihydroxy-7H-benzo[a] cycloheptene-6,8-dicarboxylate (2).

To a mixture of 7.2 g (105 mmoles) of sodium ethoxide and 12 ml (60 mmoles) of diethylphthalate **1**, 10 ml (53 mmoles) of diethylglutarate was added. The mixture was heated at 130 °C for 3 hours and then cooled; ethanol formed was eliminated by using a Dean Stark apparatus. The product was poured into 10 N aqueous solution of hydrochloric acid (0.5 L). The precipitate formed was filtered and washed with water. The residue was crystallized from ethanol and gives 10.49 g (33 mmoles) (55%) of the benzocycloheptene **2**. ^1H NMR (DMSO- d_6): δ 1.32 (6H, t, J = 7.1, 2xCH₃ ester), δ 3.29 (2H, s, CH₂), δ 4.28 (4H, q, J = 7.2, 2xCH₂ ester), δ 7.68 (2H, dd, J = 3.4, 5.9, H-2, H-3), δ 7.93 (2H, dd, J = 3.4, 5.9, H-1, H-4), δ 12.52 (2H, s, OH); ^{13}C NMR (DMSO- d_6): δ 14.5 (CH₃), δ 18.7 (C-7), δ 61.2 (CH₂), δ 104.8 (C-6, C-8), δ 128.1-130.11 (C-1, C-2, C-3, C-4), δ 134.2 (C-9a, C-4a), δ 166.5 (C-5, C-9), δ 171.7 (C=O); IR (KBr): 2990-2960 (CH₂, CH₃), 1640-1610 (C=O ester); IC-ms: m/z 319 (MH⁺).

2-[5-(3-Ethoxy-3-oxopropyl)-6-oxo-2-phenyl-1,6-dihydro-4-pyrimidinyl]benzoic Acid (**4**).

To a mixture of 1.085 g (6.9 mmoles) of benzamidine hydrochloride hydrate and 1 g (3.14 mmoles) of diester **2** in 20 ml of ethanol 38 mg (6.9 mmoles) of potassium hydroxide dissolved in 20 ml of ethanol was added. The solution was refluxed for 24 hours. Ethanol was distilled under vacuum. The product was then washed thoroughly with water and crystallized from methanol to give 670 mg (1.76 mmoles) (56%) of the pyrimidinone **4**; ^1H NMR (DMSO- d_6): δ 1.10 (3H, t, J = 7.1, CH₃ ester), δ 2.49 (4H, m, CH₂ α , CH₂ β), δ 3.96 (2H, q, J = 7.1, CH₂ ester), δ 7.20 (1H, m, H-3), δ 7.40 (1H, m, H-5), δ 7.45 (2H, m, H-3", H-5"), δ 7.54 (1H, t, J = 7.8, H-4"), δ 7.66 (1H, t, J = 7.4, H-4), δ 7.87 (1H, m, H-6), δ 8.07 (2H, d, J = 7.00, H-2", H-6") δ 10.6 (1H, br s, NH); ^{13}C NMR (DMSO- d_6): δ 14.0 (CH₃ ester), δ 22.4 (CH₂ α), δ 31.4 (CH₂ β), δ 59.7 (CH₂ ester), δ 119.5 (C-5'), δ 127.45 (C-3), δ 127.5 (C-2", C-6"), δ 128.4 (C-5), δ 128.8 (C-3", C-5"), δ 129.1 (C-1), δ 129.4 (C-6), δ 131.0 (C-4"), δ 132.2 (C-4), δ 132.9 (C-1"), δ 138.1 (C-2), δ 138.8 (C-4'), δ 153.2 (C-2'), δ 165.9 (C-6'), δ 172.2 (C=O ester), δ 172.4 (C=O acid); IR (KBr): 3350-3150 (OH, NH), 2980-2930 (CH₂, CH₃), 1715 (C=O ester), 1660 (C=O acid), 1625 (C=O pyrimidine); IC-ms: m/z 393 (MH⁺).

Methyl 2-[5-(3-Ethoxy-3-oxopropyl)-6-oxo-2-phenyl-1,6-dihydro-4-pyrimidinyl] benzoate (**5**).

