Antitumour polycyclic acridines. Part 5.[1] Synthesis of 7*H*-pyrido[4,3,2-*kl*]acridines with exploitable functionality in the pyridine ring

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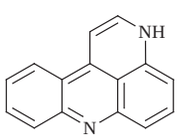
Two series of new 9-(1,2,3-triazol-1-yl)acridines 8 and 11 have been synthesised by base catalysed cyclisation reaction of 9-azidoacridine 5 with either 1,3-dicarbonyl compounds or activated acetonitriles. Ring formation occurred in a regiospecific manner indicating a stepwise ionic reaction sequence. The combination of activating base and solvent, as well as the solubility of the products, are crucial for achieving acceptable yields. Several of the 9-(1,2,3-triazol-1-yl)acridines have been converted to fluorescent 7*H*-pyrido[4,3,2-*kl*]acridines 14 by Graebe–Ullmann nitrogen-expulsion degradations employing boiling diphenyl ether as the thermolytic medium. In one case, the thermolysis of 9-[4-methoxycarbonyl-5-(4-chlorobutyl)-1,2,3-triazol-1-yl]acridine 16, the chlorobutyl side-chain participated in an additional intramolecular cyclisation step leading to the pentacyclic quinolizino[2,3,4-*kl*]acridine 18.

Introduction

Since the early days of the 20th century acridine derivatives have attracted the attention of medicinal chemists because of their broad-ranging biological properties.[2] Notably, in recent years the DNA binding propensities and topoisomerase II-inhibitory activities of acridines have been exploited in the development of clinically-active antitumour agents.[3] A series of polycyclic aromatic compounds based on 3*H*-pyrido[2,3,4-*kl*]-acridine **1** have been isolated from natural (marine) sources[4]



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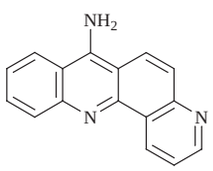

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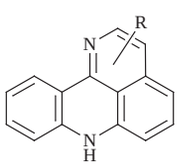

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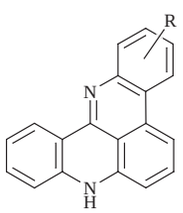

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and also shown to inhibit topoisomerase II. A derivative of a related pyridoacridine, 7-aminopyrido[2,3-*c*]acridine **2**, has been shown to inhibit human gastric carcinoma MKN 45 cells: the planar aromatic tetracycle is more active than the 5,6-dihydro analogue.[5] In our own work we have exploited the Graebe–Ullmann degradation of 1,2,3-triazoles[6] to construct examples of the 7*H*-pyrido[4,3,2-*kl*]acridine **3**[7] and 8*H*-quinolino[4,3,2-*kl*]acridine ring systems **4**[8] using appropriate 9-(1,2,3-triazolyl)acridines as starting materials.

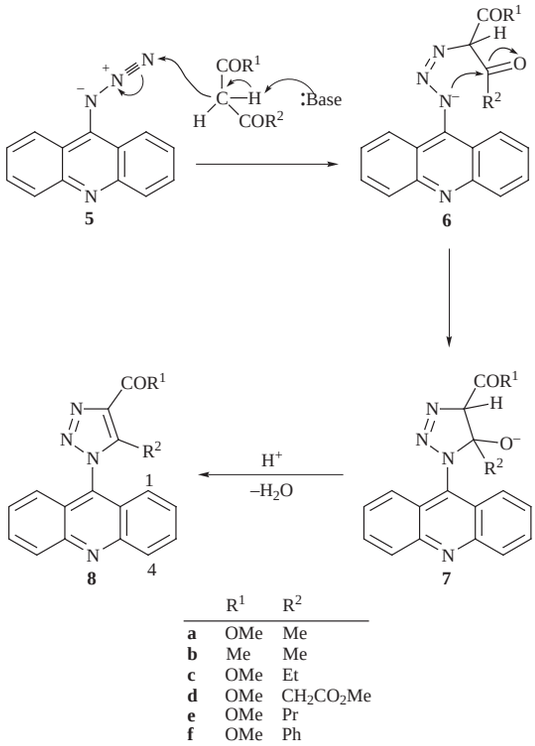
The most general and versatile synthesis of 1,2,3-triazoles comprises the pericyclic addition of organic azides to 1,3-dipolarophiles such as alkynes.[9] A problem with concerted 1,3-dipolar cycloadditions with 9-azidoacridine **5** is that unsymmetrical alkynes can give two isomeric 9-(triazolyl)acridines with poor regioselectivity, and separation of the product mixture is necessary.[7] Also, although 1*H*-1,2,3-benzotriazoles are usually obtained in a regiospecific manner from diazotised derivatives of *o*-phenylenediamines,[8] this method cannot be applied to generate 1,2,3-triazoles lacking the benzo anelland.

In the course of our project directed towards the development of new anticancer polycyclic acridines we now report a new synthesis of 9-(1,2,3-triazol-1-yl)acridines from 9-azidoacridine **5** and reactive methylenic compounds; this route has the advantage that a single triazolylacridine is formed. Certain of the products have been subjected to nitrogen expulsion under Graebe–Ullmann conditions to give pyrido[4,3,2-*kl*]-acridines which bear functionalities suitable for the attachment of additional pharmacophores.

Results and discussion

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

It is well known that organic azides undergo base-catalysed condensation reactions with activated methylenic compounds.[10] In order to generate appropriate triazolylacridine precursors for the formation of pyrido[4,3,2-*kl*]acridines we used commercially available 1,3-dicarbonyl compounds as reaction partners of 9-azidoacridine[11] **5** (Scheme 1). When a solution of the azidoacridine **5** was allowed to react with an excess of methyl acetoacetate or pentane-2,4-dione in methanolic potassium hydroxide or sodium methoxide, the corresponding 9-(1,2,3-triazol-1-yl)acridines **8a**,**b** precipitated in good yields from the reaction medium. Reactions with other methylenic esters gave triazoles **8c**–**f** which were soluble in the reaction media and were isolated in poor yields after chromatographic separation on silica gel to effect purification. For example, reaction between **5** and methyl propionylacetate gave the required triazole **8c** (23%) together with 9-methoxyacridine. The contaminant presumably arises from the reaction between **5** acting as a reactive 'pseudo halogen'[11] and methoxide ion. No cyclisation occurred if the reaction was carried out in the absence of a base and removal of the by-product water by means of molecular sieves did not improve the yields. The use of methanol as reaction medium is indispensable, as the formation of the 9-(1,2,3-triazol-1-yl)-acridines was suppressed if the reaction was performed in less

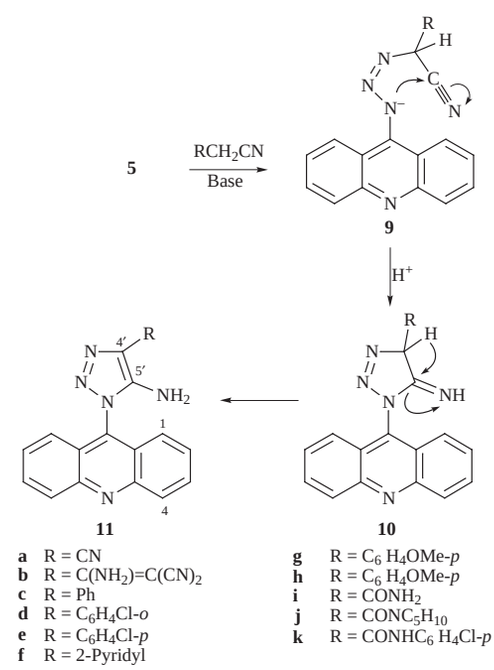


	R^1	R^2
a	OMe	Me
b	Me	Me
c	OMe	Et
d	OMe	CH_2CO_2Me
e	OMe	Pr
f	OMe	Ph

Scheme 1

polar solvents (tetrahydrofuran or dichloromethane). If the ethyl ester derivatives of reactive methylenic substrates were employed, ester exchanges were observed giving rise to the final isolation of the methyl esters **8e**,**f**.

In order to obtain the amino-substituted triazolylacridines from 9-azidoacridine **5**, activated acetonitriles were employed as the reactive methylenic partners. Thus malononitrile and malononitrile dimer (2-aminoprop-1-ene-1,1,3-tricarbonitrile) gave the aminotriazoles **11a**,**b** in 47 and 53% yields, respectively (Scheme 2). The reaction required alkoxide as base and surprisingly failed when carried out in the presence of amines such as Hünig's base. In the case of the benzylic nitriles, initially poor yields of **11c**–**h** (<5%) were obtained when the reactions were performed in a sodium methoxide–methanol system. Considerable improvements in yields were achieved if the combination sodium methoxide in ethanol was employed. Apparently the low concentration of ethoxide ion in the equilibrium was necessary to promote the reaction. Under these conditions phenylacetonitriles, with electron-withdrawing groups in the phenyl substituent, and (2-pyridyl)acetonitrile gave aminotriazoles **11c**–**f** in excellent (70–88%) yields, whereas electron-donating groups in the benzylic substrates gave poor yields of the aminotriazoles **11g** (28%) and **11h** (36%). Similarly, interaction of azidoacridine **5** and cyanoacetamide and its *N*-substituted derivatives gave only poor yields of aminotriazoles **11i**–**k**.



a	R = CN	**g**	R = C_6H_4OMe-*p*
b	R = $C(NH_2)=C(CN)_2$	**h**	R = C_6H_4OMe-*p*
c	R = Ph	**i**	R = $CONH_2$
d	R = C_6H_4Cl-*o*	**j**	R = $CONC_5H_{10}$
e	R = C_6H_4Cl-*p*	**k**	R = $CONHC_6H_4Cl$-*p*
f	R = 2-Pyridyl		

Scheme 2

The compositions of the heterocycles were confirmed by either elemental analysis or high resolution mass spectroscopy. The formation of regioisomeric mixtures was excluded by the NMR spectral data. The acridine protons appeared as the expected ABCD spin system between δ 7.25 and 8.37. Unambiguous confirmation of the regiochemistry of the condensation reaction was provided by NOE difference spectroscopy of compound **8c**, showing NOE enhancement for the acridine protons in the 1-position at δ 7.25 when the triplet signal of the ethyl substituent at δ 0.87 was irradiated. The observation of an NOE from the broad singlet at δ 6.52 in the triazolylacridine **11i** to the acridine protons in the 1-position at δ 7.35 confirmed the location of the amino group on the 5′-position of the triazole ring. As a result of the conjugation of the two cyano groups and the presence of two donor groups in the α-position the 4′-C signal of the triazole **11b** appeared at relatively high field (δ 70.4) in the ^{13}C NMR spectrum.

