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Synthesis of Cyclo-bis-intercaland Receptor Molecules with Phenanthridinium Units*

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The cyclo-bis-intercaland type of receptor molecules based on phenanthridinium units have been synthesized and their spectroscopic (NMR, electronic absorption and fluorescence) properties studied. X-ray structures of two macrocyclic bis-phenanthridine precursors of cyclo-bis-intercalands have been determined.

INTRODUCTION

Synthesis of artificial receptor molecules capable of binding and recognition of each of the major nucleotides in water presents one of the recent challenges in supramolecular chemistry. It is also of interest from the biochemical and medicinal standpoints since the recognition of nucleotides could be in many aspects related to the problem of selective interactions of small molecules with DNA, being designed either to produce biological effects or to be used as DNA structural probes or markers.[1] The most obvious approach to nucleotide recognition emerges from natural examples of gene expression where complementary nucleic bases are precisely mutually recognized by hydrogen bonding.[2] Based on such an approach the selective re-

* Dedicated to Professor Vlado Prelog on the occasion of his 90th birthday.
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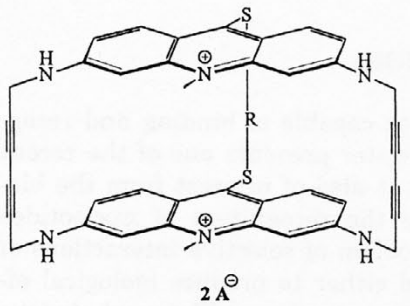
ceptor molecules able to recognize each of the major nucleic bases in lipophilic media, utilizing hydrogen bonding and stacking interactions have been prepared.[3] However, the development of receptor molecules with recognition properties for nucleotides in water, where they are most soluble, presents a more difficult problem.[4–6] The main obstacle in nucleotide recognition lies in the fact that hydrogen bonding, as an obvious nucleic base recognition mode, is highly disfavoured in aqueous media.[2] One of the possible solutions for nucleotide recognition could be anticipated by construction of water soluble receptor molecules possessing a lipophilic binding and a built-in hydrogen bonding base recognition site, both protected from water solvation. The first step on the way to such receptors must be construction of water soluble receptors able to bind the nucleic base part of a nucleotide in their lipophilic cavity. In this respect, the water soluble cyclo-bis-intercaland[7] type of receptor molecules, based on acridinium units, are of special interest (Figure 1). As it has been shown recently, such receptor molecules exhibit strong binding of various flat aromatic substrates including nucleosides and nucleotides in aqueous media. By the process of cyclointercalation,[7d] an aromatic guest or nucleic base part of a nucleotide is inserted between acridinium units of the receptor due to the favourable stacking interactions between π-systems. For nucleotides, the binding constants of 10^4 and as high as 10^8 dm^3/mol have been measured, depending on whether only stacking or simultaneous stacking and electrostatic interactions are involved.[7c,f]

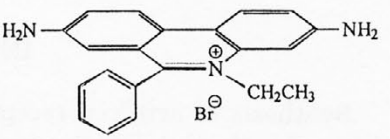
The design of cyclo-bis-intercalands has been inspired by the well known DNA intercalation phenomenon[2,8] involving insertion of flat aromatic mole-



R

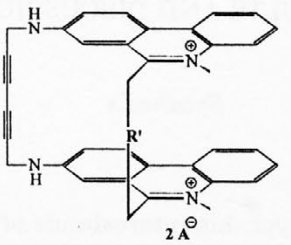
$CH_2CH_2OCH_2CH_2$

$CH_2CH_2CH_3$

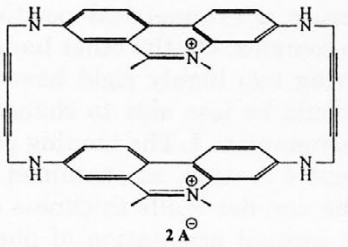


Ethidium bromide (E)

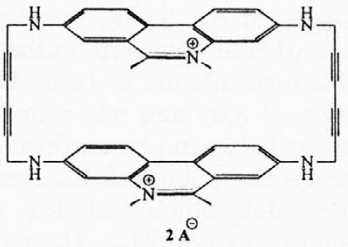
Figure 1. Acridinium type of cyclo-bis-intercalands and DNA intercalator ethidium bromide.



I



II



III

Figure 2. Phenanthridinium based cyclo-bis-intercalands of types **I**, **II** and **III**.

cules, such as acridinium dyes, between adjacent base pairs of duplex DNA. Besides the acridinium type of DNA intercalators, the phenanthridine derivative ethidium bromide (E, Figure 1) is one of the most useful intercalators in the analytical sense.[9,10] When E intercalates into duplex DNA, its intrinsic fluorescence exhibits a quantum yield increase of about 25-fold.[11] These interesting fluorescence properties, as well as a somewhat larger area in comparison with acridine system, make the phenanthridinum group an attractive unit for construction of a cyclo-bis-intercaland type of receptors. Indeed, as we have reported recently,[12] the phenanthridinium cyclo-bis-intercalands of type **I** (Figure 2) strongly bind nucleotides in water solely by stacking interactions with nucleic bases. The binding constants of 10^5–10^6 dm^3/mol were measured, being 10 to 100 times stronger than those obtained for similar acridinium receptors[7c] (Figure 1) and nucleotides. In this paper, we present a full description of the synthesis of phenanthridinium cyclo-bis-intercalands of types **I**, **II** and **III** (Figure 2), together with their spectroscopic properties and X-ray structural studies of two macrocyclic bis-phenanthridine precursors. The binding studies with cyclo-bis-intercalands of types **II** and **III** will be published elsewhere.

