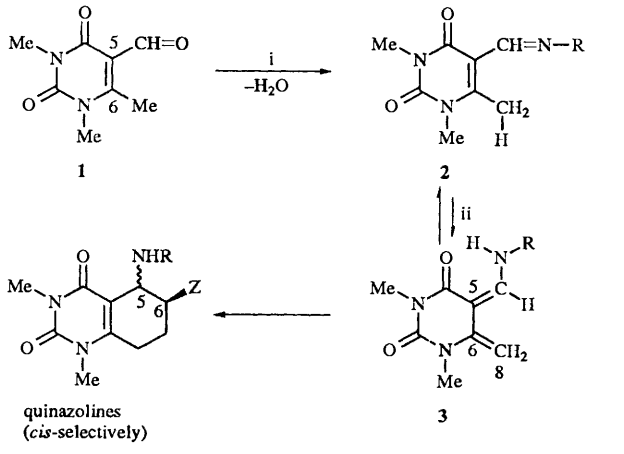
Studies on fused pyrimidine derivatives. Part 14.[1] Formation and transformation of [4 + 2] cycloadducts, cyclohepta[g]quinazoline derivatives, by the reaction of 5-(arylaminomethylene)-1,3-dimethyl-6-methyleneperhydropyrimidine-2,4-diones with tropone

Ken Ikuno,[a] Takashi Kobayashi,[a] Toshio Harada,[a] Michihiko Noguchi *[,a] and Akikazu Kakehi[b]
[a] *Department of Applied Chemistry, Faculty of Engineering, Yamaguchi University, Tokiwadai, Ube 755, Japan*
[b] *Department of Chemistry and Material Engineering, Faculty of Engineering, Shinshu University, Wakasato, Nagano 380, Japan*

The reaction of 5-(arylaminomethylene)-1,3-dimethyl-6-methyleneperhydropyrimidine-2,4-diones **3** with tropone **4** gave two diastereoisomeric [4 + 2] cycloadducts, cyclohepta[*g*]quinazolines **5** and **6**. These products correspond to *endo*- and *exo*-approach of enamine **3** to the 2,3-double bond of tropone **4**, respectively. The chemical behaviour of the *endo*- and *exo*-adducts will be discussed. The X-ray structures of 5-(4-bromoanilino)-1,3-dimethyl-2,3,4,*r*-5,*c*-5a,10,*c*-10a,11-octahydro-1*H*-cyclohepta[*g*]quinazoline-2,4,10-trione, 5-(4-bromoanilino)-1,3-dimethyl-2,3,4,*r*-5,*t*-5a,10,*t*-10a,11-octahydro-1*H*-cyclohepta[*g*]quinazoline-2,4,10-trione and 12,14-Dimethyl-*r*-6b,9,10,*c*-10a,11,12,13,14,15,*c*-15b,*c*-15c,16-dodecahydrobenzo[*c*]-cyclohepta[*kl*]pyrimido[5,4-*h*]acridine-10,13,15-trione are described.

In previous papers,[2] we described a generation of 5-(substituted aminomethylene)-1,3-dimethyl-6-methyleneperhydropyrimidine-2,4-dione intermediates **3** *via* a thermal 1,5-hydrogen shift of the corresponding 5-(substituted iminomethyl)-1,3,6-trimethyl-1,2,3,4-tetrahydropyrimidine-2,4-diones **2**. The intermediates **3** are regarded as a 1,3-diene located at the periphery of a heterocyclic system and underwent a single and regio- and stereo-selective [4 + 2] cycloaddition reaction with olefinic dienophiles to afford quinazoline derivatives (Scheme 1).



Scheme 1 *Reagents and conditions*: i, RNH_2, toluene or benzene, reflux; ii, 1,5-hydrogen shift; iii, methyl or ethyl acrylate (CH_2=CHZ)

Tropone 4 has emerged as one of the most typical multiple π-electron systems (*i.e.*, 2-, 4-, 6-, and 8π-systems) in the higher order cycloaddition reactions. Thermal reaction of simple dienes (4π) with tropone **4** proceed usually in the [4 + 6] manner utilising the 6π-component of tropone.[3] The [4 + 6] cycloaddition reaction, however, was suppressed by non-hydrogen substituents at the reaction sites, and therefore the [2 + 4] cycloaddition reaction predominated utilising the 2π-component of the diene and the 4π-component of tropone instead.[3c]

Only three examples were found for the [4 + 2] cycloaddition reaction of diene (4π) and tropone (2π); *o*-xylylene cycloadded to the 4,5-double bond of tropone to give a cyclohepta[*b*]naphthalene derivative together with the [4 + 6] cycloadduct as a minor product.[4] On the other hand, isobenzofuran reacted with tropone at its 2,3-double bond as well as giving the [4 + 6] cycloadduct.[5]

Tetrachlorocyclopentadienone ethylene ketal reacted with tropone to yield a 2:1 adduct resulting from double [4 + 2] cycloadditions on the 2,3- and 6,7-bond of tropone.[6]

We examined, therefore, the reaction of dienes **3** with tropone **4** in order to obtain further information on the reaction features of the diene.[3] The reaction of 5-(arylamino methylene)-1,3-dimethyl-6-methyleneperhydropyrimidine-2,4-diones **3** with tropone **4** gave two diastereoisomeric [4 + 2] cycloadducts, cyclohepta[*g*]quinazolines **5** and **6**, in moderate total yields. The cycloaddition of dienes **3** occurred regioselectively on the 2,3-double bond in tropone **4** and the adducts corresponded to *endo*- and *exo*-approaching products, respectively. These *endo*- and *exo*-[4 + 2] cycloadducts exhibited different behaviour toward acid treatment.

Results and discussion

[4 + 2] Cycloaddition of 5,6-dimethyleneperhydropyrimidine-2,4-diones 3 with tropone 4

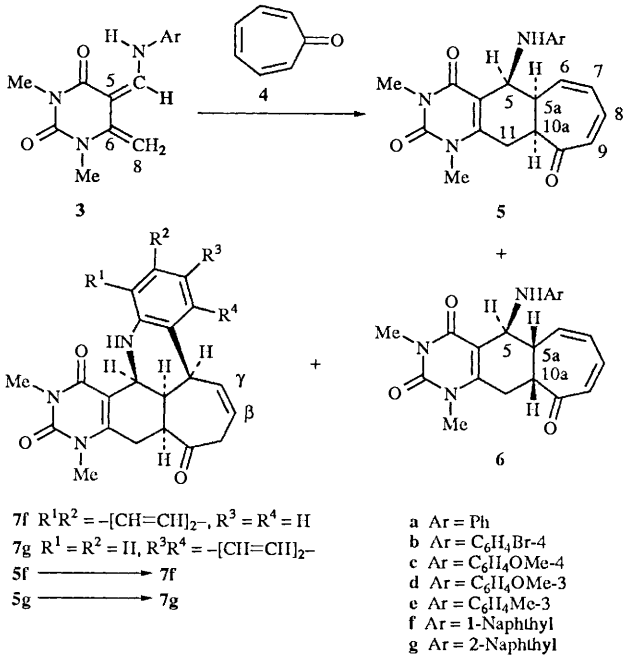
The reaction of 5-anilinomethylene-1,3-dimethyl-6-methyleneperhydropyrimidine-2,4-dione **3a**, formed *in situ* by the condensation and successive isomerisation of 1,3,6-trimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carbaldehyde **1** and aniline, with tropone **4** in 1,4-dioxane under reflux for 6 h gave two 1:1 adducts **5a** and **6a** in 26 and 25% yield, respectively, together with the formation of polymeric products (Scheme 2). The adducts **5a** and **6a** were shown to be primary products by the reaction of diene **3a** and with tropone **4** as follows; a similar reaction in benzene or tetrahydrofuran (THF) under reflux for 6 h gave almost a 1:1 mixture of **5a** and **6a** (Table 1) and no interconversion between **5a** and **6a** was observed under the above conditions.

The structures **5a** and **6a** were elucidated on the basis of spectral data. The ^{13}C NMR spectra of products **5a** and **6a** were in accord with each other over the sp^3- and sp^2-carbon ranges

Table 1 Reaction of 5-(arylaminomethylene)-1,3-dimethyl-6-methyleneperhydropyrimidine-2,4-diones **3** with tropone **4** (Scheme 2)

Entry	Ar	Solvent	Time (t/h)	Products (Yield[a]/%)		
1	Ph	1,4-dioxane	6	**5a** (26)	**6a** (25)	
2	Ph	benzene	6	**5a** (22)	**6a** (19)	
3	Ph	THF	6	**5a** (14)	**6a** (13)	
4	4-BrC_6H_4	1,4-dioxane	6	**5b** (19)	**6b** (20)	
5	4-$MeOC_6H_4$	1,4-dioxane	6	**5c** (17)	**6c** (23)	
6	3-$MeOC_6H_4$	1,4-dioxane	6	**5d** (24)	**6d** (22)	
7	3-MeC_6H_4	1,4-dioxane	6	**5e** (31)	**6e** (29)	
8	1-Naphthyl	1,4-dioxane	6	**5f** (15)	**6f** (27)	**7f** (12)
9	1-Naphthyl	1,4-dioxane	36		**6f** (25)	**7f** (27)
10	2-Naphthyl	toluene	6	**5g** and **7g** (22)[b]	**6g** (25)	
11	2-Naphthyl	1,4-dioxane	24		**6g** (15)	**7g** (15)

[a] Isolated yield. [b] Combined yield because tricycle **5g** was partly isomerised to hexacycle **7g** during purification.

