REACTIONS OF A NEW FAMILY OF AMIDE DERIVATIVES OF PHENANTHRIDINIUM AZOMETHINE YLIDES WITH DIPOLAROPHILES

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Received July 13, 1999
Accepted September 29, 1999

Dedicated to Professor Milan Kratochvíl on the occasion of his 75th birthday.

Reaction of a series of *N*-alkyl- and *N*,*N*-dialkylbromoacetamides **1a**–**1e** with phenanthridine afforded quaternary phenanthridinium salts **2a**–**2e**. These compounds treated with triethylamine form azomethine ylides which undergo a cycloaddition reaction with activated C=C bond, giving 3-(*N*-alkylcarbamoyl)-1,2,3,12b-tetrahydropyrrolo[1,2-*f*]phenanthridines **3a**–**3e**, **4c**, **5c**, **6c** or 3-(*N*-alkylcarbamoyl)-2,3-dihydropyrrolo[1,2-*f*]phenanthridine **7c**. Their stereochemistry was studied by NMR spectroscopy. The best results were obtained with fumaronitrile as a dipolarophile. It has been found that the ylides react in *syn* conformations but if 1-adamantyl moiety is bound to the ylide, it reacts in *anti* conformation, too. The azomethine ylides show a very poor reactivity towards dimethyl fumarate or dimethyl maleate. Yet we could prepare products for ylide bearing 1-adamantyl group.

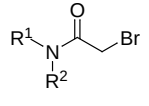
Key words: 1,3-Dipolar cycloadditions; Stereochemistry; NMR spectroscopy; Azomethine ylides; Phenanthridinium salts; Fumaronitrile; Dimethyl fumarate; Dimethyl maleate; 5-Substituted 6-phenanthridones.

Azomethine ylides derived from quaternary phenanthridinium salts have been found to exhibit versatility in 1,3-dipolar cycloadditions acting as 1,3-dipole with a series of activated alkenes (dimethyl fumarate, dimethyl maleate and fumaronitrile) affording pyrrolidino[1,2-*f*]phenanthridines[1–6]. Such cycloadditions have been observed to proceed stereoselectively accordingly to the concerted transition structure.

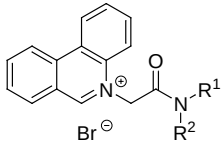
In our laboratory a great effort has been made to study stereoselectivity of 1,3-dipolar cycloadditions of those azomethine ylides[1–6]. Each of 1,3-dipoles under examination possessed a stabilising carbonyl group of an ester attached to the negatively charged dipole part. In addition, literature brings reports on a wide family of sulfonylacetamide derivatives[7–9]. Never-

theless, to the best of our knowledge, there is none paper concerning carbonyl stabilised phenanthridinium based azomethine ylides with a simple amide group although some examples concerning other type of ylides have been reported[10]. Therefore, we were interested in their preparation and reactivity with common dipolarophiles, mainly from the stereoselectivity point of view. We wished to compare their behaviour with related compounds from our previous studies.

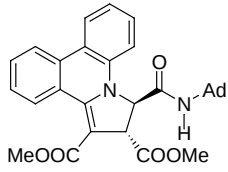
There are dozens of papers concerning preparation of *N*-alkyl- or *N*,*N*-dialkyl bromoacetamides. Central to almost all of them are classic works by Weaver[11] and Drake[12] that were used or improved by many other authors[13–22]. *N*-Alkyl- or *N*,*N*-dialkylbromoacetamides are available through a reaction of bromoacetyl bromide or bromoacetyl chloride and appropriate primary or secondary amines or amine hydrochlorides in inert solvents (1,2-dichloroethane, CH_2Cl_2, benzene) at temperatures ranging from –50 to 10 °C. In our work we used classic Weaver's procedure. Bromoacetyl bromide reacts readily and selectively on the carbonyl carbon with a series of primary and secondary aliphatic amines in CH_2Cl_2 at –20 °C to form *N*-alkyl- or *N*,*N*-dialkylbromoacetamides **1a**–**1e** in acceptable yields 45–75%. The obtained *N*,*N*-dialkylbromoacetamides **1a**, **1b** and *N*-alkyl-



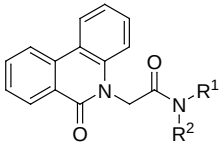
1a - 1e



2a - 2e



7c



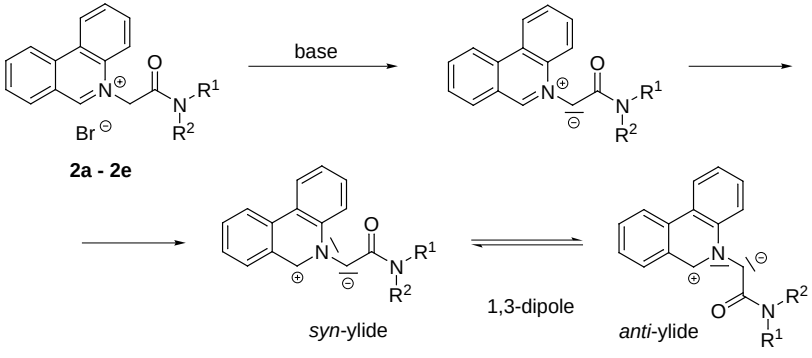
8b - 8e

	R^1	R^2
a	cyclohexyl	cyclohexyl
b	i-Pr	i-Pr
c	1-adamantyl	H
d	benzyl	H
e	(±)-1-(1-adamantyl)ethyl	H

bromoacetamides **1c**, **1d** show in FTIR spectra a very strong band at 1 635–1 651 cm^{-1} corresponding to the amide carbonyl stretching vibration (amide I). In addition, compounds **1c**–**1e** exhibit strong bands at 3 300 cm^{-1} (N–H stretching vibration, amide III) and around 1 500 cm^{-1} (amide II). In mass spectra of compounds **1a**–**1e**, molecular ions are always detectable; the parent peaks are formed from M^+ peaks by loss of HBr ($M^+ - 80$).

The prepared bromoacetamides undergo a nucleophilic substitution reaction with phenanthridine nitrogen. Such reactions are described only in our previous papers[1–6]. Reaction conditions given in works dealing with alkylations of imines[23] or dihydroisochinolines[24–26] can be also used. With phenanthridine, when CH_2Cl_2 is used as a solvent, the reaction at ambient temperature takes several weeks up to months, probably due to the poor nitrogen nucleophilicity. Yet by employing a polar aprotic solvent acetonitrile, we can shorten reaction time up to three days at reflux temperature[5,6]. Using this procedure, quaternary phenanthridinium salts **2a**–**2e** were obtained in yields above 80%. Being often insoluble in the reaction medium, they can be easily isolated. In IR spectra, the quaternary phenanthridinium salts **2a**–**2e** show a typical band 1 627 cm^{-1} belonging to the stretching vibration of $CH{=}N^+$ group. In ^{13}C NMR spectra this group with its chemical shift δ 157 ppm is difficult to detect due to bad relaxation properties of $CH{=}N^+$ carbon. ^1H NMR chemical shifts of $CH{=}N^+$ lie at very low fields at 10.5 ppm, which can be caused by the presence of a full positive charge on the nitrogen atom and by the used solvent. In mass spectra, we can find peaks $M^+ - 79$, which correspond to the cationic part of the salts.

