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A New Ring System from Photocycloaddition of 6-Chloro-1,3-dimethyluracil to *p*- and *m*-Xylene. Formation of 6-Methylene-9,11,x-trimethyl-9,11-diazapentacyclo[6.4.0.0^{1,3}.0^{2,5}.0^{4,8}]dodecane-10,12-diones

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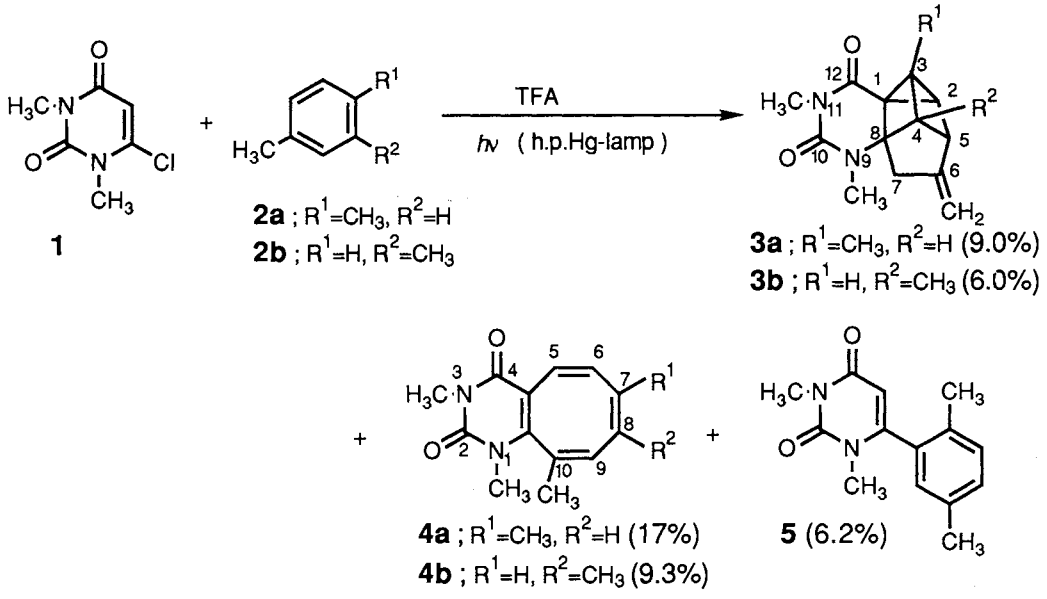
UV irradiation of 6-chloro-1,3-dimethyluracil in *p*- and *m*-xylene in the presence of trifluoroacetic acid gave the title compounds, novel cycloaddition products of the pyrimidine ring to the benzene moiety. Tetramethylcyclooctapyrimidine-2,4-diones were also yielded.

In the previous papers,[1] we reported that 1,3-dimethylcyclooctapyrimidine-2,4-diones were first produced by the photolysis of 6-chloro-1,3-dimethyluracil (**1**) in benzene and its monosubstituted derivatives in the presence of trifluoroacetic acid (TFA), probably *via ortho*-cycloaddition. In attempt to construct a new ring system consisting of a pyrimidine ring through the other possible processes including *meta*-cycloaddition,[2] we have extended our work to disubstituted benzenes. In the present paper, we describe our findings that 6-methylene-9,11,x-trimethyl-9,11-diazapentacyclo[6.4.0.0^{1,3}.0^{2,5}.0^{4,8}]dodecane-10,12-diones (**3a**; x = 3 and **3b**; x = 4) were first produced together with 1,3,n,10-tetramethylcyclooctapyrimidine-2,4-diones (**4a**; n = 7 and **4b**; n = 8) upon irradiation of **1** in *p*- and *m*-xylene (**2a**, **2b**) in the presence of TFA.



Scheme 1.

A solution of **1** (2 mmol) and TFA (4 mmol) in *p*-xylene (**2a**) (400 ml) was irradiated with a 500 W high-pressure mercury lamp through a Pyrex filter (λ>300 nm) under an argon atmosphere for 20 h to afford the pentacyclic compound **3a**[3](9.0%) and a cyclooctapyrimidine-2,4-dione **4a**[4] as the single regioisomer (17%), together with the substitution product 1,3-dimethyl-6-(*p*-xylyl)uracil (**5**)[5] (6.2%) (Scheme 1[6]). Similarly the photolysis of **1** in *m*-xylene (**2b**) in the presence of TFA afforded a pentacyclic derivative **3b**[7] in 6.0% yield, together with a cyclooctapyrimidine derivative **4b**[8] as the sole regioisomer (9.3%) (Scheme 1[6]).