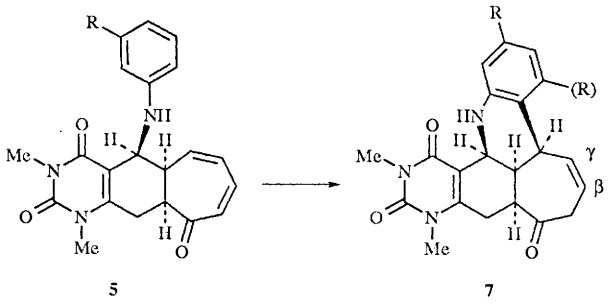


Scheme 2 Reaction of 5-(arylaminomethylene) diones **3** with tropone **4** in some refluxing solvents

except for only one sp^3-carbon signal, assigned to C-5a. The ^1H–^1H COSY spectra of compounds **5a** and **6a** revealed that both adducts had an alignment of methine (5-H), methine (5a-H), methine (10a-H), and methylene protons (11-H) as well as of olefin (9-H), olefin (8-H), olefin (7-H), olefin (6-H), and methine proton (5a-H). These findings indicate that the cycloaddition of diene **3a** occurs on the 2,3-double bond of tropone 4 and that the 5-(anilinomethylene)moiety of compound **3a** is orientated in the opposite direction to that of the tropone carbonyl group. The stereochemistry of the adducts **5a** and **6a** was assigned from the coupling constants between 5- and 5a-H; for adduct **5a** the methine proton at the 5-position was observed as a broad singlet (J ~ 0 Hz, 5,5a-*cis*), while that for **6a** appeared as a doublet (J 2.9 Hz, 5,5a-*trans*). The assignments were elucidated by nuclear overhauser enhancement (NOE) measurements of compounds **5a** and **6a**; irradiation of the 5a-H caused a remarkable enhancement of the 5-H signal for **5a** (18%) and a little for that for compound **6a** (1%). These suggest that tropone 4 adds formally to diene **3a** with a *Z*-configuration[2e] at the 5-methylene moiety in *endo*- and *exo*-manner to form 5-anilino-1,3-dimethyl-2,3,4,5,5a,10,10a,11-octahydro-1*H*-cyclohepta[*g*]quinazoline-2,4,10-triones **5a** and **6a**, respectively. More details on the reaction pathway will be discussed in the following paper.[7]

Similar reactions of 5-(4-bromoanilinomethylene)- **3b**, 5-(4-methoxyanilinomethylene)- **3c**, 5-(3-methoxyanilinomethylene)- **3d** and 5-(3-methylanilinomethylene)-substituted dione **3e** with tropone 4 gave mixtures of *endo*- and *exo*-adducts **5b–e** and **6b–e** in moderate total yields (Table 1). The structures of these adducts **5** and **6** were also assigned on the basis of their spectral data. Furthermore the structures of adducts **5b** and **6b** were unambiguously established by X-ray crystallographic analyses (see the Experimental section).

A similar reaction of 5-(1-naphthylaminomethylene)-substituted dione **3f** with tropone 4 in 1,4-dioxane under reflux for 6 h gave a mixture of three isomeric products **5f** (15%), **6f** (27%), and **7f** (12%) (Scheme 3). The proportions of the products



Scheme 3 Isomerisation of *endo*-cycloadducts **5** to acridines **7** in acid conditions (H^+ or Lewis acids)

depended upon the reaction conditions; prolonged heating (36 h) in 1,4-dioxane gave compounds **6f** (25%) and **7f** (27%). These results suggested that product **7f** was a secondary one from *endo*-adduct **5f** and, indeed, heating of compound **5f** in 1,4-dioxane under reflux gave compound **7f** (Table 2).

The structure of compound **7f** was assigned to be a benzo[*c*]cyclohepta[*kl*]pyrimido[5,4-*h*]acridine derivative on the basis of its spectral data, and was also confirmed by X-ray crystallographic analysis (see the Experimental section). These suggest that nucleophilic attack of the naphthalene π-electrons on the δ-position of the seven-membered α,β,γ,δ-unsaturated ketone moiety in compound **5f** takes place to give a hexacyclic system containing a seven-membered non-conjugated ketone (δ_{CO} 208.7).

Similar results were obtained by the reaction of 5-(2-naphthylaminomethylene)-substituted dione **3g** with tropone 4 in toluene or 1,4-dioxane under reflux which led to adducts **5g**, **6g**, and benzo[*a*]cyclohepta[*kl*]pyrimido[5,4-*h*]acridine **7g** (Scheme 2). Such transformation of tricycles **5** to hexacycles **7** was consistent with the results of PM3 calculations as described latter.

Table 2 Thermal and acid-assisted isomerisation of *endo*-adducts **5** to acridines **7**

Entry	Substrate	Solvent	Acid catalyst	Temp.	Time (t/h)	Products (Yield[a]/%)
1	**5f**	1,4-dioxane	none	reflux	6	**5f** (42), **7f** (42)
2	**5f**	EtOH	none	reflux	24	**7f** (91)
3	**5g**	EtOH	none	reflux	6	**7g** (quant.)
4	**5a**	EtOH	12 mol dm^{-3} HCl (1 drop)	reflux	2	**7a** (29)
5	**5d**	EtOH	0.5 mol dm^{-3} HCl (1 drop)	reflux	4	**7d** (61)
6	**5d**	CH_2Cl_2	$AlCl_3$ (0.2 mol equiv.)	ambient	12	**7d** (86)
7	**5e**	EtOH	0.5 mol dm^{-3} HCl (1 drop)	reflux	17	**7e** (52)[b]
8	**5e**	benzene	$BF_3(OEt_2)$ (0.1 mol equiv.)	reflux	1	**7e** (40)[b]

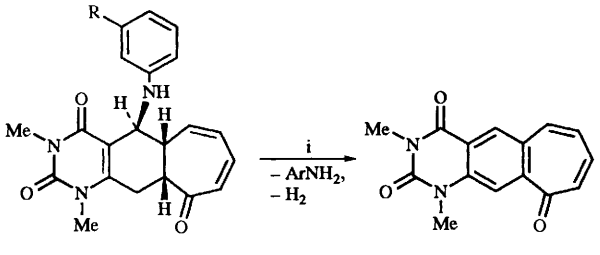
[a] Isolated yield. [b] Mixture (~ 1 : 1) of two isomers by its ^1H NMR spectrum.

The diene **3** added to the 2,3-double bond of tropone 4 regioselectively to afford *endo*- and *exo*-[4 + 2] cycloadducts **5** and **6** as mentioned above. The tropone 4, therein, behaved only as a 2π-component toward the diene 4π-system of compounds **3**. This is probably the first example reported of the thermal reactions of tropone with 4π-dienes.

Chemical behaviours of *endo*- and *exo*-[4 + 2] cycloadducts

In *endo*-adducts **5f** and **5g**, the π-electrons of the naphthylamino moiety at the 5-position underwent a nucleophilic ring closure to afford hexacyclic heterocycles **7f** and **7g** under the reaction conditions. Our next concern, therefore, was focused on the chemical behaviour of the [4 + 2] cycloadducts **5** and **6**. Other *endo*-adducts **5** than compounds **5f** and **5g** did not show any change under the reaction conditions; neither did any of the *exo*-[4 + 2] cycloadducts **6**. The isomerisation of tricycle **5f** to hexacycle **7f** was shown to proceed smoothly in ethanol under reflux (Table 2). Utilisation of proton or Lewis acids facilitated the isomerisation **5** ⟶ **7** (Scheme 3); treatment of compound **5a** with one drop of 12 mol dm^{-3} hydrochloric acid in ethanol under reflux for 2 h gave the acridine **7a** in 29% yield. Similarly, acridines **7d** and **7e** (as two regioisomers) were obtained by the treatment of *endo*-adducts **5d** and **5e** with protic and Lewis acids. The results of the transformation **5** ⟶ **7** upon acid treatment are summarised in Table 2.