When quaternary phenanthridinium salts **2a**–**2e** are treated with a base (triethylamine), proton is abstracted from the methylene attached to carbonyl, forming a 1,3-dipole (azomethine ylide) (Scheme 1). This species can

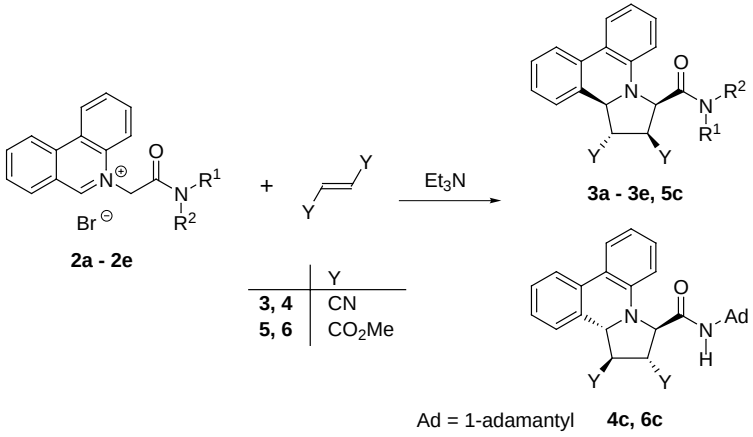


SCHEME 1

react in a cycloaddition reaction adding onto an activated multiple bond to form a five-membered ring (Scheme 2). Such reactions could proceed *via* two extreme mechanisms[27,28], a concerted one with retention of the dipolarophile configuration or a two-step zwitterionic mechanism where the obtained products lose previous dipolarophile configuration. Moreover,

phenanthridine-based azomethine ylides can undergo a conformation change through an equilibrium between *syn* and *anti* forms by a possible rotation on the partial double bond (Scheme 1).

We were interested in stereochemistry of cycloadducts **3a**–**3e**, **4c**, **5c**, **6c** (Scheme 2) as a source of the information on the transition structure arrangement. It also allows to make some conclusions about the ylide conformation.



SCHEME 2

In situ generated azomethine ylides react with fumaronitrile to form 1,2,3,12b-tetrahydropyrrolo[1,2-*f*]phenanthridines **3a**–**3e**, **4c**, **5c**, **6c**. After two-day heating in argon atmosphere, the reaction is completed (TLC) and products are triturated with benzene (see Experimental). The products were then separated on a silica column by flashing with an appropriate solvent mixture. Although we have found in all the reactions that two spots appeared in TLC, the more polar spot belongs to an unidentified decomposition product (according to the NMR analysis) with the only exception of the reaction of **2c** when two diastereoisomers **3c** and **4c** could be isolated. Relative configurations of hydrogen atoms on C2–C3 and C1–C12b atoms were solved by comparing coupling constants of the compounds with the previous results[1–6,29]. It was found that the *trans* coupling constant ranges from 3 to 5 Hz and the *cis* constant from 8 to 11 Hz. We assume that 1,3-dipolar cycloadditions on azomethine ylides proceed *via* a concerted mechanism with retention of the dipolarophile configuration. This could be proved by the $^3J(1,2)$ coupling constant provided they are similar for arbitrary configurations on C2–C3 and C1–C12b atoms. The $^3J(1,2)$ coupling

constant for compounds **3a**–**3e** ranges from 8 to 10 Hz and for compound **4c** is 8.2 Hz.

Thus, 1,3-dipolar cycloadditions of azomethine ylides generated from quaternary phenanthridinium salts **2a**–**2e** yield pyrrolo[1,2-*f*]phenanthridines **3a**–**3e**, **4c**, **5c** and **6c** with preserved configuration 1,2-*trans*. The configuration in compounds **3a**–**3e** and **5c** was 1,12b-*trans* and 2,3-*cis* and in compounds **4c** and **6c** 1,12b-*trans* and 2,3-*trans*. With compounds **2a**, **2b**, **2d** and **2e** as a result of the ylide addition in *syn* conformation, only one product of addition was isolated in about 25% yields. However, the azomethine ylide from **2c** adds on fumaronitrile both in *syn* and *anti* form as could be inferred from the product stereochemistry. The reaction of **2c** gave excellent yield of 95% related to sum of both products **3c** and **4c**.

Besides fumaronitrile, we also tried to examine some other types of dipolarophiles, particularly dimethyl fumarate and dimethyl maleate. Yet, to our great surprise, these react with ylides much worse than fumaronitrile, giving yields below 10%. The cycloadducts are contaminated with starting dipolarophiles, which impedes further effort in this field. Only the azomethine ylide generated from quaternary salt **2c** and dimethyl fumarate using the standard procedure gives two products **5c** and **6c** in the ratio 7 : 3, hence in lower yields than with **3c** and **4c**. When dimethyl maleate was treated with the ylide from **2c**, we were only able to isolate **7c**, the oxidation product on the C1–C12b bond where the stereochemical information about the additon was lost. Thus we cannot make any conclusions about the ylide configuration.

When azomethine ylides were generated from quaternary salts **2b**–**2e** by treating with triethylamine in the absence of any dipolarophile but in presence of water (wet THF solution), 5-substituted 6-phenanthridones **8b**–**8e** were isolated as the sole products in yields above 80%. Such compounds were detected as by-products[3,5], hence this approach fully proved their formation as a consequence of the presence of water in the reaction medium. 5-Substituted 6-phenanthridones **8b**–**8e** are easily available by alkylation of 6-phenanthridone with the appropriate halomethylcarbonyl compounds[30–35] in the presence of a base. Our procedure is another convenient way of their preparation.

In NMR spectra of 5-substituted 6-phenanthridones **8b**–**8d**, two carbonyl signals can be found, first at 161–162 ppm corresponding to the lactam carbonyl (at C-6) and the other in the range of 164–168 ppm, which corresponds to the aliphatic amide carbonyl. Nevertheless, in FTIR spectra, the sole band at 1 650 cm^{-1} can be found. In mass spectra, the most intensive

peaks are those formed from the molecular ions by the lost of NR^1R^2 or $O{=}CNR^1R^2$ groups. Molecular ions are also detectable.

We can conclude that when the ylide is generated by triethylamine in the presence of dipolarophile the 1,3-dipolar cycloaddition reaction proceeds in a way that dipolarophile preserves its configuration and the ylide reacts in *syn* conformation. Exception is the reaction with the ylide containing adamantyl skeleton bound directly to the amide nitrogen atom. In that case, although the configuration of the dipolarophile is again preserved, the relatively bulky group is pushing the molecule of the ylide to possess energetically more stable *anti* conformation. The fact is reflected in the configuration of the products **3c**, **4c** or **5c** and **6c**. When there is a spacer between the amide nitrogen atom and the adamantyl group, as it is in case of ylide formed from phenanthridinium **2e**, the formed product shows that the ylide reacts in *syn* conformation. The same results were observed irrespective of the dipolarophile.

EXPERIMENTAL

Melting points were measured on a Kofler hot stage (VEB Wagetechnik Rapido 79/2106) and are incorrected. IR spectra were recorded on an FTIR Ati Mattson spectrophotometer in KBr pellets (ν in cm^{-1}). NMR spectra were recorded on a Bruker Avance 500 Apparatus with working frequency 500 MHz for ^1H and 125 MHz for ^{13}C in $CDCl_3$ (unless given otherwise) with TMS as an internal standard. Chemical shifts are given in ppm (δ-scale), coupling constants *J* in Hz. Mass spectra were recorded on a Fisons Instruments Trio 1000 spectrometer in positive mode with EI ionisation. TLC was carried out on commercial silica foils (Silufol Kavalier, Czech Republic). Column chromatography was carried out on Merck silica (63–100 μm). CH_2Cl_2 (Onex, Czech Republic) was dried over CaH_2 and distilled from it. Triethylamine was dried over KOH and rectified onto a column with BaO. Dicyclohexylamine, diisopropylamine (Fluka) and benzylamine (Reachim, Russia) were dried over KOH and distilled. Bromoacetyl bromide (Fluka) was distilled under reduced pressure (b.p. 35–37 °C/2 mm Hg) prior to use. Phenanthridine, dimethyl fumarate, dimethyl maleate and fumaronitrile (Aldrich) were used as received.

Bromoacetamides **1a**–**1e**. General Procedure

Bromoacetyl bromide (10.0 g, 50.0 mmol) was added dropwise to a stirred solution of amine (100.0 mmol) in dry CH_2Cl_2 cooled to temperatures from –20 to –30 °C. A strong exothermic reaction occurred and a white solid precipitated. Reaction temperature during the addition of bromoacetyl bromide should not exceed –10 °C. After the whole amount of bromoacetyl bromide was added, stirring at the same temperature continued for additional 20 min. Finally, the reaction mixture was allowed to heat to ambient temperature and ice-cold dilute hydrochloric acid (1 : 1) was added. The organic layer was dried over anhydrous Na_2SO_4, evaporated *in vacuo* and the residue (sticky or solid) was crystallised from an appropriate solvent.

