Antitumour polycyclic acridines. Part 1. Synthesis of 7*H*-pyrido- and 8*H*-quino-[4,3,2-*kl*]acridines by Graebe–Ullmann thermolysis of 9-(1,2,3-triazol-1-yl)acridines: application of differential scanning calorimetry to predict optimum cyclisation conditions

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The thermal decomposition of a series of acridines substituted in the 9-position with 1,2,3-triazol-1-yl, benzotriazol-1-yl and naphthotriazol-1-yl groups has been studied by differential scanning calorimetry. Whereas the monocyclic triazole 7a shows a discrete melting endotherm followed by a decomposition exotherm corresponding to formation of the 7*H*-pyrido[4,3,2-*kl*]acridine 8, in the benzotriazoles 10a–e and naphthotriazole 10f these processes coincide with a single sharp exothermic transition attributed to cyclisation to polycyclic acridines 11a–f, respectively. The optimum conditions for the preparative scale synthesis of polycyclic acridines from triazole precursors utilised boiling diphenyl ether as the decomposition medium. A benzotriazol-1-ylacridine 10e substituted in the *peri* position with a methyl group behaved anomalously: as well as affording the expected 8*H*-quino[4,3,2-*kl*]acridine 11e, cyclisation also led to radical mediated loss of the methyl group to form the unsubstituted 8*H*-quino[4,3,2-*kl*]acridine 11a and H-abstraction from the methyl group leading to the benzoazepinoacridine 12. Radical cyclisation of 9-(2-iodoanilino)acridine 16 also gave 8*H*-quino[4,3,2-*kl*]acridine 11a. The crystal structure of 11a confirms the 8*H* tautomer arrangement with intermolecular N8–H · · · N13 hydrogen bonding and exhibits a polycyclic system that is planar with rms deviation 0.044 Å.

Introduction

The acridine ring system is an ideal framework for the medicinal chemist to embellish with a diversity of functional groups.[1] Derivatives and salts of acridines are characteristically highly crystalline, stable, attractively coloured, often strongly fluorescent and, rewardingly, display a range of antimicrobial properties which have given them a secure position in the history of chemotherapy.[2] Since our first venture into acridine chemistry in 1972[3] derivatives of this ring system have attracted attention in the development of cancer chemotherapeutic agents.[4] For example, *m*-AMSA **1**,[5] and other DNA binding agents, are now known to be targeted to topoisomerase II,[6,7] a DNA processing protein overexpressed in many proliferating tumour cell types, for example in breast cancer.[8]

Topoisomerase II exists in two distinct isoforms in human cells; the α- (170 kDa) and β-isoforms (180 kDa)[9] which differ in their patterns of expression and sensitivity to anticancer drugs.[10] New agents which might selectively discriminate between these isoforms could have a different clinical profile compared with standard drugs of the general topoisomerase II-inhibitory class such as amsacrine, doxorubicin and etoposide.[11] Intriguingly, a series of DNA-intercalating pyridoacridines isolated from the purple marine *Cystodytes* sp. ascidian such as the tetracycle cystodytin A **2a** and cystodytin J **2b**, the pentacyclic pyridoacridines kuanoniamine D **3** and shermilamine B **4** and the heptacycle eilatin **5** have been shown to inhibit topoisomerase II.[12] The aforementioned structures (Fig. 1) are representative of a large number of pyridoacridine based natural products.[13]

It has been shown previously that a pentacyclic acridine **11a** could be synthesised by a thermal Graebe–Ullmann reaction on the 9-(benzotriazol-1-yl)acridine **10a**.[14] Subsequently, Mitchell and Rees, as part of a comprehensive study of the photolysis of 1-aryl-1,2,3-triazoles,[15,16] obtained the same pentacycle from the photolysis of **10a** in acetonitrile.[15] In both cases recovered yields were <40%. In this paper we report the synthesis of a range of 9-(substituted-1,2,3-triazol-1-yl)acridines which have been subjected to differential scanning calorimetry (DSC) to measure the thermal parameters underlying their decomposition and cyclisation: using this information we have optimised conditions for their transformation to polycyclic acridines.

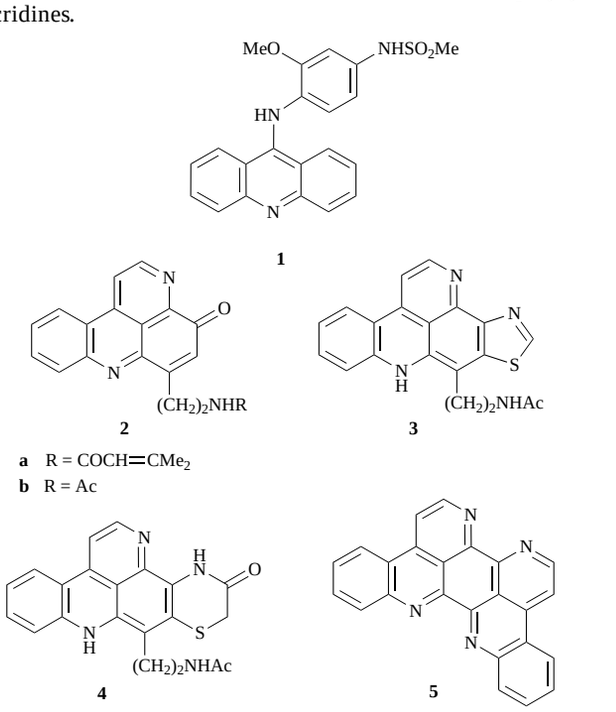
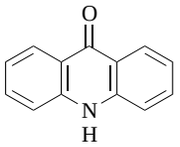


Fig. 1 Structures of representative topoisomerase II inhibitors amsacrine **1** and marine pyridoacridine alkaloids **2**–**5**

Results and discussion

Synthesis of 9-(1,2,3-triazol-1-yl)acridines

Acridin-9-one **6**[2] was the starting point for the synthesis of the required triazolylacridines. 9-(1,2,3-Triazol-1-yl)acridine **7a**



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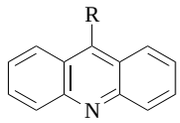

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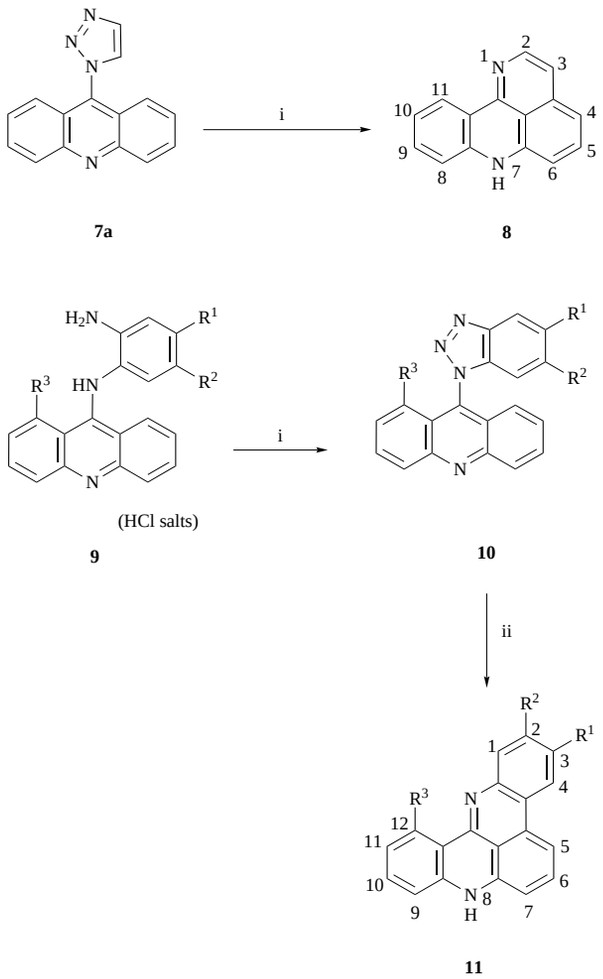
a R = 1,2,3-triazol-l-yl
b R = 1,2,3-triazol-2-yl
c R = Cl
d R = N_3
e R = NH_2