Semiempirical MO calculations indicate that the positive charge in the azido group of 9-azidoacridine **5** is localised at the central nitrogen (+0.724), not at the terminal one (−0.334).[12] Preferred nucleophilic attack of the carbanions at the terminal azido nitrogen to generate intermediate triazenyl anions **6a**–**f** and **9a**–**k** can be explained by considering the orbital interaction of the decisive frontier molecule orbitals. The reaction is most likely directed by a bonding overlap of the LUMO of **5** and the HOMO of the α-methylene carbon of the carbanions. The intermediacy of triazenyl species also explains the formation of traces (TLC) of 9-aminoacridine detected in many of these cyclisations, since monoalkyltriazenes are known to undergo heterolysis to arylamines.[13] Subsequent steps comprise either 5-*exo-trig* or 5-*exo-dig* cyclisation of the triazenyl anions to give the triazolines **7a**–**f** or **10a**–**k**, respectively. In the case of the triazolines **7a**–**f** from 1,3-dicarbonyl compounds, aromatisation to triazoles **8a**–**f** was accompanied by the elimination of water; tautomerism of the iminotriazolines **10a**–**k** produced the favoured aminotriazoles **11a**–**k**.

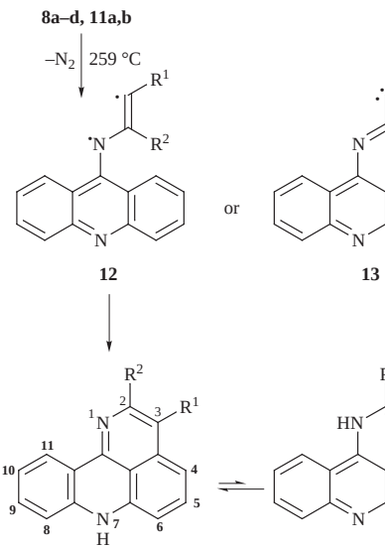
Thermal Graebe–Ullmann conversion of 9-(1,2,3-triazol-1-yl)-acridines to 7*H*-pyrido[4,3,2-*kl*]acridines

Classic Graebe–Ullmann conditions for the elimination of nitrogen from 1-aryl-1*H*-1,2,3-triazoles involve heating the triazole beyond its melting point.[6] Alternative fragmentations can be initiated photochemically[14] or by microwave irradiation of the triazoles in the presence of pyrophosphorus acid.[15]

Recently we have shown that thermal Graebe–Ullmann conversions of 9-(1,2,3-triazol-1-yl)acridines and 9-(1,2,3-benzotriazolyl)acridines to tetracyclic **3** and pentacyclic acridines **4** can be monitored by differential scanning calorimetry (DSC).[7,8] Analysis of the thermal transitions of the series of compounds prepared in the present work show, in addition to melting endotherms, singular exothermic events corresponding to dinitrogen expulsion and cyclisation (Table 1). For example, decomposition endotherms were measured at 256 and 277 °C for the triazoles **8a** and **8b**, respectively.

Following the successful experiences in our earlier work[7,8] we employed boiling diphenyl ether (bp 259 °C) as a vehicle to effect conversion of triazoles **8a**–**d** to tetracyclic acridines. Reaction was complete in 5–15 min and the highly fluorescent

products **14a**–**d** were isolated in high yields (76–86%). Of the aminotriazole series **11** only those substrates with cyano groups **11a**,**b** gave the corresponding aminopyridoacridines **14e**,**f**, respectively. The mechanism of the cyclisation involves either diradical **12** or iminocarbene **13** intermediates which insert into the C–H bond in the *peri* position of the acridine nucleus (Scheme 3) followed by an aromatising shift of the H-atom.[16]



	R^1	R^2
a	CO_2Me	Me
b	COMe	Me
c	CO_2Me	Et
d	CO_2Me	CH_2CO_2Me
e	CN	NH_2
f	$C(NH_2)=C(CN)_2$	NH_2

Scheme 3

The structures of the pyrido[4,3,2-*kl*]acridines **14a**–**f** were confirmed by elemental analysis and high resolution mass spectral data. The signals recorded in the ^{1}H NMR spectrum showed the typical pattern of the angular fused acridine system.[7,8] Further structural information was furnished by a ^{1}H–^{1}H COSY-45 NMR spectrum of compound **14b**. Thus, five pronounced cross peaks were observed demonstrating the five vicinal spin-spin interactions. Unambiguous confirmation for the presence of the 7*H*-tautomer was provided by an NOE experiment. The irradiation of the absorption of the NH hydrogen at δ 7.64 in **14b** gave rise to two NOE enhancements of the signals at δ 6.60 and 6.91, revealing the direct neighbourhood to the protons in the 6- and 8-position. Furthermore, the chemical shifts of the skeletal ^{13}C nuclei were consistent with the proposed structure for the tetracyclic system. Accordingly, seven CH signals at low field and two CH_3 signals at high field were observed in the DEPT135 experiment on **14b**. The carbon atom C-3 of the 3-cyano-substituted tetracycle **14e** experienced a pronounced shielding (δ_C 75.9) owing to the vicinity of the amino function in the 2-position.

Semiempirical MO calculations on the two possible tautomers of the tetracyclic acridines showed that the equilibrium **14** ⇌ **15** favoured the 7*H*-tautomers **14** since the calculated enthalpies of formation were in the range 43.5–59.9 kJ mol^{-1} lower in the pyridoacridines **14a**–**f** compared to the corresponding 1*H*-tautomers (Table 1).[12] This preference for the 7*H*-tautomers **14** over the 1*H*-structures **15** can be explained by steric interactions between the amino hydrogen and the *peri* H-atom at position 11 in the less stable tautomers **15**.

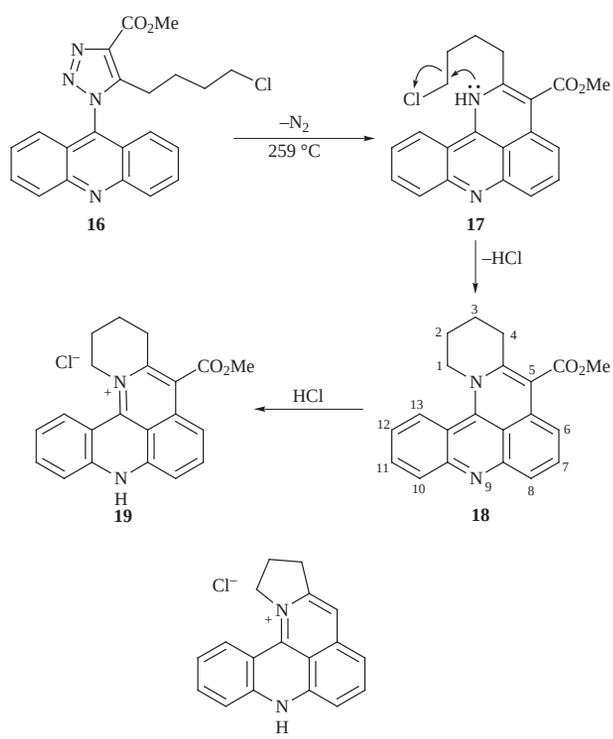
One 9-azidoacridine cyclisation with a reactive methylenic substrate gave rise to an unusual polycyclic acridine. Thus

Table 1 Differential scanning calorimetry (DSC) of the decomposition of selected triazoles **8** and semiempirical calculation of the tautomerism of the tetracycles **14/15** using the MOPAC programme[12]

DSC			MOPAC	
8→**14**	T_{dec}/°C[a]	ΔH_{dec}/kJ mol^{-1}[b]	**14**→**15**	ΔH_{calc}/kJ mol^{-1}[c]
a	256	−162	**a**	46.9
b	277	−202	**b**	44.8
c	272	−227	**c**	43.5
d	256	−253	**d**	46.0
			e	59.9
			f	55.3

[a] Decomposition process, minimum of DSC thermogram. [b] Enthalpy of decomposition process. [c] PM3 Calculated enthalpy of the tautomerisation.

interaction of **5** with methyl 7-chloro-3-oxoheptanoate in sodium methoxide–methanol gave a low yield (15%) of the triazole ester **16** contaminated with 9-amino- and 9-methoxyacridines and 2-methoxycarbonylcyclohex-1-enol,[17] the product of intramolecular cyclisation of the starting heptanoate. DSC analysis of the triazole showed an exothermic degradation at 247 °C. Preparative-scale thermolysis of the triazole in boiling diphenyl ether was complete in 10 min and gave a mixture of the yellow 2-(4-chlorobutyl)pyridoacridine ester **17** and the red pentacyclic quinolizinoacridine **18** (Scheme 4). Separation of



Scheme 4

the products was accomplished by column chromatography on silica gel. The light-sensitive tetracycle **17** gave an appropriate MH^+ ion in the ES mass spectrum at *m*/*z* 367. The ^{1}H and ^{13}C NMR spectra were consistent with an angular fused acridine structure and the DEPT135 spectrum confirmed the presence of seven CH signals at low field, four methylene absorptions and a signal for the methyl group at high field.

