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PHOTOCHEMICAL SYNTHESIS OF POLYCYCLIC PYRIMIDINES THROUGH THE ACID CATALYZED CYCLOADDITION OF 6-CHLORO-1-METHYLURACIL TO METHYL SUBSTITUTED BENZENES

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Abstract – UV-irradiation of 6-chloro-1-methyluracil with benzene in the presence of TFA resulted in 1,2-cycloaddition and susequent elimination of HCl gave a cyclooctapyrimidine-2,4-dione. Similar acid catalyzed photoreaction with substituted benzenes bearing two or three methyl groups afforded the corresponding cyclooctapyrimidines and two novel pentacyclic compounds, 9,11-diazapentacyclo[6.4.0.0^{1,3}.0^{2,5}.0^{4,8}]dodecanes and 9.11-diazapentacyclo[6.4.0.0^{1,3}.0^{2,6}.0^{4,8}]dodcanes, in fair yields.

Recently, photoreaction of nucleic bases has been received much attention from both organic chemistry and biological perspectives.[1] During the course of our continuing studies on the photochemical modification of the pyrimidine ring, we have previously reported that the acid catalyzed photoreaction of 6-chloro-1,3-dimethyluracil (6-ClDMU) with benzene derivatives proceeds by way of 1,2-cycloaddition to give cyclooctapyrimidines.[2] Certain cyclooctapyrimidines were further converted into various novel valence isomers,[3-5] by way of a variety of electrocyclic pathways depending on the reaction conditions and substituents on the cycloadducts. These reactions however, have been carried out with both *N*1 and *N*3 methyl capped uracils. Taking the biological importance of the *N*3-H moiety of the pyrimidine ring into consideration, the presence of a non-protected *N*3-H function of the pyrimidine ring

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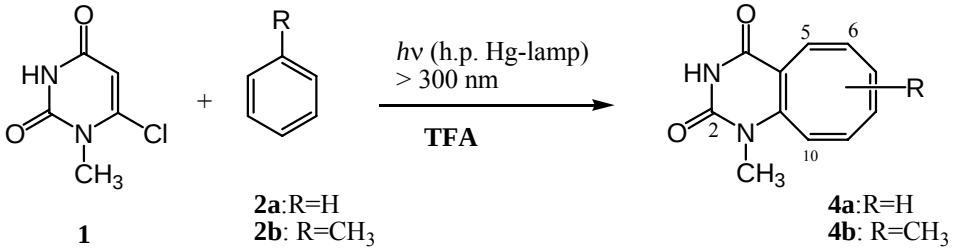
This paper is dedicated to Professor Steven M. Weinreb on the occasion of his 65th birthday.

may represent a significant pharmacophore for the development of useful chemotherapeutics. We intended to extend this photoreaction to 6-chloro-1-methyluracil (**1**) bearing an *N*3-H function. In the present paper, we describe that the photoreaction of **1** with benzene and its methyl derivatives in the presence of TFA successfully effected cycloaddition to give NH free polycyclic pyrimidines.

UV-irradiation of a solution of 6-chloro-1-methyluracil (**1**) in benzene (**2a**) with a 500 W high-pressure mercury lamp in a degassed Pyrex tube (λ>300 nm) for 16 h afforded 1-methyl-6-phenyluracil (**3a**) in low yield (3%), together with large amount of unreacted **1**. In contrast, the addition of TFA to the solution gave rise to the formation of 1-methylcyclooctapyrimidine-2,4-dione (**4a**) in appreciable yield (70%, based on 73% **1** consumed), while the substitution reaction was significantly attenuated (3%) (Scheme 1).



Scheme 1

The structural assignment of **4a** was made on the basis of detailed MS and the NMR spectroscopic studies. The coupling constants for the vinyl protons of **4a**, $J_{5,6,}$ $J_{7,8,}$ $J_{9,10}$ = 11.5 Hz, and $J_{6,7,}$ $J_{8,9,}$ = 3.5-4 Hz, revealed the configurations to be all *cis*.