(49%) together with the isomeric 9-(1,2,3-triazolyl-2-yl)acridine **7b** (26%) were prepared by interaction of 9-chloroacridine **7c**, obtained from **6** and phosphorus oxychloride,[3] with the anion of 1,2,3-triazole generated using sodium hydride in dry DMF. Interaction of 9-chloroacridine or 1-methyl-9-chloroacridine with a range of anilines afforded the anilinoacridines **9a**–**e**, isolated as their hydrochloride salts. In the case of the reaction with 2-amino-4-methylaniline the major product isolated was the anilinoacridine **9d** but NMR analysis of the reaction mixture indicated the presence of a minor product, presumably the isomer (**9**: $R^1 = R^3 = H$, $R^2 = Me$) in a 5:1 ratio. The naphthylaminoacridine **9f** was similarly formed from 2,3-diaminonaphthalene. Nitrosation of the series **9a**–**f** in hydrochloric acid furnished the insoluble benzotriazoles **10a**–**e** and naphthotriazole **10f** in high yields (Scheme 1). Compound **10a** has been prepared previously from the cycloaddition reaction between 9-azidoacridine **7d** and benzyne.[15,17] Attempts to synthesise the amine **10g** by reduction of 9-(6-nitrobenzotriazol-1-yl)acridine **10c** under a range of conditions were not successful because of reductive fission of the acridine–benzotriazole bond.

The triazolylacridines were readily hydrolysed to acridin-9-one **6** in hot aqueous mineral acids and effervesced at their melting-points indicative of triazole ring fragmentation (Graebe–Ullmann reaction).



7a **8** **9** (HCl salts) **10** **11**

	R^1	R^2	R^3
a	H	H	H
b	Cl	H	H
c	H	NO_2	H
d	Me	H	H
e	H	H	Me
f	CH=CH–CH=CH		H
g	H	NH_2	H

Scheme 1 *Reagents and conditions*: i, Sodium nitrite in 2 M HCl, 0 °C, then aq. NH_3; ii, boiling PhOPh, 2 h. Numbering shown for compound **11** applies to **11a**–**e** and **11g** only.

Differential scanning calorimetry (DSC)

Temperature changes in solid materials can induce a number of chemical (*e.g.* degradation) and physical (*e.g.* melting, recrystallisation) effects. Characterisation of these changes may be achieved by thermal analysis.[18] In practice, DSC involves placing a small amount of a sample in a DSC pan and increasing/decreasing the temperature at a predetermined rate. The flow of heat into this pan is adjusted to ensure that the temperature of the sample pan is identical to that of the reference pan which has no sample present. Thus, in the examination of melting properties (an endothermic process), as the sample melts more energy in the form of heat must be provided to the sample pan to maintain the temperature at an equivalent value to the reference pan. The thermogram of 9-(1,2,3-triazol-1-yl)acridine **7a** [Fig. 2(a)] shows a melting endotherm at 212.1 °C with enthalpy of fusion of 813.3 J g^{-1}, a range representing a molten phase (approx. 215–247 °C) and a sharp exothermic transition at 249.8 °C (−2414 J g^{-1}) corresponding to thermolytic cyclisation to the pyridoacridine **8**. The sharpness of the transition indicates that the latter process is relatively free of competing reactions. In contrast, the thermogram of the isomeric 9-(1,2,3-triazol-2-yl)acridine **7b** reveals no melting (or decomposition) at <300 °C (data not shown).

In the thermogram of 9-(benzotriazol-1-yl)acridine **10a** [Fig. 2(b)] it is apparent that only one enthalpy change occurs on heating the sample. Melting and thermolytic cyclisation coincide to give an overall exotherm centred at 245.6 °C (−714.9 J g^{-1}). As in the monocyclic triazole example, the sharpness and singularity of the exothermic transition confirms that formation of the pentacyclic acridine **11a** occurs over a very narrow temperature range and does not involve a complex sequence of reactions with the potential to generate significant impurities. A sample of pure pentacyclic acridine **11a**, prepared independently (see later), melted at 286.8 °C [Fig. 2(b), inset]. When the sample of **10a** was mixed with diphenyl ether (1 mol equiv.) the shape of the exotherm was changed [Fig. 2(c)] and the temperature of maximum energy release, corresponding to cyclisation, was lowered to 230.1 °C. However, the overall energy release was comparable (−692.8 J g^{-1}) to that liberated during cyclisation of the unadulterated sample of **10a**, showing that the diphenyl ether was not perturbing the reaction pathway. The thermogram monitoring the decomposition of 9-(benzotriazol-1-yl)-1-methylacridine **10e** (data not shown) shows a much broader exothermic transition than that for **10a** with peak irregularities. These features, together with the pronounced baseline drift, were predictive of the generation of a mixture of products in the preparative thermolysis of **10e**.

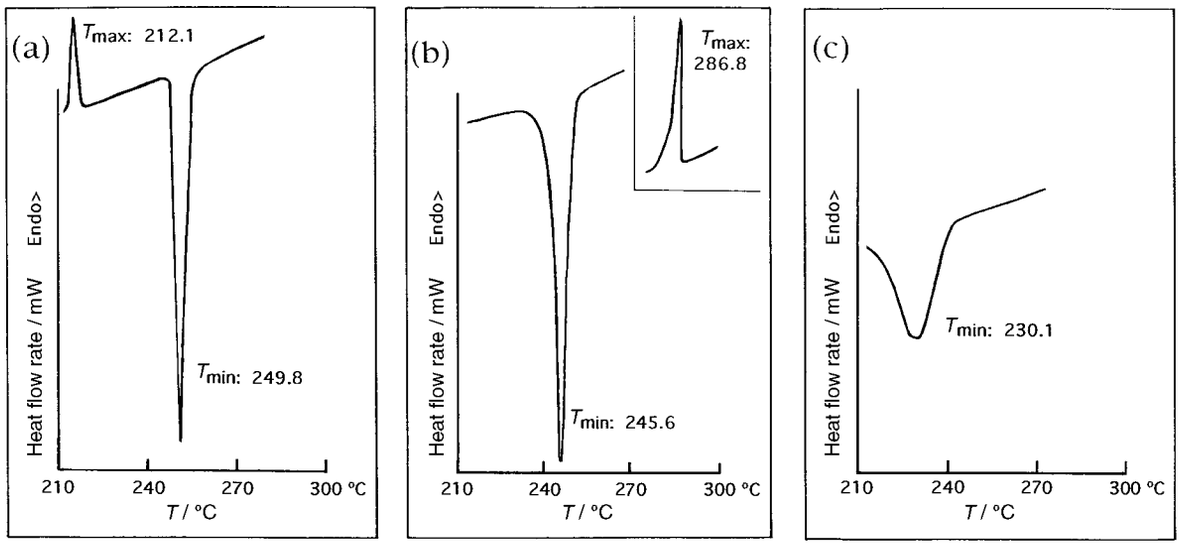


Fig. 2 Thermograms monitoring melting and decomposition of: (a) 9-(1,2,3-triazol-1-yl)acridine **7a**; (b) 9-(benzotriazol-1-yl)acridine **10a** with (inset) melting of 8*H*-quino[4,3,2-*kl*]acridine **11a**; (c) melting and decomposition of 9-(benzotriazol-1-yl)acridine **11a** with diphenyl ether (1 mol equiv.)

Preparative thermolysis of 9-(1,2,3-triazol-1-yl)acridines

Using the DSC, the precise decomposition temperatures of the series of 9-(benzotriazolyl)acridines **10a–f** were determined (Table 1). Clearly the optimum conditions for cyclisation to pyridoacridines **11a–f** should be solid state thermolysis at those individual temperatures. However, for reactions on a preparative scale which are exothermic and involve rapid nitrogen release, it was more convenient (and safer) to conduct the thermolyses in boiling diphenyl ether (bp 259 °C for 1 h). Also this approach allowed us to exploit the lowering of the cyclisation temperature because of the solvation effect of the solvent.