On the other hand, treatment of *exo*-adducts **6a**, **6d** and **6e** with Lewis acids under similar conditions gave intractable mixtures of products. Prolonged heating of compounds **6a**, **6d** and **6e** in ethanol containing a higher concentration of hydrochloric acid led to 1,3-dimethyl-2,3,4,10-tetrahydro-1*H*-cyclohepta[*g*]quinazoline-2,4,10-trione **8** in low to fair yields along with mixtures of unidentified products (Scheme 4). The results of conversion **6** ⟶ **8** are demonstrated in Table 3. 1,4-Elimination of the arylamine, accompanied by dehydrogenation, from substitute **5** was postulated for the formation of cycloheptaquinazoline **8**.



6 **8**

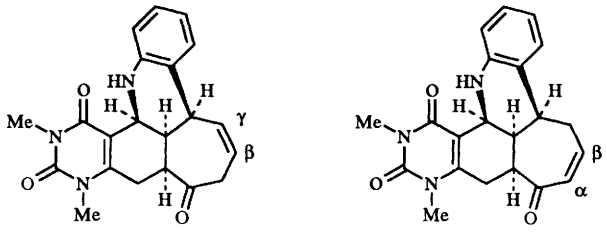
Scheme 4 *Reagent and conditions*: i, EtOH, hydrochloric acid, reflux

In order to obtain further information on the chemical behaviour of [4 + 2] cycloadducts **5** and **6**, PM3 molecular orbital calculations were examined. The structure optimisations of adducts **5a** and **6a** were performed by utilising the structures of compounds **5b** and **6b** as initial geometries. These revealed that the isomerisation of *endo*-adduct **5a** to hexacycle **7a** was a possible process and that, on the other hand, the nucleophilic attack of the anilino π-electrons in compound **6a** on the seven-membered unsaturated ketone moiety was impossible on structural grounds. The formation of the seven-membered β,γ-unsaturated ketone system in compounds **7** was also confirmed by the PM3 calculations; the heat of formation for compound **7a** (β,γ-unsaturated) was lower than that estimated for the regioisomer **7a'** (α,β-unsaturated) by 2.7 kcal mol^{-1}† (Fig. 1).

Table 3 Acid treatment of *exo*-adducts **6** leading to the cycloheptaquinazoline **8**

Entry	Substrate	Acid catalyst	Time (t/h)	Product (Yield[a]/%)
1	**6a**	12 mol dm^{-3} HCl (10 drops)	24	**8** (29)
2	**6d**	12 mol dm^{-3} HCl (1 drop)	20	**8** (48)
3	**6e**	12 mol dm^{-3} HCl (1 drop)	20	**8** (40)

[a] Isolated yield.



7a -54.31 kcal mol^{-1} **7a'** -51.61 kcal mol^{-1}

Fig. 1 Heats of formation for acridine derivatives **7a** and **7a'**. 1 cal = 4.184 J.

In conclusion, we have reported here that 5-(arylamino methylene)-6-methyleneperhydropyrimidine-2,4-dione intermediates **3** cycloadd to the 2,3-double bond of tropone 4 regioselectively to afford *endo*- and *exo*-[4 + 2] cycloadducts **5** and **6**. In *endo*-adduct **5** the π-electrons of the arylamino moiety attack the δ-position of α,β,γ,δ-unsaturated ketone system derived from the tropone to afford the acridine **7** under both neutral and acidic conditions.

Experimental

Mps were measured on a Yanagimoto micro melting point apparatus and are uncorrected. IR spectra were measured on a JASCO IR-Report-100 spectrophotometer from samples as

† 1 cal = 4.184 J.

KBr pellets. ^{1}H NMR and ^{13}C NMR spectra were measured on JEOL GSX-400 and/or 270 spectrometers for solutions in deuteriochloroform unless otherwise stated. Tetramethylsilane was used as internal standard and *J*-values are given in Hz; Splitting pattern ov indicates signals overlapping with each other. Mass spectra were determined on a JEOL JMS-021G-2 or JMS-D spectrometer. Elemental analyses were performed on a Hitachi 026 CHN analyser. All non-aqueous reactions were run under a positive pressure of argon. All solvents were dried by standard methods before use. The progress of reactions was monitored by TLC (Silica Gel 60F-254, Merck). Chromatographic purification was performed with Wakogel C-200 (100–200 mesh, Wako Pure Chemical Industries) and/or Silica Gel 60 (230–400 mesh, Merck).

Reaction of 5-anilinomethylene-1,3-dimethyl-6-methyleneperhydropyrimidine-2,4-dione 3a with tropone 4. General procedures

To a refluxing solution of tropone 4 (1.16 g, 10.0 mmol) in 1,4-dioxane (5 cm^3) were added solutions of 1,3,6-trimethyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidine-5-carbaldehyde **1** (0.182 g, 1.0 mmol) and aniline (0.109 cm^3, 1.3 mmol) in 1,4-dioxane (2.5 cm^3 each) *via* a double-barrelled microfeeder over a period of 3 h. The reaction mixture was heated under reflux for an additional 6 h and the solvent was then evaporated off under reduced pressure. The residue was subjected to column chromatography on silica gel with hexane–ethyl acetate (1 : 1) to give a mixture of the [4 + 2] cycloadducts **5a** and **6a** (0.188 g; **5a**:**6a** ~ 1:1). Flash chromatography of the mixture with hexane–ethyl acetate (2 : 1) gave *endo*- **5a** (26%) and *exo*-adduct **6a** (25%), respectively.

5-*Anilino*-1,3-*dimethyl*-2,3,4,r-5,c-5a,10,c-10a,11-*octahydro*-1H-*cyclohepta*[g]*quinazoline*-2,4,10-*trione* **5a** was obtained as orange plates from ethanol; mp 205–207 °C (Found: C, 69.2; H, 5.9; N, 11.4. $C_{21}H_{21}N_3O_3$ requires C, 69.40; H, 5.83; N, 11.56%); ν_{max}/cm^{-1} 3350 (NH) and 1680 and 1640 (CO); δ_H(270 MHz) 2.49 (1 H, dd, *J* 5.9 and 17.6, 11-H), 2.86 (1 H, br s, 5a-H), 3.10 (1 H, br, NH), 3.31 and 3.52 (each 3 H, each s, 1- and 3-Me), 3.43 (1 H, d, *J* 17.6, 11-H), 3.67 (1 H, m, 10a-H), 4.81 (1 H, br, 5-H), 5.89 (1 H, dd, *J* 7.8 and 11.7, 7-H), 6.00 (1 H, d, *J* 12.2, 9-H), 6.30–6.39 (2 H, ov, 6- and 8-H) and 6.56, 6.65 and 7.08 (total 5 H, Ph); δ_C (68 MHz) 27.4 (C-11), 28.2 (1-Me), 31.2 (3-Me), 43.4 (C-5a), 44.4 (C-10a), 49.4 (C-5), 108.4 (C-4a), 113.5, 117.7, 128.8 and 148.1 (Ph-C), 126.9 and 129.9 (C-7 and -9), 136.4 and 138.4 (C-6 and -8), 149.0 (C-11a), 151.9 (C-2), 161.5 (C-4) and 201.6 (C-10); *m*/*z* 364 (M$^+$).

5-*Anilino*-1,3-*dimethyl*-2,3,4,r-5,t-5a,10,t-10a,11-*octahydro*-1H-*cyclohepta*[g]*quinazoline*-2,4,10-*trione* **6a** was obtained as yellow plates from ethanol; mp 208–210 °C (Found C, 69.7; H, 5.7; N, 11.6%); ν_{max}/cm^{-1} 3380 (NH) and 1700, 1650 and 1640 (CO); δ_H(270 MHz) 2.62–2.72 (2 H, ov, 11-H$_2$), 3.21–3.28 (3 H, ov, 5a- and 10-H and NH), 3.28 and 3.39 (each 3 H, each s, 1- and 3-Me), 4.59 (1 H, d, *J* 2.9, 5-H), 5.89 (1 H, d, *J* 11.2, 6-H), 6.08 (1 H, d, *J* 12.7, 9-H), 6.17 (1 H, ddd, *J* 2.9, 7.3 and 11.2, 7-H), 6.60–6.65 (4 H, ov, 8-H and Ph) and 7.12 (2 H, Ph); δ_C(68 MHz) 23.3 (C-11a), 26.7 (1-Me), 29.5 (3-Me), 33.5 (C-5a), 44.1 (C-10a), 49.4 (C-5), 105.9 (C-4a), 111.2, 115.6, 125.9 and 145.8 (Ph-C), 127.9 and 129.2 (C-7 and -9), 136.4 and 138.1 (C-6 and -8), 149.7 (C-11a), 150.1 (C-2), 160.4 (C-4) and 199.0 (C-10); *m*/*z* 364 (M$^+$).