RESULTS AND DISCUSSION

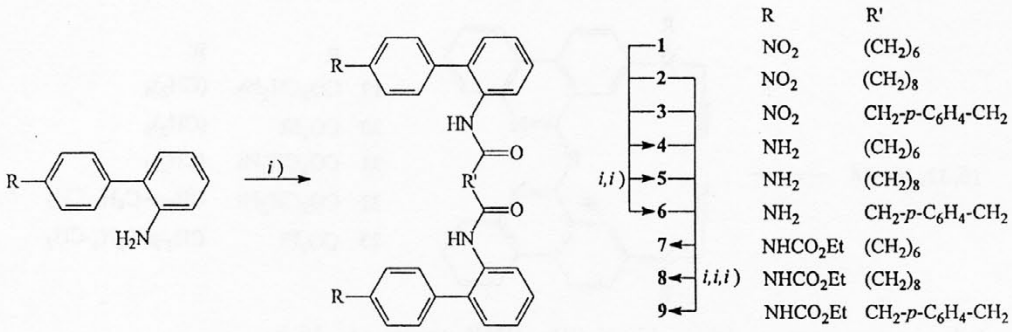
Synthesis

Construction Principles

The phenanthridinium cyclo-bis-intercalands of types **I**, **II** and **III** differ in the flexibility and mutual orientation of phenanthridinium units. Those of type **I** contain one rigid hexadiyne bridge at 8,8'-amino- and a flexible hexa- or octa-methylene bridge at 6,6'-phenanthridinium positions. Such a construction mode is expected to provide considerable flexibility to **I** and, consequently, some degree of its adaptability to different substrates. The presence of 6,6'-bridge is important to ensure a symmetrical position of phenanthridinium units in the intercalative complex. On the other hand, cyclo-bis-intercalands of types **II** and **III** having two highly rigid hexadiyne bridges at 3,3'- and 8,8'-amino-positions, should be less able to change the distance between phenanthridinium units compared to **I**. The binding pocket between the phenanthridinium units is about 4 Å wide, as examined from CPK models which is slightly wider than the van der Walls thickness of an aromatic system. Also, **II** and **III** differ in mutual orientation of phenanthridinium units (Figure 2). The examination of CPK models shows that phenanthridinium units in **II** and **III** may rotate more or less freely around phenanthridinium 3,3'-, 8,8'-amino single bonds. Considering the positive charges on quaternary nitrogens and the interaction with close counterions, the existence of **II** and **III** predominantly in *trans*-conformations (with respect to charged nitrogens) may be anticipated. In such a case, the overall π-surface available for interaction with intercalated substrate would be somewhat larger in *trans*- than in *cis*-conformation of both **II** and **III**. This, together with different positions of charged nitrogens, may result in enhanced binding and recognition of specific substrates.

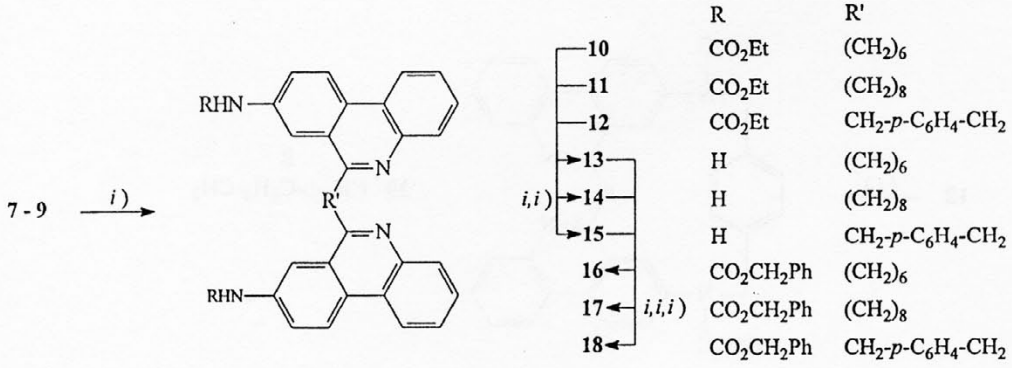
Synthesis of 6,6'- and 8,8'-Bridged Macrocyclic Bis-phenanthridines

The key step in the synthesis of **I** as well as **II**, **III** consists of the well established Cu(II) promoted oxidative coupling of propargyl derivatives in high-dilution conditions yielding macrocyclic structures with hexadiyne bridges.[7,13,14] Consequently, the starting synthetic steps were directed towards preparation of phenanthridine derivatives substituted by propargyl groups at positions planned for introduction of hexadiyne bridges. A functionalized phenanthridine system can be conventionally prepared by the Morgan-Walls reaction[15] based on the middle pyridine ring formation by intramolecular electrophilic cyclization of 2-amidobiphenyl derivatives using $POCl_3$ or polyphosphoric acid. Also, the preparation of bis-3,8-diaminophenanthridine derivatives bridged at 6,6'-positions has been reported by the

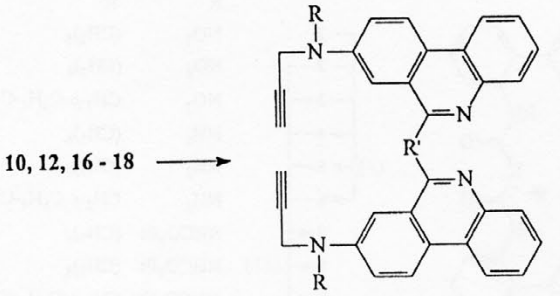


Scheme 1. *i*) $ClCO(CH_2)_6COCl$, $ClCO(CH_2)_8COCl$ or $ClCOCH_2$-*p*-C_6H_4-CH_2COCl, dry C_6H_6, reflux; *i,i*) H_2, 10% Pd/C, DMF/ETOH (3 : 1), 50 bar, 70 °C; *i,i,i*) $ClCO_2Et$, *N,N'*-dimethylaniline, dry EtOH.

same reaction starting from the corresponding bis-biphenylyl diamides.[16] For construction of **I** the bis-phenanthridines functionalized by amino groups only at 8,8'-positions are needed (Figure 2). The starting 2-amino-4'-nitrobiphenyl (Scheme 1) was obtained in high yield by selective nitration of 2-aminobiphenyl (KNO_3/H_2SO_4, 0 °C).[17] Its reaction with suberoyl, sebacoyl or *p*-phenylene diacetyl chloride (molar ratio 2 : 1) gave bis-biphenyl derivatives **1–3** in yields exceeding 80%. The catalytic hydrogenation of **1–3** using 10% Pd/C in DMF-EtOH at 50 bar and 70 °C, gave the corresponding amino-bis-biphenyls **4–6** in 90–100% yield. Protection of amino groups by ethyl chloroformate in dry EtOH in the presence of dimethylaniline yielded

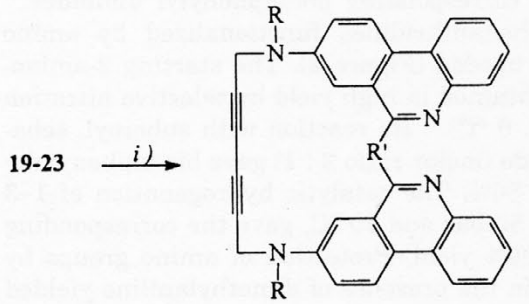


Scheme 2. *i*) $POCl_3$, reflux, 2 h; *i,i*) 70% H_2SO_4, 140 °C, 30 min; *i,i,i*) $ClCO_2CH_2Ph$, K_2CO_3, DMF, 0 °C, 30 min.