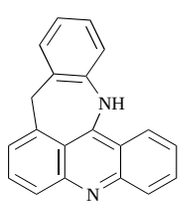
Preparative scale thermolysis of 9-(1,2,3-triazol-1-yl)acridine **7a** in boiling diphenyl ether gave the red tetracycle **8** in 75% isolated yield after chromatographic purification (Scheme 1). The isomeric (triazol-2-yl)acridine **7b** was recovered unchanged from boiling diphenyl ether as predicted from the DSC analysis. The unsubstituted benzotriazole **10a** afforded the 8*H*-quino-[4,3,2-*kl*]acridine **11a** in boiling diphenyl ether in an isolated yield (84%) superior to that recorded in earlier solid state[14] or photolytic Graebe–Ullmann cyclisations.[15] Interestingly, reasonable yields of γ-carbolines have been reported for Graebe–Ullmann reactions on 4-(benzotriazol-1-yl)pyridines conducted in pyrophosphoric acid under microwave irradiation.[19] Analogues **10b–f** cyclised thermally to the corresponding substituted quinoacridines **11b–f** in moderate yields ranging from 50–65% after chromatographic purification. In the case of the 1-methylacridine **10e** the major product **11e** (60%) was accompanied by the demethylated pentacycle **11a** (12%) and a trace (<1%) of a product isomeric with **11e**. This compound is assigned, tentatively, the benzoazepinoacridine structure **12** since its EI mass spectrum showed a base peak at $M^+ - 14$ (CH_2) mass units contrasting with $M^+ - 15$ (Me) for the isomer **11e**. Lack of sufficient material thwarted full characterisation of this product. Catalytic hydrogenation of the 2-nitroquinoacridine **11c** gave the corresponding amine **11g** (58%).

The mechanism of the photolytic counterpart of the transformation **10a** to **11a** has been interpreted by Mitchell and Rees[15] as involving an initial triplet diradical **13** which gives rise to a singlet carbene which, in its 'dipolar form' **14**, attacks the acridine 1- (or 8-) position in an electrophilic process (Scheme 2). In the present thermal variant of this cyclisation it is proposed that rotation of the phenyl–amine bond positions the aryl radical to initiate *homolytic* substitution at the acridine 1- (or 8-) position. The pentacyclic diradical **15** would then

Table 1 Thermal analysis of 9-(benzotriazol-1-yl)acridines **10** using differential scanning calorimetry

Compound	Decomposition temperature (T/°C)[a]	Energy release (E/J g^{-1})
10a	245.6	−714.9
10a[b]	230.1	−692.8
10b	242.3	−593.3
10c	261.9	−636.8
10d	242.1	−596.6
10e	220.2	−312.9
10f	255.2	−1808.2

[a] Minimum point on the exotherm (T_{min}). [b] Mixed with diphenyl ether (1 mol equiv.).



(or tautomer)

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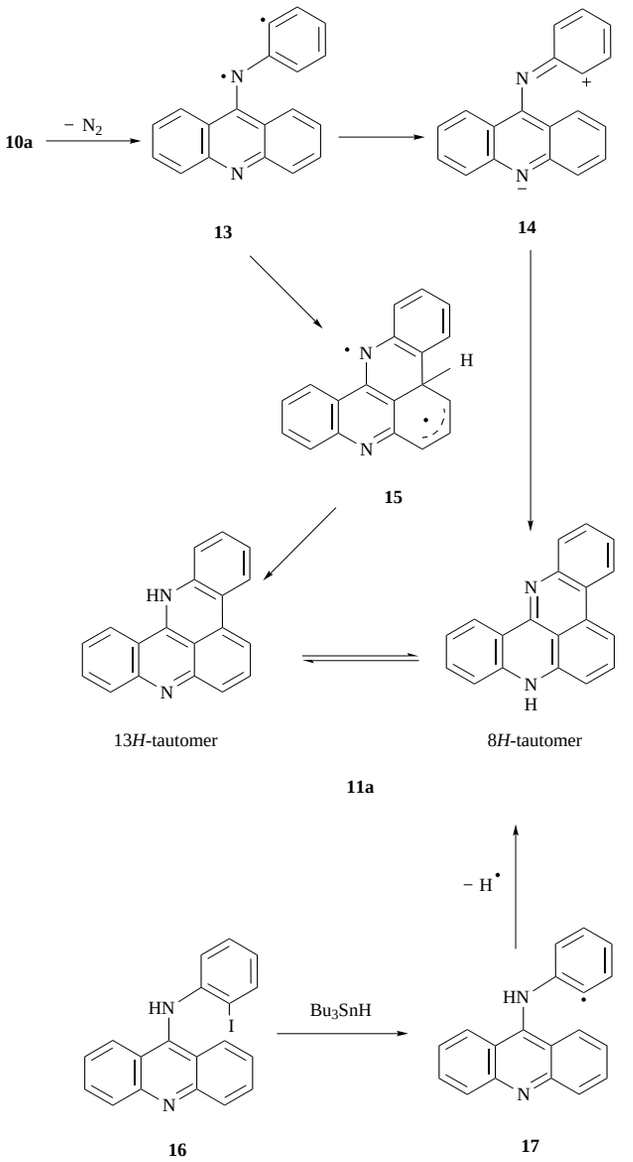
aromatise to the 13*H*-tautomer of the observed 8*H*-quino-[4,3,2-*kl*]acridine **11a**. (For a discussion on the tautomeric structures of **11a**, see later.)

Two pieces of evidence support this mechanism. The minor loss of a methyl group in the thermolysis of acridine **10e**, yielding the unsubstituted quinoacridine **11a**, can be accounted for by homolysis of the C–Me bond (**15**; Me for H); also, the benzoazepine structure **12** probably formed in the same decomposition could arise by H-abstraction from the methyl group. More convincingly, 2-iodoanilinoacridine **16** formed from 9-chloroacridine and 2-iodoaniline, undergoes radical coupling to yield **11a** (32%, unoptimised) *via* the aryl radical **17** generated with tributyltin hydride–AIBN. In contrast, the iodoaniline was stable in boiling diphenyl ether (3 h) without radical initiation.

Properties and structure of 8*H*-quino[4,3,2-*kl*]acridine

Mitchell and Rees assigned the 8*H*-tautomeric structure to the quinoacridine **11a** on the basis of NOE difference and 2D spectra but no details were given.[15] We have confirmed this assign-



Scheme 2

ment for **11a** in both solution and the solid state. Thus 2D COSY studies were used to analyse the three- and four-spin systems in the polycyclic nucleus and NOE enhancements (Fig. 3) to identify the terminal protons. Irradiation of the absorptions for H-7 and H-9 (see Scheme 1 for numbering system) elicited an 8% enhancement of the NH signal at δ 10.8; irradiation of the NH absorption gave a 10% and 9% enhancement of the protons at positions 7 and 9, respectively. The NOE enhancements were reduced by exchange of the amine proton with water in the DMSO. The most significant NOE enhancement (24%) was obtained when the signals for protons 4 and 5 were irradiated; this is indicative of their close proximity in the pentacycle. NMR and MS analyses were used to confirm the structures of other polycyclic acridines described in this paper since microanalytical data were unreliable due to the propensity of acridines to undergo solvation.[2]

The pyridoacridine **8** (pK_a 6.08, measured by the UV–visible spectroscopic method) and the unsubstituted pentacycle **11a** (pK_a 6.30) and hexacycle **11f** (pK_a 6.17) are bases of comparable strength but slightly weaker bases than the reference 9-anilinoacridine *m*-AMSA **1** (pK_a 7.19).[20] 9-Aminoacridine **7e** is approximately 10 000-fold a stronger base (pK_a 9.99)[2] than the new heterocycles. In the quinoacridine series **11** the presence of a 2-nitro group in **11c** has a dramatic base-weakening effect (pK_a 4.22) whereas the effect of a 2-amino group in **11g** is only marginal (pK_a 6.18). As expected, the presence of an electron-