5-(4-*Bromoanilino*)-1,3-*dimethyl*-2,3,4,r-5,c-5a,10,c-10a,11-*octahydro*-1H-*cyclohepta*[g]*quinazoline*-2,4,10-*trione* **5b** was obtained as orange plates from ethanol; mp 206–208 °C (Found: C, 57.2; H, 4.6; N, 9.4. $C_{21}H_{20}BrN_3O_3$ requires C, 57.02; H, 4.57; N, 9.50%); ν_{max}/cm^{-1} 3360 (NH) and 1690 and 1650 (CO); δ_H(270 MHz) 2.50 (1 H, dd, *J* 5.9 and 17.6, 11-H), 2.84 (1 H, m, 5a-H), 3.07 (1 H, br, NH), 3.30 and 3.52 (each 3 H, each s, 1- and 3-Me), 3.43 (1 H, d, *J* 17.6, 11-H), 3.69 (1 H, m, 10a-H), 4.75 (1 H, dd, *J* 3.3 and 7.3, 5-H), 5.89 (1 H, dd, *J* 7.7 and 11.7, 7-H), 5.99 (1 H, d, *J* 12.8, 9-H), 6.30–6.37 (2 H, ov, 6- and 8-H) and 6.44 and 7.15 (total 4 H, ArH); δ_C(68 MHz) 27.3 (C-11), 28.2 (1-Me), 31.1 (3-Me), 43.3 (C-5a), 44.1 (C-10a), 49.3 (C-5), 107.9 (C-4a), 109.2, 114.9, 131.5 and 147.2 (Ph-C), 136.2 and 138.0 (C-6 and -8), 149.1 (C-11a), 151.8 (C-2), 161.5 (C-4) and 201.6 (C-10); *m*/*z* 443 and 441 (M$^+$).

5-(4-*Bromoanilino*)-1,3-*dimethyl*-2,3,4,r-5,t-5a,10,t-10a,11-*octahydro*-1H-*cyclohepta*[g]*quinazoline*-2,4,10-*trione* **6b** was obtained as pale yellow plates from ethanol; mp 200–203 °C (Found: C, 56.8; H, 4.6; N, 9.2%); ν_{max}/cm^{-1} 3350 (NH) and 1690 and 1650 (CO); δ_H(270 MHz) 2.54–2.69 (2 H, ov, 11-H$_2$), 3.21–3.29 (2 H, ov, 5a-H and NH), 3.35 and 3.38 (each 3 H, each s, 1- and 3-Me), 3.83 (1 H, br d, *J* 4.0, 10a-H), 5.59 (1 H, br, 5-H), 5.89 (1 H, br d, *J* 13.2, 6-H), 6.13–6.21 (2 H, ov, 7- and 9-H), 6.61 (1 H, dd, *J* 7.0 and 12.5, 8-H) 6.52 and 7.25 (total 4 H, ArH); δ_C(68 MHz) 24.8 (C-11), 28.3 (1-Me), 31.0 (3-Me), 35.0 (C-5a), 46.1 (C-10a), 51.7 (C-5), 107.2 (C-4a), 110.1, 114.9, 132.9 and 145.5 (Ph-C), 137.7 and 138.7 (C-6 and -8), 151.2 and 151.5 (C-2 and -11a), 162.0 (C-4) and 200.3 (C-10); *m*/*z* 443 and 441 (M$^+$).

Structures of compounds **5b** and **6b** were confirmed by X-ray crystal-structure analyses and their crystal data are summarised in Table 4 (see below).

5-(4-*Methoxyanilino*)-1,3-*dimethyl*-2,3,4,r-5,c-5a,10,c-10a,11-*octahydro*-1H-*cyclohepta*[g]*quinazoline*-2,4,10-*trione* **5c** was obtained as orange plates from ethanol; mp 192–194 °C (Found: C, 67.4; H, 6.0; N, 10.8. $C_{22}H_{23}N_3O_4$ requires C, 67.16; H, 5.89; N, 10.68%); ν_{max}/cm^{-1} 3350 (NH) and 1690 and 1640 (CO); δ_H(270 MHz) 2.49 (1 H, dd, *J* 6.2 and 17.6, 11-H), 2.85 (1 H, br, 5a-H), 3.30 and 3.51 (each 3 H, each s, 1- and 3-Me), 3.40 (1 H, d, *J* 17.6, 11-H), 3.62 (1 H, br, 10a-H), 3.71 (3 H, s, OMe), 3.30–3.71 (1 H, br, NH), 4.69 (1 H, br, 5-H), 5.91 (1 H, dd, *J* 7.7 and 11.5, 7-H), 5.99 (1 H, d, *J* 12.5, 9-H), 6.30–6.40 (2 H, ov, 6- and 8-H) and 6.56 and 6.69 (total 4 H, ArH); δ_C(68 MHz) 27.3 (C-11), 28.2 (1-Me), 31.1 (3-Me), 43.1 and 44.5 (C-5a and -10a), 50.9 (C-5), 55.7 (OMe), 108.7 (C-4a), 114.4, 115.2, 142.4 and 152.3 (Ph-C), 126.7 and 130.3 (C-7 and -9), 136.3 and 138.5 (C-6 and -8), 149.0 (C-11a), 151.9 (C-2), 161.6 (C-4) and 201.4 (C-10); *m*/*z* 393 (M$^+$).

5-(4-*Methoxyanilino*)-1,3-*dimethyl*-2,3,4,r-5,t-5a,10,t-10a,11-octahydro-1H-*cyclohepta*[g]*quinazoline*-2,4,10-*trione* **6c** was obtained as pale orange plates from ethanol; mp 192–194 °C (Found: C, 67.3; H, 6.0; N, 10.7%); ν_{max}/cm^{-1} 3380 (NH) and 1700, 1660 and 1640 (CO); δ_H(270 MHz) 2.53–2.71 (2 H, ov, 11-H$_2$), 3.30–3.38 (3 H, ov, 5a- and 10a-H and NH), 3.36 and 3.38 (each 3 H, each s, 1- and 3-Me), 3.73 (3 H, s, OMe), 4.56 (1 H, d, *J* 2.6, 5-H), 5.86 (1 H, d, *J* 11.4, 6-H), 6.11–6.18 (2 H, ov, 7- and 9-H), 6.58 (1 H, dd, *J* 7.0 and 12.5, 8-H) and 6.65 and 6.78 (total 4 H, ArH); δ_C(68 MHz) 24.9 (C-11), 28.2 (1-Me), 31.0 (3-Me), 35.1 (C-5a), 45.9 (C-10a), 52.9 (C-5), 55.8 (OMe), 107.8 (C-4a), 115.0, 115.6, 140.7 and 153.0 (Ph-C), 127.5 and 131.0 (C-7 and -9), 137.6 and 139.3 (C-6 and -8), 151.1 and 151.6 (C-2 and -11a), 162.2 (C-4) and 200.5 (C-10); *m*/*z* 393 (M$^+$).

5-(3-*Methoxylanilino*)-1,3-*dimethyl*-2,3,4,r-5,c-5a,10,c-10a,11-*octahydro*-1H-*cyclohepta*[g]*quinazoline*-2,4,10-*trione* **5d** was obtained as yellow prisms from ethanol; mp 191–193 °C (Found: C, 67.5; H, 5.9; N, 10.5%); ν_{max}/cm^{-1} 3350 (NH) and 1690, 1650 and 1640 (CO); δ_H(270 MHz) 2.49 (1 H, dd, *J* 6.2 and 17.6, 11-H), 2.86 (1 H, br, 5a-H), 3.13 (1 H, br, NH), 3.30 and 3.51 (each 3 H, each s, 1- and 3-Me), 3.41 (1 H, d, *J* 17.6, 11-H), 3.65 (1 H, br, 10a-H), 3.72 (3 H, s, OMe), 4.78 (1 H, br, 5-H), 5.91 (1 H, dd, *J* 7.7 and 11.4, 7-H), 5.99 (1 H, d, *J* 13.1, 9-H), 6.31–6.40 (2 H, ov, 6- and 8-H) and 6.11–6.24 and 6.99 (total 4 H, ArH); δ_C(68 MHz) 27.3 (C-11), 28.2 (1-Me), 31.1 (3-Me), 43.2 (C-5a), 43.2 and 44.5 (C-5a and -10a), 49.5 (C-5), 55.0 (OMe), 99.8, 102.8, 106.7, 129.4, 149.1 and 160.3 (Ph-C), 108.2 (C-4a), 126.8 and 129.9 (C-7 and -9), 136.5 and 138.3 (C-6

and -8), 149.5 (C-11a), 151.9 (C-2), 161.6 (C-4) and 201.4 (C-10); *m/z* 393 (M^+).