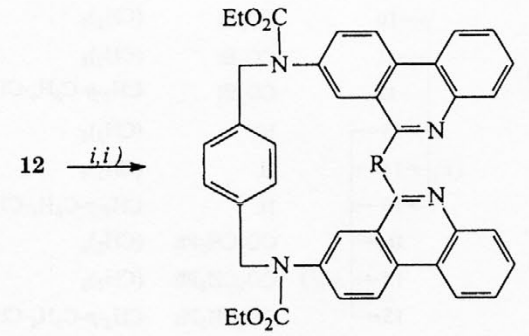


	R	R'
19	CO_2CH_2Ph	$(CH_2)_6$
20	CO_2Et	$(CH_2)_6$
21	CO_2CH_2Ph	$(CH_2)_8$
22	CO_2CH_2Ph	CH_2-*p*-C_6H_4-CH_2
23	CO_2Et	CH_2-*p*-C_6H_4-CH_2

Scheme 3. *i*) propargyl bromide K_2CO_3, DMF, argon, r.t., 48 h.



	R	R'
24	CO_2CH_2Ph	$(CH_2)_6$
25	CO_2Et	$(CH_2)_6$
26	CO_2CH_2Ph	$(CH_2)_8$
27	CO_2CH_2Ph	CH_2-*p*-C_6H_4-CH_2
28	CO_2Et	CH_2-*p*-C_6H_4-CH_2



	R
29	CH_2-*p*-C_6H_4-CH_2

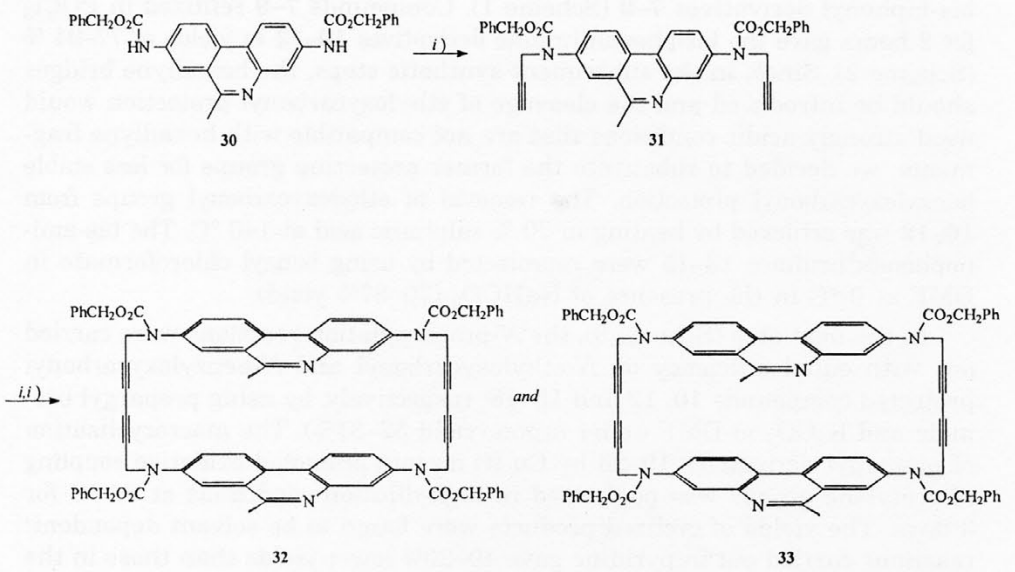
Scheme 4. *i*) $Cu(OAc)_2 \times H_2O$, pyridine/CH_3CN (5 : 1), high dilution, 60 °C, 3 d; *i,i*) α,α'-dibromo-*p*-xylene, K_2CO_3, DMF, 80 °C, 5 d.

bis-biphenyl derivatives **7–9** (Scheme 1). Compounds **7–9** refluxed in $POCl_3$ for 2 hours gave the bis-phenanthridine derivatives **10–12** in yields of 77–94 % (Scheme 2). Since, in the subsequent synthetic steps, the hexadiyne bridges should be introduced and the cleavage of ethyloxycarbonyl protection would need strongly acidic conditions that are not compatible with hexadiyne fragments, we decided to substitute the former protecting groups for less stable benzyloxycarbonyl protection. The removal of ethyloxycarbonyl groups from **10–12** was achieved by heating in 70 % sulphuric acid at 140 °C. The bis-aminophenanthridines **13–15** were reprotected by using benzyl chloroformate in DMF at 0 °C in the presence of $NaHCO_3$ (70–87% yield).

In the next step (Scheme 3), the *N*-propargylation reactions were carried out with equal efficiency on *N*-ethyloxycarbonyl and *N*-benzyloxycarbonyl protected compounds **10**, **12** and **16–18**, respectively, by using propargyl bromide and K_2CO_3 in DMF under argon (yield 52–81%). The macrocyclization of propargyl derivatives **19–23** by Cu(II) acetate promoted oxidative coupling of acetylene groups was performed in high-dilution conditions at 60 °C for 3 days. The yields of cyclized products were found to be solvent dependent: reactions carried out in pyridine gave 10–20% lower yields than those in the pyridine-acetonitrile 5 : 1 solvent mixture (yields 40–50%). The same effect of acetonitrile on yields of macrocyclization reactions was also observed by Vögtle[18] and attributed to the template function of acetonitrile molecule. Besides the macrocyclic bis-phenanthridines **24–28** having $(CH_2)_6$, $(CH_2)_8$ and *p*-xylylene bridges at 6,6'-positions, the macrocyclic bis-phenanthridine **29** having *p*-xylylene bridges at both positions was also prepared. The reaction of **22** with *p*-xylylene dibromide, K_2CO_3 in high-dilution conditions (DMF, 80 °C) gave only 9% of **29** after 5 days.

Synthesis of 3,3'- and 8,8'-Bridged Macrocyclic Bis-phenanthridines

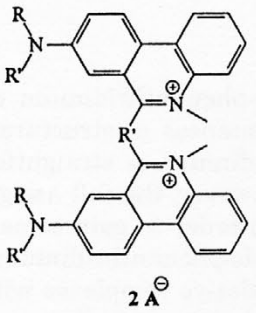
The 1 : 1 macrocyclization of dipropargyl phenanthridine derivative **31** should give two macrocyclic products, **32** and **33**, with different orientation of phenanthridine units (Scheme 5). The synthesis started from amino protected 6-methylphenanthridine **30** which was propargylated in the same way as described for **19–23**, giving **31** in 73% yield. The 1 : 1 macrocyclization of **31** by Cu(II) acetate promoted coupling of acetylene groups was performed under high-dilution conditions (0.002 M solution of **31**) in dry acetonitrile. The reaction was monitored by t.l.c. (CH_2Cl_2/MeOH, 95 : 5) which showed formation of a single product with R_f = 0.40. The product was isolated and its purity checked by t.l.c. in various solvent systems. The sixfold development of t.l. chromatograms in the CH_2Cl_2/EtOH/EtOAc (48 : 1 : 1) solvent system revealed however two spots with R_f = 0.67 and R_f = 0.63. The products have been separated by multiple repetition of preparative t.l.c. and tentatively assigned as diastereoisomers **32** and **33** (Scheme 5) on the basis of their ^{1}H-NMR spectra as discussed in the next paragraph.