N,N-Dicyclohexylbromoacetamide (**1a**). Yield 7.54 g (50%), colourless needles (cyclohexane); m.p. 121–122 °C. FTIR: 2 931, 2 858, 1 635 (C=O), 1 459, 1 371, 1 319, 1 114, 1 056, 1 000, 894. ^{1}H NMR: 1.07–1.82 m, 20 H (10 × CH_2); 2.90 m, 1 H (CH); 3.40 m, 1 H (CH); 3.77 s, 2 H (CH_2Br). ^{13}C NMR: 24.97; 25.05; 25.65; 26.25; 28.83; 29.24; 30.91 (7 × CH_2); 56.21 (2 × CH); 165.30 (C=O). EI MS: 304 (M^+ + 2, 5), 302 (M^+, 5), 224 (5), 223 (19), 222 (100), 180 (5), 178 (8), 176 (7), 141 (9), 140 (74), 138 (15), 99 (5), 98 (22), 81(20), 84 (7), 83 (22), 81 (21), 56 (19), 56 (9), 55 (19).

N,N-Diisopropylbromoacetamide (**1b**). Yield 10.0 g (45%), colourless leaflets (ligroin); m.p. 57–59 °C. FTIR: 2 967, 2 934, 2 873, 1 634 (C=O), 1 476, 1 373, 1 343, 1 212, 1 138, 1 098, 1 043, 912. ^{1}H NMR: 1.23 d, 6 H, J = 4.5 (CH_3); 1.36 d, 6 H, J = 4.5 (CH_3); 3.42 m, 1 H (CH); 3.79 s, 2 H (CH_2Br); 3.94 m, 1 H (CH). ^{13}C NMR: 19.97; 20.53 (2 × CH_3); 28.45 (CH_2Br); 46.11; 50.21 (2 × CH); 165.17 (C=O). EI MS: 224 (M^+ + 2, 3), 222 (M^+, 3), 208 (32), 206 (30), 166 (43), 164 (45), 143 (7), 142 (100), 87 (4), 86 (95), 72 (3), 70 (12), 58 (22), 57 (18), 44 (16), 43 (18).

N-(1-Adamantyl)bromoacetamide (**1c**). Yield 8.2 g (63%), colourless needles (benzene); m.p. 124–126 °C. FTIR: 3 266 (NH, amide III), 3 081, 2 904, 2 856, 1 656 (C=O), 1 563 (amide II), 1 454, 1 402, 1 305, 1 211, 1 093, 998, 914, 750, 696. ^{1}H NMR: 1.69 s, 6 H (3 × CH_2); 2.02 s, 6 H (3 × CH_2); 2.10 s, 3 H (3 × CH); 3.77 s, 2 H (CH_2Br); 6.15 bs, 1 H (NH). ^{13}C NMR: 30.01 (CH); 36.35 (CH_2); 41.31 (CH_2); 52.68 (C_q); 164.24 (C=O). EI MS: 273 (M^+ + 2, 23), 271 (M^+, 22), 216 (38), 214 (41), 194 (5), 193 (18), 192 (100), 151 (3), 150 (15), 137 (3), 136 (18), 135 (97), 123 (10), 121 (13), 119 (7), 107 (16), 105 (12), 95 (14), 94 (36), 93 (43), 92 (38), 91 (39), 81 (16), 79 (32), 77 (29).

N-Benzylbromacetamide (**1d**). Yield 8.4 g (75%), colourless needles (toluene); m.p. 105–107 °C. FTIR: 3 278 (NH, amide III), 3 071, 3 017, 2 952, 1 646 (C=O), 1 553 (amide II), 1 453, 1 421, 1 321, 1 210, 1 006, 749, 698. ^{1}H NMR: 3.88 s, 2 H (CH_2Br); 4.45 d, 2 H, J = 5.8 (CH_2Ph); 6.80 br s, 1 H (NH); 7.25–7.35 m, 5 H (CH_{ar}). ^{13}C NMR: 28.87 (CH_2Br); 44.09 (CH_2Ph); 127.58; 127.63; 128.68 (3 × CH_{ar}); 137.24 ($C_{q\ ar}$); 165.28 (C=O). EI MS: 230 (M^+ + 2, 5), 228 (M^+, 5), 150 (3), 149 (8), 148 (100), 108 (5), 107 (58), 106 (45), 92 (8), 91 (71), 79 (32), 77 (27), 44 (8), 42 (16).

(±)-N-[1-(1-Adamantyl)ethyl]bromoacetamide (**1e**). Yield 9.48 g (60%), colourless needles (toluene); m.p. 128–129 °C. FTIR: 3 294 (NH, amide III), 3 044, 2 902, 2 847, 1 647 (NH, amide I), 1 559 (amide II), 1 449, 1 386, 1 340, 1 212, 1 160, 1 125, 1 023, 722. ^{1}H NMR: 1.04 d, 3 H, J = 6.9 (CHC**H**$_3$); 1.36 d, 1 H, J = 6.9 (C**H**CH_3); 1.53 dd, 6 H, J = 34.7, J = 12.0 (3 × CH_2); 1.62 t, 6 H, J = 11.1 (3 × CH_2); 1.99 s, 3 H (3 × CH); 3.63 m, 1 H (NH); 3.89 s, 2 H (CH_2Br). ^{13}C NMR: 14.12 (CH_3); 28.13 (3 × CH); 34.70 (CH_2Br); 35.74 (C_q); 36.86 (CH_2); 38.21 (CH_2); 53.90 (CH); 164.46 (C=O). EI MS: 302 (M^+ + 2, 9), 300 (M^+, 9), 223 (3), 221 (16), 220 (91), 179 (3), 178 (23), 137 (3), 136 (23), 135 (100), 123 (7), 121 (9), 119 (7), 107 (42), 105 (12), 94 (8), 93 (75), 91 (31), 85 (46), 81 (31), 79 (78), 77 (28), 69 (26), 67 (33), 57 (29), 55 (23), 44 (58).

Synthesis of Quaternary Phenanthridinium Salts **2a**–**2d**. General Procedure

A chloroform solution of phenanthridine (3.0 g, 16.7 mmol) was added to a hot solution of appropriate bromacetamide **1a**–**1e** (16.7 mmol) in acetonitrile (50 ml) and the solution was refluxed for 5 days. During the heating, a yellowish solid precipitated and the solution turned orange. The reaction mixture was concentrated under reduced pressure, the residue

was collected, washed consecutively with chloroform and diethyl ether, and dried at room temperature.

5-[(N,N-Dicyclohexylcarbamoyl)methyl]phenanthridinium bromide (**2a**). Yield 0.43 g (85%), yellowish needles; not melting up to 300 °C. FTIR: 2 958, 2 929, 2 852, 1 654 (C=O), 1 629 (CH=N^+), 1 448, 1 305, 1 267, 1 240, 1 155, 995, 800, 763. ^{1}H NMR (DMSO-d_6): 1.00–2.21 m, 22 H (cyclohexyl); 6.39 s, 2 H (CH_2C=O); 8.22–9.25 m, 8 H (CH_{ar}); 10.37 s, 1 H (CH=N^+). ^{13}C NMR (DMSO-d_6): 24.78; 25.16; 25.56; 28.82; 29.63; 30.73 (6 × CH_2); 55.73; 57.24 (2 × CH); 59.83 (CH_2C=O); 119.97; 123.51; 125.67; 130.45; 132.10; 133.16; 138.81 (8 × CH_{ar}); 124.97; 130.71; 134.49; 134.95 (4 × $C_{q\ ar}$). EI MS: 402 (M^+ – 79, 1), 401 (2), 223 (6), 222 (38), 194 (17), 193 (13), 180 (42), 179 (100), 178 (38), 152 (14), 151 (16), 150 (9), 140 (31), 138 (17), 98 (22), 83 (18), 81 (18), 56 (15), 55 (39), 41 (29).