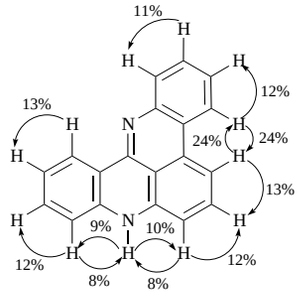
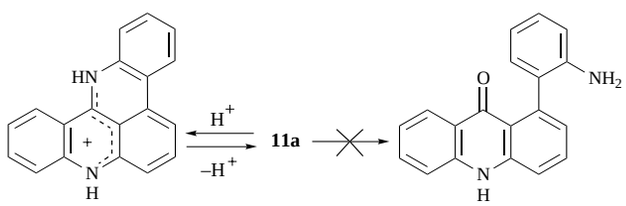


Fig. 3 Selected NOE enhancements in 8*H*-quino[4,3,2-*kl*]acridine **11a**

withdrawing chloro group **11b** in the 3-position is significantly base-weakening (pK_a 5.32) and a 3-methyl group **11d** base-strengthening (pK_a 6.85).

The monocation **18** formed from **11a** readily dissociates in water to afford the highly fluorescent free base. Unlike 9-chloro- and 9-azido-acridine[4] and the anilinoacridines and triazolylacridines described herein which readily hydrolyse to acridin-9-one **6**, especially in acids, compound **11a** is stable in 5 M hydrochloric acid or sodium hydroxide. The potential product of such hydrolysis might have been anticipated to be the 1-arylacridinone **19** (Scheme 3). Also compound **11a** failed to afford



Scheme 3

an ethiodide salt when boiled in excess ethyl iodide (24 h). Clearly these properties are incompatible with a 13*H*-tautomeric ('tethered' 9-anilinoacridine) structure for **11a**.

The electronic absorption spectrum of *m*-AMSA **1** in ethanol is relatively simple and shows three bands at 240, 340 and 433 nm; the long wavelength band is shifted to 461 nm on protonation. In contrast the spectra of the pyridoacridine **8** and the quinoacridines **11a**–**g** display considerable fine structure (Table 2) and the long wavelength absorptions of the free bases in the range 443–475 nm undergo significant bathochromic shifts (to 488–500 nm) on protonation.

In order to confirm the structure of **11a** and facilitate subsequent interpretation of physicochemical and molecular modelling studies on the intercalative interactions of polycyclic acridines and DNA, an X-ray structure determination was completed. The molecular structure of **11a** is shown in Fig. 4. Several pieces of crystallographic evidence unanimously indicate that the 8*H*-tautomer is present in the crystalline state. A hydrogen atom site 0.96(4) Å from N8 was located in a difference electron density map and successfully refined. While both ring bonds to N8 are relatively long, C7a–N8 and N8–C8a being 1.370(5) Å and 1.389(4) Å respectively, the much shorter N13–C13a [1.324(4) Å] shows double bond character which militates against protonation there. The C–N–C bond angles of 122.6(3)° at N(8) and 117.5(3) at N13 show the expected compression by a lone pair at N13. A hydrogen bond links N8 as donor to N13 of a molecule in equivalent position x, $0.5 - y$, $-0.5 + z$ with H···N contact distance 2.08(4) Å, N···N 3.036(4) Å, and N–H···N angle 175(4)°. Since, notwithstanding the above evidence, this hydrogen bond could provide a low-energy pathway for proton transfer from N8 to N13 in some molecules, heats of formation were calculated for both tautomers after optimisation of geometry starting from the crystal structure. Semi-empirical molecular orbital calculations

Table 2 Electronic absorption spectra of 7*H*-pyrido- and 8*H*-quino-[4,3,2-*kl*]acridines

Compound	Absorbance maxima (λ/nm)	
	Neutral species[a]	Protonated species[b]
1 (*m*-AMSA)	240, 340, 433	240, 342, 461
8	231, 250, 267,* 307,* 319, 409,* 429, 453	238, 278, 301,* 315, 356, 375, 438,* 463, 490
11a	236, 260,* 288, 300, 334, 373, 426, 443	236, 274, 288, 318, 361, 431,* 460, 488
11b	238, 264, 286,* 289, 339, 381, 429, 446	238, 256, 277, 289, 367, 434,* 460, 489
11c	235, 271, 292,* 329,* 342, 423, 449	233, 263, 292,* 325,* 409, 433,* 459, 490
11d	239, 260,* 286, 289, 300,* 336, 375, 425, 444	239, 277, 289, 319, 363, 435,* 461, 490
11f	262, 295, 326, 352, 370,* 382, 399, 421,* 447, 475	267, 294,* 308, 352, 371, 440,* 468, 500
11g	235, 275, 326, 434,* 453	235, 247, 255, 275, 290, 363, 434,* 460, 490

[a] Measured in ethanol. [b] Measured in ethanol containing 4 M hydrochloric acid. * Shoulder.

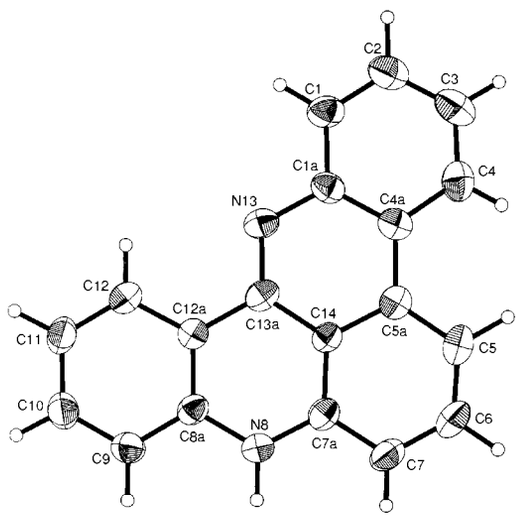


Fig. 4 ORTEP[22] drawing of 8*H*-quino[4,3,2-*kl*]acridine **11a** and the crystallographic numbering scheme

with AM1 parameters in GAMESS[21] yielded ΔH_f values 6.6 kcal mol^{-1} lower for the 8*H*- than for the 13*H*-tautomer.

The heterocyclic framework of **11a** is planar within 0.09 Å with rms deviation 0.044 Å. The acridine ring is slightly creased along a line approximately from C7 to C12. Thus the fragment C9 C10 C11 C12 C12a C8a N8 C7a C7 has rms deviation of only 0.013 Å and makes a dihedral angle of 3.0(2)° to another planar fragment comprising C5a C5 C6 C7 C7a C14 C13a C12a C12 with rms deviation 0.011 Å. In turn the phenyl ring C1 C2 C3 C4 C4a C1a, also with rms deviation 0.011 Å, is twisted from the latter plane by 3.1(2)°.

We will report on the intriguing biological properties of these polycyclic systems, and related structures, in future papers in this series.

Experimental

Melting points were obtained on a Gallenkamp melting point apparatus and are uncorrected. IR Spectra were measured in KBr on a Mattson 2020 Galaxy Series FT-IR spectrometer. UV Spectra were measured in 95% ethanol on a Cecil 1020S scanning spectrometer. ^{1}H and ^{13}C NMR Spectra were recorded on a Bruker ARX250 spectrometer operating at 250.13 and 62.9 MHz, respectively. ^{13}C Assignments (C = quaternary carbon) were based on DEPT135 and DEPT90 experiments. Mass spectra were recorded on an AEI MS-902, a VG Micromass 7070E or a VG Platform spectrometer. Silica gel C60H (40–60 mm) was used for flash chromatography. TFA = trifluoroacetic acid.