5-(3-*Methoxylanilino*)-1,3-*dimethyl*-2,3,4,r-5,t-5a,10,t-10a,11-*octahydro*-1H-*cyclohepta*[g]*quinazoline*-2,4,10-*trione* **6d** was obtained as pale yellow plates from ethanol; mp 165–167 °C (Found: C, 67.14; H, 5.80; N, 10.6%); ν_{max}/cm^{-1} 3360 (NH) and 1700, 1690 and 1650 (CO); δ_H(270 MHz) 2.53–2.72 (2 H, ov, 11-H_2), 3.24–3.39 (2 H, ov, 5a- and 10a-H), 3.36 and 3.39 (each 3 H, each s, 1- and 3-Me), 3.75 (3 H, s, OMe), 4.64 (1 H, d, *J* 2.6, 5-H), 5.87 (1 H, d, *J* 3.3 and 12.5, 6-H), 6.12–6.32 (5 H, ov, 7- and 9-H and ArH), 6.59 (1 H, dd, *J* 7.0 and 12.5, 8-H) and 7.09 (1 H, t, *J* 8.1, ArH); δ_C(68 MHz) 24.9 (C-11), 28.3 (1-Me), 31.0 (3-Me), 35.1 (C-5a), 46.2 (C-10a), 51.6 (C-5), 55.1 (OMe), 99.7, 103.2, 106.4, 130.2, 147.8 and 160.8 (Ph-C), 107.5 (C-4a), 127.6 and 131.0 (C-7 and -9), 137.7 and 139.0 (C-6 and -8), 151.1 and 151.6 (C-2 and -11a), 162.0 (C-4) and 200.4 (C-10); *m/z* 393 (M^+).

1,3-*Dimethyl*-5-(m-*toluidino*)-2,3,4,r-5,c-5a,10,c-10a,11-*octahydro*-1H-*cyclohepta*[g]*quinazoline*-2,4,10-*trione* **5e** was obtained as orange prisms from ethanol; mp 199 °C (Found: C, 70.1; H, 6.2; N, 11.0. $C_{22}H_{23}N_3O_3$ requires C, 70.01; H, 6.14; N, 11.12%); ν_{max}/cm^{-1} 3350 (NH) and 1690 and 1640 (CO); δ_H(270 MHz) 2.21 (3 H, s, Me), 2.49 (1 H, dd, *J* 5.9 and 18.0, 11-H), 2.87 (1 H, br, 5a-H), 3.08 (1 H, br, NH), 3.30 and 3.51 (each 3 H, each s, 1- and 3-Me), 3.40 (1 H, d, *J* 17.6, 11-H), 3.64 (1 H, br, 10a-H), 4.79 (1 H, br, 5-H), 5.90 (1 H, dd, *J* 8.1 and 11.7, 7-H), 5.99 (1 H, d, *J* 12.5, 9-H), 6.30–6.49 (5 H, ov, 6- and 8-H and ArH), 6.98 (1 H, dd, *J* 7.3 and 7.8, ArH); δ_C(68 MHz) 21.7 (Me), 27.3 (C-11), 28.2 (1-Me), 31.1 (3-Me), 43.2 (C-5a), 44.5 (C-10a), 49.6 (C-5), 108.4 (C-4a), 110.6, 114.5, 118.8, 128.5, 138.3 and 148.1 (Ph-C), 136.3 and 138.4 (C-6 and -8), 149.0 (C-11a), 151.9 (C-2), 161.5 (C-4) and 201.5 (C-10); *m/z* 377 (M^+).

1,3-*Dimethyl*-5-(m-*toluidino*)-2,3,4,r-5,t-5a,10,t-10a,11-*octahydro*-1H-*cyclohepta*[g]*quinazoline*-2,4,10-*trione* **6e** was obtained as yellow needles from ethanol; mp 214–215 °C (Found: C, 69.7; H, 6.2; N, 10.9%); ν_{max}/cm^{-1} 3350 (NH) and 1690, 1650 and 1640 (CO); δ_H(270 MHz) 2.26 (3 H, s, Me), 2.49–2.70 (2 H, ov, 11-H_2), 3.25–3.36 (3 H, ov, 5a- and 10a-H and NH), 3.36 and 3.39 (each 3 H, each s, 1- and 3-Me), 4.66 (1 H, d, *J* 2.6, 5-H), 5.89 (1 H, br d, *J* 10.4, 6-H), 6.13–6.20 (2 H, ov, 7- and 9-H), 6.44–6.46 (2 H, ArH), 6.56–6.63 (2 H, ov, 8-H and ArH) and 7.07 (1 H, dd, *J* 7.3 and 7.7, ArH); δ_C(68 MHz) 21.7 (Me), 24.9 (C-11), 28.3 (1-Me), 31.0 (3-Me), 35.1 (C-5a), 46.1 (C-10a), 51.6 (C-5), 107.6 (C-4a), 110.4, 114.2, 119.4, 129.3, 139.1, and 146.5 (Ph-C), 127.6 and 131.0 (C-7 and -9), 137.6 and 139.1 (C-6 and -8), 151.0 and 151.6 (C-2 and -11a), 162.0 (C-4) and 200.4 (C-10); *m/z* 377 (M^+).

1,3-*Dimethyl*-5-(1-*naphthylamino*)-2,3,4,r-5,c-5a,10,c-10a,11-*octahydro*-1H-*cyclohepta*[g]*quinazoline*-2,4,10-*trione* **5f** was obtained as orange crystals and was subjected to analytical treatment without recrystallisation; mp 160–162 °C (Found: C, 72.2; H, 5.7; N, 9.9. $C_{25}H_{23}N_3O_3$ requires C, 72.62; H, 5.61; N, 10.16%); ν_{max}/cm^{-1} 3400 (NH) and 1700, 1650 and 1640 (CO); δ_H(270 MHz) 2.52 (1 H, dd, *J* 5.9 and 17.6, 11-H), 2.96 (1 H, m, 5a-H), 3.27 and 3.53 (each 3 H, each s, 1- and 3-Me), 3.27–3.53 (2 H, ov, 11-H and NH), 3.71 (1 H, m, 10a-H), 5.09 (1 H, br, 5-H), 5.76 (1 H, dd, *J* 7.7 and 11.7, 7-H), 5.89 (1 H, d, *J* 12.1, 9-H), 6.11 (1 H, dd, *J* 7.7 and 12.1, 8-H), 6.33 (1 H, dd, *J* 6.6 and 11.7, 6-H) and 6.85, 7.14–7.42 and 7.67–7.71 (total 7 H, ArH); δ_C(68 MHz) 27.4 (C-11), 28.1 (1-Me), 31.0 (3-Me), 43.4 and 44.5 (C-5a and -10a), 48.2 (C-5), 108.2 (C-4a), 106.0, 117.4, 120.5, 123.9, 124.5, 125.4, 126.1, 128.3, 134.4 and 143.1 (naphthyl-C), 126.5 and 130.0 (C-7 and -9), 136.1 and 138.4 (C-6 and -8), 149.6 and 151.8 (C-2 and -11a), 161.6 (C-4) and 201.8 (C-10); *m/z* 413 (M^+).

1,3-*Dimethyl*-5-(1-*naphthylamino*)-2,3,4,r-5,t-5a,10,t-10a,11-*octahydro*-1H-*cyclohepta*[g]*quinazoline*-2,4,10-*trione* **6f** was obtained as yellow needles from ethanol–chloroform; mp 224–225 °C (Found: C, 72.5; H, 5.6; N, 10.2%); ν_{max}/cm^{-1} 3400 (NH) and 1700, 1660 and 1640 (CO); δ_H(270 MHz) 2.58–2.78 (2 H, ov, 11-H_2), 3.41 and 3.51 (each 3 H, each s, 1- and 3-Me), 3.36–3.50 (3 H, ov, 5a- and 10a-H and NH), 4.88 (1 H, d, *J* 2.2, 5-H), 5.95 (1 H, br d, *J* 11.4, 6-H), 6.11–6.22 (2 H, ov, 7- and 9-H), 6.59 (1 H, dd, *J* 7.0 and 12.5, 8-H) and 6.76, 7.26–7.46 and 7.76–7.79 (total 7 H, naphthyl-H); δ_C(68 MHz) 25.1 (C-11), 28.3 (1-Me), 31.0 (3-Me), 34.3 (C-5a), 46.6 (C-10a), 51.7 (C-5), 107.4 (C-4a), 105.6, 118.8, 120.2, 124.1, 124.9, 125.8, 126.3, 128.6, 134.4 and 141.5 (naphthyl-C), 127.7 and 131.1 (C-7 and -9), 137.6 and 139.0 (C-6 and -8), 151.4 and 151.6 (C-2 and -11a), 162.2 (C-4) and 200.5 (C-10); *m/z* 413 (M^+).