5-[(N,N-Diisopropylcarbamoyl)methyl]phenanthridinium bromide (**2b**). Yield 5.37 g (80%), yellowish needles; not melting up to 300 °C. FTIR: 2 994, 2 966, 2 926, 1 651 (C=O), 1 629 (CH=N^+), 1 534, 1 448, 1 352, 1 317, 1 264, 1 208, 1 156, 1 039, 803, 760. ^{1}H NMR (DMSO-d_6): 1.26 d, 6 H, J = 6.6 (2 × CH_3); 1.39 d, 6 H, J = 6.5 (2 × CH_3); 3.64 septet, 1 H, J = 6.6 (CH); 4.20 septet, 1 H, J = 6.5 (CH); 6.27 s, 2 H (CH_2C=O); 8.11–9.21 m, 8 H (CH_{ar}); 10.31 s, 1 H (CH=N^+). ^{13}C NMR (DMSO-d_6): 20.62; 20.95 (2 × CH_3); 46.08; 48.84 (2 × CH); 59.80 (CH_2C=O); 120.12; 123.45; 125.25; 130.71; 130.99; 132.44; 133.42; 139.07 (8 × CH); 123.70; 125.86; 134.63; 135.11 (4 × $C_{q\ ar}$); 157.64 (CH=N^+); 162.61 (C=O). EI MS: 322 (M^+ – 79, 5), 321 (15), 194 (18), 193 (38), 180 (42), 179 (100), 178 (23), 165 (18), 164 (11), 152 (14), 151 (18), 150 (9), 142 (15), 141 (12), 99 (11), 98 (17), 86 (28), 84 (26), 58 (21), 57 (12), 44 (42), 43 (49).

5-{[N-(1-Adamantyl)carbamoyl]methyl}phenanthridinium bromide (**2c**). Yield 6.0 g (80%), yellowish crystals; m.p. 228–230 °C. FTIR: 3 187 (N–H, amide III), 3 037, 2 904, 2 848, 1 683 (C=O, amide I), 1 625 (CH=N^+), 1 552 (amide II), 1 450, 1 359, 1 259, 1 220, 1 089, 746, 695. ^{1}H NMR (DMSO-d_6): 1.61 s, 6 H (3 × CH_2); 2.01 d, 6 H, J = 8.75 (3 × CH_2); 3.30 s, 3 H (3 × CH); 5.93 s, 2 H (CH_2C=O); 8.11–9.19 m, 8 H (CH_{ar}); 10.40 s, 1 H (CH=N^+). ^{13}C NMR (DMSO-d_6): 30.72 (CH); 37.79 (CH_2); 42.75 (CH_2); 54.03 (C_q); 120.96; 125.25; 127.00; 132.33; 132.50; 134.12; 134.92; 140.47 (8 × CH_{ar}); 125.14; 124.41; 135.61; 136.42 (4 × $CH_{q\ ar}$); 155.36 (CH=N^+); 164.52 (C=O). EI MS: 372 (M^+ – 79, 2), 370 (2), 273 (5), 271 (5), 216 (7), 214 (7), 194 (18), 193 (100), 192 (29), 180 (17), 179 (50), 178 (16), 167 (2), 166 (5), 165 (18), 135 (22), 94 (7), 93 (10), 92 (7), 91 (9), 79 (13), 77 (8), 41 (6).

5-[(N-Benzylcarbamoyl)methyl]phenanthridinium bromide (**2d**). Yield 6.0 g (88%), beige needles; m.p. 293–295 °C. FTIR: 3 202 (N–H, amide III), 3 047, 2 959, 1 683 (C=O, amide I), 1 627 (CH=N^+), 1 547 (amide II), 1 452, 1 421, 1 352, 1 262, 1 222, 1 150, 1 066, 1 005, 939, 758, 708. ^{1}H NMR (DMSO-d_6): 4.39 d, 2 H, J = 5.7 (CH_2Ph); 6.05 s, 2 H (CH_2C=O); 7.26–7.36 m, 5 H (CH_{ar}); 8.09–8.15 m, 3 H (CH_{ar} + NH); 8.39–9.44 m, 6 H (CH_{ar}); 10.47 s, 1 H (CH=N^+). ^{13}C NMR (DMSO-d_6): 43.11 (CH_2Ph); 59.58 (CH_2C=O); 119.64; 123.75; 125.47; 127.48; 127.78; 128.75; 130.81; 131.00; 132.56; 133.47; 139.04 (11 × CH_{ar}); 123.68; 125.90; 134.09; 134.98; 138.73 (5 × $C_{q\ ar}$); 157.68 (CH=N^+); 164.50 (C=0). EI MS: 328 (M^+ – 79, 3), 326 (4), 235 (28), 234 (13), 194 (25), 193 (52), 180 (83), 179 (100), 166 (18), 165 (34), 152 (19), 151 (27), 148 (48), 107 (21), 105 (15), 91 (82), 65 (13), 63 (12), 51 (11), 50 (8).

(±)-5-({N-[1-(1-Adamantyl)ethyl]carbamoyl}phenanthridinium bromide (**2e**). Yield 5.84 g (73%), yellowish needles; m.p. 175–177 °C. FTIR: 3 206 (NH, amide III), 3 054, 2 901, 2 847, 1 683 (C=O, amide I), 1 626 (CH=N^+), 1 600 (C=C), 1 552 (amide II), 1 505, 1 451, 1 384, 1 261, 1 219, 1 137, 1 079, 758. ^{1}H NMR (DMSO-d_6): 1.18 d, 3 H, J = 6.9 (CH_3); 1.64 m, 9 H (3 × CH_2 + 3 × CH); 2.03 d, 6 H, J = 15.9 (3 × CH_2); 3.59 m, 1 H (C**H**CH_3); (5.98 and 6.10)

AB_q, 2 H, *J* = 16 (CH_2C=O); 8.19–9.28 m, 9 H (8 × CH_{ar} + NH); 10.42 (CH=N^+). ^{13}C NMR (DMSO-d_6): 13.07 (CH_3); 27.81 (3 × CH); 34.45 (C_q); 36.07 (3 × CH_2); 36.93 (3 × CH_2); 53.93 ($CHCH_3$); 59.72 (CH_2C=O); 119.45; 123.75; 125.53; 130.84; 131.11; 132.40; 133.44; 138.99 (8 × CH_{ar}); 123.64; 125.91; 133.97; 134.89 (4 × $C_{q\ ar}$); 163.58 (C=O). EI MS: 400 (M^+ – 79, 1), 399 (1), 263 (17), 261 (4), 222(1), 221 (6), 220 (39), 180 (18), 179 (98), 178 (22), 153 (4), 152 (11), 151 (18), 136 (12), 135 (100), 107 (12), 105 (5), 93 (24), 85 (15), 79 (25), 44 (24).

Preparation of Cycloadducts **3a**–**3e**, **4c**, **5c**, **6c**, and **7c**. General Procedure

To a suspension of 1.0 g of appropriate quaternary salt **2a**–**2d** in dry CH_2Cl_2, an equivalent of fumaronitrile, dimethyl fumarate or dimethyl maleate was added and argon was introduced under stirring at ambient temperature for 5 min. Then an equivalent of dry triethylamine was added under argon and the reaction mixture was refluxed for 2 days. The solvent was removed *in vacuo* and the residue was triturated with benzene. Benzene was evaporated and the residue was analysed by TLC and ^{1}H NMR. Products were separated by column chromatography on silica.