A solution of 500 mg (1.37 mmoles) of **4** in 20 ml of MeOH was added to a solution of 3 ml of concentrated sulfuric acid in 20

ml of MeOH. The resulting solution was refluxed for 12 hours, evaporated to dryness and the residue was dissolved in water. The solution was neutralised with sodium hydrogen carbonate and extracted with chloroform. The organic layer was washed with water, dried over anhydrous sodium sulfate, and evaporated to afford crystals which were recrystallised from MeOH, to give 405 mg (1 mmole) (73%) of **5**; ^1H NMR (CD₃OD): δ 1.16 (3H, t, J = 7.1, CH₃ ester), δ 2.49 (2H, m, CH₂ β), δ 2.67 (2H, m, CH₂ α), δ 3.71 (3H, s, O-CH₃), δ 4.02 (2H, q, J = 7.1, CH₂ ester) δ 7.43 (1H, d, J = 7.5, H-3), δ 7.50 (2H, m, H-3", H-5"), δ 7.54 (1H, d, J = 7.2, H-4"), δ 7.57 (1H, t, J = 7.7, H-5), δ 7.67 (1H, t, J = 7.1, H-4), δ 7.95 (2H, d, J = 7.3, H-2", H-6"), δ 8.03 (1H, d, J = 7.7, H-6); ^{13}C NMR (CD₃OD): δ 14.5 (CH₃ ester), δ 23.5 (CH₂ α), δ 33.2 (CH₂ β), δ 52.7 (O-CH₃), δ 61.6 (CH₂ ester), δ 117.1 (C-5'), δ 122.7 (C-1), δ 128.9 (C-2", C-6"), δ 130.0 (C-3", C-5"), δ 130.2 (C-3), δ 130.8 (C-5), δ 131.5 (C-2), δ 131.5 (C-3), δ 131.6 (C-6), δ 132.9 (C-4"), δ 133.9 (C-1") δ 133.4 (C-4), δ 140.6 (C-4'), δ 156.5 (C-2'), δ 168.8 (C-6'), δ 174.6 (C=O); IR (KBr): 3350-3100 (NH), 2990-2930 (CH₂, CH₃), 1735-1730 (C=O ester), 1634 (C=O pyrimidine); IC-ms: m/z 407 (MH⁺).

Ethyl 2-[5-(3-Ethoxy-3-oxopropyl)-2-phenyl-1,6-dihydro-4-pyrimidinyl]benzoate (**6**).

A solution of 1 g (2.74 mmoles) of **4** in 20 ml of EtOH was added to a solution of 3 ml of concentrated sulfuric acid in 20 ml of EtOH. The resulting solution was refluxed for 24 hours, cooled and neutralised with 1 N aqueous sodium hydroxide. The precipitate formed was isolated by filtration and washed with diethyloxide. Crystals were recrystallised from ethyl acetate to give 1.06 g (2.52 mmoles) (92%) of compound **6**; ^1H NMR (DMSO- d_6): δ 0.98 (3H, t, J = 7.1, CH₃ ester), δ 1.11 (3H, t, J = 7.1, CH₃ ester), δ 2.43 (2H, br t, J = 7.0, CH₂ β), δ 2.57 (2H, br t, J = 7.3, CH₂ α), δ 3.97 (2H, q, J = 7.1, CH₂ ester), δ 4.04 (2H, q, J = 7.1, CH₂ ester), δ 7.48 (1H, m, H-3), δ 7.49 (1H, m, H-4"), δ 7.54 (2H, m, H-3", H-5"), δ 7.59 (1H, dt, J = 1.0-7.4, H-5), δ 7.69 (1H, dt, J = 0.95-7.4, H-4), δ 7.92 (1H, d, J = 7.5, H-6), δ 8.02 (2H, d, J = 7.5, H-2", H-6"), δ 12.89 (1H, br s, NH); ^{13}C NMR (DMSO- d_6): δ 13.4 (CH₃ ester), δ 13.45 (CH₃ ester), δ 22.1 (CH₂ α), δ 31.5 (CH₂ β), δ 59.8 (CH₂ ester), δ 60.6 (CH₂ ester), δ 120.6 (C-5), δ 127.4 (C-2", C-6"), δ 127.5 (C-1), δ 128.6 (C-3", C-5"), δ 129.2 (C-3), δ 129.8 (C-5), δ 130.2 (C-6), δ 131.4 (C-2), δ 131.5 (C-4), δ 131.8 (C-4"), δ 132.2 (C-1"), δ 138.9 (C-4'), δ 163.2 (C-2'), δ 166.6 (C-4), δ 172.0 (C=O); IR (KBr): 3470-3060 (NH), 2980 (CH₂, CH₃), 1712 (C=O ester), 1638 (C=O pyrimidine); IC-ms: m/z 421 (MH⁺).