12,14-*Dimethyl*-r-6b,9,10,c-10a,11,12,13,14,15,c-15b,c-15c,16-*dodecahydrobenzo*[c]*cyclohepta*[kl]*pyrimido*[5,4-h]*acridine*-10,13,15-*trione* **7f** was obtained as pale brown plates from ethanol–dichloromethane; mp 241–243 °C (Found: C, 72.7; H, 5.6; N, 10.2%); ν_{max}/cm^{-1} 3380 (NH) and 1700, 1680 and 1660 (CO); δ_H(270 MHz) 2.39 (1 H, dd, *J* 6.2 and 18.3, 11-H), 2.57 (1 H, dd, *J* 8.1 and 19.8, 9-H), 2.74–2.86 (2 H, ov, 9- and 15c-H), 3.31 (1 H, dd, *J* 1.1 and 18.3, 11-H), 3.41 and 3.51 (each 3 H, each s, 12- and 14-Me), 3.78 (1 H, dd, *J* 6.2 and 6.4, 10a-H), 4.39 (1 H, d, *J* 3.7, 15b-H), 4.44 (1 H, t, *J* 9.9, 6b-H), 4.86 (1 H, br, NH), 5.91 (1 H, ddd, *J* 4.4, 8.1, and 10.4, 8-H), 6.59 (1 H, ddd, *J* 2.9, 9.9, and 10.4, 7-H), 7.15 (1 H, d, *J* 8.4, 5-H), 7.26 (1 H, d, *J* 8.4, 1-H), 7.37–7.44 (2 H, ov, 2- and 3-H) and 7.63–7.75 (2 H, ov, 4- and 6-H); δ_C(68 MHz) 26.6 (C-11), 28.2 (12-Me), 31.0 (14-Me), 37.1 and 38.0 (C-9 and -15c), 41.5 and 43.8 (C-6b and -10a), 48.9 (C-15b), 107.3 (C-15a), 117.6 (C-6a), 119.4 and 119.9 (C-1 and -5), 122.8 (C-16b), 125.5 and 125.6 (C-2 and -3), 127.4, 128.2, 128.4 and 132.6 (C-4, -6, -7 and -8), 135.4 (C-4a), 140.8 (C-16a), 149.9 and 151.9 (C-11a and -13), 162.7 (C-15), and 208.7 (C-10); *m/z* 413 (M^+).

The reaction mixture of 5-(2-naphthylamino)-substituted dione **3g** with tropone 4 was heated under reflux for 6 h. Usual work-up with short-column chromatography on silica gel gave a mixture of *endo*- **5g** and *exo*-adduct **6g** (in total yield of 47%). *endo*-Adduct **5g** was partly isomerised to the acridine **7f** during further purification.

1,3-*Dimethyl*-5-(2-*naphthylamino*)-2,3,4,r-5,c-5a,10,c-10a,11-*octahydro*-1H-*cyclohepta*[g]*quinazoline*-2,4,10-*trione* **5g** was obtained as orange crystals and was subjected to analytical treatment without recrystallisation; mp 203–205 °C (Found: C, 72.2; H, 5.8; N, 9.7%); ν_{max}/cm^{-1} 3380 (NH) and 1700, 1660 and 1650 (CO); δ_H(270 MHz) 2.48 (1 H, dd, *J* 5.9 and 17.6, 11-H), 2.91 (1 H, m, 5a-H), 3.30 and 3.52 (each 3 H, each s, 1- and 3-Me), 3.42 (1 H, br d, *J* 17.6, 11-H), 3.30–3.52 (1 H, ov, NH), 3.67 (1 H, m, 10a-H), 4.96 (1 H, br, 5-H), 5.81 (1 H, dd, *J* 7.8 and 11.7, 7-H), 6.00 (1 H, d, *J* 12.2, 9-H), 6.26 (1 H, dd, *J* 7.8 and 12.2, 8-H), 6.40 (1 H, dd, *J* 6.8 and 11.7, 6-H) and 6.73, 6.90, 7.15, 7.31 and 7.52–7.62 (total 7 H, naphthyl-H); δ_C(68 MHz) 27.4 (C-11), 28.3 (1-Me), 31.0 (3-Me), 43.4 and 44.5 (C-5a and -10a), 48.2 (C-5), 108.2 (C-4a), 106.2, 117.4, 120.5, 123.9, 124.5, 125.4, 126.1, 134.4 and 143.1 (naphthyl-C), 126.5 and 130.0 (C-7 and -9), 128.3 (C-3), 136.1 and 138.4 (C-6 and -8), 149.6 (C-11a), 151.8 (C-2), 161.6 (C-4) and 201.8 (C-10); *m/z* 413 (M^+).

1,3-*Dimethyl*-5-(2-*naphthylamino*)-2,3,4,r-5,t-5a,10,t-10a,11-*octahydro*-1H-*cyclohepta*[g]*quinazoline*-2,4,10-*trione* **6g** was obtained as yellow needles from ethanol–chloroform; mp 172–174 °C (Found: C, 72.5; H, 5.8; N, 9.9%); ν_{max}/cm^{-1} 3350 (NH) and 1720, 1700 and 1650 (CO); δ_H(270 MHz) 2.53–2.70 (2 H, ov, 11-H_2), 3.24–3.34 (1 H, ov, 5a-H), 3.34 and 3.35 (each 3 H, each s, 1- and 3-Me), 3.46 (1 H, m, 10a-H), 3.98 (1 H, br, NH), 4.78 (1 H, d, *J* 2.2, 5-H), 5.93 (1 H, br d, *J* 11.4, 6-H), 6.09–6.20 (2 H, ov, 7- and 9-H), 6.56 (1 H, dd, *J* 7.0 and 12.5, 8-H) and 6.83–6.87, 7.20, 7.35 and 7.59–7.66 (total 7 H, naphthyl-H); δ_C(68 MHz) 24.8 (C-11), 28.2 (1-Me), 30.9 (3-Me), 34.7 (C-5a), 46.2 (C-10a), 51.6 (C-5), 107.2 (C-4a), 105.1, 118.2, 122.3, 126.0,

126.3, 127.5, 127.9, 130.9, 134.9 and 144.0 (naphthyl-C), 127.6 and 130.9 (C-7 and -9), 137.6 and 139.0 (C-6 and -8), 151.2 and 151.4 (C-2 and -11a), 162.0 (C-4) and 200.3 (C-10); *m/z* 413 (M^+).

10,12-*Dimethyl*-r-4c,7,8,c-8a,9,10,11,12,13,c-13b,c-13c,14-*dodecahydrobenzo*[a]*cyclohepta*[kl]*pyrimido*[5,4-h]*acridine*-8,11,13-*trione* **7g** was obtained as prisms from ethanol–dichloromethane; mp 260 °C (decomp.) (Found: C, 72.4; H, 5.5; N, 9.85%); ν_{max}/cm^{-1} 3350 (NH) and 1690 and 1650 (CO); $\delta_H(CF_3CO_2D$; 270 MHz) 2.62 (1 H, br d, *J* 19.5, 9-H), 3.09–3.24 (2 H, ov, 7-H_2), 3.47 (1 H, d, *J* 19.5, 9-H), 3.60 and 3.72 (each 3 H, each s, 10- and 12-Me), 3.60–3.84 (2 H, ov, 13c-H and NH), 4.54 (1 H, br, 8a-H), 5.08 (1 H, t, *J* 8.3, 4b-H), 5.28 (1 H, br s, 13b-H), 6.05 (1 H, m, 6-H), 6.93 (1 H, m, 5-H), 7.45 (1 H, d, *J* 8.8, 15-H), 7.71 (2 H, ov, 2- and 3-H), 8.01 (2 H, ov, 1- and 4-H) and 8.11 (1 H, br d, *J* 7.3, 16-H); *m/z* 413 (M^+).

Conversion of *endo*-adducts 5 into acridines 7

General procedures for treatment with hydrochloric acid. A solution of *endo*-adduct **5a** (0.100 g, 0.28 mmol) in ethanol (5 cm^3) containing one drop of 12 mol dm^{-3} hydrochloric acid was heated under reflux for 12 h. Usual work-up with column chromatography gave the acridine **7a** (0.029 g, 29%).