The structure of **3a** was determined by X-ray crystallographic analysis.[9] The structure includes a uracil ring condensed with a tetracyclooctane system, consisting of 3, 4, 4, and 5-membered rings (Fig. 1).

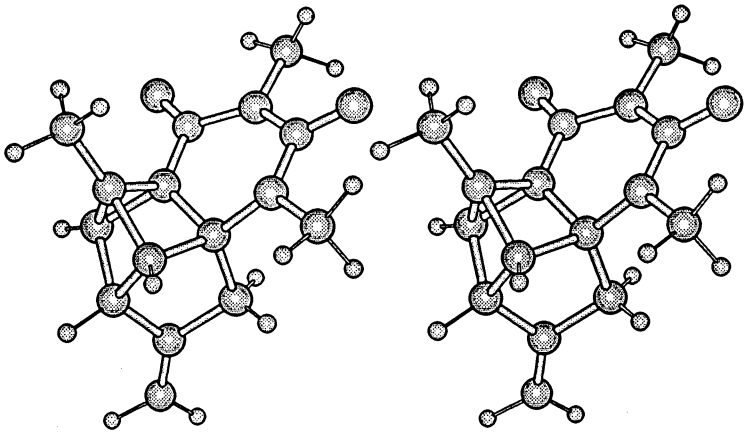


Fig. 1. Stereoscopic view of **3a**.

The structure of **3b** was deduced from the spectral analogy with **3a**. The nuclear Overhauser effect (NOE) experiments confirmed the structural assignment of **3b** (Fig. 2). The structure was supported by The ^{1}H-detected heteronuclear multiple-bond connectivity (HMBC) spectrum, wherein each signal due to protons showed long-range correlation with the corresponding carbons; H-7^{a} with C-1, C-4, C-6, C-8, and C^{6}=$\underline{C}H_2$; H-7^{b} with C-1 and C-6; H-2 with C-4; *exo*-methylene protons (=C$\underline{H}^{a}$, =C$\underline{H}^{b}$) with C-5 and C-7; H-3 with C-12, C-1, C-4, C-5, C-6 and C-7; H-5 with C-1, C-2, C-4, C^{6}=$\underline{C}H_2$, C-7, C-8, and C^{4}-$\underline{C}H_3$; C^{4}-CH_3 with C-3, C-4, C-5, and C-8; N^{9}-CH_3 with C-8; N^{11}-CH_3 with C-12.

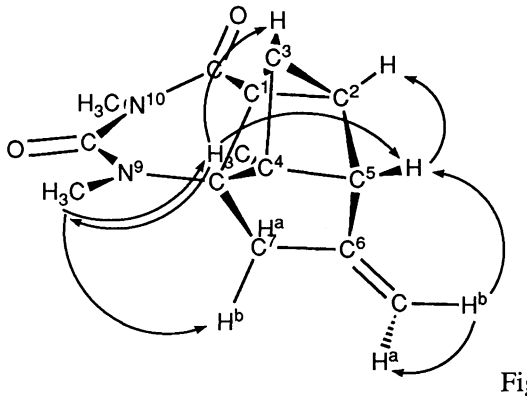
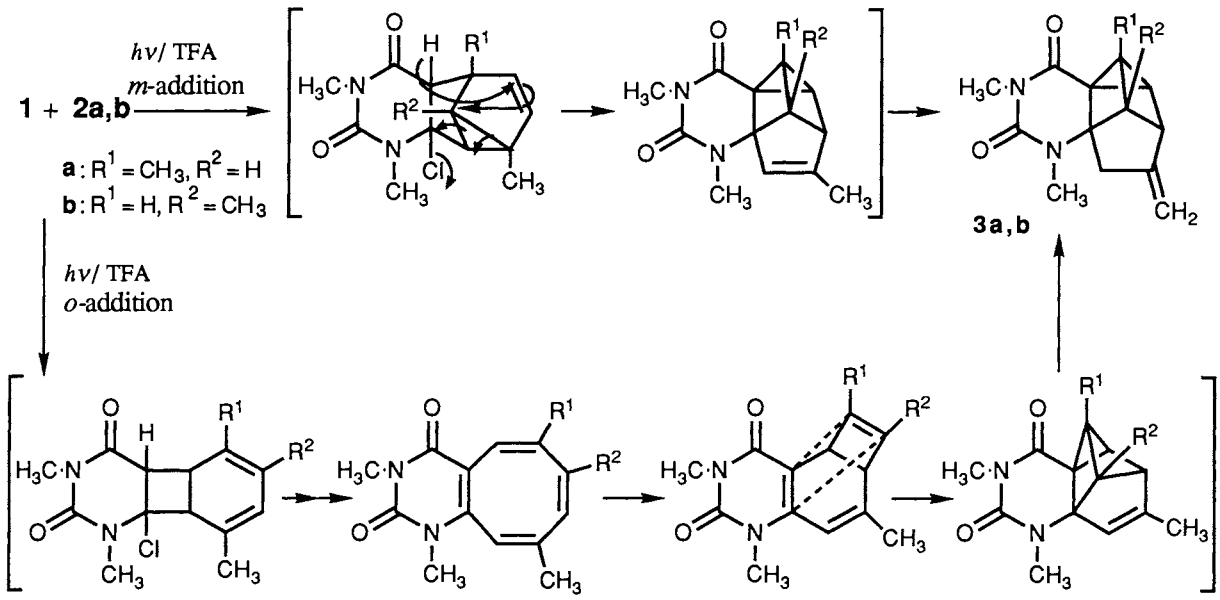