Differential scanning calorimetry

Differential scanning calorimetry was performed with a Perkin-Elmer DSC-4 instrument using the Thermal Analysis Data Station (TADS) for data collection, handling and presentation. Samples for thermal analysis were weighed (1–4 mg) into an aluminium pan and covered with an aluminium lid which was then crimped into position. The pan was placed in the DSC oven together with a blank, prepared in exactly the same way but without the sample. The sample and blank were purged continuously with nitrogen gas at a flow-rate of 25 cm^3 min^{-1} (1.4 kg cm^{-2}) and the thermograms were recorded over a temperature range of 40–290 °C with a programmed heating rate of 10 °C min^{-1}. Temperature calibration was made with an indium standard (onset temperature 156.6 °C) and temperatures are quoted as those of peak maximum (T_{max}) or minimum (T_{min}).

9-(1,2,3-Triazol-1-yl)acridine 7a

To a mixture of 95% sodium hydride (0.14 g, 5.5 mmol) in dry DMF (15 cm^3) was added 1*H*-1,2,3-triazole (0.38 g, 5.5 mmol) at 25 °C. The mixture was stirred (30 min) and a solution of 9-chloroacridine[2] (1.07 g, 5.0 mmol) in dry DMF (5 cm^3) was added slowly (15 min). After being stirred at 60 °C (2 h) the mixture was poured into ice–water (100 cm^3) and products were collected. Flash chromatographic separation (hexane–ethyl acetate, 1:1) gave a slow moving fraction comprising the triazole **7a** which crystallised from ethyl acetate as greenish needles (0.6 g, 49%), mp 212 °C; ν_{max}(KBr)/cm^{-1} 3096, 1560, 1449, 1233, 1071, 1007, 756, 637; λ_{max}(EtOH)/nm 209.5, 248.0, 361.0; δ_H([^{2}H$_6$]DMSO) 8.96 (d, 1 H, H-5′), 8.33 (m, 3 H, H-4,4′,5), 8.00 (m, 2 H, H-3,6), 7.74 (m, 2 H, H-2,7), 7.36 (d, 2 H, H-1,8); δ_C([^{2}H$_6$]DMSO) 149.5 (C), 138.4 (C), 134.9 (CH), 132.1 (CH), 130.3 (CH), 130.2 (CH), 129.4 (CH), 123.2 (CH), 122.6 (C) (Found: C, 72.9; H, 4.05; N, 22.8; MH$^+$ [CI], 247. $C_{15}H_{10}N_4$ requires C, 73.1; H, 4.1; N, 22.8%; *M*H, 247).

The fast moving fraction gave 9-(1,2,3-triazol-2-yl)acridine **7b** (0.32 g, 26%), mp >300 °C; ν_{max}(KBr)/cm^{-1} 1553, 1520, 1481, 1406, 922, 818, 750, 637; δ_H([^{2}H$_6$]DMSO) 8.50 (s, 2 H, H-4′,5′), 8.33 (dd, 2 H, H-4,5), 7.99 (m, 2 H, H-3,6), 7.72 (m, 2 H, H-2,7), 7.52 (d, 2 H, H-1,8); δ_C([^{2}H$_6$]DMSO) 149.7 (C), 138.1 (CH), 132.0 (CH), 130.2 (CH), 129.2 (CH), 123.6 (CH), 122.3 (C) (Found: C, 73.1; H, 4.0; N, 22.5; MH$^+$ [CI], 247. $C_{15}H_{10}N_4$ requires C, 73.1; H, 4.1; N, 22.8%; *M*H, 247).

9-(2-Aminoanilino)acridine hydrochloride 9a

1,2-Diaminobenzene (1.08 g) in boiling dry methanol (50 cm^3) was treated with 9-chloroacridine (2.14 g) over 30 min. The mixture was refluxed for a further 1 h, cooled and diethyl ether (20 cm^3) was added. The anilinoacridine hydrochloride (2.06 g, 64%) was collected and had mp 319–320 °C (lit.,[14] 320–322 °C); ν_{max}(KBr)/cm^{-1} 2799, 1632, 1549, 1501, 1474, 1261, 1157, 751; λ_{max}(EtOH)/nm 212.3, 248.3, 395.3; δ_H([^{2}H$_6$]DMSO) 14.74 (br s, 1 H, NH), 11.26 (br s, 1 H, NH), 8.26 (d, 2 H, H-1,8), 8.16 (d, 2 H, H-4,5), 8.01 (m, 2 H, H-3,6), 7.44 (m, 2 H, H-2,7), 7.29 (t, 1 H, H-4′), 7.17 (d, 1 H, H-6′), 7.00 (d, 1 H, H-3′), 6.74 (t, 1 H, H-5′), 5.75 (br s, 2 H, NH$_2$).

The following acridines were prepared similarly.

9-(2-Amino-4-chloroanilino)acridine hydrochloride 9b. From 9-chloroacridine and 3,4-diaminochlorobenzene (88%), mp 298–300 °C (from methanol); ν_{max}(KBr)/cm^{-1} 2895, 1637, 1583, 1551, 1519, 1265, 1160, 746; λ_{max}(EtOH)/nm 212.7, 249, 394.5;

δ_H([$^2H_6$]DMSO) 14.72 (br s, 1 H, NH), 11.06 (br s, 1 H, NH), 8.29 (d, 2 H, H-1,8), 8.11 (d, 2 H, H-4,5), 7.97 (m, 2 H, H-3,6), 7.44 (m, 2 H, H-2,7), 7.14 (d, 1 H, H-6′), 6.96 (d, 1 H, H-3′), 6.64 (t, 1 H, H-5′), 5.98 (br s, 2 H, NH_2).

9-(2-Amino-5-nitroanilino)acridine hydrochloride 9c. From 2-amino-4-nitroaniline (57%), mp 303–306 °C (from acetonitrile); ν_{max}(KBr)/cm^{-1} 3411, 3300, 3186, 1637, 1585, 1517, 1475, 1309; λ_{max}(EtOH)/nm 220, 251.5, 409; δ_H([$^2H_6$]DMSO) 14.81 (br s, 1 H, NH), 11.12 (br s, 1 H, NH), 8.28 (d, 2 H, H-1,8), 8.14 (m, 2 H, H-4′,6′), 8.09 (d, 2 H, H-4,5), 7.99 (m, 2 H, H-3,6), 7.46 (t, 2 H, H-2,7), 7.18 (br s, 2 H, NH_2), 6.98 (d, 1 H, H-3′).

9-(2-Amino-4-methylanilino)acridine hydrochloride 9d. From 2-amino-4-methylaniline (91%), mp 273–275 °C (from acetonitrile–methanol); ν_{max}(KBr)/cm^{-1} 2706, 1637, 1583, 1553, 1520, 1475, 1158, 748; λ_{max}(EtOH)/nm 215.4, 247.2, 400; δ_H([$^2H_6$]DMSO) 14.50 (br s, 1 H, NH), 11.24 (br s, 1 H, NH), 8.30 (d, 2 H, H-1,8), 8.06 (d, 2 H, H-4,5), 7.94 (m, 2 H, H-3,6), 7.38 (t, 2 H, H-2,7), 6.94 (d, 1 H, H-6′), 6.73 (d, 1 H, H-3′), 6.46 (dd, 1 H, H-5′), 2.29 (s, 3 H, CH_3).

9-(2-Aminoanilino)-1-methylacridine hydrochloride 9e. From 9-chloro-1-methylacridine[23] and 1,2-diaminobenzene (78%), mp 255–257 °C (from methanol); ν_{max}(KBr)/cm^{-1} 1632, 1579, 1551, 1474, 1421, 1384, 758; λ_{max}(EtOH)/nm 216.3, 247.2, 390; δ_H([$^2H_6$]DMSO) 13.97 (br s, 1 H, NH), 10.43 (br s, 1 H, NH), 7.84 (m, 5 H, H-3,4,5,6,8), 7.17 (m, 3 H, H-2,4′,7), 6.95 (d, 1 H, H-6′), 6.76 (d, 1 H, H-3′), 6.58 (t, 1 H, H-5′), 5.61 (br s, 2 H, NH_2), 2.74 (s, 3 H, CH_3).