(1R,2S*,3R*,12bS*)-1,2-Dicyano-N,N-dicyclohexyl-1,2,3,12b-tetrahydropyrrolo[1,2-f]phenanthridine-3-carboxamide* (**3a**). Yield 0.28 g (25%), eluted with Et_2O, yellow powder; m.p. 160–163 °C. FTIR: 3 069, 2 929, 2 856, 2 244 (CN), 1 643 (C=O, amide I), 1 494, 1 446, 1 368, 1 299, 1 270, 1 120, 1 017, 893, 754. ^{1}H NMR: 1.21–1.97 m, 20 H (10 × CH_2); 3.03 m, 1 H (CH); 3.35 dd, 1 H, *J*(2,3) = 9.7, *J*(1,2) = 8.2 (H-2); 3.73 m, 1 H (CH); 4.01 dd, 1 H, *J*(1,2) = 8.2, *J*(1,12b) = 3.4 (H-1); 5.10 d, 1 H, *J*(2,3) = 9.7 (H-3); 5.18 d, 1 H, *J*(1,12b) = 3.4 (H-12b); 6.63–7.83 m, 8 H (8 × CH_{ar}). ^{13}C NMR: 25.06; 25.17; 25.61; 25.69; 26.41; 26.46; 29.41; 29.72; 31.18; 31.56 (10 × CH_2); 33.98 (C-2); 39.49 (C-1); 57.18; 58.36 (2 × CH); 63.53 (C-3); 63.94 (C-12b); 117.24; 118.52 (2 × CN); 112.26; 119.11; 122.84; 124.21; 125.73; 128.23; 129.36; 129.62 (8 × CH_{ar}); 113.95; 129.92; 130.05; 140.00 (4 × $C_{q\ ar}$); 166.40 (C=O). EI MS: 479 (M^+ + 1, 1), 478 (M^+, 2), 450 (2), 449 (6), 271 (5), 270 (18), 269 (11), 268 (10), 267 (8), 244 (3), 243 (10), 242 (16), 220 (4), 219 (15), 218 (100), 180 (7), 179 (24), 178 (6), 165 (9), 83 (21), 81 (6), 56 (7), 55 (54), 54 (7). For $C_{31}H_{34}N_4O$ (478.6) calculated: 77.79% C, 7.16% H, 13.85% N; found: 78.03% C, 7.56% H, 13.95% N.

(1R,2S*,3R*,12bS*)-1,2-Dicyano-N,N-diisopropyl-1,2,3,12b-tetrahydropyrrolo[1,2-f]phenanthridine-3-carboxamide* (**3b**). Yield 0.27 g (27%), eluted with $CHCl_3$–Et_2O (4 : 1), yellowish powder (diethyl ether); m.p. 213–215 °C. FTIR: 3 065, 2 970, 2 932, 2 247 (CN), 1 641 (C=O, amide I), 1 603 (C=C), 1 495, 1 445, 1 379, 1 302, 1 209, 1 122, 1 040, 751. ^{1}H NMR: 1.25 d, 3 H, *J* = 6.6 (CH_3); 1.36 d, 3 H, *J* = 6.6 (CH_3); 1.41 d, 3 H, *J* = 6.7 (CH_3); 1.46 d, 3 H, *J* = 6.7 (CH_3); 3.34 dd, *J*(2,3) = 9.6, *J*(1,2) = 8.2 (H-2); 3.51 septet, 1 H, *J* = 6.7 (CH); 4.05 dd, 1 H, *J*(1,2) = 8.2, *J*(1,12b) = 3.5 (H-1); 4.21 septet, 1 H, *J* = 6.7 (CH); 5.08 d, 1 H, *J*(2,3) = 9.6 (H-3); 5.20 d, 1 H, *J*(1,12b) = 3.5 (H-12b); 6.61–7.43 m, 8 H (CH_{ar}). ^{13}C NMR: 20.12; 20.25; 20.51; 21.07 (4 × CH_3); 33.84 (C-2); 39.36 (C-1); 46.92; 49.41 (2 × CH); 63.56 (C-3); 63.89 (C-12b); 117.04; 118.30 (2 × CN); 112.01; 120.91; 122.75; 124.16; 125.72; 128.13; 129.30; 129.64 (8 × CH_{ar}); 128.95; 129.92; 140.01 (3 × $C_{q\ ar}$); 166.14 (C=O). EI MS: 398 (M^+, 2), 270 (17), 268 (7), 244 (3), 243 (6), 242 (5), 219 (18), 218 (100), 180 (8), 179 (9), 165 (7), 99 (4), 98 (4), 86 (8), 44 (42), 43 (49). For $C_{25}H_{26}N_4O$ (398.5) calculated: 75.35% C, 6.58% H, 14.06% N; found: 75.61% C, 6.35% H, 13.87% N.

(1R,2S*,3R*,12bS*)-N-(1-Adamantyl)-1,2-dicyano-1,2,3,12b-tetrahydropyrrolo[1,2-f]-phenanthridine-3-carboxamide* (**3c**). Yield 0.62 g (60%), less polar compound eluted with CH_2Cl_2–Et_2O (4 : 1), yellow crystals; m.p. 133–135 °C. FTIR: 3 342 (NH, amide III), 3 061,

2 909, 2 851, 2 247 (CN), 1 678 (C=O, amide I), 1 602 (C=C), 1 518 (amide II), 1 444, 1 263, 1 094, 755. ^{1}H NMR: 1.66 d, 6 H, *J* = 2.9 (CH_2); 1.97 d, 6 H, *J* = 3.1 (CH_2); 2.07 br s, 3 H (CH); 3.19 t, 1 H, *J*(2,3) = *J*(1,2) = 9.7 (H-2); 3.93 dd, 1 H, *J*(1,2) = 9.7, *J*(1,12b) = 4.7 (H-1); 4.63 d, 1 H, *J*(2,3) = 9.7 (H-3); 4.85 d, 1 H, *J*(1,12b) = 4.7 (H-12b); 6.40 br s, 1 H (NH); 6.79–7.87 m, 8 H, (8 × CH_{ar}). ^{13}C NMR: 29.25 (CH); 33.54 (C-2); 36.01 (CH_2); 41.05 (C-1); 41.33 (CH_2); 52.56 (C_q); 64.20 (C-3); 69.53 (C-12b); 117.87; 119.69 (2 × CN); 113.31; 121.97; 122.73; 123.87; 127.05; 128.37; 129.94; 130.36 (8 × CH_{ar}); 116.28; 126.58; 129.19; 140.74 (4 × $C_{q\ ar}$); 166.70 (C=O). EI MS: 449 (M^+ + 1, 1), 448 (M^+, 2), 421 (1), 419 (1), 371 (1), 370 (1), 369 (1), 271 (2), 270 (9), 220 (3), 219 (16), 218 (100), 194 (1), 193 (3), 180 (9), 179 (2), 150 (2), 149 (2), 136 (2), 135 (13), 120 (2), 93 (2), 79 (2). For $C_{29}H_{28}N_4O$ (448.6) calculated: 77.65% C, 6.29% H, 12.49% N; found: 77.35% C, 6.45% H, 12.61% N.

(1R,2S*,3R*,12bS*)-N-Benzyl-1,2-dicyano-1,2,3,12b-tetrahydropyrrolo[1,2-f]phenanthridine-3-carboxamide* (**3d**). Yield 0.25 g (25%), eluted with $CHCl_3$–Et_2O (4 : 1), yellowish powder (diethyl ether); m.p. 171–173 °C. FTIR: 3 292 (NH, amide III), 3 064, 2 932, 2 864, 2 246 (CN), 1 667 (C=O, amide I), 1 602 (C=C), 1 522 (amide II), 1 494.9, 1 445, 1 387, 1 294, 1 213, 1 171, 1 066, 1 028, 950, 756, 700. ^{1}H NMR: 3.20 dd, 1 H, *J*(2,3) = 10.05, *J*(1,2) = 9.5 (H-2); 3.97 dd, 1 H, *J*(1,2) = 9.5, *J*(1,12b) = 4.6 (H-1); 4.49 m, 2 H (CH_2NH); 4.63 d, 1 H, *J*(2,3) = 10.05 (H-3); 5.01 d, 1 H, *J*(1,12b) = 4.6 (H-12b); 6.79 d, 1 H, *J* = 8.1 (CH_{ar}); 7.03 t, 1 H, *J* = 7.6 (CH_{ar}); 7.17 br t, 1 H, *J* = 5.8 (NH); 7.24–7.86 m, 11 H (CH_{ar}). ^{13}C NMR: 33.68 (C-1); 40.89 (C-2); 43.88 (CH_2NH); 64.32 (C-3); 68.96 (C-12b); 117.75; 119.70 (2 × CN); 113.27; 122.07; 122.72; 123.91; 127.04; 127.68; 127.87; 128.39; 128.83; 129.98; 130.35 (11 × CH_{ar}); 116.14; 126.35; 129.11; 136.97; 140.49 (5 × $C_{q\ ar}$); 168.11 (C=O). EI MS: 406 (M^+ + 2, 2), 405 (M^+ + 1, 6), 404 (M^+, 6), 314 (2), 313 (6), 243 (16), 242 (14), 219 (6), 218 (27), 217 (8), 188 (11), 187 (38), 180 (100), 179 (25), 166 (3), 165 (11), 164 (3), 92 (7), 91 (85). For $C_{26}H_{20}N_4O$ (404.5) calculated: 77.21% C, 4.98% H, 13.85% N; found: 77.38% C, 4.92% H, 13.56% N.