Presumably the pentacycle **18** is formed by intramolecular cyclisation of the precursor **17** accompanied by dissociation of the hydrochloride salt under the thermolytic conditions. The presence of the additional heteroalicyclic ring in **18** was confirmed by the strong NOE enhancement of the proton at C-13 that occurs when the signal of the methylene protons at the

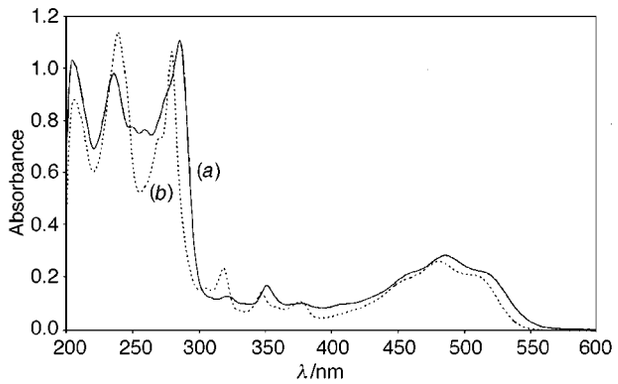


Fig. 1 Electronic absorption spectra of (*a*) the quinolizinoacridinium chloride **19** and (*b*) the indolizinoacridinium salt **20** in ethanol

1-position was irradiated. The protons at the 1-position experience a marked deshielding (δ 4.29) because of the ring current effect of the acridine nucleus. Also, a weak NOE effect was observed between the protons of the methyl group and the proton at C-6. The expected spin system for the ^{1}H and ^{13}C nuclei of **18** was seen in both the ^{1}H–^{1}H COSY-45 and in the inverse correlated ^{13}C–^{1}H NMR spectra.

The neutral, insoluble pentacyclic acridine **18** was converted to a water-soluble hydrochloride salt **19** which, as expected, had a qualitatively similar electronic absorption spectrum to that of the indolizinoacridinium salt **20** which we have synthesised previously from the cycloaddition reaction between 9-azidoacridine and 5-chloropent-1-yne (Fig. 1).[7]

In summary we have demonstrated that the base-catalysed cycloaddition reaction of activated methylene compounds with 9-azidoacridine, as well as the Graebe–Ullmann reaction of the resulting triazolylacridines, are controlled by the substitution pattern of the corresponding precursors. Taken in conjunction with our previous papers[7,8] this new pathway represents a potentially adaptable third major route to antitumour polycyclic acridines. We will publish the biological results on these intriguing compounds separately.

Experimental

All NMR spectra were measured on a Bruker ARX 250 instrument at room temperature unless otherwise stated. Chemical shifts are reported in δ units and referenced to the solvent as internal standard; coupling constants (*J* values) are in Hz. Melting points were obtained on a Gallenkamp melting point apparatus and are uncorrected. IR spectra were measured on a Mattson 2020 Galaxy Series FT-IR spectrometer. UV Spectra were measured on a Pharmacia Biotech Ultraspec 2000 UV/visible Spectrophotometer. Mass spectra were recorded on a Micromass Platform spectrometer. High resolution mass data were collected on a VG Autospec instrument. Differential scanning calorimetry was performed with a Perkin-Elmer DSC-4 instrument as reported previously.[8] Merck silica gel 60 (0.040–0.063 mm) was used for chromatography.

9-(4-Methoxycarbonyl-5-methyl-1,2,3-triazol-1-yl)acridine 8a

To a solution of potassium hydroxide (84 mg, 1.50 mmol) in dry methanol (3 cm^3) was added dropwise a solution of methyl acetoacetate (174 mg, 1.50 mmol) in dry methanol (1 cm^3). After 4 h a solution of 9-azidoacridine[11] **5** (165 mg, 0.75 mmol) in dry methanol (5 cm^3) was added dropwise. After about 20 min crystals precipitated. To complete the reaction the mixture was stirred for 12 h in the dark. The crystals were filtered off and washed with a little methanol and water and recrystallised from boiling ethyl acetate to give the triazole **8a** as colourless crystals (179 mg, 75%), mp 240–241 °C (decomp.) (Found: C, 67.76; H, 4.39; N, 17.51. $C_{18}H_{14}N_4O_2$ requires C, 67.92; H, 4.43; N, 17.60%); ν_{max}(KBr)/cm^{-1} 2951, 1723 (CO), 1441, 1221, 1198, 1101, 772 and 748; δ_H(250.13 MHz; $CDCl_3$) 2.31 (3 H, s, Me), 4.06 (3 H, s, OMe), 7.25 (2 H, ddd, *J* 8.7, 1.3 and 0.8), 7.59 (2 H, ddd, *J* 8.7, 6.7 and 1.0), 7.86 (2 H, ddd, *J* 8.8, 6.7 and 1.3) and 8.36 (2 H, ddd, *J* 8.8, 1.0 and 0.8); δ_C(62.90 MHz; [$^2H_6$]DMSO) 9.2 (CH_3), 52.1 (CH_3), 122.1 (C), 122.3 (CH), 129.3 (CH), 129.8 (CH), 131.6 (CH), 135.1 (C), 136.2 (C), 142.4 (C), 148.9 (C) and 161.5 (C); *m*/*z* (APCI) 319 (MH$^+$, 100%) and 291 (85, MH − N_2).

9-(4-Acetyl-5-methyl-1,2,3-triazol-1-yl)acridine 8b

To a solution of sodium methoxide (81 mg, 1.50 mmol) in dry methanol (3 cm^3) was added pentane-2,4-dione (150 mg, 1.50 mmol). After 4 h a solution of 9-azidoacridine **5** (165 mg, 0.75 mmol) in dry methanol (5 cm^3) was added dropwise. The mixture was stirred for 24 h in the dark. The resulting suspension was concentrated and filtered. The white residue was washed with a little methanol and water. Recrystallisation from boiling ethyl acetate–hexane furnished the triazole **8b** as colourless crystals (141 mg, 62%), mp 203–205 °C (decomp., effervescent) (Found: C, 71.36; H, 4.49; N, 18.72. $C_{18}H_{14}N_4O$ requires C, 71.51; H, 4.67; N, 18.53%); ν_{max}(KBr)/cm^{-1} 3067, 1686 (CO), 1551, 1431, 1279, 1142, 953 and 760; δ_H(250.13 MHz; $CDCl_3$) 2.31 (3 H, s, Me), 2.88 (3 H, s, Me), 7.25 (2 H, d, *J* 8.5), 7.60 (2 H, ddd, *J* 8.5, 6.6 and 1.1), 7.86 (2 H, ddd, *J* 8.7, 6.6 and 1.3) and 8.37 (2 H, d, *J* 8.7); δ_C(62.90 MHz; $CDCl_3$) 9.3 (CH_3), 28.0 (CH_3), 121.8 (CH), 122.5 (C), 128.7 (CH), 130.2 (CH), 130.9 (CH), 135.2 (C), 140.6 (C), 143.4 (C), 149.4 (C) and 194.3 (C); *m*/*z* (APCI) 302 (MH$^+$, 100%) and 275 (55, MH − N_2).

9-(4-Methoxycarbonyl-5-ethyl-1,2,3-triazol-1-yl)acridine 8c

To a solution of *N*-ethyldiisopropylamine (1.0 cm^3, 6.00 mmol) in dry methanol (1 cm^3) was added methyl propionylacetate (0.75 cm^3, 6.00 mmol). After 30 min a solution of 9-azidoacridine **5** (0.66 g, 3.00 mmol) in dry methanol (10 cm^3) was added dropwise and the mixture was stirred for 12 h in the darkness. The resulting solution was evaporated and subjected to column chromatography on silica gel using hexane–diethyl ether (3:7) as eluent. The first fraction contained the excess of the keto ester. 9-Methoxyacridine was eluted as second fraction. Evaporation of the third fraction gave a white powder which was recrystallised from boiling acetone–hexane to give colourless crystals of **8c** (0.23 g, 23%), mp 177–179 °C (effervescent at 210 °C) (Found: C, 68.39; H, 4.73; N, 17.01. $C_{19}H_{16}N_4O_2$ requires C, 68.66; H, 4.85; N, 16.86%); ν_{max}(KBr)/cm^{-1} 3067, 2992, 1734 (CO), 1452, 1215, 1194, 1020, 772 and 746; δ_H(250.13 MHz; $CDCl_3$) 0.87 (3 H, t, *J* 7.5, CH_2CH_3), 2.73 (2 H, q, *J* 7.5, CH_2CH_3), 4.06 (3 H, s, OCH_3), 7.25 (2 H, d, $J_{1,2}$ 8.6, 1-H), 7.58 (2 H, ddd, $J_{2,1}$ 8.6, $J_{2,3}$ 6.7 and $J_{2,4}$ 1.0, 2-H), 7.86 (2 H, ddd, $J_{3,4}$ 8.8, $J_{3,2}$ 6.7 and $J_{3,1}$ 1.3, 3-H) and 8.36 (2 H, d, $J_{4,3}$ 8.8, 4-H); δ_C(62.90 MHz; $CDCl_3$) 13.1 (CH_3), 17.1 (CH_2), 52.3 (CH_3), 121.8 (CH), 122.7 (C), 128.6 (CH), 130.0 (CH), 131.0 (CH), 135.4 (C), 135.9 (C), 147.5 (C), 149.2 (C) and 161.7 (C); *m*/*z* (ES) 331 (MH$^+$, 100%).