9-(3-Amino-2-naphthylamino)acridine hydrochloride 9f. From 9-chloroacridine and 2,3-diaminonaphthalene (68%), mp 267–269 °C; ν_{max}(KBr)/cm^{-1} 3418, 1636, 1584, 1553, 1507, 1476, 1383, 745; λ_{max}(EtOH)/nm 221.5, 276, 402; δ_H([$^2H_6$]DMSO) 14.88 (br s, 1 H, NH), 11.40 (br s, 1 H, NH), 8.29 (d, 2 H, H-1,8), 8.14 (d, 2 H, H-4,5), 7.95 (m, 2 H, H-3,6), 7.75 (s, 1 H, H-8′), 7.68 (d, 1 H, H-4′), 7.61 (d, 1 H, H-7′), 7.37 (t, 3 H, H-2,6′,7), 7.25 (s, 1 H, H-1′), 7.16 (t, 1 H, H-5′), 5.92 (br s, 2 H, NH_2).

9-(Benzotriazol-1-yl)acridine 10a. 9-(2-Aminoanilino)-acridine hydrochloride **9a** (1.61 g), suspended in 2 M hydrochloric acid (50 cm^3) at 0–5 °C was treated (30 min) with a solution of sodium nitrite (0.7 g, 2 mol equiv.) in water (5 cm^3). The suspension was stirred at 0 °C for 1 h, basified with concentrated aqueous ammonia–ice and the product collected and crystallised from aqueous DMF. The benzotriazole was formed as cream crystals (1.01 g, 69%), mp 245.7 °C (decomp.) (lit.,[15] 250 °C, decomp.); ν_{max}(KBr)/cm^{-1} 3048, 1554, 1491, 1426, 1058, 752, 748; λ_{max}(EtOH)/nm 200, 249, 362; δ_H([^{2}H]TFA) 8.24 (d, 2 H, H-1,8), 8.05 (m, 3 H, H-2,4′,7), 7.59 (t, 2 H, H-3,6), 7.44 (m, 4 H, H-4,5,5′,7′), 7.01 (d, 1 H, H-6′); δ_C([^{2}H]TFA) 141.0 (C), 139.4 (CH), 136.0 (C), 132.3 (CH), 131.0 (CH), 129.1 (CH), 123.9 (CH), 123.1 (C), 119.9 (CH), 118.3 (CH), 110.2 (CH).

The following triazolyl-substituted acridines were prepared similarly.

9-(5-Chlorobenzotriazol-1-yl)acridine 10b. From **9b** as yellow needles (84%), mp 220 °C (decomp.); ν_{max}(KBr)/cm^{-1} 3050, 1554, 1487, 1431, 1050, 825, 751; λ_{max}(EtOH)/nm 203.5, 248.5, 361.5; δ_H([^{2}H]TFA) 8.25 (d, 2 H, H-1,8), 8.09 (m, 3 H, H-2,4′,7), 7.65 (t, 2 H, H-3,6), 7.42 (m, 3 H, H-4,5,7′), 6.95 (dd, 1 H, H-6′); δ_C([^{2}H]TFA) 146.0 (C), 141.0 (C) 139.3 (CH), 134.8 (C), 134.4 (C), 132.6 (CH), 130.9 (CH), 123.9 (CH), 123.0 (C), 119.9 (CH), 118.4 (CH), 110.8 (CH) (Found: C, 68.7; H, 3.2; N, 17.0; MH$^+$ [CI], 331, 333. $C_{19}H_{11}N_4Cl$ requires C, 69.1; H, 3.4; N, 17.0%; *M*H, 331, 333).

9-(6-Nitrobenzotriazol-1-yl)acridine 10c. From **9c** as yellow needles (55%), mp 261.8 °C (decomp.); ν_{max}(KBr)/cm^{-1} 2991, 1552, 1489, 1344, 1234, 1061, 752, 748; λ_{max}(EtOH)/nm 230, 362; δ_H([^{2}H]TFA) 8.23 (m, 4 H, H-1,4′,5′,8), 8.04 (t, 2 H, H-2,7), 7.91 (s, 1 H, H-7′), 7.58 (t, 2 H, H-3,6), 7.35 (d, 2 H, H-4,5); δ_C([^{2}H]TFA) 149.0 (C), 141.1 (C), 139.5 (CH), 135.6 (C), 131.3 (CH), 123.7 (CH), 123.4 (CH), 121.9 (CH), 121.3 (CH), 120.1 (CH), 107.3 (CH) (Found: C, 64.8; H, 3.0; N, 19.95; MH$^+$ [CI], 341. $C_{19}H_{11}N_5O_2 \cdot 0.5H_2O$ requires C, 65.1; H, 3.4; N, 20.0%; *M*H, 341).

9-(5-Methylbenzotriazol-1-yl)acridine 10d. From **9d** as cream flakes (56%), mp 242.1 °C (decomp.); ν_{max}(KBr)/cm^{-1} 3042, 1555, 1498, 1432, 1232, 1065, 750; λ_{max}(EtOH)/nm 203, 248, 361; δ_H([^{2}H]TFA) 8.22 (d, 2 H, H-1,8), 8.05 (t, 2 H, H-2,7), 7.72 (s, 1 H, H-4′), 7.60 (t, 2 H, H-3,6), 7.38 (m, 3 H, H-4,5,7′), 6.95 (d, 1 H, H-6′), 2.51 (s, 3 H, CH_3); δ_C([^{2}H]TFA) 143.4 (C), 140.9 (C), 139.5 (CH), 135.5 (CH), 134.9 (C), 131.4 (CH), 129.9 (C), 123.0 (CH), 120.1 (CH), 115.6 (CH), 110.2 (CH), 20.1 (CH_3) (Found: C, 77.6; H, 4.5; N, 18.2; MH$^+$ [CI], 311. $C_{20}H_{14}N_4$ requires, C, 77.4; H, 4.55; N, 18.05%; *M*H, 311).

9-(Benzotriazol-1-yl)-1-methylacridine 10e. From **9e** as yellow crystals (84%), mp 220 °C (decomp.); ν_{max}(KBr)/cm^{-1} 1579, 1474, 1421, 1258, 1093, 758; λ_{max}(EtOH)/nm 200, 253, 362.5; δ_H([^{2}H]TFA) 7.70 (m, 5 H), 7.41 (m, 4 H), 7.07 (m, 2 H), 2.87 (s, 3 H, CH_3); δ_C([^{2}H]TFA) 163.9 (C), 144.2 (C), 142.9 (C), 139.5 (CH), 138.8 (CH), 135.3 (C), 133.1 (CH), 130.3 (CH), 128.9 (CH), 127.6 (CH), 121.9 (C), 120.2 (CH), 119.2 (C), 117.6 (C), 25.4 (CH_3).

9-(Naphtho[2,3-*d*]triazol-1-yl)acridine 10f. From **9f** as amber needles (59%), mp 255.2 °C (decomp.); ν_{max}(KBr)/cm^{-1} 3036, 1553, 1460, 1424, 1275, 1044, 883, 750; λ_{max}(EtOH)/nm 215, 247, 320, 361; δ_C([^{2}H]TFA) 141.0 (C), 139.3 (CH), 135.3 (C), 133.2 (C), 130.7 (CH), 129.3 (CH), 129.0 (CH), 127.6 (CH), 127.3 (CH), 124.2 (CH), 123.1 (C), 119.9 (CH), 117.2 (CH), 106.8 (CH) (Found: C, 79.2; H, 3.9; N, 16.0; MH$^+$ [CI], 346. $C_{23}H_{14}N_4O_2$ requires C, 79.7; H, 4.1; N, 16.2%; *M*H, 346).