(1R,2S*,3R*,12bS*)-N-[1-(1-Adamantyl)ethyl]-1,2-dicyano-1,2,3,12b-tetrahydropyrrolo-[1,2-f]phenanthridine-3-carboxamide* (**3e**). Yield 0.15 g (26%), elution with ethyl acetate, light yellow crystals; m.p. 195–197 °C. FTIR: 3 299 (NH, amide III), 3 061, 2 903, 2 847, 2 247 (CN), 1 674 (C=O, amide I), 1 603 (C=C), 1 522 (amide II), 1 495, 1 444 , 1 383, 1 297, 1 260, 1 212, 1 159, 1 093, 1 023, 946, 750. ^{1}H NMR: 1.04 d, 3 H, *J* = 6.9 (CHC**H**$_3$); 1.36 d, 1 H, *J* = 6.9 (C**H**CH_3); 1.53 dd, 6 H, *J* = 34.7, *J* = 12.0 (3 × CH_2); 1.62 t, 6 H, *J* = 11.1 (3 × CH_2); 1.99 s, 3 H (3 × CH); 3.25 m, 1 H (H-2); 3.68 d(dd), 1 H, *J* = 32.9, *J*(1,2) = 9.95, *J*(1,12b) = 4.6 (H-1); 4.72 dd, 1 H, *J* = 13.3, *J*(2,3) = 9.95 (H-3); 4.97 dd, 1 H, *J* = 22.03, *J*(1,12b) = 4.6 (H-12b); 6.48 br s, 1 H (NH); 6.82–7.90 m, 8 H (8 × CH_{ar}). ^{13}C NMR: 14.45 (CH_3); 28.13 (3 × CH); 33.89 (C-2); 35.85 (C_q); 36.72 (3 × CH_2); 38.28 (3 × CH_2); 41.07 (C-1); 53.54 (CH); 63.90 (C-3); 69.05 (C-12b); 1117.79; 119.53 (2 × CN); 113.22; 121.74; 122.71; 123.75; 126.73; 128.34; 129.78; 130.21 (8 × CH_{ar}); 113.61; 126.65; 129.05; 140.38 (4 × $C_{q\ ar}$); 167.07 (C=O). EI MS: 478 (M^+ + 2, 1), 477 (M^+ + 1, 1), 476 (M^+, 3), 270 (21), 245 (10), 243 (12), 242 (8), 220 (5), 219 (21), 218 (100), 193 (16), 180 (27), 179 (18), 165 (13), 163 (8), 135 (11), 79(11). For $C_{31}H_{32}N_4O$ (476.6) calculated: 78.12% C, 6.77% H, 11.75% N; found: 78.07% C, 6.63% H, 11.81% N.

(1R,2R*,3R*,12bR*)-N-(1-Adamantyl)-1,2-dicyano-1,2,3,12b-tetrahydropyrrolo[1,2-f]-phenanthridine-3-carboxamide* (**4c**). Yield 0.49 g (35%), more polar compound eluted with CH_2Cl_2–Et_2O (4 : 1), yellow crystals; m.p. 157–159 °C. FTIR: 3 361 (NH, amide III), 3 064, 2 907, 2 851, 2 247 (CN), 1 674 (C=O, amide I), 1 603 (C=C), 1 522 (amide II), 1 446, 1 263, 1 094, 746. ^{1}H NMR: 1.68 br s, 6 H (CH_2); 2.06 d, 6 H, *J* = 2.7 (CH_2); 2.09 br s, 3 H (CH);

3.67 d, 1 H, *J*(2,3) = 4.1 (H-3); 3.99 dd, 1 H, *J*(1,2) = 8.3, *J*(1,12b) = 4.1 (H-1); 4.57 d, 1 H, *J*(1,2) = 8.3, *J*(2,3) = 4.1 (H-2); 5.54 d, 1 H, *J*(1,12b) = 4.1 (H-12b); 6.48 br s, 1 H (NH); 6.50–7.92 m, 8 H (8 × CH_{ar}). ^{13}C NMR: 29.28 (CH); 36.65 (C-2); 36.06 (CH_2); 41.26 (CH_2); 42.96 (C-1); 52.59 (C_q); 62.94 (C-3); 68.81 (C-12b); 114.99; 115.98 (2 × CN); 113.01; 121.04; 122.66; 123.14; 126.60; 128.34; 129.66; 130.03 (8 × CH_{ar}); 118.89; 126.01; 130.00; 142.09 (4 × $C_{q\ ar}$); 166.08 (C=O). EI MS: 449 (M^+ + 1, 1), 448 (M^+, 2), 421 (1), 419 (1), 371 (1), 370 (1), 369 (1), 271 (2), 270 (9), 220 (3), 219 (16), 218 (100), 194 (1), 193 (3), 180 (9), 179 (2), 150 (2), 149 (2), 136 (2), 135 (13), 120 (2), 93 (2), 79 (2). For $C_{29}H_{28}N_4O$ (448.6) calculated: 77.65% C, 6.29% H, 12.49% N; found: 77.71% C, 6.34% H, 12.52% N.

(1R,2S*,3R*,12bS*)-Dimethyl 3-[N-(1-adamantyl)]carbamoyl-1,2,3,12b-tetrahydropyrrolo[1,2-f]-phenanthridine-1,2-dicarboxylate* (**5c**). Yield 0.46 g (35%), less polar compound eluted with CH_2Cl_2–Et_2O (5 : 1), yellowish crystals; m.p. 191–193 °C. FTIR: 3 300 (NH, amide III), 3 035, 2 908, 2 849, 1 730 (C=O ester), 1 675 (C=O, amide I), 1 603 (C=C), 1 519 (amide II), 1 497, 1 449, 1 358, 1 306, 1 233, 1 167 (C–O), 1 102, 1 026, 806, 741. ^{1}H NMR: 1.67 s, 6 H (3 × CH_2); 1.97 d, 6 H, *J* = 2.9 (3 × CH_2); 2.07 s, 3 H (3 × CH); 3.38 t, 1 H, *J* = 9.4 (H-2); 3.68 s, 3 H (OCH_3); 3.73 s, 3 H (OCH_3); 3.75 dd, 1 H, *J*(1,2) = 9.4, *J*(1,12b) = 5.1 (H-1); 4.79 d, 1 H, *J*(2,3) = 9.4 (H-3); 4.97 d, 1 H, *J*(1,12b) = 5.1 (H-12b); 6.44 br s, 1 H (N-H); 6.69–8.65 m, 8 H (8 × CH_{ar}). ^{13}C NMR: 29.32 (CH); 36.17 (CH_2); 41.41 (CH_2); 50.37 (C-2); 51.87 (C_q); 52.17 (OCH_3); 52.27 (OCH_3); 55.18 (C-1); 64.02 (C-3); 68.53 (C-12b); 113.50; 119.98; 122.23; 123.15; 126.03; 127.47; 128.56; 129.72 (8 × CH_{ar}); 119.82; 130.19; 133.28; 142.98 (4 × $C_{q\ ar}$); 169.54 (C=O, amide); 171.81; 172.05 (2 × C=O, ester). EI MS: 516 (M^+ + 2, 1), 515 (M^+ + 1, 1), 514 (M^+, 2), 336 (3), 334 (3), 302 (11), 277 (8), 276 (35), 275 (8), 253 (2), 252 (17), 251 (100), 244 (18), 220 (5), 219 (36), 217 (18), 136 (2), 135 (19), 93 (10), 79(8).