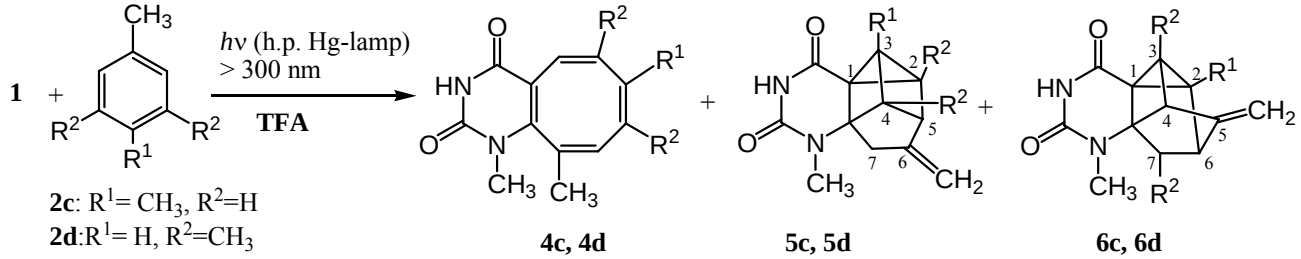
The photoreaction with toluene (**2b**) under the above conditions afforded five isomeric 1,*n*-dimethyl-cyclooctapyrimidines (*n*=6,7,8,9,10) in fair yield (**4b$_6$**:23%, **4b$_7$**: 16%, **4b$_8$**: 25%, **4b$_9$**: 7%, **4b$_{10}$**: 18%) (Scheme1). The structural assignments, including the stereochemistry of **4b** were made on the basis of the similarity to **4a** in their ^{1}H-NMR spectroscopic data. Methyl substituted sites on the cycloocta-tetraene moiety were determined by NOE experiments.

Thus, analogous to the case of the reaction with 6-ClDMU and **2a**,**b**, UV excitation of **1** undergoes 1,2-cycloaddition with **2a**,**b** to produce cyclooctapyrimidines *via* the concomitant elimination of hydrogen chloride which is then followed by an electrocyclic ring opening reaction.

We then investigated the photoreaction with *p*-xylene (**2c**) under the same conditions. HPLC separation of the reaction mixture afforded three types of cycloadducts as single regioisomers namely, 1, 7,10-trimethylcyclooctapyrimidine-2,4-dione (**4c**) in 31% yield along with two novel pentacyclic compounds, 6-methylene-3,9-dimethyl-9,11-diazapentacyclo[6.4.0.0^{1,3}.0^{2,5}.0^{4,8}]dodecane-10,12-dione (**5c**) and 5-methylene-2,9-dimethyl-9,11-diazapentacyclo[6.4.0.0^{1,3}.0^{2,6}.0^{4,8}]dodecane-10,12-dione (**6c**)

in 15% and 13 % yield respectively. Conversely, the reaction with toluene gave the cyclooctapyrimidines with poor regioselectivity (Scheme 2).

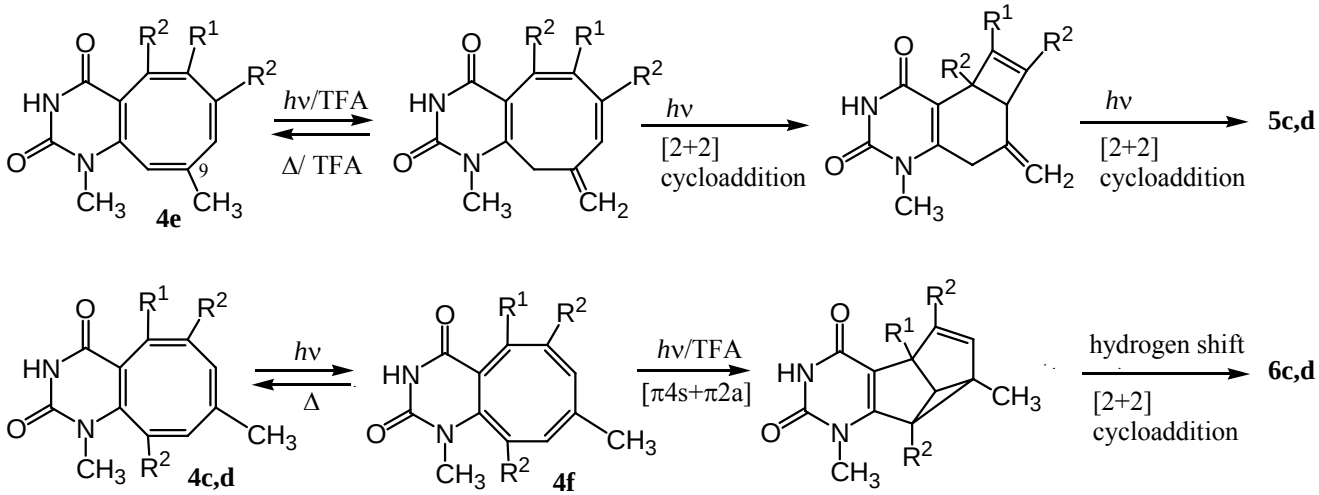
The structures of **5c** and **6c** were determined by comparison with the NMR data for *N*3-methyl penta-