9-(4-Methoxycarbonyl-5-methoxycarbonylmethyl-1,2,3-triazol-1-yl)acridine 8d

To a solution of *N*-ethyldiisopropylamine (0.17 ml, 1.00 mmol) in dry methanol (1 cm^3) was added dimethyl 3-oxopentane-1,5-dioate (1.74 g, 10.00 mmol). After 10 min a solution of 9-azidoacridine **5** (1.10 g, 5.00 mmol) in dry methanol (8 cm^3) was added dropwise. After approximately 2 h yellow needles precipitated. The solid was filtered off after 12 h and washed with little methanol to give **8d** as bright yellow needles (0.70 g, 37%), mp 184–186 °C (decomp.) (Found: C, 63.56; H, 4.14; N, 15.03. $C_{20}H_{16}N_4O_4$ requires C, 63.83; H, 4.28; N, 14.89%); ν_{max}(KBr)/cm^{-1} 2955, 2905, 1730 (CO), 1489, 1462, 1439, 1416, 1387, 1346, 1325, 1275, 1233, 1200, 1179, 1144, 1069, 756 and 746; δ_H(250.13 MHz; $CDCl_3$) 3.36 (3 H, s, CH_3), 3.78 (2 H, s, CH_2), 4.05 (3 H, s, OCH_3), 7.30 (2 H, ddd, *J* 8.7, 1.3 and 0.7), 7.60 (2 H, ddd, *J* 8.7, 6.6 and 1.1), 7.86 (2 H, ddd, *J* 8.8, 6.6 and

1.3) and 8.36 (2 H, ddd, *J* 8.8, 1.1 and 0.7); δ_C(62.90 MHz; $CDCl_3$) 29.3 (CH_2), 52.4 (CH_3), 52.5 (CH_3), 121.9 (CH), 122.5 (C), 128.7 (CH), 130.0 (CH), 131.0 (CH), 134.6 (C), 137.6 (C), 138.8 (C), 149.2 (C), 161.5 (C) and 166.9 (C); *m*/*z* (ES) 377 (MH^+, 100%).

9-(4-Methoxycarbonyl-5-propyl-1,2,3-triazol-1-yl)acridine 8e

To a solution of sodium methoxide (81 mg, 1.50 mmol) in dry methanol (3 cm^3) was added a solution of ethyl butyrylacetate (237 mg, 1.50 mmol) in dry methanol (2 cm^3). After 1 h a solution of 9-azidoacridine **5** (165 mg, 0.75 mmol) in dry methanol (5 cm^3) was added dropwise. The mixture was stirred for 24 h in the dark. The resulting solution was evaporated and subjected to column chromatography on silica gel. Using hexane–diethyl ether (1 : 1) as eluent, small amounts of 9-methoxyacridine were separated. Further elution with hexane–diethyl ether (1 : 1) gave a reddish fraction containing the triazole **8e**, which was recrystallised from boiling ethyl acetate–hexane to furnish colourless crystals (39 mg, 15%), mp 139–140 °C (effervescence at 240 °C) (Found: C, 69.48; H, 5.34; N, 15.92. $C_{20}H_{18}N_4O_2$ requires C, 69.35; H, 5.24; N, 15.92%); ν_{max}(KBr)/cm^{-1} 2969, 1726 (CO), 1460, 1327, 1117, 1030 and 754; δ_H(250.13 MHz; $CDCl_3$) 0.62 (3 H, t, *J* 7.3, CH_2CH_3), 1.20–1.29 (2 H, m), 2.67–2.74 (2 H, m), 4.06 (3 H, s, OCH_3), 7.25 (2 H, d, *J* 8.7), 7.59 (2 H, ddd, *J* 8.7, 6.6 and 1.1), 7.87 (2 H, ddd, *J* 8.8, 6.6 and 1.3) and 8.36 (2 H, d, *J* 8.8); δ_C(62.90 MHz; $CDCl_3$) 13.6 (CH_3), 21.9 (CH_2), 25.2 (CH_2), 52.2 (CH_3), 121.8 (CH), 122.6 (C), 128.6 (CH), 130.1 (CH), 131.0 (CH), 135.4 (C), 136.3 (C), 146.2 (C), 149.3 (C) and 161.8 (C); *m*/*z* (APCI) 347 (MH^+, 100%) and 319 (20, $MH - N_2$).

9-(4-Methoxycarbonyl-5-phenyl-1,2,3-triazol-1-yl)acridine 8f

To a solution of sodium methoxide (81 mg, 1.50 mmol) in dry methanol (3 cm^3) was added a solution of ethyl benzoylacetate (288 mg, 1.50 mmol) in dry methanol (2 cm^3). After 1 h a solution of 9-azidoacridine **5** (165 mg, 0.75 mmol) in dry methanol (5 cm^3) was added dropwise. The mixture was stirred for 24 h in the dark. The resulting solution was evaporated and subjected to column chromatography on silica gel. Using diethyl ether as eluent, excess ethyl benzoylacetate and small amounts of 9-methoxyacridine were separated. Further elution with diethyl ether gave the triazole **8f** as colourless crystals after recrystallisation from boiling ethyl acetate–hexane (57 mg, 20%), mp 211–213 °C (effervescence at 240 °C) (Found: C, 72.67; H, 4.17; N, 14.68. $C_{23}H_{16}N_4O_2$ requires C, 72.62; H, 4.24; N, 14.73%); ν_{max}(KBr)/cm^{-1} 3061, 2949, 1726 (CO), 1437, 1209, 1057 and 756; δ_H(250.13 MHz; [$^2H_6$]DMSO) 3.84 (3 H, s, OCH_3), 7.09–7.26 (5 H, m), 7.59 (2 H, d, *J* 8.6), 7.70 (2 H, ddd, *J* 8.6, 6.5 and 1.0), 7.94 (2 H, ddd, *J* 8.6, 6.5 and 1.3) and 8.27 (2 H, d, *J* 8.6); δ_C(62.90 MHz; [$^2H_6$]DMSO) 52.1 (CH_3), 122.3 (C), 122.6 (CH), 124.8 (C), 128.2 (CH), 129.2 (CH), 129.3 (CH), 129.6 (CH), 130.3 (CH), 131.6 (CH), 135.7 (C), 136.4 (C), 144.3 (C), 148.6 (C) and 160.9 (C); *m*/*z* (APCI) 381 (MH^+, 100%) and 353 (30, $MH - N_2$).

9-(5-Amino-4-cyano-1,2,3-triazol-1-yl)acridine 11a

To malononitrile (73 mg, 1.10 mmol) in dry methanol (2 cm^3) was added a solution of sodium methoxide (59 mg, 1.10 mmol) in dry methanol (3 cm^3). A solution of 9-azidoacridine **5** (220 mg, 1.00 mmol) in dry methanol (3 cm^3) was added dropwise and a yellow solid started to precipitate. The mixture was stirred for 24 h in the dark. The suspension was filtered and the residue was washed with water and methanol. The resulting yellow powder was purified by column chromatography on silica gel. Using hexane–diethyl ether (1 : 2) as eluent, small amounts of impurities were separated. The fraction from diethyl ether furnished the triazole **11a** as a lemon yellow powder (135 mg, 47%), mp 248–250 °C (decomp.); ν_{max}(KBr)/cm^{-1} 3391, 3082, 2226, 1651, 1588, 1501, 1422, 1009 and 750; δ_H(250.13 MHz; [$^2H_6$]DMSO) 7.30 (2 H, br s, NH_2), 7.52 (2 H, d, *J* 8.6), 7.73 (2 H, ddd, *J* 8.6, *J* 6.6 and *J* 1.1), 7.99 (2 H, ddd, *J* 8.7, *J* 6.6 and *J* 1.3) and 8.35 (2 H, d, *J* 8.7); δ_C(62.90 MHz; [$^2H_6$]DMSO) 100.9 (C), 113.6 (C), 122.6 (CH), 122.7 (C), 128.8 (CH), 129.8 (CH), 131.3 (CH), 134.2 (C), 149.3 (C) and 150.3 (C); *m*/*z* (APCI) 287 (MH^+, 100%) and 259 (65, $MH - N_2$) [Found: *m*/*z* (CI), 287.1059 (MH^+). $C_{16}H_{11}N_6$ requires 287.1045].