Hydrolysis of 9-(triazol-1-yl)acridines

Hydrolysis of 9-(1,2,3-triazol-1-yl)acridine **7a** (0.1 g) in boiling 2 M hydrochloric acid (2 h) gave a precipitate of acridone **6** (0.06 g)[3] when the cooled mixture was adjusted to pH 5. Similarly, hydrolysis of 9-(benzotriazol-1-yl)acridine **10a** gave a mixture of acridone and benzotriazole (1:1).

7*H*-Pyrido[4,3,2-*kl*]acridine 8

9-(1,2,3-Triazol-1-yl)acridine **7a** (0.24 g) was mixed with diphenyl ether (10 g) and the mixture was heated at reflux temperature until TLC analysis showed that all the triazole had been consumed (generally 2 h). The mixture was added to the top of a silica gel column and the column eluted with hexane to remove diphenyl ether. The product was then eluted with EtOH–ethyl acetate (1:1), solvent evaporated and the residue crystallised from aqueous DMF to give red–brown crystals (0.16 g, 75%), mp 281–282 °C; ν_{max}(KBr)/cm^{-1} 3449, 3015, 1638, 1547, 1466, 1433, 1343, 762 cm^{-1}; δ_H([$^2H_6$]DMSO) 10.73 (br s, 1 H, NH), 8.32 (d, 1 H, H-11), 8.12 (d, 1 H, H-2), 7.43 (m, 2 H, H-5,9), 7.14 (m, 2 H, H-3,8), 7.04 (t, 1 H, H-10), 6.98 (d, 1 H, H-4), 6.78 (d, 1 H, H-6); δ_C([$^2H_6$]DMSO) 152.0 (C), 145.0 (CH), 141.0 (C), 140.8 (C), 138.5 (C), 132.7 (CH), 132.3 (CH), 125.1 (CH), 121.0 (CH), 119.9 (C), 117.0 (CH), 116.5 (CH), 113.2 (CH), 106.2 (CH) (Found: C, 82.3; H, 4.7; N, 12.65; M$^+$ [EI], 218. $C_{15}H_{10}N_2$ requires C, 82.6; H, 4.6; N, 12.8%; *M*, 218).

Similarly prepared were the following compounds.

8*H*-Quino[4,3,2-*kl*]acridine 11a (with C. K. Wong). From **10a**, in 84% yield, mp 285–287 °C (from aqueous DMF) (lit.,[15] >280 °C); ν_{max}(KBr)/cm^{-1} 1628, 1597, 1460, 1384, 1331, 1154, 745; δ_H([$^2H_6$]DMSO) 10.78 (br s, 1 H, NH), 8.56 (d, 1 H, H-12), 8.39 (d, 1 H, H-4), 7.91 (d, 1 H, H-5), 7.83 (d, 1 H, H-1), 7.67 (t, 1 H, H-6), 7.70 (t, 1 H, H-2), 7.48 (t, 1 H, H-10), 7.41 (t, 1 H, H-3), 7.22 (d, 1 H, H-9), 7.13 (m, 2 H, H-7,11); δ_C([$^2H_6$]DMSO) 150.4 (C), 145.5 (C), 139.9 (C), 132.1 (CH), 131.7 (CH), 129.2 (CH), 128.6 (CH), 124.8 (CH), 122.9 (CH), 122.8 (C), 121.1 (CH), 119.7 (C), 115.9 (CH), 115.1 (C), 110.4 (CH), 109.7 (CH) (Found: C, 84.8; H, 4.4; N, 10.2; MH$^+$ [CI], 269. Calc. for $C_{19}H_{12}N_2$: C, 85.0; H, 4.5; N, 10.45%; *M*H, 269).

3-Chloro-8*H*-quino[4,3,2-*kl*]acridine 11b. From **10b**, in 50% yield, mp 240–241 °C (from aqueous DMF); ν_{max}(KBr)/cm^{-1}

3396, 1625, 1605, 1543, 1466, 1329, 1155, 743; δ_H([$^2H_6$]DMSO) 10.90 (br s, 1 H, NH), 8.54 (d, 1 H, H-12), 8.24 (s, 1 H, H-4), 7.92 (d, 1 H, H-5), 7.73 (m, 2 H, H-1,6), 7.46 (m, 2 H, H-2,10), 7.22 (d, 1 H, H-9), 7.13 (m, 2 H, H-7,11); δ_C([$^2H_6$]DMSO) 150.5 (C), 140.9 (C), 140.7 (C), 135.9 (C), 134.5 (C), 132.8 (CH), 132.4 (CH), 131.6 (CH), 129.0 (CH), 125.5 (CH), 123.4 (C), 123.3 (CH), 121.8 (CH), 116.7 (CH), 116.0 (C), 111.2 (CH), 110.2 (C), 109.8 (CH) (Found: C, 75.2; H, 3.4; N, 9.2; M^+ [EI], 302, 304. $C_{19}H_{11}ClN_2$ requires C, 75.4; H, 3.6; N, 9.25%; *M*, 302, 304).

2-Nitro-8*H*-quino[4,3,2-*kl*]acridine 11c. From **10c**, in 65% yield, mp >300 °C (from aqueous DMF); ν_{max}(KBr)/cm^{-1} 3368, 1626, 1561, 1463, 1437, 1383, 1343, 742; δ_H([$^2H_6$]DMSO) 11.82 (br s, 1 H, NH), 8.24 (m, 2 H, H-4,12), 8.14 (d, 1 H, H-1), 7.88 (dd, 1 H, H-3), 7.74 (m, 2 H, H-5,6), 7.57 (t, 1 H, H-10), 7.20 (m, 3 H, H-7,9,11); δ_C([$^2H_6$]DMSO) 151.7 (C), 151.2 (C), 142.8 (C), 139.8 (CH), 137.0 (C), 133.4 (C), 132.2 (C), 130.2 (C), 128.5 (CH), 127.9 (CH), 124.7 (CH), 123.9 (CH), 121.4 (CH), 118.8 (CH), 118.0 (CH), 117.3 (CH), 115.8 (C), 113.4 (C) (Found: C, 62.4; H, 3.7; N, 11.4; M^+ [EI], 313. $C_{19}H_{11}N_3O_2\cdot 3H_2O$ requires C, 62.1; H, 4.3; N, 11.5%; *M*, 313).

3-Methyl-8*H*-quino[4,3,2-*kl*]acridine 11d. From **10d** in 50% yield, mp 230–232 °C (from aqueous DMF); ν_{max}(KBr)/cm^{-1} 2989, 1627, 1600, 1536, 1466, 1330, 1154, 743; δ_H([$^2H_6$]DMSO) 10.83 (br s, 1 H, NH), 8.57 (dd, 1 H, H-12), 8.23 (s, 1 H, H-4), 7.78 (d, 1 H, H-5), 7.73 (m, 2 H, H-1,6), 7.47 (m, 2 H, H-2,10), 7.19 (d, 1 H, H-9), 7.14 (m, 2 H, H-7,11), 2.52 (s, 3 H, CH_3); δ_C([$^2H_6$]DMSO) 149.6 (C), 143.8 (C), 140.2 (C), 140.0 (C), 134.3 (C), 133.9 (C), 132.0 (CH), 131.7 (CH), 130.9 (CH), 128.7 (CH), 124.8 (C), 122.7 (C), 122.6 (CH), 121.0 (CH), 120.0 (CH), 116.0 (CH), 115.3 (C), 110.4 (CH), 109.6 (CH), 21.4 (CH_3) (Found: C, 84.75; H, 4.9; N, 10.1; M^+ [EI], 282. $C_{20}H_{14}N_2$ requires C, 85.1; H, 5.0; N, 9.9%; *M*, 282).