Scheme 2

cyclic derivatives which had given X-ray crystallographic data in detail.[6] The ^{1}H and ^{13}C-nmr spectra including ^{13}C-^{1}H COSY showed signals due to two methyl groups, two methylene groups, three methine groups and six quaternary carbon atoms. HMBC spectrum and NOE experiments provided the information to enable us to construct pentacyclic compounds consisting of 3, 4, 4, and 5-membered rings for **5c** and 3, 4, 5, and 5-membered rings for **6c**.

Similarly the photoreaction with mesitylene (**2d**) afforded 1,6,8,10-tetramethyl-cyclooctapyrimidine-2,4-dione (**4d**) (21%) and the two pentacyclic compounds, 6-methylene-2,4,9-trimethyl-9,11-diazapentacyclo[6.4.0.$0^{1,3}$.$0^{2,5}$.$0^{4,8}$]dodecane-10,12-dione (**5d**) (18%) and 5-methylene-3,7,9-trimethyl-9,11-diazapentacyclo[6.4.0.$0^{1,3}$.$0^{2,6}$.$0^{4,8}$] dodecane-10,12-dione (**6d**) (8%) (Scheme 2).



Scheme 3

The reaction pathway for the formation of the pentacyclic compound is inferred on the basis of the established pathway[7] for the formation of *N*3-methyl derivative respectively as depicted in Scheme 3. It

is suggested that compound **5** could be derived from 9-methylcyclooctapyrimidine (**4e**) *via* a multi-step transformation starting with a [1,3] sigmatropic rearrangement of 9-methyl group followed by subsequent double [2 + 2] cycloaddition processes. The formation of compound **6** can be explained by the rearrangement of cyclooctapyrimidine tautomer (**4f**) involving a [π4s +π2a] process.

These results provide the first example of the formation of various cycloadducts between *N*3-H chlorouracil and benzenes. Interestingly in this reaction methyl substituents on the benzene ring are effective auxiliaries in achieving subsequent electrocyclic rearrangement of photoadducts including forming highly strained pentacyclic cage compounds.

It is noteworthy that reactions involving *N*3 free 6-chlororouracil in place of dimethyluracil derivatives, would provide synthons for the synthesis of singular polycyclic systems including a *N*3 non-substituted pyrimidine ring.

EXPERMENTAL

NMR spectra were measured with a JEOL JNM-EA500 (500 MHz) spectrometer, and ^{1}H-NMR chemical shifts are given on the δ (ppm) scale based on those of the signals of solvents. MS spectra and high-resolution MS (HRMS) spectra were recorded with JEOL JMS-FABmate (EI). Reverse-phase liquid chromatography (RP-HPLC) was carried out on a Shim-pac PREP-ODS (25 cm x 20 mm *i.d.*) (Shimadzu) with aqueous methanol, using a Shimadzu LC-6A apparatus with monitoring at 254 nm. Silica gel LC (Si-HPLC) was conducted on a Shim-pac PREP-Sil (H) (25 cm x 20 mm *i.d.*) (silica gel), using the same apparatus. UV-Irradiation was carried out externally with a 500 W high-pressure mercury (h. p. Hg) lamp (Eiko-sha, Osaka) in a degassed Pyrex tube (> 300 nm) on a merry-go-round apparatus.