9-[5-Amino-4-(1-amino-2,2-dicyanoethenyl)-1,2,3-triazol-1-yl]-acridine 11b

To a solution of 2-aminoprop-1-ene-1,1,3-tricarbonitrile (145 mg, 1.10 mmol) in dry methanol (2 cm^3) was added a solution of sodium methoxide (59 mg, 1.10 mmol) in dry methanol (3 cm^3). 9-Azidoacridine **5** (220 mg, 1.00 mmol) in dry methanol (3 cm^3) was added dropwise. The mixture was stirred for 24 h in the dark and the solid was collected and washed with water and methanol to give the triazole **11b** as a white powder (127 mg, 53%), mp 173–178 °C (decomp.); ν_{max}(KBr)/cm^{-1} 3408, 3329, 3181, 2205, 1640, 1593, 1514, 1437, 1094 and 760; δ_H(250.13 MHz; [$^2H_6$]DMSO) 6.87 (2 H, br s, NH_2), 7.45 (2 H, d, *J* 8.6), 7.69 (2 H, ddd, *J* 8.6, *J* 6.7 and *J* 0.9), 7.99 (2 H, ddd, *J* 8.7, *J* 6.7 and *J* 1.2), 8.22 (2 H, br s, NH_2) and 8.36 (2 H, d, *J* 8.7); δ_C(62.90 MHz; [$^2H_6$]DMSO) 70.4 (C), 116.3 (C), 121.8 (C), 122.8 (C), 123.3 (CH), 128.5 (CH), 129.5 (CH), 131.4 (CH), 136.3 (C), 149.0 (C), 150.9 (C), 151.8 (C) and 162.5 (C); *m*/*z* (APCI) 353 (MH^+, 100%) [Found: *m*/*z* (CI), 353.1263. $C_{19}H_{13}N_8$ requires 353.1263].

9-(5-Amino-4-phenyl-1,2,3-triazol-1-yl)acridine 11c

To a solution of 9-azidoacridine **5** (220 mg, 1.00 mmol) and phenylacetonitrile (1.17 g, 10.0 mmol) in dry ethanol (6 cm^3) was added dropwise a solution of sodium methoxide (54 mg, 1.00 mmol) in dry ethanol (2 cm^3). The suspension was stirred for 24 h in the dark. The precipitate was collected and washed with water and hot methanol to give the triazolylacridine **11c** as a bright yellow powder (256 mg, 76%), mp 207–209 °C (decomp.); ν_{max}(KBr)/cm^{-1} 3426, 3289, 3163, 1638, 1510, 1424, 1269, 980 and 756; δ_H(250.13 MHz; [$^2H_6$]DMSO) 6.00 (2 H, br s, NH_2), 7.30 (1 H, tt, *J* 7.4 and 1.3), 7.45–7.53 (4 H, m), 7.72 (2 H, ddd, *J* 8.7, 6.6 and 1.1), 7.92–8.01 (4 H, m) and 8.35 (2 H, ddd, *J* 8.5, 1.1 and 1.0); δ_C(62.90 MHz; [$^2H_6$]DMSO) 123.0 (C), 123.1 (CH), 124.9 (CH), 126.1 (C), 126.2 (CH), 128.2 (CH), 128.9 (CH), 129.7 (CH), 131.1 (CH), 132.1 (C), 135.8 (C), 142.4 (C) and 149.3 (C); *m*/*z* (APCI) 338 (MH^+, 100%) and 310 ($MH - N_2$, 35%) [Found: *m*/*z* (CI), 338.1406. $C_{21}H_{16}N_5$ requires 338.1406].

9-[5-Amino-4-(2-chlorophenyl)-1,2,3-triazol-1-yl]acridine 11d

Compound **11d** (73%) was prepared as above as a yellow crystalline powder; mp 167–169 °C (decomp.) (Found: C, 67.69; H, 3.64; N, 18.67. $C_{21}H_{14}N_5Cl$ requires C, 67.84; H, 3.80; N, 18.83%); ν_{max}(KBr)/cm^{-1} 3435, 3283, 3165, 1628, 1561, 1510, 1439, 1420, 988 and 754; δ_H(250.13 MHz; [$^2H_6$]DMSO) 5.85 (2 H, br s, NH_2), 7.46–7.65 (5 H, m), 7.71–7.79 (3 H, m), 7.98 (2 H, ddd, *J* 8.6, 6.6 and 1.2) and 8.35 (2 H, d, *J* 8.6); δ_C(62.90 MHz; [$^2H_6$]DMSO) 122.9 (C), 123.2 (CH), 124.7 (C), 127.4 (CH), 128.2 (CH), 129.7 (CH), 129.7 (CH), 129.9 (CH), 130.5 (C), 131.1 (CH), 132.4 (CH), 133.2 (C), 136.0 (C), 143.4 (C) and 149.3 (C); *m*/*z* (ES) 372 (MH^+, 100%).

9-[5-Amino-4-(4-chlorophenyl)-1,2,3-triazol-1-yl]acridine 11e

To a solution of sodium methoxide (54 mg, 1.00 mmol) in dry ethanol (2 cm^3) was added (4-chlorophenyl)acetonitrile (1.51 g, 10.0 mmol). A solution of 9-azidoacridine **5** (220 mg, 1.00 mmol) in dry ethanol (2 cm^3) was added dropwise. The mixture was stirred for 24 h in the dark. The resulting suspension was filtered and the solid product was washed with water and methanol to give the triazole **11e** as a yellow solid (327 mg, 88%), mp 204–205 °C (decomp.) (Found: C, 67.70; H, 3.60; N, 18.70. $C_{21}H_{14}N_5Cl$ requires C, 67.84; H, 3.80; N, 18.83%);

ν_{max}(KBr)/cm^{-1} 3422, 3293, 3154, 1640, 1562, 1505, 1424, 1265, 1096, 988, 824 and 750; δ_H(250.13 MHz; [$^2H_6$]DMSO) 6.09 (2 H, br s, NH_2), 7.49–7.55 (4 H, m), 7.72 (2 H, dd, *J* 8.0 and 7.0), 7.93–7.80 (4 H, m), 7.97 (2 H, dd, *J* 8.5 and 6.6) and 8.35 (2 H, d, *J* 8.7); δ_C(62.90 MHz; [$^2H_6$]DMSO; 308 K) 122.9 (C), 123.0 (CH), 125.1 (C), 126.5 (CH), 128.1 (CH), 128.7 (CH), 129.6 (CH), 130.5 (C), 130.9 (C), 131.0 (CH), 135.5 (C), 142.5 (C) and 149.2 (C); *m/z* (ES) 372 (MH^+, 20%) and 221 (100).

9-[5-Amino-4-(2-pyridyl)-1,2,3-triazol-1-yl]acridine 11f

To a solution of (2-pyridyl)acetonitrile (591 mg, 5.00 mmol) in dry methanol (2 cm^3) was added a solution of sodium methoxide (270 mg, 5.00 mmol) in dry methanol (5 cm^3). This mixture was treated dropwise with a solution of 9-azidoacridine **5** (991 mg, 4.50 mmol) in dry methanol (13 cm^3). The colour changed to green and a yellow powder precipitated. The resulting suspension was filtered (after 24 h) and the residue was washed with water and methanol to give compound **11f** as a light yellow solid (1.07 g, 70%), mp 277–279 °C (decomp.); ν_{max}(KBr)/cm^{-1} 3441, 3364, 3057, 1647, 1611, 1553, 1532, 1414, 1227, 1080 and 754; δ_H(250.13 MHz; [$^2H_6$]DMSO) 6.88 (2 H, br s, NH_2), 7.37–7.45 (3 H, m), 7.64–7.78 (3 H, m), 8.04–8.08 (4 H, m), 8.56 (1 H, d, *J* 8.8) and 9.30 (1 H, d, *J* 7.0); δ_C(62.90 MHz; [$^2H_6$]DMSO) 117.2 (CH), 119.0 (C), 120.0 (CH), 124.0 (CH), 125.0 (CH), 126.6 (CH), 129.1 (CH), 129.4 (CH), 130.1 (CH), 132.2 (C), 132.9 (C), 149.2 (C), 149.5 (C) and 154.3 (C); *m/z* (ES) 339 (MH^+, 100%) and 311 (45, MH − N_2) [Found: *m/z* (CI), 339.1358 (MH^+). $C_{20}H_{15}N_6$ requires 339.1358].

The triazole can be transformed into its hydrochloride salt with 10 M hydrochloric acid. Lemon yellow powder, mp 248–250 °C (decomp.); ν_{max}(KBr)/cm^{-1} 3443, 3084, 2992, 2515, 1640, 1574, 1535, 1368, 1242 and 758; δ_H(250.13 MHz; D_2O) 7.03 (1 H, dd, *J* 8.0 and 7.0), 7.12 (1 H, dd, *J* 8.0 and 7.0), 7.72–7.83 (4 H, m), 7.94–7.98 (3 H, m) and 8.68 (1 H, d, *J* 7.0); δ_C(62.90 MHz; [$^2H_6$]DMSO) 118.1 (CH), 118.4 (C), 119.7 (CH), 119.8 (CH), 126.1 (CH), 127.0 (CH), 127.3 (CH), 130.6 (C), 130.8 (CH), 133.9 (C), 136.9 (CH), 140.5 (C), 151.6 (C) and 166.4 (C); *m/z* (FAB, Cs^+, 3-nitrobenzyl alcohol) 339 (MH^+ − Cl).

9-[5-Amino-4-(4-methoxyphenyl)-1,2,3-triazol-1-yl]acridine 11g

Compound **11g** (28%) was prepared like compound **11e** as a yellow powder; mp 201–203 °C (decomp.) (Found: C, 71.76; H, 4.56; N, 18.76. $C_{22}H_{17}N_5O$ requires C, 71.92; H, 4.66; N, 19.06%); ν_{max}(KBr)/cm^{-1} 3432, 3289, 3146, 1638, 1572, 1518, 1424, 1246, 828 and 754; δ_H(250.13 MHz; [$^2H_6$]DMSO) 3.82 (3 H, s, CH_3), 5.87 (2 H, br s, NH_2), 7.06 (2 H, d, *J* 8.6), 7.51 (2 H, d, *J* 8.4), 7.72 (2 H, dd, *J* 8.4 and 6.6), 7.86 (2 H, d, *J* 8.6), 7.97 (2 H, dd, *J* 8.5 and 6.6) and 8.34 (2 H, d, *J* 8.5); δ_C(62.90 MHz; [$^2H_6$]DMSO) 55.3 (CH_3), 114.3 (CH), 123.0 (C), 123.2 (CH), 124.6 (C), 126.2 (C), 126.4 (CH), 128.2 (CH), 129.7 (CH), 131.1 (CH), 136.0 (C), 141.7 (C), 149.3 (C) and 157.9 (C); *m/z* (ES) 368 (MH^+, 20%), 340 (30, MH − N_2) and 279 (100).