10,12-*Dimethyl*-r-4b,7,8,c-8a,9,10,11,12,13,c-13b,c-13c,14-*dodecahydrocyclohepta*[mn]*pyrimido*[4,5-c]*acridine*-8,11,13-*trione* **7a** was obtained as plates from ethanol–chloroform; mp 268 °C (decomp.) (Found: C, 69.1; H, 5.85; N, 11.5. $C_{21}H_{21}N_3O_3$ requires C, 69.40; H, 5.83; N, 11.56%); ν_{max}/cm^{-1} 3350 (NH) and 1690, 1650 and 1645 (CO); δ_H(270 MHz) 2.39 (1 H, dd, *J* 7.3 and 18.3, 9-H), 2.66 (1 H, dd, *J* 7.3 and 19.8, 7-H), 2.77 (1 H, ddd, *J* 3.7, 5.9 and 9.5, 13c-H), 2.90 (1 H, ddd, *J* 2.9, 4.4 and 19.8, 7-H), 3.31 (1 H, d, *J* 18.3, 9-H), 3.37 and 3.50 (each 3 H, each s, 10- and 12-Me), 3.76 (1 H, dd, *J* 5.9 and 7.3, 8a-H), 3.88 (1 H, br, NH), 4.27–4.34 (2 H, ov, 4b- and 13b-H), 5.93 (1 H, ddd, *J* 4.4, 7.3 and 10.3, 6-H), 6.53–6.61 (2 H, ov, 1- and 5-H), 6.75 (1 H, t, *J* 7.3, 3-H) and 6.97–7.05 (2 H, ov, 2- and 4-H); *m/z* 363 (M^+).

General procedures for treatment with lewis acids. A solution of *endo*-adduct **5d** (0.050 g, 0.13 mmol) and aluminium chloride (0.004 g, 0.12 mmol) in dry dichloromethane (3 cm^3) was stirred at room temperature for 12 h. The reaction mixture was washed with water and the aqueous layer was extracted with dichloromethane. The combined organic layer was dried ($MgSO_4$) and evaporated to dryness. The residue was subjected to column chromatography on silica gel with hexane–ethyl acetate (1 : 2) which gave the acridine **7d** (0.043 g, 86%).

2-Methoxy-10,12-dimethyl-*r*-4b,7,8,*c*-8a,9,10,11,12,13,*c*-13b,*c*-13c,14-dodecahydrocyclohepta[*mn*]pyrimido[4,5-*c*]acridine-8,11,13-trione **7d** was obtained as pale yellow prisms from ethanol–chloroform; mp 231–233 °C; ν_{max}/cm^{-1} 3340 (NH) and 1690, 1650 and 1640 (CO); δ_H(270 MHz) 2.39 (1 H, dd, *J* 7.3 and 18.1, 9-H), 2.66 (1 H, dd, *J* 7.8 and 19.5, 7-H), 2.74 (1 H, ddd, *J* 3.4, 6.4 and 9.8, 13c-H), 2.90 (1 H, ddd, *J* 2.9, 4.4 and 19.5, 7-H), 3.30 (1 H, dd, *J* 1.5 and 18.1, 9-H), 3.37 and 3.49 (each 3 H, each s, 10- and 12-Me), 3.71 (3 H, s, OMe), 3.74 (1 H, dd, *J* 6.4 and 7.3, 8a-H), 3.71–3.74 (1 H, br, NH), 4.23 (1 H, t, *J* 9.8, 4b-H), 4.34 (1 H, d, *J* 3.4, 13b-H), 5.91 (1 H, ddd, *J* 4.4, 7.8 and 10.3, 6-H), 6.06 (1 H, d, *J* 2.4, 1-H), 6.34 (1 H, dd, *J* 2.4 and 8.3, 3-H), 6.55 (1 H, ddd, *J* 2.9, 9.8 and 10.3, 5-H) and 6.92 (1 H, d, *J* 8.3, 4-H); δ_C(68 MHz) 26.3 (C-9), 28.1 (10-Me), 30.9 (12-Me), 36.0 and 38.1 (C-7 and -13c), 41.7 and 43.5 (C-4b and -8a), 48.2 (C-13b), 55.1 (OMe), 99.4 (C-1), 107.3 and 107.2 (C-3 and -13a), 116.0 (C-4a), 127.9 and 130.0 (C-5 and -6), 136.0 (C-4), 146.9 (C-14a), 149.9 (C-9a), 151.8 (C-11), 158.5 (C-2), 162.4 (C-13) and 208.9 (C-8); *m/z* 393 (M^+).

A similar conversion of *endo*-adduct **5e** gave a ~ 1 : 1 mixture of 2,10,12-trimethyl-(**7e-1**) and 4,10,12-trimethyl-*r*-4b,7,8,*c*-8a,9,10,11,12,13,*c*-13b,*c*-13a,14-dodecahydrocyclohepta[*mn*]-pyrimido[4,5-*c*]acridine-8,11,13-trione (**7e–2**). These isomers could not be separated from each other by the usual procedures. The acridine **7e** was obtained as pale yellow prisms from ethanol–chloroform; mp 273–275 °C (decomp.) (Found: C, 70.1; H, 6.1; N, 11.0. $C_{22}H_{23}N_3O_3$ requires C, 70.01; H, 6.14; N, 11.13%); ν_{max}/cm^{-1} 3350 (NH) and 1690, 1650 and 1640 (CO); *m/z* 377 (M^+); δ_H(270 MHz) 2.21 and 2.29 (each 3 H, each s, Me), 2.30–2.42 (total 2 H, ov, 2 × 9-H), 2.60–2.68 (total 2 H, ov, 2 × 7-H), 2.74 (1 H, ddd, *J* 2.2, 4.9 and 19.5, 13c-H) and 2.83 (1 H, ddd, *J* 3.4, 5.4 and 19.1, 13c-H), 2.93 (1 H, ddd, *J* 2.9, 4.4 and 19.5, 7-H) and 3.17 (1 H, ddd, *J* 2.9, 4.9 and 19.1, 7-H), 3.24 (1 H, dd, *J* 1.0 and 18.1, 9-H) and 3.30 (1 H, dd, *J* 1.0 and 18.1, 9-H), 3.37, 3.38, 3.45 and 3.51 (each 3 H, each s, 10- and 12-Me), 3.73 (1 H, dd, *J* 6.0 and 6.8, 8a-H) and 3.78 (1 H, dd, *J* 5.4 and 6.0, 8a-H), 3.88 (total 2 H, ov, 2 × NH), 4.16 (1 H, d, *J* 2.9, 13b-H) and 4.30 (1 H, d, *J* 2.9, 13b-H), 4.23–4.29 (total 2 H, ov, 2 × 4b-H), 5.81–5.93 (2 H, ov, 2 × 6-H), 6.37 (1 H, s, 1-H) and 6.47 (1 H, d, *J* 7.8, 1-H), 6.50–6.59 (total 3 H, ov, ArH), 6.67 (1 H, d, *J* 7.3, 3-H) and 6.91–6.95 (total 2 H, ov, ArH); δ_C(68 MHz) 20.6 and 21.1 (Me), 26.5 and 27.0 (C-9), 28.1 and 28.2 (10-Me), 31.0 and 31.7 (12-Me), 35.7, 36.4, 38.4 and 39.6 (C-7 and -13c), 41.0, 41.7, 43.7 and 43.9 (C-4b and -8a), 48.6 and 49.4 (C-13b), 107.0 and 107.4 (C-13a), 113.9 and 115.9 (C-1), 121.0, 121.1, 122.9 and 123.4 (C-3 and -4a), 126.6, 127.5, 128.1 and 129.2 (C-5 and -6), 134.5, 136.0, 136.6 and 136.8 (C-2 and -4), 146.1 and 147.5 (C-14a), 149.9 and 150.1 (C-9a), 152.0 (C-11), 162.5 (C-13) and 208.9 (C-8).

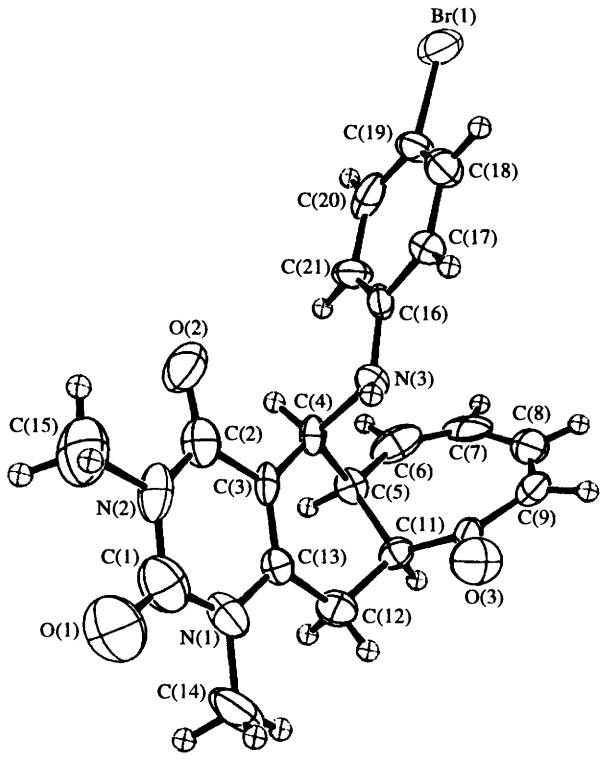


Fig. 2 ORTEP drawing of compound **5b** with crystallographic numbering scheme

Conversion of *exo*-adducts 6 into cycloheptaquinazoline 8

General procedures. A solution of *exo*-adduct **6a** (0.100 g, 0.28 mmol) in ethanol (5 cm^3) containing three drops of 12 mol dm^{-3} hydrochloric acid was heated under reflux for 24 h. The mixture was evaporated to dryness and the residue was extracted with dichloromethane (3 × 15 cm^3). Usual work-up with column chromatography gave the cycloheptaquinazoline **8** (0.021 g, 29%).