Scheme 5. *i*) propargyl bromide, K_2CO_3, DMF, argon; r.t., 48 h; *i,i*) $Cu(OAc)_2 \times H_2O$, CH_3CN, high dilution, 60 °C, 3 d.

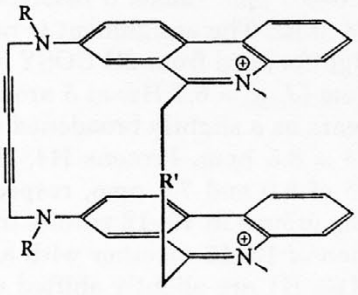
Preparation of Acyclic and Macrocyclic Bis-intercalands of Types ***I, II*** *and* ***III***

Various acyclic and macrocyclic bisphenanthridinium intercalands (Charts 1 and 2) were prepared by quaternization of phenanthridine 5,5'-nitrogens of the corresponding 8-amino protected acyclic and 3,8-amino protected macrocyclic bis-phenanthridines by using the excess of methyl trifluoromethylsulphonate in dichloroethane,[7c] which precipitated the products as trifluoromethylsulphonate salts. The *N*-benzyloxycarbonyl protected salts were either suspended in dry dichloromethane and treated with trifluoromethylsulphonic acid at room temperature or treated directly without isolation in the quaternization step, giving bis-phenanthridinium trifluoromethylsulphonate salts **36–38** and **43–45**, **49** and **51**. These salts are still relatively lipophilic substances soluble in acetonitrile and alcohols but not in water. The exchange of relatively lipophilic trifluoromethylsulphonate anion for more hydrophilic hydrogensulphate was performed by mixing the solutions of bis-phenanthridinium trifluoromethylsulphonate and the excess of tetrabutylammonium hydrogensulphate in acetonitrile which precipitated bis-phenanthridinium hydrogensulphate salts **39**, **40**, **46–48**, **50** and **52**. The *N*-deprotected bis-phenanthridinium hydrogensulphates were found to be of sufficient water solubility, which allowed for **46–48** the binding studies with nucleotides to be executed using the fluorescence method.[12b]



	R	R'	R''	$A^{\ominus}$
34	$CH_2C{\equiv}CH$	CO_2Et	$(CH_2)_6$	$CF_3SO_3^-$
35	$CH_2C{\equiv}CH$	CO_2Et	CH_2-*p*-C_6H_4-CH_2	$CF_3SO_3^-$
36	$CH_2C{\equiv}CH$	H	$(CH_2)_6$	$CF_3SO_3^-$
37	H	H	$(CH_2)_6$	$CF_3SO_3^-$
38	H	H	$(CH_2)_8$	$CF_3SO_3^-$
39	$CH_2C{\equiv}CH$	H	$(CH_2)_6$	HSO_4^-
40	H	H	$(CH_2)_6$	HSO_4^-

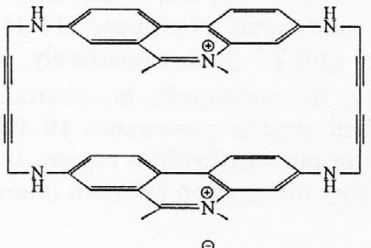
$2\,A^{\ominus}$



	R	R'	$A^{\ominus}$
41	CO_2Et	$(CH_2)_4$	$CF_3SO_3^-$
42	CO_2Et	*p*-C_6H_4	$CF_3SO_3^-$
43	H	$(CH_2)_4$	$CF_3SO_3^-$
44	H	$(CH_2)_6$	$CF_3SO_3^-$
45	H	*p*-C_6H_4	$CF_3SO_3^-$
46	H	$(CH_2)_4$	HSO_4^-
47	H	$(CH_2)_6$	HSO_4^-
48	H	*p*-C_6H_4	HSO_4^-

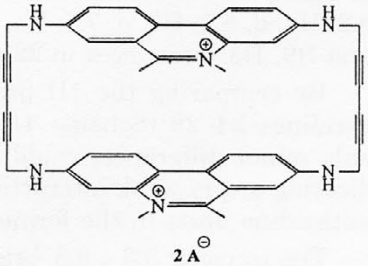
$2\,A^{\ominus}$

Chart 1.



$2\,A^{\ominus}$

$A^{\ominus}$	
49	$CF_3SO_3^-$
50	HSO_4^-



$2\,A^{\ominus}$

$A^{\ominus}$	
51	$CF_3SO_3^-$
52	HSO_4^-

Chart 2.

Spectra

^{1}H-NMR Spectra

In the series of bis-phenanthridine and bis-phenanthridinium derivatives prepared, the assignment of ^{1}H-NMR resonances of structural fragments, except for phenanthridine or phenanthridinium, is straightforward and hence is not discussed, except for **49–52**. However, the full assignment of heteroaromatic resonances is of importance in order to gain some structural information on bis-phenanthridine or bis-phenanthridinium compounds and especially for studies of their intercalative complexes with aromatic guests, where complexation induced shifts may give valuable informations on their structures.[4b]

The acyclic 8,8'-aminoprotected bis-phenanthridine derivatives **10–12** and **16–18** (Scheme 2) show in the δ = 7.6–8.8 ppm range, 5 resolved resonances for protons of both phenanthridine units. The assignment is not possible from 1D spectra, however, it is straightforward from 2D COSY spectra giving the positions of H10 and H1 doublets (J_{ortho} = 6.5 Hz) at δ around 8.8 and 8.6 ppm, respectively. Proton H7 appears as a slightly broadened singlet due to small *meta*-coupling with H9 at δ = 8.5 ppm. Protons H4, H9 and H3, H2 give two multiplets centered at δ of 8.0 and 7.6 ppm, respectively. The removal of ethyloxycarbonyl protecting groups in **10–12** results in a different pattern in the phenanthridine region of **13–15** together with a slight upfield shift of all resonances. Protons H10, H1 are slightly shifted upfield and partly overlapped giving the multiplet at δ = 8.5 ppm. Protons H4 (doublet) and H3, H2 (multiplet) appear at δ of 7.9 and 7.5 ppm, respectively. The largest upfield shifts are observed for H7 (δ = 7.5 ppm) and H9 (δ = 7.3 ppm), resulting from their *ortho*-positions to 8-amino groups.