Photoreaction of 1 with 2 in the presence of TFA----- A solution of **1** (56 mg, 0.35 mmol) and TFA (10 equiv. mol: 260 μl) in benzenes (**2a-d**) (100 mL) was put portion-wise (10 mL each) into ten degassed Pyrex tubes and irradiated externally at room temperature for 16 h.

Typical procedure for the isolation of the cycloadduct----- After the photoreaction according to the general procedure, the reaction mixtures in several Pyrex tubes were put together, and evaporated *in vacuo*. The residual oil was passed through a short column of silica gel with AcOEt. The eluate was submitted to HPLC with following solvent systems; 30% MeOH-H_2O on RP-HPLC for **4a**, 15% AcOEt-hexane on Si-HPLC for **4b**, **4d**, **5d**, and **6d**, and 25% AcOEt- hexane on Si-HPLC for **4c**, **5c**, and **6c**.

1-Methylcyclooctapyrimidine-2,4-dione(**4a**): Yellow crystals, mp 243-246 °C (*i*-PrOH). ^{1}H–NMR

(C_6D_6) δ; 2.45 (3H, s, N^1-CH_3), 4.92 (1H, d, *J*=11.5 Hz, H-10), 5.41 (1H, dd, *J*=11.5, 3.5 Hz, H-9), 5.47 (1H, dd, *J*=11.5, 3.5 Hz, H-8), 5.58 (1H, dd, *J*=11.5, 4.0 Hz, H-7), 5.66 (1H, dd, *J*=11.5, 4.0 Hz, H-6), 6.24 (1H, d, *J*=11.5 Hz, H-5), 9.13 (1H, brs, N^3-H). NOE; H-10 with N^1-CH_3 , H-9; H-5 with H-6; N^1-CH_3 with H-10. ^{13}C-NMR (C_6D_6); 30.47 (N^1-CH_3), 110.83 (4a), 125.74 (10), 127.55 (5), 129.33 (9), 130.79 (6), 133.05 (7), 135.39 (8), 149.16 (10a), 150.68 (2), 161.00 (4). MS *m/z* (%):202 (M^+, 100), 159 (55), 131 (42), 116 (32). *Anal*. Calcd for $C_{11}H_{10}N_2O_2$: C, 65.34; H, 4.98; N, 13.85. Found: C, 65.27; H, 4.99; N, 13.77.

1,6-Dimethylcyclooctapyrimidine-2,4-dione(4b$_6$): Yellow crystals, mp 220-223 °C (acetone). ^{1}H-NMR($CDCl_3$) δ; 1.86 (3H, s, C^6-CH_3), 3.28 (3H, s, N^1-CH_3), 5.89 (1H, s, H-5), 5.94 (1H, dd, *J*=11.5, 3.5 Hz, H-8), 6.01 (1H, d, *J*=11.5 Hz, H-7), 6.01 (1H, d, *J*=11.5 Hz, H-10), 6.31 (1H, dd, *J*=11.5, 3.5 Hz, H-9), 8.38 (1H,brs,N^3-H). NOE; H-10 with N^1-CH_3, H-9; H-9 with H-10, H-8; H-8 with H-9, H-7; H-7 with H-8, C^6-CH_3 ; C^6-CH_3 with H-7, H-5. ^{13}C-NMR($CDCl_3$) δ; 23.45 (C^6-CH_3), 31.88 (N^1-CH_3), 112.50 (4a), 121.63 (5), 125.56 (10), 127.86 (8), 136.44 (7), 136.93 (9), 140.93 (6), 149.79 (10a), 151.03 (2), 161.79 (4). MS *m/z* (%):216 (M^+, 100), 201 (11), 173 (38), 158 (18), 145 (39), 115 (14), 104 (18). HRMS; Calcd for $C_{12}H_{12}N_2O_2$: 216.0899. Found: 216.0902.