9-[5-Amino-4-(4-methylphenyl)-1,2,3-triazol-1-yl]acridine 11h

Compound **11h** (36%) was prepared in a similar method to compound **11e** as a light yellow solid; mp 202–203 °C (decomp.); ν_{max}(KBr)/cm^{-1} 3424, 3289, 3163, 1638, 1578, 1518, 1425, 1265, 986, 818 and 754; δ_H(250.13 MHz; [$^2H_6$]DMSO) 2.37 (3 H, s, CH_3), 5.94 (2 H, br s, NH_2), 7.30 (2 H, d, *J* 8.0), 7.52 (2 H, d, *J* 8.5), 7.72 (2 H, dd, *J* 8.5 and 6.8), 7.83 (2 H, d, *J* 8.0), 7.97 (2 H, dd, *J* 8.4 and 6.8) and 8.35 (2 H, d, *J* 8.4); δ_C(62.90 MHz; [$^2H_6$]DMSO; 318 K) 20.7 (CH_3), 122.9 (C), 123.0 (CH), 124.8 (CH), 126.3 (C), 127.9 (CH), 129.1 (C), 129.2 (CH), 129.5 (CH), 130.8 (CH), 135.2 (C), 135.7 (C), 141.9 (C) and 149.2 (C); *m/z* (ES) 352 (MH^+, 60%), 324 (25, MH − N_2), 221 (100%) [Found: *m/z* (CI), 352.1562 (MH^+). $C_{22}H_{18}N_5$ requires 352.1562].

9-(5-Amino-4-carbamoyl-1,2,3-triazol-1-yl)acridine 11i

To a solution of 9-azidoacridine **5** (220 mg, 1.00 mmol) in dry ethanol (7 cm^3) was added a solution of 2-cyanoacetamide (92 mg, 1.10 mmol) in dry ethanol (3 cm^3). The resulting mixture was treated dropwise with a 21% solution of sodium ethoxide in ethanol (357 mg, 1.10 mmol). A yellow powder precipitated and the suspension was stirred for 24 h in the dark. The precipitate was filtered off and washed with water and hot methanol to give compound **11i** as a bright yellow powder (134 mg, 44%), mp 265–267 °C (decomp., effervescent); ν_{max}(KBr)/cm^{-1} 3484, 3405, 3343, 3208, 3150, 1672, 1622, 1588, 1557, 1510, 1400, 1354, 1304, 1007 and 754; δ_H(250.13 MHz; [$^2H_6$]DMSO) 6.52 (2 H, br s, NH_2), 7.35 (1 H, br s, CONH), 7.47 (2 H, d, $J_{1,2}$ 8.5, 1-H), 7.72 (2 H, ddd, $J_{2,1}$ 8.5, $J_{2,3}$ 6.6 and $J_{2,4}$ 1.0, 2-H), 7.80 (1 H, br s, CONH), 7.97 (2 H, ddd, $J_{3,4}$ 8.7, $J_{3,2}$ 6.6 and $J_{3,1}$ 1.3, 3-H) and 8.34 (2 H, d, $J_{4,3}$ 8.7, 4-H); δ_C(62.90 MHz; [$^2H_6$]DMSO) 120.7 (C), 122.8 (C), 122.9 (CH), 128.4 (CH), 129.7 (CH), 131.2 (CH), 135.3 (C), 147.5 (C), 149.3 (C) and 164.3 (C); *m/z* (APCI) 305 (MH^+, 100%) and 195 (40) [Found: *m/z* (CI), 305.1151 (MH^+). $C_{16}H_{13}N_6O$ requires 305.1151].

9-[5-Amino-4-(piperidin-1-ylcarbonyl)-1,2,3-triazol-1-yl]-acridine 11j

To a solution of 9-azidoacridine **5** (220 mg, 1.00 mmol) and 2-cyanoacetylpiperidine (167 mg, 1.10 mmol) in dry methanol (40 cm^3) was added dropwise a solution of sodium methoxide (59 mg, 1.10 mmol) in methanol (3 cm^3). The mixture was stirred for 24 h in the dark. The yellow product was collected. The residue was washed with water and hot methanol to give the triazole **11j** as a yellow powder (97 mg, 26%), mp 230–232 °C (decomp.); ν_{max}(KBr)/cm^{-1} 3403, 3256, 2936, 2849, 1615, 1508, 1414, 1316, 1119, 993 and 752; δ_H(250.13 MHz; [$^2H_6$]DMSO; 343 K) 1.71 (6 H, br), 4.07 (4 H, br), 6.48 (2 H, br s, NH_2), 7.48 (2 H, d, *J* 8.5), 7.71 (2 H, ddd, *J* 8.5, *J* 6.6 and *J* 1.2), 7.96 (2 H, ddd, *J* 8.8, *J* 6.6 and *J* 1.4) and 8.34 (2 H, d, *J* 8.8); δ_C(62.90 MHz; [$^2H_6$]DMSO; 313 K; DEPT135) 24.0 (CH_2), 25.5 (CH_2), 25.7 (CH_2), 122.4 (CH), 127.8 (CH), 129.3 (CH) and 130.6 (CH); *m/z* (APCI) 373 (MH^+, 100%) and 282 (80) [Found: *m/z* (CI), 373.1777 (MH^+). $C_{21}H_{21}N_6O$ requires 373.1777].

9-{5-Amino-4-[*N*-(4-chlorophenyl)carbamoyl]-1,2,3-triazol-1-yl}-acridine 11k

Compound **11k** (15%) was prepared in a similar method to compound **11j** as a yellow solid; mp 231–233 °C (decomp., effervescence); ν_{max}(KBr)/cm^{-1} 3389, 3092, 3067, 1669, 1630, 1593, 1555, 1510, 1491, 1402, 1235, 833 and 756; δ_H(250.13 MHz; [$^2H_6$]DMSO; 313 K) 6.66 (2 H, br s, NH_2), 7.41 (2 H, d, *J* 8.9), 7.53 (2 H, d, *J* 8.7), 7.73 (2 H, dd, *J* 8.8 and *J* 6.5), 7.93–8.00 (4 H, m), 8.35 (2 H, d, *J* 8.8) and 10.45 (1 H, br s, NH); δ_C(62.90 MHz; [$^2H_6$]DMSO; 313 K) 120.6 (C), 121.9 (CH), 122.9 (CH), 122.9 (C), 127.0 (C), 128.5 (CH), 128.7 (CH), 129.8 (CH), 131.3 (CH), 135.1 (C), 138.2 (C), 148.1 (C), 149.3 (C) and 160.9 (C); *m/z* (APCI) 415 (MH^+, 100%) and 387 (20, MH − N_2) [Found: *m/z* (CI), 415.1074 (MH^+). $C_{22}H_{16}N_6OCl$ requires 415.1074].

3-Methoxycarbonyl-2-methyl-7*H*-pyrido[4,3,2-*kl*]acridine 14a

A well stirred suspension of the triazole **8a** (318 mg, 1.00 mmol) in diphenyl ether (10 cm^3) was slowly heated and refluxed for 15 min in the dark. The red solution was allowed to cool to ambient temperature and was subjected to column chromatography on silica gel. Diphenyl ether was eluted with hexane–diethyl ether (10:1). The fraction resulting from elution with diethyl ether gave the light sensitive and fluorescent product as an orange solid. Crystallisation from hexane–toluene gave pure tetracycle **14a** as an orange powder (247 mg, 85%), mp 182–184 °C (Found: C, 74.25; H, 4.71; N, 9.72. $C_{18}H_{14}N_2O_2$ requires C, 74.47; H, 4.86; N, 9.65%); ν_{max}(KBr)/cm^{-1} 3354, 3065, 2949, 1692 (CO), 1632, 1601, 1578, 1534, 1460, 1435, 1339, 1271, 1258, 1233, 1166, 779, 746 and 660; δ_H(250.13 MHz; $CDCl_3$) 2.64 (3 H, s), 3.99 (3 H, s), 6.60 (1 H, dd, *J* 7.8 and 0.7), 6.89

(1 H, dd, *J* 8.2 and 0.7), 7.09 (1 H, ddd, *J* 8.0, 7.2 and 1.0), 7.10 (1 H, dd, *J* 8.5 and 1.0), 7.37 (1 H, ddd, *J* 8.5, 7.2 and 1.4), 7.41 (1 H, dd, *J* 8.2 and 7.8), 7.54 (1 H, br s, NH) and 8.53 (1 H, dd, *J* 8.0 and 1.4); δ_C(62.90 MHz; $CDCl_3$) 23.8 (CH_3), 52.0 (CH_3), 104.9 (CH), 111.5 (CH), 114.9 (CH), 117.3 (C), 118.2 (C), 120.6 (C), 121.7 (CH), 125.6 (CH), 131.8 (CH), 132.2 (CH), 135.9 (C), 139.2 (C), 139.4 (C), 152.1 (C), 152.4 (C) and 169.7 (C); *m*/*z* (ES) 291 (MH^+, 100%).