(1R,2R*,3R*,12bR*)-Dimethyl 3-[N-(1-adamantyl)]carbamoyl-1,2,3,12b-tetrahydropyrrolo[1,2-f]-phenanthridine-1,2-dicarboxylate* (**6c**). Yield 0.36 g (27%), more polar compound eluted with CH_2Cl_2–Et_2O (5 : 1), yellowish crystals; m.p. 208–210 °C. FTIR: 3 399 (NH, amide III), 3 035, 2 909, 2 855, 1 729 (C=O ester), 1 647 (C=O, amide I), 1 608 (C=C), 1 547 (amide II), 1 497, 1 450, 1 358, 1 306, 1 233, 1 168 (C–O), 1 102, 1 026, 806, 741. ^{1}H NMR: 1.68 s, 6 H (3 × CH_2); 1.99 d, 6 H, *J* = 2.9 (3 × CH_2); 2.06 s, 3 H (3 × CH); 3.10 s, 3 H (OCH_3); 3.37 d, 1 H, *J*(1,2) = 5.5 (H-2); 3.74 m, 1 H (H-1); 3.76 s, 3 H (OCH_3); 4.72 d, 1 H, *J*(2,3) = 5.5 (H-3); 5.69 d, 1 H, *J*(1,12b) = 5.7 (H-12b); 6.55 br s, 1 H (N-H); 6.81–8.64 m, 8 H (8 × CH_{ar}). ^{13}C NMR: 29.45 (CH); 36.32 (CH_2); 41.38 (CH_2); 46.17 (C-2); 52.38 (C_q); 52.41 (OCH_3); 52.56 (OCH_3); 55.79 (C-1); 63.31 (C-3); 71.36 (C-12b); 112.75; 119.48; 121.76; 122.04; 127.45; 127.57; 128.48; 129.81 (8 × CH_{ar}); 118.77; 128.87; 129.92; 144.42 (4 × $C_{q\ ar}$); 169.02 (C=O, amide); 171.22; 172.90 (2 × C=O, ester). EI MS: 516 (M^+ + 2, 1), 515 (M^+ + 1, 1), 514 (M^+, 2), 336 (3), 334 (3), 302 (11), 277 (8), 276 (35), 275 (8), 253 (2), 252 (17), 251 (100), 244 (18), 220 (5), 219 (36), 217 (18), 136 (2), 135 (19), 93 (10), 79 (8).

(2R,3R*)-Dimethyl 3-[N-(1-adamantyl)carbamoyl]-1,2-dihydropyrrolo[1,2-f]phenanthridine-1,2-dicarboxylate* (**7c**). Yield 0.45 g (34%), eluted with CH_2Cl_2–Et_2O (2 : 1), yellowish crystals; m.p. 189–192 °C. FTIR: 3 342 (NH, amide III), 3 061, 2 908, 2 851, 1 748 (C=O ester), 1 654 (C=O, amide I), 1 607 (C=C), 1 532 (amide II), 1 440, 1 363, 1 260, 1 212, 1 169, 1 098 (C–O), 1 026, 803, 750. ^{1}H NMR: 1.60 d, 6 H, *J* = 3 (3 × CH_2); 1.88 d, 6 H, *J* = 2.9 (3 × CH_2); 1.99 s, 3 H (3 × CH); 3.73 s, 3 H (OCH_3); 3.76 s, 3 H (OCH_3); 4.21 d, 1 H, *J*(2,3) = 5.0 (H-2); 4.79 d, 1 H, *J*(2,3) = 5.0 (H-3); 6.15 br s, 1 H (N-H); 6.82–8.53 m, 8 H (8 × CH_{ar}). ^{13}C NMR: 29.22 (CH); 36.13 (CH_2); 41.25 (CH_2); 49.17 (C_q); 52.00 (OCH_3); 52.32 (C-2); 52.58 (OCH_3); 65.53 (C-3); 95.28; 119.31; 120.65; 124.92; 136.20; 137.20 (6 × $C_{q\ ar}$); 113.06; 115.94; 121.86; 123.14; 128.10; 128.85; 129.79; 132.92 (8 × CH_{ar}); 166.92 (C=O, amide); 167.42

(C=O, ester, conjug.); 173.50 (C=O, ester, free). EI MS: 514 (M^+ + 2, 1), 513 (M^+ + 1, 2), 512 (M^+, 3), 387 (8), 302 (10), 236 (7), 235 (5), 211 (1), 210 (17), 209 (100), 195 (3), 180 (9), 178 (28), 152 (8), 135 (17), 93 (8), 79 (8), 67 (4).

Preparation of 5-Substituted 6-Phenanthridones **8b**–**8e**. General Procedure

To a suspension of 1.0 g of quaternary salt **2b**–**2e** in THF, an equivalent of TEA and 1.0 ml of water were added. The mixture was refluxed for 4–6 h. The phenanthridinium salt gradually dissolved during the heating and triethylammonium bromide precipitated upon cooling. THF was removed under reduced pressure, the residue was triturated with water. The solid was sucked off, dried at 100 °C and crystallised from an appropriate solvent.

N,N-Diisopropyl-2-[6(5H)-oxophenanthridin-5-yl]acetamide (**8b**). Yield 0.57 g (85%), yellow powder (cyclohexane); m.p. 203–205 °C. FTIR: 3 073, 2 994, 2 965, 2 931, 1 648 (C=O), 1 448, 1 353, 1 312, 1 212, 1 131, 1 042, 802, 750, 720. ^{1}H NMR: 1.43 d, 6 H, J = 6.3 (CH_3); 1.48 d, 6 H, J = 6.6 (CH_3); 3.63 septet, 1 H, J = 6.3 (CH); 4.27 septet, 1 H, J = 6.6 (CH); 5.31 s, 2 H (CH_2C=O); 7.24–8.62 m, 8 H (CH_{ar}). ^{13}C NMR: 20.51 (CH_3); 20.93 (CH_3); 45.51 (CH_2C=O); 46.25 (CH); 48.05 (CH); 115.09; 121.53; 122.53; 123.23; 127.68; 128.89; 129.33; 132.47 (8 × CH_{ar}); 119.97; 125.17; 133.86; 137.75 (4 × $C_{q\ ar}$); 161.50 (C=O, lactam); 164.93 (C=O). EI MS: 338 (M^+ + 2, 3), 336 (M^+, 8), 237 (9), 236 (43), 235 (9), 210 (4), 209 (22), 208 (48), 180 (16), 179 (23), 178 (88), 153 (7), 152 (28), 151 (12), 129 (4), 128 (42), 101 (8), 100 (100), 98 (10), 87 (7), 86 (98), 44 (7), 43 (81).

N-(1-Adamantyl)-2-[6(5H)-oxophenanthridin-5-yl]acetamide (**8c**). Yield 0.69 g (81%), yellowish powder (methanol–ethanol, 1 : 1); m.p. 205–207 °C. FTIR: 3 276 (NH, amide III), 3 070, 2 904, 2 848, 1 648 (C=O), 1 604 (C=C), 1 548 (amide II), 1 434, 1 363, 1 257, 1 162, 1 064, 1 007, 796, 719. ^{1}H NMR: 1.54 t, 6 H, J = 2.8 (3 × CH_2); 1.85 d, 6 H, J = 2.8 (3 × CH_2); 1.93 m, 3 H (3 × CH); 4.82 s, 2 H (CH_2C=O); 6.08 br s, 1 H (NH); 7.28–8.46 m, 8 H (8 × CH_{ar}). ^{13}C NMR: 29.25 (CH); 36.13 (CH_2); 41.25 (CH_2); 49.17 (C_q); 52.00 (CH_2C=O); 115.93; 121.73; 123.13; 127.97; 128.85; 129.96; 132.91 (7 × CH_{ar}); 119.90; 124.92; 133.87; 137.21 (4 × $C_{q\ ar}$); 161.98 (C=O, lactam); 166.99 (C=O). EI MS: 385 (M^+, 5), 237 (2), 123 (9), 235 (8), 211 (4), 210 (18), 209 (100), 196 (3), 195 (7), 181 (6), 180 (15), 179 (15), 178 (25), 153 (5), 152 (21), 151 (11), 135 (18), 94 (6), 93 (18), 91 (8), 79 (19), 77 (10). For $C_{25}H_{26}N_2O_2$ (385.5) calculated: 77.69% C, 6.78% H, 7.25% N; found: 77.73% C, 6.81% H, 7.24% N.