1,7-Dimethylcyclooctapyrimidine-2,4-dione(4b$_7$): Yellow crystals, mp 227-230 °C (*i*-PrOH). ^{1}H-NMR($CDCl_3$) δ; 1.78 (3H, s, C^7-CH_3), 3.28 (3H, s, N^1-CH_3), 5.74 (1H, m, H-8), 5.92 (1H, d, *J*=11.5 Hz, H-10), 5.97 (1H, d, *J*=11.5 Hz, H-6), 6.09 (1H, d, *J*=11.5 Hz, H-5), 6.27 (1H, dd, *J*=11.5, 3.5 Hz, H-9), 8.64 (1H, brs, N^3-H9). NOE; H-10 with N^1-CH_3, H-9; H-9 with H-10, H-8; H-8 with H-9, C^7-CH_3; C^7-CH_3 with H-8, H-6. ^{13}C-NMR ($CDCl_3$); 23.38 (C^7-CH_3), 31.80 (N^1-CH_3), 111.51 (4a), 124.47 (10), 124.90 (8), 124.93 (5), 135.49 (6), 137.91 (9), 141.83 (7), 150.63 (10a), 151.05 (2), 161.51 (4). MS *m/z* (%):216 (M^+, 100), 201 (15), 173 (27), 158 (18), 145 (33), 130 (22), 115 (9), 104 (22). *Anal*. Calcd for $C_{12}H_{12}N_2O_2$ C, 66.65; H, 5.59; N, 12.96. Found: C, 65.90; H, 5.52; N, 12.51.

1,8-Dimethylcyclooctapyrimidine-2,4-dione(4b$_8$): Yellow crystals, mp 207-210 °C (*i*-PrOH). ^{1}H-NMR($CDCl_3$) δ; 1.82 (3H, s, C^8-CH_3), 3.29 (3H, s, N^1-CH_3), 5.77 (1H, m, H-7), 5.93 (1H, d, *J*=11.5 Hz, H-10), 6.00 (1H, dd, *J*=11.5, 3.5 Hz, H-6), 6.10 (1H, d, *J*=11.5 Hz, H-5), 6.23 (1H, d, *J*=11.5 Hz, H-9). NOE; H-10 with N^1-CH_3 , H-9; H-9 with H-10, C^8-CH_3; C^8-CH_3 with H-9, H-7; H-7 with C^8-CH_3, H-6; H-6 with H-7, H-5; N^1-CH_3 with H-10. ^{13}C-NMR ($CDCl_3$) δ; 22.48 (C^8-CH_3), 31.73 (N^1-CH_3), 111.60 (4a), 123.73 (10), 125.72 (5), 127.85 (7), 133.03 (6), 138.37 (8), 140.02 (9), 150.17 (10a), 151.26 (2), 161.77 (4). MS *m/z* (%):216 (M^+, 100), 201 (11), 176 (23), 173 (26), 158 (14), 145 (37), 144 (34), 130 (32), 115 (12), 104 (30). HRMS; Calcd for $C_{12}H_{12}N_2O_2$: 216.0899. Found: 216.0895.

1,9-Dimethylcyclooctapyrimidine-2,4-dione(4b$_9$): Yellow crystals, mp 245-247 °C (acetone). ^{1}H-

NMR($CDCl_3$) δ; 1.92 (3H, s, C^9-CH_3), 3.28 (3H, s, N^1-CH_3), 5.75 (1H, s, H-10), 5.94-6.00 (2H, m, H-7 and H-8), 6.06 (1H, dd, *J*=10.9, 3.5 Hz, H-6), 6.18 (1H, d, *J*=10.9 Hz, H-5), 8.43 (1H, brs, N^3-H). NOE; H-10 with N^1-CH_3, C^9-CH_3; C^9-CH_3 with H-10, H-8; H-6 with H-7, H-5; N^1-CH_3 with H-10. ^{13}C-NMR ($CDCl_3$) δ; δ; 23.90 (C^9-CH_3), 31.91 (N^1-CH_3), 111.13 (4a), 120.60 (10), 127.13 (5), 131.14 (8), 132.21 (6), 133.07 (7), 146.29 (9), 150.87 (10a), 151.15 (2), 161.69 (4). MS *m/z* (%):216 (M^+, 100), 201 (13), 176 (5), 173 (30), 158 (11), 130 (24), 115 (11), 104 (15). HRMS; Calcd for $C_{12}H_{12}N_2O_2$: 216.0899. Found: 216.0903.