The presence of protecting and propargyl groups on 8,8'-nitrogens of **19–23** (Scheme 3) results in an appearance of 7 well resolved resonances for protons of both phenanthridine units in **19–21** (δ/ppm: H10, d, 8.6; H1, d, 8.5; H7, s, 8.2; H4, d, 8.1; H9, d, 7.8; H3, t, 7.7; H2, t, 7.6) and partly overlapped H7, H4 and H9, H3 resonances in **22** and **23** at δ of 8.1 and 7.7 ppm, respectively.

By comparing the 1D proton NMR spectra of macrocyclic bis-phenanthridines **24–29** (Scheme 4) with those of their acyclic precursors **19–23**, only minor differences could be observed in the phenanthridine region, indicating a very weak interaction or absence of any interaction between phenanthridine units in the former.

The isomeric 3,3'-, 8,8'-bridged bis-phenanthridines prepared as outlined in Scheme 5 show different pattern of phenanthridine resonances. The analysis of their COSY spectra gives alternative assignments for H10, H1 and H9, H2 phenanthridine protons. However, an unambigous assignment of all phenanthridine resonances could be achieved by a combined analysis of NOESY and COSY spectra. In NOESY spectra two NOE interac-

tions could be observed, the first between H7 and 6-CH_3 and the second between H4, H7 and methylene protons from hexadiyne bridges. This reveals the chemical shifts of H7 and H4 unambigously. In COSY spectra, weak interactions from *meta*-coupling between H7, H9 and H4, H2 could be observed, which gives the chemical shifts of H9 and H2 and identifies their *ortho*-coupling partners H10 and H1, respectively. Comparison of 1D spectrum of the isomer with m.p. 215–217 °C and higher R_f value with those of 6,6'- and 8,8'-bridged bisphenanthridines **24–28** shows that the chemical shifts of phenanthridine protons are almost identical for both types of macrocyclic compounds (Figure 3). In contrast, the isomer with m.p. 127–128 °C and lower R_f value shows a completely different pattern of phenanthridine resonances. Protons H10, H1 appear as a quasi triplet due to the partial overlap of two doublets, centred at δ = 8.5 ppm. Similarly, H7 and H4 singlets are partially overlapped at δ = 8.1 ppm. Slightly broadened doublets of H9 and H2 are located at δ of 7.75 and 7.67 ppm, respectively. The observed chemical shift differences for phenanthridine protons of the isomer with lower m.p. suggest their different mutual orientation with respect to the higher melting isomer and the series of 6,6'-, 8,8'-bridged bis-phenanthridines. On that basis, the structure **32** could be assigned to the higher melting and structure **33** to the lower melting isomer.

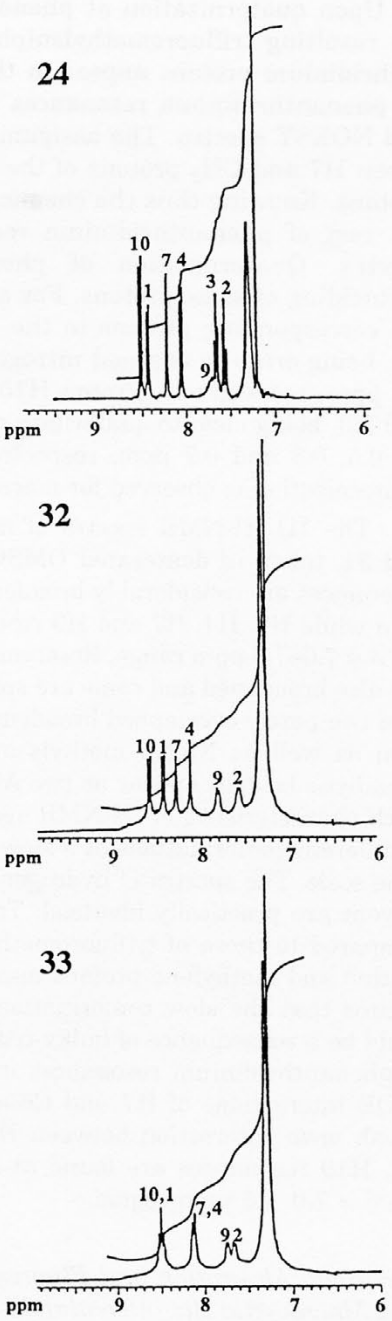


Figure 3. The ^{1}H-NMR regions of phenanthridine resonances of **24**, **32** and **33**.

Upon quaternization at phenanthridine N5, in the ^{1}H-NMR spectra of the resulting trifluoromethylsulphonate salts **34–37** and **41–45**, the phenanthridinium protons appear in the δ = 7.5–9.0 ppm range. Assignment of all phenanthridinium resonances was achieved from the analysis of COSY and NOESY spectra. The assignments were based on NOE interactions between H7 and CH_2 protons of the hexadiyne bridge and H4 and N5-methyl protons. Knowing thus the chemical shifts of H7 and H4, the assignment of the rest of phenanthridinium resonances is straightforward from COSY spectra. Quaternization of phenanthridine N5 produces considerable deshielding of some protons. For example, comparison of chemical shifts for the corresponding protons in the spectra of **36** and **20** shows that H2 and H4, being *ortho* to charged nitrogen, are shifted downfield in **36** by 1.3 and 0.3 ppm, respectively. Proton H10 is also deshielded for 0.2 ppm while H1 and H3, being *meta* to quaternary nitrogen as well as H7 are strongly shielded for 0.5, 0.8 and 0.7 ppm, respectively. The same trend of shifts induced by quaternization is observed for macrocyclic bis-phenanthridinium derivative **43**.