12-Methyl-8*H*-quino[4,3,2-*kl*]acridine 11e. From **10e**, in 60% yield, mp 185–187 °C (from aqueous DMF); ν_{max}(KBr)/cm^{-1} 3404, 1621, 1600, 1534, 1460, 1384, 1180, 763; δ_H([$^2H_6$]DMSO) 10.80 (br s, 1 H, NH), 8.40 (d, 1 H, H-4), 7.89 (d, 1 H, H-5), 7.82 (d, H, H-1), 7.64 (m, 2 H, H-2,6), 7.40 (t, 1 H, H-3), 7.29 (t, 1 H, H-10), 7.08 (m, 2 H, H-7,9), 6.88 (d, 1 H, H-11), 3.12 (s, 3 H, CH_3); δ_C([$^2H_6$]DMSO) 157.2 (C), 150.0 (C), 146.7 (C), 144.1 (C), 139.0 (C), 136.2 (CH), 135.2 (CH), 133.5 (2 × CH), 129.6 (CH), 129.3 (CH), 127.2 (CH), 126.7 (C), 122.8 (C), 120.2 (C), 118.7 (CH), 114.6 (C), 113.6 (CH), 30.9 (CH_3) (Found: C, 82.7; H, 4.9; N, 9.7; M^+ [EI], 282. $C_{20}H_{14}N_2\cdot 0.5H_2O$ requires C, 82.5; H, 5.15; N, 9.6%; *M*, 282). Also isolated by flash chromatography of the crude thermolysis mixture were 8*H*-quino[4,3,2-*kl*]acridine **11a** (12%), identical (mp; IR, UV, ^{1}H and ^{13}C NMR and mass spectra) and a product (<1%) tentatively identified as the benzoazepinoacridine **12** with M^+ (EI) 282 and 268 ($M^+ - CH_2$).

4*H*-Benzo[6,7]quino[4,3,2-*kl*]acridine 11f. Prepared by thermolysis of **10f**, in 60% yield, mp 313–315 °C (from aqueous DMF); ν_{max}(KBr)/cm^{-1} 3449, 1626, 1597, 1535, 1468, 1385, 1155, 739; δ_H([$^2H_6$]DMSO) 10.95 (br s, 1 H, NH), 8.93 (s, 1 H), 8.51 (dd, 1 H), 8.23 (s, 1 H), 8.08 (d, 1 H), 7.97 (dd, 1 H), 7.91 (dd, 1 H), 7.68 (t, 1 H), 7.39 (m, 3H), 7.16 (d, 2 H), 7.06 (t, 1 H); δ_C([$^2H_6$]DMSO) 152.0 (C), 140.7 (C), 140.6 (C), 134.5 (C), 134.1 (C), 133.0 (CH), 132.8 (CH), 131.4 (C), 129.0 (C), 125.5 (CH), 128.2 (CH), 127.0 (CH), 125.9 (CH), 125.7 (CH), 123.6 (C), 122.7 (CH), 122.0 (CH), 117.1 (CH), 114.6 (C), 112.6 (CH) (Found: C, 83.7; H, 4.3; N, 8.5; M^+ [EI], 318. $C_{23}H_{14}N_2\cdot 1H_2O$ requires C, 84.1; H, 4.8; N, 8.5%; *M*, 318).

2-Amino-8*H*-quino[4,3,2-*kl*]acridine 11g

A suspension of 2-nitro-8*H*-quino[4,3,2-*kl*]acridine **11c** in methanol (100 cm^3) was hydrogenated over activated palladium–carbon (0.05 g) for 3 h at 30 psi and 25 °C. Removal of catalyst through Celite, followed by evaporation of solvent gave the aminoquinoacridine **11g** (58% yield, red crystals, from aqueous DMF), mp >300 °C (decomp.); ν_{max}(KBr)/cm^{-1} 3439, 1630, 1600, 1470, 1384, 1330, 1112, 773; δ_H([$^2H_6$]DMSO) 10.87 (br s, 1 H, NH), 8.72 (d, 1 H, H-12), 8.13 (d, 1 H, H-4), 7.67 (d, 1 H, H-5), 7.51 (t, 1 H, H-6), 7.45 (t, 1 H, H-10), 7.20 (d, 1 H, H-9), 6.97 (m, 4 H, H-1,3,7,11), 5.54 (br s, 2 H, NH_2); δ_C([$^2H_6$]DMSO) 150.0 (C), 147.4 (C), 140.1 (C), 134.9 (C), 131.9 (CH), 131.5 (CH), 124.8 (CH), 123.7 (CH), 120.8 (CH), 116.2 (C), 115.9 (CH), 115.1 (CH), 113.4 (C), 109.7 (CH), 109.1 (CH), 107.0 (CH); M^+ (EI) 283.

9-(2-Iodoanilino)acridine 16

To a solution of 2-iodoaniline (1.20 g) in refluxing anhydrous methanol (35 cm^3) was added 9-chloroacridine (1.07 g) over 0.5 h. The mixture was boiled (10 h), cooled and excess diethyl ether added. The precipitated iodoanilinoacridine hydrochloride salt (75%) was collected (Found: M^+ [EI], 396. $C_{19}H_{13}IN_2$ requires *M*, 396).

The free base, mp 186–188 °C (from methanol), was obtained from the hydrochloride salt by trituration with aqueous ammonia; ν_{max}(KBr)/cm^{-1} 3372, 1626, 1590, 1528, 1474, 1146, 1009, 752; λ_{max}(EtOH)/nm 223, 244, 410; δ_H([$^2H_6$]DMSO) 11.25 (br s, 1 H, NH), 8.07 (d, 2 H, H-1,8), 7.70 (t, 2 H, H-3,6), 7.52 (m, 4 H), 6.98 (m, 4 H); δ_C([$^2H_6$]DMSO) 155.6 (C), 151.6 (C), 141.0 (C), 140.0 (CH), 132.5 (CH), 130.4 (CH), 127.9 (C), 123.7 (CH), 122.0 (CH), 118.7 (CH), 117.6 (CH), 91.2 (C).

The free base (0.4 g) was dissolved in dry toluene (5 cm^3). Tributyltin hydride (2.5 cm^3) was added, the mixture was heated to reflux under nitrogen and a solution of 2,2′-azoisobutyronitrile (0.012 g) in dry toluene (1 cm^3) was added dropwise. The mixture was boiled (12 h) with light exclusion, cooled, diluted with diethyl ether (20 cm^3). The precipitated mixture was separated by flash chromatography (hexanes–ethyl acetate, 1:1) into unreacted iodoanilinoacridine and 8*H*-quino[4,3,2-*kl*]acridine **11a** (0.09 g, 32%), identical (mp; UV, IR, ^{1}H and ^{13}C NMR spectra) to a sample prepared by thermolysis of 9-(benzotriazol-1-yl)acridine **10a** (see above).

X-Ray crystal structure determination

Crystal data: $C_{19}H_{12}N_2$, M_r 268.31, monoclinic, space group $P2_1/c$, a = 7.169(1), b = 14.401(3), c = 12.397(3) Å, β = 93.92(2)°, V = 1276.9(4) Å^3, Z = 4, D_x = 1.396 g cm^{-3}. On an Enraf-Nonius CAD4 diffractometer with Mo-Kα radiation (λ = 0.71 073 Å) 4778 reflections were collected, of which 2257 were independent (R_{int} = 0.0972) and 896 were considered observed [$I > 2\sigma(I)$]. The structure was solved by direct methods,[24] all hydrogen atoms were located in difference electron density maps, and positional parameters of all atoms together with appropriate displacement parameters were refined by the full-matrix least-squares method.[25] The final discrepancy indices were R = 0.048 for observed reflections and $wR(F^2)$ = 0.102 for all data. The final difference electron density synthesis showed no feature greater than ±0.18 e Å^{-3}.†

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† Atomic coordinates, thermal parameters and bond lengths and angles have been deposited at the Cambridge Crystallographic Data Centre (CCDC). See Instructions for Authors, *J. Chem. Soc., Perkin Trans. 1*, 1997, Issue 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 207/133.

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