1,10-Dimethylcyclooctapyrimidine-2,4-dione(4b$_{10}$): Orange oil. ^{1}H-NMR($CDCl_3$) δ; 1.94 (3H, s, C^{10}-CH_3), 3.27 (3H, s, N^1-CH_3), 5.96 (1H, dd, *J*=10.9, 3.5 Hz, H-7), 6.02 (2H, m, H-8 and H-9), 6.06 (1H, dd, *J*=10.9, 2.3 Hz, H-6), 6.28 (1H, d, *J*=10.9 Hz, H-5). NOE; C^{10}-CH_3 with N^1-CH_3, H-9; H-6 with H-5, H-7; N^1-CH_3 with C^{10}-CH_3. ^{13}C-NMR ($CDCl_3$) δ; 21.68 (C^{10}-CH_3), 32.62 (N^1-CH_3), 110.51 (4a), 126.38 (5), 130.40 (8), 132.01 (7), 132.09 (9), 132.35 (6), 133.82 (10), 151.75 (10a), 153.90 (2), 161.88 (4). MS *m/z* (%):216 (M^+, 100), 201 (17), 176 (6), 173 (32), 158 (28), 145 (37), 115 (14), 104 (23). HRMS; Calcd for $C_{12}H_{12}N_2O_2$: 216.0899. Found: 216.0899.

1,7,10-Trimethylcyclooctapyrimidine-2,4-dione(4c): Colorless crystals. mp 245-247 °C (*i*-PrOH). ^{1}H-NMR((acetone-d_6)) δ; 1.68 (3H, s, C^7-CH_3), 1.91 (3H, s, C^{10}-CH_3), 3.19 (3H, s, N^1-CH_3), 5.81 (1H, m, H-8), 5.91 (1H, brd, *J*=11.5 Hz, H-6), 6.00 (1H, m, H-9), 6.12 (1H, d, *J*=11.5 Hz, H-5). NOE; H-9 with C^{10}-CH_3, H-8; C^7-CH_3 with H-8, H-6; H-6 with C^7-CH_3 , H-5; N^1-CH_3 with C^{10}-CH_3. ^{13}C-NMR ($CDCl_3$) (acetone-d_6) δ; 20.65 (C^{10}-CH_3), 22.25 (C^7-CH_3), 31.85 (N^1-CH_3), 109.89 (4a), 125.42 (5), 125.87 (8), 132.42 (9),133.23 (10), 134.22 (6), 139.57 (7), 151.50 (2), 153.82 (10a), 161.44 (4). MS *m/z* (%):230 (M^+, 100), 215 (27), 190 (19), 187 (13), 144 (37), 129 (6). *Anal*. Calcd for $C_{13}H_{14}N_2O_2$ C, 67.81; H, 6.13; N, 12.17. Found: C, 67.66; H, 6.13; N, 12.15.