The 1D ^{1}H-NMR spectra of isomeric trifluoromethylsulphonate salts **49** and **51**, taken in deuterated DMSO, are very similar. The phenanthridinium resonances are considerably broadened; H1, H10 give a broad signal at δ = 8.55 ppm while H2, H4, H7 and H9 resonances appear as a broadened multiplet in the δ = 7.0–7.5 ppm range. Resonances of other than phenanthridinium protons are also broadened and some are split. The phenanthridinium 6-methyl protons give two partly overlapped broadened singlets of different intensities at δ = 3.1 ppm as well as N5,N5'-methyls at δ = 4.2 ppm. The methylene protons of hexadiyne bridges appear as two AB systems located at δ of 4.35 and 4.7 ppm. Such characteristics of ^{1}H-NMR spectra of **49** and **51** point to the equilibrium of different conformations at a slow interconversion rate compared to the NMR time scale. The spectra of hydrogensulphate salts **50** and **52** taken in the same solvent are practically identical. The resonances are much less broadened, as compared to those of trifluoromethyl-sulphonate salts, and the resonances of methyl and methylene protons appear as slightly broadened singlets. This indicates that the slow conformational interconversion rate in the former case could be a consequence of bulky trifluoromethylsulphonate anions. Assignment of phenanthridinium resonances in **50** and **52** is also achieved from NOESY (NOE interactions of H7 and C6-methyl and H4 and N5-methyl) and COSY (weak *meta* interaction between H7 and H9) spectra. The phenanthridinium H1, H10 resonances are found at δ = 8.5 ppm and the rest of resonances in the δ = 7.0–7.5 ppm region.

*Electronic Absorption and Fluorescence Spectra of Acyclic and Macrocyclic Bis-intercalands **39, 46, 50** and **52***

The electronic absorption spectra of monomeric 8-aminopropargyl-5,6-dimethylphenanthridinium hydrogensulphate, acyclic **39**, macrocyclic 6,6'- and

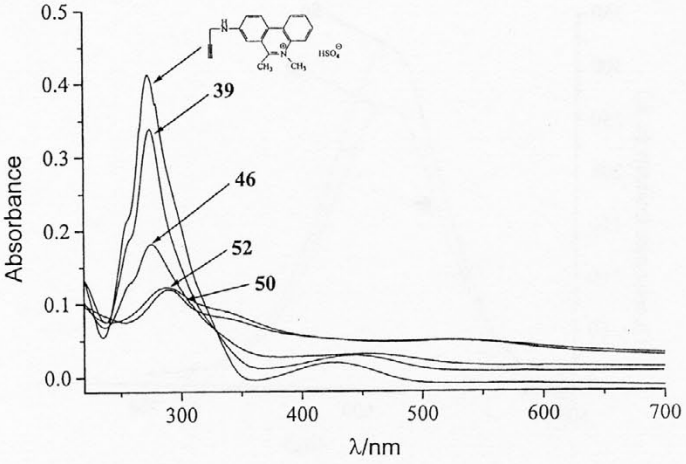


Figure 4. The electronic absorption spectra of monomeric phenanthridinium hydrogensulphate ($c = 1.2 \times 10^{-5}$ mol/dm^3), **39**, **46**, **50** and **52** ($c = 6 \times 10^{-6}$ mol/dm^3) taken in aqueous buffer (pH = 6, sodium cacodylate).

8,8'-bridged **46** and isomeric 3,3'- and 8,8'-bridged **50**, **52** bis-phenanthridinium compounds, taken in aqueous buffer (pH = 6) are shown in Figure 4. The acyclic **39** (λ_{max} = 275 nm, ε = 63266) and macrocyclic **46** (λ_{max} = 276 nm,

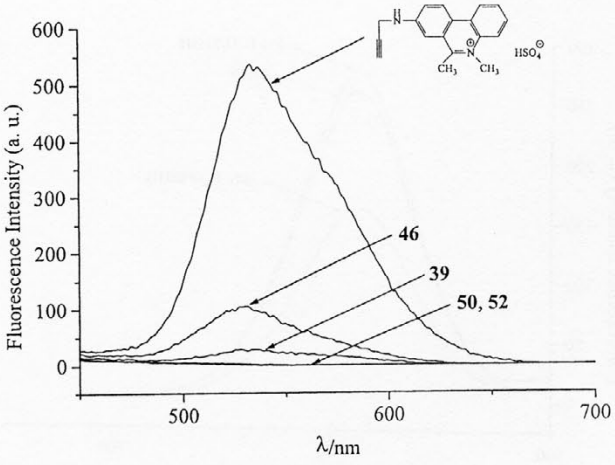


Figure 5. The fluorescence emission spectra of monomeric phenanthridinium hydrogensulphate ($c = 2.4 \times 10^{-6}$ mol/dm^3) **46**, **39** (λ_{excit} = 278 nm) and **50**, **52** ($c = 1.2 \times 10^{-6}$ mol/dm^3, λ_{excit} = 288 nm) taken in aqueous buffer (pH = 6, sodium cacodylate).

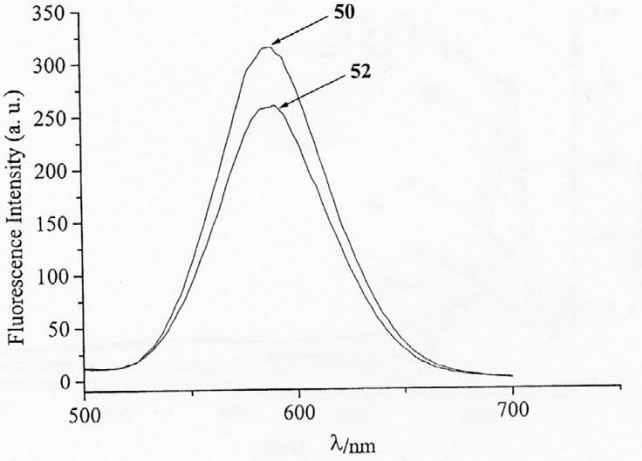


Figure 6. The emission spectra of **50** and **52** ($\lambda_{excit.}$ = 295 nm) in ethanol (c = 1.1 × 10^{-6} mol/dm^3).

ε = 36781), **50** (λ_{max} = 289 nm, ε = 21250) and **52** (λ_{max} = 288 nm, ε = 20990) bis-phenanthridinium compounds show strong hypochromism. As we have reported recently, the ratios of molar extinction coefficients for the series **46–48** and monomeric phenanthridinium hydrogensulphate were ε_{39} / $\varepsilon_{monomer}$ = 1.62, ε_{46} / $\varepsilon_{monomer}$ = 0.95, ε_{47} / $\varepsilon_{monomer}$ = 1.37 and ε_{48} / $\varepsilon_{monomer}$ = 1.18, show-