The pyridoacridine **14a** was transformed into its hydrochloride salt by adding 1 M hydrochloric acid (2 cm^3) to a solution of the tetracycle **14a** (29 mg, 0.10 mmol) in methanol (1 cm^3). The mixture was stirred for 1 h and the solvent was removed to give a red hydrochloride salt in quantitative yield: mp >300 °C (decomp.); λ_{max}(EtOH)/nm 206, 232, 268, 309, 321, 424 and 447; ν_{max}(KBr)/cm^{-1} 3407, 3003, 1721 (CO), 1649, 1634, 1489, 1341, 1159 and 785; δ_H(250.13 MHz; D_2O) 1.83 (3 H, s), 3.77 (3 H, s), 6.18 (1 H, d, *J* 8.3), 6.47 (1 H, d, *J* 8.0), 6.53 (1 H, d, *J* 8.2), 6.95 (1 H, dd, *J* 8.0 and 7.1), 7.15 (1 H, dd, *J* 8.3 and 8.2), 7.30 (1 H, d, *J* 8.0) and 7.34 (1 H, dd, *J* 8.0 and 7.1); δ_C(62.90 MHz; D_2O) 17.6 (CH_3), 53.5 (CH_3), 109.1 (C), 110.6 (CH), 113.0 (CH), 113.5 (C), 117.6 (C), 117.8 (CH), 122.3 (CH), 125.0 (CH), 131.5 (C), 136.7 (CH), 137.2 (CH), 138.0 (C), 138.7 (C), 141.6 (C), 146.1 (C) and 166.6 (C).

3-Acetyl-2-methyl-7*H*-pyrido[4,3,2-*kl*]acridine 14b

Compound **14b** (85%) was prepared in a similar method by thermolysis of triazole **8b** in boiling diphenyl ether and formed dark red crystals, mp 206–208 °C (hexane–ethyl acetate) (Found: C, 78.66; H, 5.06; N, 10.11. $C_{18}H_{14}N_2O$ requires C, 78.81; H, 5.14; N, 10.21%); ν_{max}(KBr)/cm^{-1} 3345, 3059, 1692 (CO), 1628, 1601, 1576, 1543, 1532, 1462, 1339, 1252, 1223, 1175, 770, 762 and 665; δ_H(250.13 MHz; $CDCl_3$) 2.54 (3 H, s, CH_3), 2.59 (3 H, s, CH_3), 6.60 (1 H, dd, $J_{6,5}$ 7.8 and $J_{6,4}$ 0.7, 6-H), 6.75 (1 H, dd, $J_{4,5}$ 8.2 and $J_{4,6}$ 0.7, 4-H), 6.91 (1 H, dd, $J_{8,9}$ 8.4 and $J_{8,10}$ 0.9, 8-H), 7.08 (1 H, ddd, $J_{10,11}$ 8.1, $J_{10,9}$ 7.2 and $J_{10,8}$ 0.9, 10-H), 7.36 (1 H, ddd, $J_{9,8}$ 8.4, $J_{9,10}$ 7.2 and $J_{9,11}$ 1.3, 9-H), 7.36 (1 H, dd, $J_{5,4}$ 8.2 and $J_{5,6}$ 7.8, 5-H), 7.64 (1 H, br s, NH) and 8.50 (1 H, dd, $J_{11,10}$ 8.1 and $J_{11,9}$ 1.3, 11-H); δ_C(62.90 MHz; $CDCl_3$) 22.8 (CH_3), 31.9 (CH_3), 105.1 (CH, 6-C), 110.6 (CH, 4-C), 115.1 (CH, 8-C), 117.2 (C), 120.5 (C), 121.8 (CH, 10-C), 125.3 (CH, 11-C), 127.4 (C), 131.7 (CH, 9-C), 132.2 (CH, 5-C), 134.7 (C), 139.3 (C), 139.4 (C), 147.9 (C), 151.4 (C) and 206.6 (C); *m*/*z* (ES) 275 (MH^+, 100%).

3-Methoxycarbonyl-2-ethyl-7*H*-pyrido[4,3,2-*kl*]acridine 14c

Similarly prepared, from the triazole **8c**, this pyridoacridine (86%) formed red crystals, mp 194–195 °C (ethyl acetate) (Found: C, 74.84; H, 5.25; N, 9.01. $C_{19}H_{16}N_2O_2$ requires C, 74.98; H, 5.30; N, 9.20%); ν_{max}(KBr)/cm^{-1} 3297, 3250, 2976, 1688 (CO), 1632, 1603, 1578, 1532, 1493, 1464, 1431, 1335, 1279, 1262, 1235, 1179, 1154, 789, 756 and 662; δ_H(250.13 MHz; [$^2H_6$]DMSO) 1.29 (3 H, t, *J* 7.5), 2.74 (2 H, q, *J* 7.5), 3.92 (3 H, s), 6.87–6.91 (2 H, m), 7.10 (1 H, dd, *J* 7.7 and 7.6), 7.20 (1 H, d, *J* 8.1), 7.45–7.57 (2 H, m), 8.41 (1 H, d, *J* 7.9) and 11.07 (1 H, br s, NH); δ_C(62.90 MHz; [$^2H_6$]DMSO) 14.2 (CH_3), 29.4 (CH_2), 52.3 (CH_3), 105.9 (CH), 110.1 (CH), 116.1 (CH), 116.8 (C), 117.6 (C), 119.4 (C), 121.3 (CH), 124.8 (CH), 132.3 (CH), 133.0 (CH), 135.3 (C), 140.1 (C), 140.4 (C), 151.9 (C), 155.5 (C) and 169.0 (C); *m*/*z* (ES) 305 (MH^+, 100%).

3-Methoxycarbonyl-2-methoxycarbonylmethyl-7*H*-pyrido-[4,3,2-*kl*]acridine 14d

Compound **14d** (76%) was prepared in a similar way from triazole **8d** and formed red crystals; mp 189–191 °C (methanol–ethyl acetate) (Found: C, 68.72; H, 4.62; N, 7.60. $C_{20}H_{16}N_2O_4$ requires C, 68.96; H, 4.63; N, 8.04%); ν_{max}(KBr)/cm^{-1} 3295, 2947, 1721 (CO), 1701 (CO), 1634, 1599, 1580, 1530, 1433, 1341, 1254, 1206, 1179, 1154, 772 and 669; δ_H(250.13 MHz; [$^2H_6$]DMSO) 3.64 (3 H, s), 3.87 (3 H, s), 3.95 (2 H, s), 6.93 (1 H, d, *J* 7.9), 7.12 (1 H, dd, *J* 8.0 and 7.9), 7.20 (1 H, d, *J* 8.0), 7.21 (1 H, d, *J* 8.0), 7.51 (1 H, dd, *J* 8.0 and 7.9), 7.60 (1 H, dd, *J* 8.0 and 7.9), 8.33 (1 H, d, *J* 8.0) and 11.17 (1 H, br s, NH); δ_C(62.90 MHz; [$^2H_6$]DMSO) 43.1 (CH_2), 51.9 (CH_3), 52.2 (CH_3), 106.5 (CH), 110.9 (CH), 116.2 (CH), 117.5 (C), 117.7 (C), 119.2 (C), 121.5 (CH), 125.0 (CH), 132.6 (CH), 133.2 (CH), 135.6 (C), 140.1 (C), 140.4 (C), 149.7 (C), 152.5 (C), 168.0 (C) and 170.9 (C); *m*/*z* (ES) 349 (MH^+, 100%).

2-Amino-3-cyano-7*H*-pyrido[4,3,2-*kl*]acridine 14e

Compound **14e** (55%, reflux time 5 min) was prepared in a similar method from triazole **11a** as an orange powder from acetone; mp 318–322 °C (decomp.); ν_{max}(KBr)/cm^{-1} 3480, 3383, 3306, 2185 (CN), 1638, 1603, 1576, 1534, 1346, 768, 746 and 662; δ_H(250.13 MHz; [$^2H_6$]acetone) 6.24 (2 H, br s, NH_2), 6.73 (1 H, dd, *J* 7.9 and 0.9), 6.93 (1 H, dd, *J* 8.1 and 0.9), 7.09 (1 H, ddd, *J* 8.1, 7.9 and 1.0), 7.28 (1 H, dd, *J* 8.1 and 1.0), 7.53 (1 H, dd, *J* 8.1 and 7.9), 7.54 (1 H, ddd, *J* 8.1, 7.9 and 1.6), 8.48 (1 H, dd, *J* 8.1 and 1.6) and 10.35 (1 H, br s, NH); δ_C(62.90 MHz; [$^2H_8$]THF) 75.9 (C), 103.9 (CH), 110.2 (CH), 113.9 (C), 116.7 (CH), 118.3 (C), 120.7 (C), 122.0 (CH), 126.6 (CH), 133.1 (CH), 134.5 (CH), 140.8 (C), 141.5 (C), 141.9 (C), 155.6 (C) and 161.6 (C); *m*/*z* (ES) 259 (MH^+, 100%) [Found: *m*/*z* (CI), 259.0984 (MH^+). $C_{16}H_{11}N_4$ requires 259.0984].