Fig.2. NOE Correlation for **3b**.

The formation of the pentacyclic compounds (**3a,b**) could be explained by the mechanism involving either *meta*- or *ortho*-cycloaddition[10] (Scheme 2). Isolation of the intermediate would provide the determinate evidence, but is unsuccessful at the present stage.[11]



Scheme 2.

The photoreaction of **1** in *p*-xylene (**2a**) under similar conditions but in the absence of TFA gave **5** (1.4%) and barely detectable **4a** (<0.1% on HPLC), together with a large amount of unreacted **1** (92%). No formation of **3a** was detected. The UV spectrum of **1** (λ_{max} 262 nm) (0.08 mmol • dm^{-3}) shifted *ca.* 6 nm to the red in cyclohexane by the addition of TFA (9 equiv. molar). This new spectrum was insensible to the added **2a**, whereas the fluorescence of this solution was quenched efficiently with **2a**. Taking into consideration that the incident light (λ>300 nm) is absorbed preferentially by **1** (87% at λ302 nm) under the conditions empolyed, the present reaction may result from the initial excitation of protonated **1** or the charge transfer complex of **1** and TFA.

Although the reaction pathway leading to **3** remains unclear, it is noteworthy that the present reaction provides the first construction of a pentacyclic system involving the pyrimidine ring fused to the tetracyclooctane moiety in the manner as to generate the *exo*-methylene group at the C-6.

Further studies on the scope and the mechanisms of the present photoreaction are in progress.

References

1) K. Seki, N. Kanazashi, and K. Ohkura, *Heterocycles*, **32**, 229 (1991); K. Ohkura, N. Kanazashi, and K. Seki, *Chem. Pharm. Bull.*, **41**, 239 (1993).

2) It is well recognized that photolysis of benzene and its simple derivatives produces *ortho*, *meta*, and less commonly *para*-cycloadducts with ethylenes: J. Mattay, *J. Photochem.*, **37**, 167 (1987); A. Gilbert, *Pure Appl. Chem.*, **52**, 2669 (1980).

3) **3a**: Mp 106-107 °C, recrystallized from ether. MS *m/z* (%): 244 (M^+, 28), 243 (100), 229 (63), 204 (94), 187 (18), 172 (20), 159 (16), 158 (37), 147 (80), 144 (33). ^{1}H-NMR (400 MHz, CD_3OD, TMS): δ = 1.45

(3H, s, C^3-$C\underline{H}_3$), 2.42 (1H, dt, J = 16.9, 2.5 Hz, H-7^a), 2.52 (1H, dt, J = 16.9, 2.5 Hz, H-7^b), 2.78 (1H, dd, J = 5.1, 4.4 Hz, H-4), 2.82 (1H, dd, J = 5.1, 2.6 Hz, H-2), 2.98 (3H, s, N^9-$C\underline{H}_3$), 3.20 (3H, s, N^{11}-$C\underline{H}_3$), 3.65 (1H, dd, J = 4.4, 2.6 Hz, H-5), 4.73 (1H, t, J = 2.5 Hz, C^6=CH^a),and 4.90 (1H, t, J = 2.5 Hz, C^6=CH^b). High-resolution (HR) MS: Anal. Found: 244.1212. Calcd for $C_{14}H_{16}N_2O_2$: 244.1211.