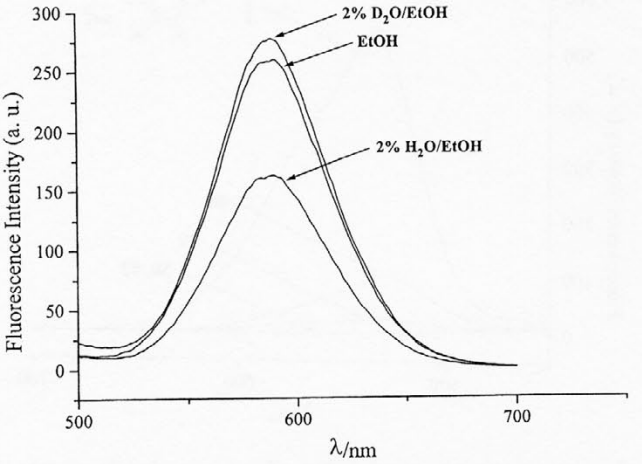


Figure 7. The effects of added D_2O and H_2O on the intensity of emission spectra of **52** dissolved in ethanol (c = 1.1 × 10^{-6} mol/dm^3).

ing the greatest hypochromic effect for **46**, having the shortest 6,6'-bridge.[12b] The isomeric doubly hexadiyne bridged cyclointercalands **50** and **52** exhibited even smaller molar extinction coefficients than **46–48**. Strong hypochromic effects have been observed for similar charged π-systems and explained by intramolecular π-π stacking interactions.[19] The observed hypochromicity for **46–48** and **50**, **52**, however, cannot be explained solely on the basis of intramolecular stacking of phenanthridinium units since in such a case the hypochromicity should be more pronounced for flexible **39** than for the more rigid **46** or **48**.

The fluorescence emission spectra of monomeric phenanthridinium hydrogensulphate, acyclic **39** and macrocyclic **46**, **50** and **52** hydrogensulphates taken in aqueous buffer at pH = 6, are shown in Figure 5. The low quantum yields of **46** and **39** relative to monomeric phenanthridinium derivative have been observed ($\phi_{46} / \phi_{monomer} = 0.18$, $\phi_{39} / \phi_{monomer} = 0.04$). Since the emission of flexible **39** is more quenched than that of **46**, the observed effects could be attributed to some degree of weak interactions between phenanthridinium units. However, the observation that, under the same conditions, **50** and **52** showed no emission suggested that some other quenching mechanism may also be operative. Kearns has shown that the low quantum yield of ethidium bromide in water is mainly due to the quenching by hydrogen transfer from 3,8-amino groups to water molecules.[20] This quenching mechanism has been established from the observations that ethidium emission was enhanced in less polar solvents and that deuteration of amine groups led to an increase of emission intensity while the addition of water in EtOH solution of ethidium had a strong quenching effect. We observed similar effects of D_2O and H_2O on the emission intensity of **50** and **52** dissolved in ethanol (Figures 6 and 7). Addition of 2% (v/v) of water to ethanol solution of **52** (Figure 7) caused an almost 50% decrease of emission intensity. On the other hand, addition of the same volume of D_2O increased significantly the emission intensity. Apparently, quenching by hydrogen transfer to water molecules is predominantly operative for **50** and **52** having 4 secondary amino groups. Most probably, the same quenching mechanism together with weak intramolecular stacking is responsible for the relatively low fluorescence quantum yields of **39** and **46**.

Structural Studies

Crystallizations of cyclo-bis-intercalands **46–48** and **50**, **52** from various solvents in order to obtain crystals suitable for X-ray structural analysis were unsuccessful. However, suitable crystals of macrocyclic precursors **24** and **26** were obtained by crystallizations from the CH_2Cl_2-acetone solvent mixture. The molecular structures are shown in Figures 8 and 9; the ORTEP II[21] drawings were prepared with the thermal ellipsoids scaled at a 30% probability level. Interatomic distances, bond and presented torsion angles are

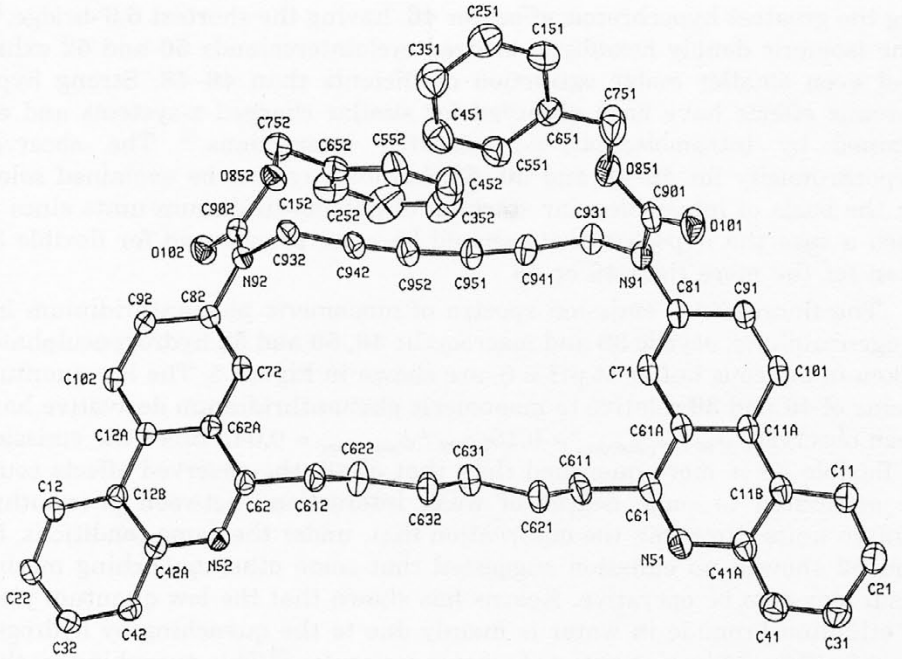


Figure 8. The ORTEP drawing of **24** with the atomic numbering.

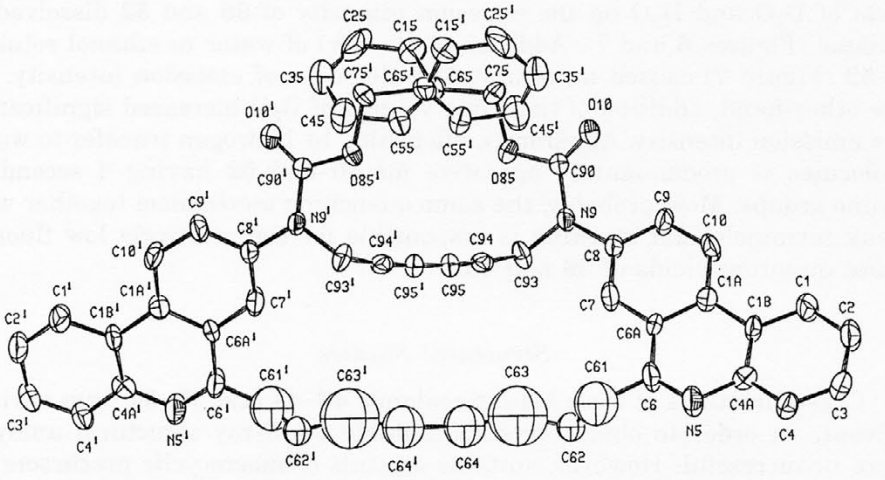


Figure 9. The ORTEP II drawing of **26** with the atomic numbering. The large thermal motion is associated with the disorder detected in octamethylene chain; only one orientation for each group is shown.