9,11-Diaza-3,9-dimethyl-6-methylenepentacyclo[6.4.0.0^{1,3}.0^{2,5}.0^{4,8}]dodecane-10,12-dione(5c): colorless crystals. mp 215-217 °C (*i*-PrOH). ^{1}H-NMR ($CDCl_3$) δ; 1.48 (3H, s, C^3-CH_3), 2.45 (1H, dt, *J*=16.9, 2.6 Hz, H-7b), 2.55 (1H, dt, *J*=16.9, 2.0 Hz, H-7a), 2.80(1H, t, *J*=4.6 Hz, H-4), 2.86 (1H, dd, *J*=4.6, 2.9 Hz,H-2), 2.96 (3H, s, N^9-CH_3), 3.68 (1H, dd, *J*=4.6, 2.9 Hz, H-5), 4.75 (1H, brs, C^6=CHb), 4.91 (1H, t-like, C^6=CHa), 7.48 (1H, brs, N^{11}-H). NOE; H-2 with H-5, C^3-CH_3; H-4 with C^3-CH_3 , N^9-CH_3 , H-5; H-5 with H-7a, H-7b, H-6b; H-6b with H-5, H-6a; H-6a with H-6b, H-7a; H-7a with H-6b, H-7b; H-7b with H-7a, N^9-CH_3 ; N^9-CH_3 with H-7b. ^{13}C-NMR ($CDCl_3$) δ; 10.58(C3-CH_3), 29.37(N9-CH_3), 32.4(3), 34.80 (2), 47.29 (1), 50.60 (4), 51.38 (5), 68.62 (8), 107.37 (C^6=CH_2), 147.07 (6), 154.11 (10), 167.10 (12). MS *m/z* (%):229 ([M-H]$^+$, 82), 215 (69), 190 (100), 172 (20), 158 (33),147 (75),144 (38), 129 (13), 119 (89), 91 (29). HRMS; Calcd for $C_{13}H_{13}N_2O_2$; 229.0977. Found; 229.0980.

9,11-Diaza-2,9-dimethyl-5-methylenepentacyclo[6.4.0.0^{1,3}.0^{2,6}.0^{4,8}]dodecane-10,12-dione (**6c**): colorless crystals. mp 172-174 °C (acetone-hexane).^{1}H-NMR ($CDCl_3$) δ; 1.57 (1H, d, *J*=9.8 Hz, H-7a), 1.62 (3H, s, C^2-CH_3), 1.75 (1H, dt, *J*=9.8, 2.3 Hz, H-7b), 2.70 (1H, brt, H-6), 2.80 (1H, t, *J*=2.3, 2.9 Hz, H-4), 2.86 (3H, s, N^9-CH_3), 2.89 (1H, d, *J*=2.9 Hz ,H-3), 4.53 (1H, s, C^5=CHb),4.64 (1H, s, C^5=CHa). NOE; C^2-CH_3 with H-6, H-3; H-4 with H-3, H-5b; H-5a with H-5b; H-6 with H-5a, H-7a , C^2-CH_3 ; H-7a with H-7b; H-7b with H-7a, N^9-CH_3; N^9-CH_3 with H-7b. ^{13}C-NMR ($CDCl_3$) δ; 12.43 (C^2-CH_3), 29.37 (N^9-CH_3), 40.17 (2), 41.76 (3), 45.78 (7), 46.21 (6), 46.25 (4), 48.67 (1), 65.86 (8), 98.45 (C^5=CH_2), 152.37 (10), 157.34 (5), 167.81 (12). MS *m/z* (%):230 (M^+, 7), 215 (100), 172 (59), 144 (26), 129 (5), 115 (9), 91 (18), 77 (9). HRMS; Calcd for $C_{13}H_{14}N_2O_2$; 230.1055. Found; 230.1055.

1, 6, 8, 10-Tetramethylcyclooctapyrimidine-2, 4-dione (**4d**): orange oil. ^{1}H-NMR (C_6D_6) δ; 1.79 (3H, s, C^8-CH_3), 1.81 (3H, s, C^6-CH_3), 1.90 (3H, s, C^{10}-CH_3), 3.27 (3H, s, N^1-CH_3), 5.61 (1H, s, H-7), 5.95 (1H, s, H-5), 5.97 (1H, s, H-9), 9.20 (1H, brs, N^3-H). NOE; C^{10}-CH_3 with N^1-CH_3, H-9; H-9 with C^{10}-CH_3, C^8-CH_3; C^8-CH_3 with H-9, H-7; C^6-CH_3 with H-7 H-5; N^1-CH_3 with C^{10}-CH_3 .^{13}C-NMR (C_6D_6) δ; 21.37 (C^{10}-CH_3), 22.55 (C^8-CH_3), 23.78 (C^6-CH_3), 32.52 (N^1-CH_3), 112.09 (4a), 120.07 (5), 129.91 (7), 131.76 (10), 135.21 (9), 137.22 (8), 142.06 (6), 151.97 (10a), 152.93 (2), 160.89 (4). MS *m/z* (%): 244 (M^+, 100), 229 (76), 201 (5), 186 (45), 173 (23), 158 (35), 144 (15), 129 (10). HRMS; Calcd for $C_{14}H_{16}N_2O_2$; 244.1212. Found; 244.1209.