2-Amino-3-(1-amino-2,2-dicyanoethenyl)-7*H*-pyrido[4,3,2-*kl*]-acridine 14f

Prepared from the triazole **11b**, this pyridoacridine **14f** formed an orange powder (66%, from aqueous DMF), mp >350 °C; ν_{max}(KBr)/cm^{-1} 3466, 3366, 3322, 3079, 3042, 2191 (CN), 1624, 1576, 1562, 1530, 1489, 1466, 1425, 1337, 1319, 1296, 1229 and 611; δ_H(250.13 MHz; [$^2H_6$]DMSO) 6.57 (2 H, br s, NH_2), 6.76 (2 H, br s, NH_2), 7.02 (1 H, d, *J* 8.0), 7.16 (1 H, dd, *J* 8.0 and 7.7), 7.28 (1 H, d, *J* 8.0), 7.55 (1 H, dd, *J* 8.0 and 7.9), 7.66 (1 H, dd, *J* 8.0 and 8.0), 7.79 (1 H, d, *J* 7.9), 8.45 (1 H, d, *J* 7.7) and 11.26 (1 H, br s, NH); *m*/*z* (ES) 325 (MH^+, 100%) [Found: *m*/*z* (CI), 325.1200 (MH^+). $C_{19}H_{13}N_6$ requires 325.1202].

9-[4-Methoxycarbonyl-5-(4-chlorobutyl)-1,2,3-triazol-1-yl]-acridine 16

To a solution of sodium methoxide (0.21 g, 0.52 mmol) in dry methanol (5 cm^3) was added dropwise a solution of methyl 7-chloro-3-oxoheptanoate[18] (1.00 g, 0.52 mmol) in dry methanol (10 cm^3). A solution of 9-azidoacridine **5** (1.14 g, 0.52 mmol) in dry methanol (40 cm^3) was added dropwise and the mixture was stirred for 24 h in the dark. The resulting solution was evaporated and subjected to column chromatography on silica gel. Unreacted 9-azidoacridine and by-products 2-methoxycarbonylcyclohex-1-enol and 9-methoxyacridine were eluted with hexane–diethyl ether (2:1 or 1:2). Further elution with hexane–diethyl ether (1:2) gave a reddish fraction containing the triazole **16**. Recrystallisation from boiling ethyl acetate–hexane provided the pure triazole as colourless needles (0.31 g, 15%), mp 94–96 °C (Found: C, 63.64; H, 4.77; N, 14.06. $C_{21}H_{19}N_4O_2Cl$ requires C, 63.88; H, 4.85; N, 14.19%); ν_{max}(KBr)/cm^{-1} 2947, 1744 (CO), 1449, 1196, 1142 and 758; δ_H(250.13 MHz; $CDCl_3$) 1.31–1.51 (4 H, m), 2.74 (2 H, t, *J* 7.7), 3.16 (2 H, t, *J* 6.1), 4.05 (3 H, s), 7.23 (2 H, d, *J* 8.0, 1-H), 7.58 (2 H, ddd, *J* 8.0, 6.7 and 1.1, 2-H), 7.86 (2 H, ddd, *J* 8.4, 6.7 and 1.4, 3-H) and 8.35 (2 H, d, *J* 8.4, 4-H); δ_C(62.90 MHz; $CDCl_3$) 22.5 (CH_2), 25.5 (CH_2), 31.3 (CH_2), 43.6 (CH_2), 52.3 (CH_3), 121.7 (CH), 122.6 (C), 128.7 (CH), 130.1 (CH), 130.9 (CH), 135.1 (C), 136.4 (C), 145.5 (C), 149.3 (C) and 161.8 (C); *m*/*z* (APCI) 395 (MH^+, 40%) and 367 (100, MH − N_2).

3-Methoxycarbonyl-2-(4-chlorobutyl)-7*H*-pyrido[4,3,2-*kl*]-acridine 17 and 5-methoxycarbonyl-1,2,3,4-tetrahydroquinolizino[2,3,4-*kl*]acridine 18

A well stirred solution of the triazole **16** (200 mg, 0.51 mmol) in diphenyl ether (20 cm^3) was refluxed for 5–10 min in the dark until no starting material was detected by TLC (silica gel;

diethyl ether). During this time the colour of the mixture changed from yellow to dark red. The mixture was allowed to cool to ambient temperature and was subjected to column chromatography on silica gel avoiding exposure to light. Diphenyl ether was removed by elution with hexane. The fraction resulting from elution with diethyl ether gave the light sensitive and highly fluorescent tetracycle **17** as a yellow solid (60 mg, 32%); mp 168–170 °C (Found: C, 69.00; H, 5.37; N, 7.46. $C_{21}H_{19}N_2O_2Cl$ requires C, 68.76; H, 5.22; N, 7.64%); ν_{max}(KBr)/cm^{-1} 2942, 1715 (CO), 1589, 1543, 1343, 1254 and 1240; δ_H(250.13 MHz; $CDCl_3$) 1.86–2.06 (4 H, m), 2.88 (2 H, t, *J* 7.1), 3.61 (2 H, t, *J* 6.7), 4.00 (3 H, s), 6.67 (1 H, d, *J* 7.8), 6.92 (1 H, dd, *J* 8.1 and 0.6), 7.05 (1 H, dd, *J* 8.3 and 0.8), 7.10 (1 H, ddd, *J* 8.1, 8.1 and 1.1), 7.38 (1 H, ddd, *J* 8.3, 7.2 and 1.5), 7.43 (1 H, dd, *J* 8.2 and 8.2), 7.54 (1 H, s br, NH) and 8.55 (1 H, dd, *J* 8.0 and 1.4); δ_C(62.90 MHz; $CDCl_3$) 26.6 (CH_2), 32.3 (CH_2), 35.5 (CH_2), 45.0 (CH_2), 52.1 (CH_3), 105.3 (CH), 111.7 (CH), 115.0 (CH), 117.2 (C), 118.6 (C), 120.6 (C), 121.8 (CH), 125.6 (CH), 131.8 (CH), 132.3 (CH), 135.7 (C), 139.2 (C), 139.4 (C), 151.9 (C), 154.6 (C) and 169.6 (C); *m*/*z* (ES) 367 (MH^+, 66%).

The column was washed with ethyl acetate before methanol was utilised to elute the pentacycle **18** as a slow moving fraction. Recrystallisation from hexane–dichloromethane gave red needles (51 mg, 30%), mp 158–160 °C (Found: C, 75.87; H, 5.38; N, 8.31. $C_{21}H_{18}N_2O_2$ requires C, 76.34; H, 5.49; N, 8.48%); λ_{max}(EtOH)/nm 203, 237, 259, 279, 288, 350 and 484; ν_{max}(KBr)/cm^{-1} 2947, 1715 (CO), 1628, 1561, 1541, 1277 and 760; δ_H(250.13 MHz; D_3COD) 1.85–2.02 (4 H, m, 2-H and 3-H), 2.88 (2 H, t, $J_{4,3}$ 7.0, 4-H), 3.98 (3 H, s, OCH_3), 4.29 (2 H, t, $J_{1,2}$ 5.3, 1-H), 6.88 (1 H, dd, $J_{6,7}$ 7.3 and $J_{6,8}$ 1.0, 6-H), 7.21 (1 H, ddd, $J_{12,13}$ 8.4, $J_{12,11}$ 6.6 and $J_{12,10}$ 1.0, 12-H), 7.49 (1 H, dd, $J_{8,7}$ 8.7 and $J_{8,6}$ 1.0, 8-H), 7.56–7.63 (1-H, m, 11-H), 7.60 (1 H, dd, $J_{7,8}$ 8.7 and $J_{7,6}$ 7.3, 7-H), 7.75 (1 H, dd, $J_{10,11}$ 8.8 and $J_{10,12}$ 1.0, 10-H) and 7.95 (1 H, d, $J_{13,12}$ 8.4, 13-H); δ_C(62.90 MHz; D_3COD) 20.8 (CH_2), 24.5 (CH_2), 26.8 (CH_2-4), 52.7 (CH_3), 55.0 (CH_2-1), 110.9 (CH-6), 115.1 (C), 117.2 (C), 120.4 (C), 120.6 (CH-8), 122.3 (CH-12), 126.5 (CH-13), 128.3 (CH-10), 131.7 (C), 132.0 (CH-11), 133.1 (CH-7), 147.3 (C), 149.7 (C), 150.0 (C), 152.5 (C) and 169.1 (C); *m*/*z* (APCI) 331 (MH^+, 100%) [Found: *m*/*z* (CI), 331.1447 (MH^+). $C_{21}H_{19}N_2O_2$ requires 331.1447].

The quinolizino[2,3,4-*kl*]acridinium chloride **19** was formed, upon treatment of the pentacycle **18** with 10 M hydrochloric acid and removal of the solvent, in quantitative yield, mp 292–296 °C, λ_{max}(EtOH)/nm 204, 236, 285, 351 and 485; ν_{max}(KBr)/cm^{-1} 3424, 2965, 1721 (CO), 1640, 1588, 1541, 1481, 1277, 1094 and 799; δ_H(250.13 MHz; D_2O) 1.60 (2 H, m), 1.79 (2 H, m), 2.71 (2 H, t, *J* 7.0), 3.91 (3 H, s, OCH_3), 4.20 (2 H, br s), 6.66–6.72 (2 H, m), 7.19 (1 H, dd, *J* 7.0 and 6.9), 7.41 (1 H, dd, *J* 7.2 and 7.1) and 7.57–7.66 (2 H, m); δ_C(62.90 MHz; D_2O) 17.6 (CH_2), 21.7 (CH_2), 25.0 (CH_2), 53.2 (CH_3), 54.4 (CH_2), 110.1 (CH), 111.3 (C), 111.8 (CH), 115.9 (C), 117.4 (CH), 118.7 (C), 122.4 (CH), 126.8 (CH), 129.9 (C), 135.2 (CH), 135.5 (CH), 137.1 (C), 140.7 (C), 145.8 (C), 151.1 (C) and 167.0 (C).

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