Table 4 Crystal data for compounds **5b**, **6b** and **7f**

	5b	**6b**	**7f**
Molecular formula	$C_{21}H_{20}BrN_3O_3$	$C_{21}H_{20}BrN_3O_3$	$C_{25}H_{23}N_3O_3$
Relative molecular mass	442.31	442.31	413.48
Crystal system	Monoclinic	Monoclinic	Monoclinic
Space group	$P2_1/c$ (#14)	$P2_1/c$ (#14)	$P2_1/c$ (#14)
Cell constants			
a(Å)	11.169(2)	10.790(3)	8.02(2)
b(Å)	13.513(2)	11.126(4)	11.015(6)
c(Å)	13.471(2)	17.003(2)	22.443(7)
β(°)	108.72(1)	107.16(1)	97.69(6)
V(Å^3)	1925.6(4)	1950.2(8)	1964(4)
Z	4	4	4
D_c (g cm^{-3})	1.526	1.506	1.398

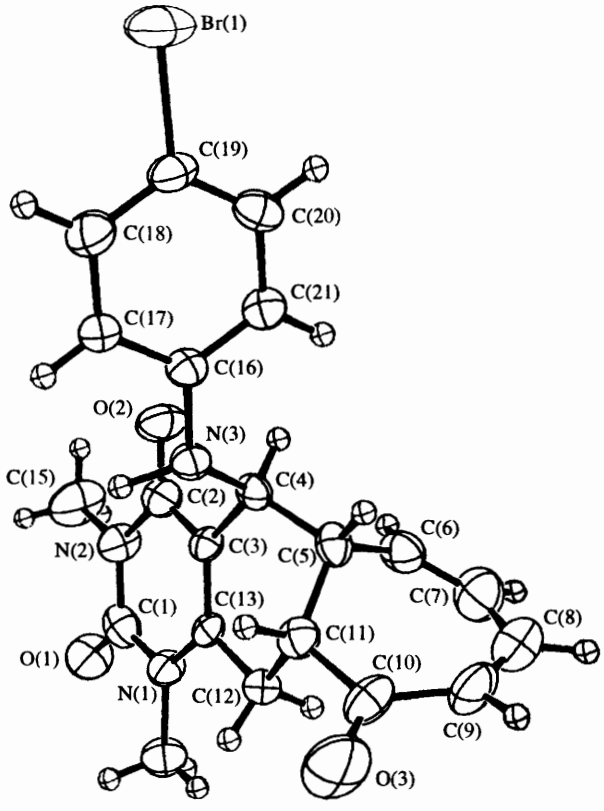


Fig. 3 ORTEP drawing of compound **6b** with crystallographic numbering scheme

1,3-*Dimethyl*-2,3,4,10-*tetrahydro*-1H-*cyclohepta*[g]*quinazoline*-2,4,10-*trione* **8** was obtained as yellow needles from ethanol–chlorofom; mp 210–212 °C (Found: C, 67.0; H, 4.6; N, 10.2. $C_{15}H_{12}N_2O_3$ requires C, 67.15; H, 4.51; N, 10.44%); ν_{max}/cm^{-1} 1700 and 1650 (CO); δ_H(270 MHz) 3.53 and 3.74 (each 3 H, each s, 1- and 3-Me), 6.74 (1 H, ddd, J 1.1, 8.1 and 11.4, 7-H), 6.97 (1 H, dd, J 1.1 and 12.1, 9-H), 7.16 (1 H, ddd, J 1.1, 8.1 and 12.1, 8-H), 7.44 (1 H, d, J 11.4, 6-H), 8.35 (1 H, s, 5-H) and 8.58 (1 H, s, 11-H); δ_C(68 MHz) 28.8 (1-Me), 31.3 (3-Me), 115.5 (C-8), 118.4 (C-4a), 126.1 (C-6), 130.8 (C-5a), 134.9, 136.1 and 136.8 (C-5, -7, and -11), 138.7 (C-9), 140.7 (C-10a), 143.0 (C-11a), 150.9 (C-2), 161.1 (C-4) and 187.1 (C-10); m/z 268 (M^+).

Single-crystal X-ray structure determinations

Single crystals (prisms) of compound **5b**, **6b** and **7f** for X-ray diffraction studies were recrystallised from ethanol. A crystal of approximate dimensions of 0.240 × 0.460 × 0.540 mm was used for data collection of compound **5b**, one of 0.240 × 0.240 × 0.260 mm of compound **6b** and one of 0.040 × 0.0400 × 0.460 mm of compound **7f**. All measurements were made on a Rigaku AFC5S diffractometer by employing graphite-monochromated Mo-Kα radiation. The unit-cell dimensions were obtained by least-squares analysis of 24 or 25 reflections within the range 37.25 < 2θ < 39.69° for compound **5b**, 34.49 < 2θ < 39.88° for compound **6b** and 20.24 < 2θ < 25.22 for compound **7f**, respectively. Summaries of the crystal data for compound **5b**, **6b** and **7f** are given in Table 4. The ω–2θ scan technique to a maximum 2θ-value of 55° was used. Scans of (1.42 + 0.30 tan θ)° were made at a speed of 32.0° min^{-1} (in omega) for compound **5b**, of (0.79 + 0.30 tan θ)° at a speed of 32.0° min^{-1} for compound **6b**, and of (1.00 + 0.30 tan θ)° at a speed of 32.0° min^{-1} for compound **7f**. A total of 4848 observed reflections (unique: 4620; R_{int} 0.082) for compound **5b**, 4955 (unique: 4711; R_{int} 0.063) for compound **6b**, and 5098 (unique: 4766; R_{int} 0.127) for compound **7f** were collected. All calculations were performed using the TEXSAN program.[8] Atoms other than hydrogen were refined anisotropically. The structures were solved by direct methods (MITHRIL)[9] and refined by least squares to R 0.072 (compound **5b**), 0.059 (compound **6b**) and 0.061 (compound **7f**). ORTEP[10] drawings of compounds **5b**, **6b** and **7f** are shown in Figs. 2, 3 and 4, respectively.‡

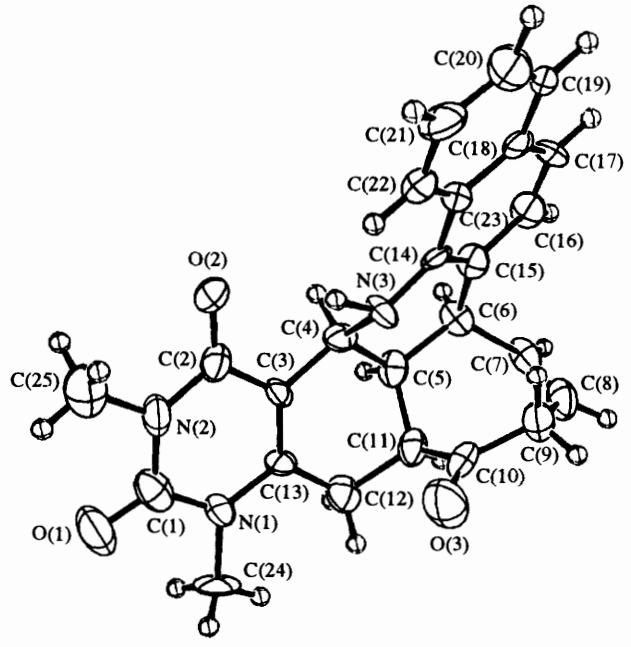


Fig. 4 ORTEP drawing of compound **7f** with crystallographic numbering scheme

‡ Tables of atomic coordinates, bond lengths and bond angles have been deposited at the Cambridge Crystallographic Data Centre. See *Instructions for Authors* (1995), Issue 1.

Computational procedure. The structural data of compounds **5b** and **7f**, confirmed by X-ray structure analyses, were used as initial geometries, and the structures of the parent heterocycles **5a** and **7a** were fully optimerised individually by the PM3 method[11] using the MOPAC program (Version 6.00)[12] on the VAX 4000 in Ube Laboratory, Corporate Research & Development, Ube Industries Ltd. The calculated heats of formation are summarised in Fig. 1.

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