2-[5-(2-Carboxyethyl)-6-oxo-2-phenyl-1,6-dihydro-4-pyrimidinyl]benzoic Acid (**7**).

A solution of 1 g (2.74 mmoles) of compound **4** in 30 ml of 1 N methanolic potassium hydroxide was stirred at room temperature for 12 hours. The resulting solution was poured into a 10 N aqueous solution of hydrochloric acid (5 ml). The precipitate formed was isolated by filtration and crystallised from methanol-water (80-20) giving 795 mg (2.2 mmoles) (80%) of compound **7**; ^1H NMR (DMSO- d_6): δ 2.37 (2H, m, CH₂ β), δ 2.45 (2H, m, CH₂ α), δ 7.42 (1H, d, J = 7.4, H-3), δ 7.49 (2H, m, H-3", H-5"), δ 7.54 (1H, m, H-4"), δ 7.56 (1H, m, H-5), δ 7.65 (1H, br t, J = 7.3, H-4), δ 7.92 (1H, d, J = 7.5, H-6), 8.04 (2H, d, J = 7.3, H-2", H-6"), δ 12.57 (4H, br s, NH+OH); ^{13}C NMR (DMSO- d_6): δ 22.4 (CH₂ α), δ 31.5 (CH₂ β), δ 120.6 (C-5), δ 127.6 (C-2", C-6"), δ 128.6 (C-3", C-5"), δ 128.64 (C-3), δ 129.3 (C-4'), δ 129.9 (C-6), δ 130.9 (C-1), 131.4 (C-4"), δ 131.5 (C-4), δ 132.4 (C-1"), δ 139.2 (C-2), δ 153.6 (C-4'),

δ 161.7 (C-2'), δ 163.4 (C-6'), δ 167.9 (C=O), δ 173.8 (C=O); IR (KBr): 3400-3050 (OH, NH), 2980-2930 (CH₂), 1715-1735 (C=O acid), 1638 (C=O pyrimidine); IC-ms: m/z 365 (MH⁺).

Ethyl 7-hydroxy-4-oxo-2-phenyl-4,5-dihydro-3H-benzo[6-7]-cyclohepta[1,2-d]pyrimidine-6-carboxylate (**3**).

A solution of 1 g (2.38 mmol) of **6** in 15 ml of dry toluene was added dropwise to 970 mg (15 mmol) dry powdered sodium ethoxide. The mixture was heated at 120 °C for 4 hours (ethanol formed was eliminated by using a Dean Stark apparatus). After addition of water, the resulting mixture was acidified with 10 N acetic acid and extracted with ethyl acetate. The organic layer was washed with water, dried over anhydrous sodium sulfate, and evaporated to afford crystals which were recrystallised from propanol to give 275 mg (0.74 mmol) (31%) of compound **3**; ¹H NMR (DMSO-*d*₆): δ 1.33 (3H, t, J = 7.0, CH₃ ester), δ 3.32 (2H, br s, CH₂), δ 4.32 (2H, q, J = 7.0, CH₂ ester), δ 7.53 (1H, m, H-11), δ 7.55 (2H, m, H-3', H-5'), δ 7.68 (1H, m, H-4'), δ 7.73 (1H, br t, J = 6.6, H-9), δ 7.95 (1H, br d, J = 7.2, H-10), δ 8.16 (2H, d, J = 7.3, H-2', H-6'), δ 8.23 (1H, d, J = 7.4, H-8) δ 12.70 (1H, br s, NH), δ 12.88 (1H, br s, OH); ¹³C NMR (DMSO-*d*₆): δ 13.8 (CH₃ ester), δ 17.2 (C-5), δ 60.8 (CH₂ ester), δ 102.7 (C-6), δ 127.2 (C-4a), δ 127.4 (C-2', C-6'), δ 128.3 (C-3', C-5'), δ 129.8-129.3 (C-8, C-11), δ 131.0 (C-9, C-10), δ 131.3 (C-1'), δ 132.1 (C-4'), δ 133.1 (C-8a), δ 136.7 (C-11a), δ 154.3 (C-1a), δ 161.1 (C-2), δ 166.0 (C-7), δ 168.4 (C=O ester), δ 170.6 (C-4); IR (KBr): 3400-3200 (NH, OH), 2980 (CH₂, CH₃), 1710 (C=O ester), 1634 (C=O pyrimidine); IC-ms: m/z 375 (MH⁺).

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