N-Benzyl-2-[6(5H)-oxophenanthridin-5-yl]acetamide (**8d**). Yield 0.82 g (82%), yellow powder (methanol–ethanol, 1 : 1); m.p. 204–206 °C. FTIR: 3 284 (NH, amide III), 3 071, 3 032, 2 954, 2 929, 1 652 (C=O), 1 608 (C=C), 1 549 (amide II), 1 433, 1 364, 1 240, 1 169, 1 078, 1 009, 751, 723. ^{1}H NMR: 4.42 d, 2 H, J = 5.9 (CH_2Ph); 5.07 s, 2 H (CH_2C=O); 6.82 br s, 1 H (NH); 7.13–7.25 m, 5 H (CH_{ar}); 7.37–8.49 m, 8 H (CH_{ar}). ^{13}C NMR: 43.26 (CH_2Ph); 48.05 (CH_2C=O); 115.58; 121.77; 123.27; 123.31; 127.24; 127.28; 128.08; 128.47; 130.03; 133.04 (10 × CH_{ar}); 119.40; 124.80; 137.03; 137.67 (4 × $CH_{q\ ar}$); 162.12 (C=O, lactam); 168.09 (C=O). EI MS: 342 (M^+, 18), 238 (3), 237 (16), 236 (82), 210 (13), 209 (76), 208 (62), 196 (45), 195 (10), 194 (5), 181 (8), 180 (28), 179 (26), 178 (100), 153 (11), 152 (45), 151 (31), 107 (5), 106 (28), 91 (31), 77 (12), 65 (11).

(±)-N-[1-(1-Adamantyl)ethyl]-2-[6(5H)-oxophenanthridin-5-yl]acetamide (**8e**). Yield 0.43 g (87%), yellowish powder (methanol–ethanol, 1 : 1); m.p. 214–216 °C. FTIR: 3 309 (NH, amide III), 3 047, 2 974, 2 901, 2 845, 1 657 (C=O, amide I), 1 609 (C=C), 1 587, 1 553 (amide II), 1 492, 1 438, 1 364, 1 316, 1 254, 1 163, 1 095 , 998, 753, 724. ^{1}H NMR: 0.92 d, 3 H, J = 10 (CHC**H**$_3$); 1.26 and 1.33 AB quartet, 6 H, J = 10 (3 × CH_2); 1.38 and 1.55 AB quartet, 6 H, J =

10 (3 × CH_2); 1.79 s, 3 H (3 × CH); 3.63 m, 1 H (C**H**CH_3); (4.83 and 5.19) AB quartet, 2 H, *J* = 15 (CH_2C=O); 6.34 d, 1 H, *J* = 10 (NH); 7.35–8.55 m, 8 H (8 × CH_{ar}). ^{13}C NMR: 14.29 ($CHCH_3$); 28.14 (3 × CH); 35.82 (C_q); 36.87 (3 × CH_2); 38.15 (3 × CH_2); 48.34 (CH_2C=O); 53.15 ($CHCH_3$); 116.19; 121.89; 123.28; 128.18; 128.95; 130.08; 133.13 (7 × CH_{ar}); 119.38; 124.93; 133.94; 137.09 (4 × $C_{q\ ar}$); 162.21 (C=O, lactam); 167.54 (C=O). EI MS: 416 (M^+ + 2, 2), 414 (M^+, 4), 238 (1), 237 (9), 236 (100), 209 (58), 208 (33), 195 (10), 180 (12), 178 (43), 153 (1), 152 (7), 151 (2), 135 (13), 93 (5), 81 (4), 79 (5), 57 (4), 55 (4), 44 (1), 43 (3).

This work was supported by the Grant of Ministry of Education (CEZ:J07/98:143100011)

REFERENCES

1. Potáček M., Topinka T., Dostál J., Humpa O.: *Collect. Czech. Chem. Commun.* **1995**, *60*, 1191.
2. Potáček M., Topinka T., Dostál J., Marek J.: *Collect. Czech. Chem. Commun.* **1994**, *59*, 2641.
3. Dostál J., Potáček M., Humpa O., Marek J.: *Bull. Soc. Chim. Belg.* **1994**, *103*, 343.
4. Topinka T.: *M.S. Thesis*. Masaryk University, Brno 1995.
5. Dostál J.: *Ph.D. Thesis*. Masaryk University, Brno 1993.
6. Trávníček M.: *M.S. Thesis*. Masaryk University, Brno 1998.
7. Garner P., Ho V. B.: *J. Org. Chem.* **1990**, *55*, 3973.
8. Kim B. H., Curran D. P.: *Tetrahedron* **1993**, *49*, 293.
9. Oppolzer W., Chapuis C., Bernardinelli G.: *Helv. Chim. Acta* **1984**, *67*, 1397.
10. Katritzky A. R., Grzeskowiak N. H.: *J. Chem. Soc., Perkin Trans. 1* **1981**, 1180.
11. a) Weaver W. E., Whaley W. M.: *J. Am. Chem. Soc.* **1947**, *69*, 515; b) Weaver W. E., Whaley W. M.: *J. Am. Chem. Soc.* **1947**, *69*, 1144.
12. Drake M. L., Eaker C. M., Shenk W.: *J. Am. Chem. Soc.* **1948**, *70*, 677.
13. Winn M., Geldern T. W., Opgenorth T. J.: *J. Med. Chem.* **1996**, *39*, 1039.
14. Bordwell F. G., Zhang S., Zhang X.-M., Liu W.-Y.: *J. Am. Chem. Soc.* **1995**, *117*, 7092.
15. Aquino C. J., Armorer D. R., Berman J. M.: *J. Med. Chem.* **1996**, *39*, 562.
16. Ciommer B., Frenking G., Schwarz H.: *Chem. Ber.* **1981**, *114*, 1503.
17. Pullukkody K. P., Norman T. J., Parker D., Doyle L.: *J. Chem. Soc., Perkin Trans. 2* **1993**, *4*, 605.
18. Vloon W. J., Kruk C., Pandit U. K., Hofs H. P.: *J. Med. Chem.* **1987**, *30*, 20.
19. Dupont V., Lecoq A., Mangeot J.-P., Aubry A.: *J. Am. Chem. Soc.* **1993**, *115*, 8898.
20. Lowe J. A., Hageman D. L., Drozda S. E.: *J. Med. Chem.* **1994**, *37*, 3789.
21. Walter H.: *Heterocycles* **1995**, *41*, 2427.
22. Kruglik L. I., Gololobov Y. G.: *Zh. Org. Khim.* **1978**, *14*, 747.
23. Jones R. C., Nichols J. R., Cox M. T.: *Tetrahedron Lett.* **1991**, *31*, 2333.
24. Tischer T., Kádas I., Bende Z., Töke T.: *J. Heterocycl. Chem.* **1991**, *28*, 867.
25. Bende Z., Töke T., Weber L., Tóth G., Janke F., Csonka F.: *Tetrahedron* **1984**, *40*, 369.
26. Bende Z., Simon K., Tóth G., Töke T., Weber L.: *Liebigs Ann. Chem.* **1982**, 924.
27. Wiley J.: *1,3-Dipolar Reaction Chemistry*, Vol. 1. Wiley, New York 1994.
28. Huisgen R. in: *Advances in Cycloaddition* (D. P. Curran, Ed.), Vol. 1, p. 1. JAI Press, Greenwich (Con.) 1988.
29. Woller P. B., Cromwell N. H.: *J. Org. Chem.* **1970**, *35*, 888.

30. DeRuiter J., Swearingen B. E., Wanderkar V., Mayfield C. A.: *J. Med. Chem.* **1989**, *32*, 1033.
31. Collina G., Forlani L., Mezzina E., Sintoni M., Todesco P. E.: *Gazz. Chim. Ital.* **1987**, *117*, 281.
32. Nakano H., Tomisawa H., Hongo H.: *Heterocycles* **1992**, *33*, 195.
33. DeRuiter J., Brubaker A. N., Whitmer L., Stein J. L.: *J. Med. Chem.* **1986**, *29*, 2024.
34. Begley W. J., Lowe G., Cheetham A. K., Newsam J. M.: *J. Chem. Soc., Perkin Trans. 1* **1981**, 2620.
35. Singh P., Deep K., Singh H.: *J. Chem. Res., Miniprint* **1984**, *3*, 636.