4) **4a**: Mp 104-105 °C (recrystallized from 2-propanol); MS *m/z* (%) 244 (M^+, 100), 229 (30); ^{1}H-NMR (400 MHz, acetone-d_6, TMS):[12] δ = 1.70 (3H, m, C^7-$C\underline{H}_3$), 1.93 (3H, t, J = 1.5 Hz, C^{10}-$C\underline{H}_3$), 3.22 (3H, s, N^3-$C\underline{H}_3$), 3.27 (3H, s, N^1-CH_3), 5.83 (1H, dd, J = 3.4, 1.0 Hz, H-8), 5.93 (1H, d, J = 11.2 Hz, H-6), 6.04 (1H, d, J = 3.4 Hz, H-9), 6.18 (1H, dd, J = 11.2, 1.0 Hz, H-5). Anal. Found: C, 68.80; H, 6.51; N, 11.45. Calcd for $C_{14}H_{16}N_2O_2$: C, 68.83; H, 6.60; N, 11.47.

5) K. Seki, K. Matsuda, Y. Bando, and K. Ohkura, *Chem. Pharm. Bull.*, **36**, 4737 (1988).

6) Yields are given on the basis of **1** consumed; 69% for **2a** and 43% for **2b**, respectively.

7) **3b**: Mp 132-134 °C, recrystallized from benzene-hexane. MS *m/z* (%): 244 (M^+, 43), 243 (100), 229 (54), 204 (36), 187 (26), 186 (14), 172 (22), 159 (31), 158 (49), 147 (38), 144 (38).^{1}H-NMR (400 MHz, acetone-d_6, TMS): δ = 1.18 (3H, s, C^4-$C\underline{H}_3$), 2.53 (1H, dt, J = 17.1, 2.3 Hz, H-7^a), 2.66 (1H, dt, J = 17.1, 2.3 Hz, H-7^b), 2.81 (1H, dd, J = 3.4, 2.4 Hz, H-2), 2.96 (3H, s, N^9-$C\underline{H}_3$), 3.08 (3H, s, N^{11}-$C\underline{H}_3$), 3.28 (1H, d, J = 2.4 Hz, H-5), 3.38 (1H, d, J = 3.4 Hz, H-3), 4.76 (1H, t, J = 2.3 Hz, C^6=CH^a), and 4.92 (1H, t, J = 2.3 Hz, C^6=CH^b). HRMS: Anal. Found: 244.1235. Calcd for $C_{14}H_{16}N_2O_2$: 244.1211.

8) **4b**: Mp 139-141 °C from 2-propanol. MS *m/z* (%) 244 (M^+, 100), 229 (29), 172 (44); ^{1}H-NMR (400 MHz, $CDCl_3$, TMS):[12] δ = 1.82 (3H, m, C^8-CH_3), 1.93 (3H, d, J = 1.5 Hz, C^{10}-CH_3), 3.32 (3H, s, N^1-CH_3), 3.35 (3H, s, N^3-CH_3), 5.70 (1H, d, J = 4.0 Hz, H-7), 5.97 (1H, d, J = 1.1 Hz, H-9), 6.02 (1H, ddd, J = 11.4, 4.0, 1.1 Hz, H-6), 6.26 (1H, d, J = 11.4 Hz, H-5). HRMS: Anal. Found: 244.1213. Calcd for $C_{14}H_{16}N_2O_2$: 244.1211.

9) X-Ray crystallography of **3a**: molecular formula, $C_{14}H_{16}N_2O_2$; molecular weight, 244.29; space group $P2_1/a$ (Z = 4), a = 15.089 (3), b = 14.652 (2), c = 7.672 (2) Å, β = 131.24 (1)°, V = 1275.3 (5) Å^3, Dx = 1.27 g/cm^3. Final R factor = 1601θ < 120°, | Fo | ≥ 2.67 σ.

10) A. H. A. Tinnemans and C. Neckers, *J. Am. Chem. Soc.*, **99**, 6460 (1977).

11) Photolysis of a solution of **4a** in **2a** in the presence of TFA afforded no pentacyclic derivative, suggesting that cyclooctapyrimidine derivatives are not involved as the intermediate leading to **3**, or that the presence of a methyl group of the cyclooctapyrimidine ring at C-9 may be essential for the formation of **3**.

12) The spin coupling constants were determined by the triple resonance method with irradiation at the peaks due to two methyl groups.

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