9,11-Diaza-2,4,9-trimethyl-6-methylenepentacyclo[6.4.0.0^{1,3}.0^{2,5}.0^{4,8}]dodecane-10,12-dione (**5d**): colorless crystals. mp 231-233 °C (EtOH).^{1}H-NMR ($CDCl_3$) δ; 1.16 (3H, s, C^4-CH_3), 1.57 (3H, s, C^2-CH_3), 2.49 (1H, dt, *J*=16.7, 2.5 Hz, H-7b), 2.58 (1H, dt, *J*=16.7, 2.5 Hz, H-7a), 2.94 (3H, s, N^9-CH_3), 2.96 (1H, s, H-5), 3.33 (1H, s, H-3), 4.84 (1H, brs, C^6=CHb), 4.93 (1H, t, *J*=2.5 Hz, C^6=CHa), 7.32 (1H, brs, N^{11}-H). NOE; C^2-CH_3 with H-5, H-3; H-3 with C^2-CH_3, C^4-CH_3; C^4-CH_3 with H-3, H-5, N^9-CH_3; H-6a with H-6b, N^9-CH_3 ; N^9-CH_3 with H-7a, C^4-CH_3. ^{13}C-NMR ($CDCl_3$) δ; 11.10 (C^2-CH_3), 14.44 (C^4-CH_3), 30.24 (1), 30.44 (N^9-CH_3), 34.99 (7), 38.74 (2), 44.78 (3), 56.46 (4), 62.63 (5), 70.77 (8), 108.31 (C^6=CH_2), 145.03 (6), 154.42 (10), 168.04 (12). MS *m/z* (%):243 ($[M-H]^+$, 13), 229 (100), 204 (24), 186 (29), 172 (20), 158 (45), 133 (29), 117 (18). HRMS; Calcd for $C_{14}H_{16}N_2O_2$; 244.1212. Found; 244.1194.

9, 11-Diaza-3, 7, 9-trimethyl-5-methylenepentacyclo[6.4.0.0^{1,3}.0^{2,6}.0^{4,8}]dodecane-10, 12-dione (**6d**): colorless crystals. mp 181-183 °C (acetone-hexane).^{1}H-NMR ($CDCl_3$) δ; 0.84 (3H, d, *J*=6.3 Hz, C^7-CH_3), 1.41 (3H, s, C^3-CH_3), 1.97 (1H, brq, *J*=6.3 Hz, H-7), 2.64 (1H, m,H-6), 2.74 (1H, m, H-2), 2.81 (3H, s, N^9-CH_3), 2.94 (1H, s, H-4), 4.50 (1H, s, C^5=CHa), 4.61 (1H, s, C^5=CHb). NOE; C^3-CH_3 with H-2, H-6 ; H-5a with H-6 , H-5b; H-5b with H-5a, H-6; H-6 with H-5a, H-5b, H-4, H-2, N^9-CH_3,

C^3-CH_3, C^7-CH_3; C^7-CH_3 with H-7, H-6, N^9-CH_3; N^9-CH_3 with H-6, H-7. ^{13}C-NMR ($CDCl_3$) δ; 8.43 (C^7-CH_3), 12.62 (C^3-CH_3), 29.60 (N^9-CH_3), 39.83 (2), 46.61 (6), 47.83 (3), 50.52 (4), 50.65 (1), 51.36 (7), 66.31 (8), 98.35 (C^5=CH_2), 153.13 (10), 156.44 (5), 167.21 (12). MS *m/z* (%):244 (M^+, 56), 229 (100), 201 (14), 200 (11), 186 (51), 173 (9), 158 (39), 144 (9), 129 (12), 116 (8). HRMS; Calcd for $C_{14}H_{16}N_2O_2$; 244.1212. Found; 244.1216.

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