TABLE I

Selected bond lengths/Å for **24**[a] and **26**[b]

	24	**26**
	phenanthridine units	
C1-C2	1.373(5)	1.37(3)
C2-C3	1.393(5)	1.40(2)
C3-C4	1.366(5)	1.38(2)
C4-C4A	1.405(5)	1.37(2)
C4A-N5	1.389(4)	1.39(2)
N5-C6	1.305(4)	1.28(1)
C6-C6A	1.458(4)	1.43(1)
C6A-C7	1.408(4)	1.38(2)
C7-C8	1.371(4)	1.40(2)
C8-C9	1.403(4)	1.36(2)
C9-C10	1.364(4)	1.38(2)
C10-C1A	1.410(4)	1.41(2)
C1A-C1B	1.441(4)	1.46(2)
C1B-C1	1.405(4)	1.41(2)
C4A-C1B	1.411(4)	1.39(2)
C6A-C1A	1.411(4)	1.41(2)
	methylene bridge	
C6-C61	1.540(4)	1.5*
C61-C62	1.529(5)	1.22(2)
C62-C63	1.510(5)	1.34(6)
C631-C632**	1.514(5)	
C63-C64		1.34(5)
C64-C64^{i}		1.62*
C61-C66		1.21(2)
C66-C67		1.22(4)
C64-C67		1.21(2)
	hexadiyne bridge	
N9-C93	1.466(5)	1.47(2)
C93-C94	1.464(4)	1.46(2)
C94-C95	1.186(4)	1.23(2)
C95-C95$^{(i)}$	1.396(4)	1.37(2)
	benzyloxycarbonyl groups***	
C8-N9	1.433(4)	1.48(2)
N9-C90	1.373(4)	1.36(2)
C90-O10	1.207(4)	1.17(2)
C90-O85	1.341(4)	1.36(2)
O85-C75	1.450(5)	1.46(2)
C75-C65	1.488(5)	1.50(2)

[a] The values of chemically analogous bonds in **24** related by noncrystallographic two-fold axis are averaged (*e.g.* C11-C21 and C12-C22) and the particular bond was named as the chemically analogous one in **26** (*e.g.* C1-C2).

[b] Symmetry code: i) $-x$, y, $1/2-z$.

* Treated as a rigid group because of the disorder.

** No analogous parameter, single value.

*** Average value for phenyl rings is 1.395(3) Å.

TABLE II

Selected bond angles/° for **24**[a] and **26**[b]

	24	**26**
	phenanthridine units	
C1-C2-C3	120.6(3)	119(2)
C2-C3-C4	119.8(3)	120(2)
C3-C4-C4A	121.0(3)	121(1)
C4-C4A-C1B	119.5(3)	121(1)
C4A-C1B-C1	118.4(3)	118(1)
C1B-C1-C2	120.9(3)	122(2)
C4A-N5-C6	119.5(2)	120(1)
N5-C6-C6A	122.7(3)	123.5(8)
C6-C6A-C1A	118.6(2)	119(1)
C6A-C1A-C1B	118.4(2)	116(1)
C1A-C1B-C4A	118.0(2)	120(1)
C1B-C4A-N5	122.9(2)	121(1)
C6A-C7-C8	121.0(3)	123(1)
C7-C8-C9	120.0(2)	119(1)
C8-C9-C10	120.4(3)	121(1)
C9-C10-C1A	121.4(3)	121(1)
C10-C1A-C6A	118.2(2)	119(1)
C1A-C6A-C7	119.4(3)	117(1)
	methylene bridge	
C61-C6-C6A	120.6(3)	117.8(6)
C61-C6-N5	116.7(3)	118.6(6)
C6-C61-C62	111.8(3)	128(1)
C61-C62-C63	114.2(3)	109(4)
C621-C631-C632*	113.9(3)	
C62-C63-C64		158(7)
C63-C64-C64^{i}		159(3)
C6-C61-C66		160(2)
C61-C66-C67		162(4)
C66-C67-C64		141(3)
C67-C64-C64^{i}		115(1)
	hexadiyne bridge	
C8-N9-C93	119.6(3)	118(1)
C90-N9-C93	120.5(3)	121(1)
N9-C93-C94	114.6(3)	109(1)
C93-C94-C95	175.2(3)	175(1)
C94-C95-C95^{i}	174.5(3)	178(2)
	benzyloxycarbonyl groups**	
C8-N9-C90	119.7(3)	121(1)
N9-C90-O10	125.0(3)	128(1)
O10-C90-O85	125.2(3)	125(1)
C90-O85-C75	116.1(3)	115(1)
O85-C75-C65	111.1(3)	107(1)
C75-C65-C55	121.6(3)	121(1)
C75-C65-C15	118.4(2)	119(1)

[a] The values of chemically analogous angles related by noncrystallographic two-fold axes are averaged (*e.g.* C11-C21-C31 and C12-C22-C32), and the particular angle was named as the chemically analogous one in **26** (*e.g.* C1-C2-C3).

[b] Symmetry code: i) $-x$, y, $1/2-z$.

* No analogous parameter, single value.

** Average value for phenyl rings is 120.0(2)°.

TABLE III

Selected torsion angles/° for **24** and **26**[a]

24		**26**	
C61A-C61-C611-C621	–87.1(4)	C6A-C6-C61-C62	78(2)
C61-C611-C621-C631	164.5(3)	C6-C61-C62-C63	–143(4)
C611-C621-C631-C632	179.4(3)	C61-C62-C63-C64	–133(2)
C621-C631-C632-C622	–173.5(3)	C62-C63-C64-C64^{i}	126(1)
C631-C632-C622-C612	–172.3(3)	C63-C64-C64^{i}-C63^{i}	159(3)
C632-C622-C612-C62	–168.1(3)	C6A-C6-C61-C66	–54(6)
C622-C612-C62-C62A	–76.8(4)	C6-C61-C66-C67	132(1)
C612-C62-C62A-C72	1.9(4)	C61-C66-C67-C64	–22(2)
C62-C62A-C72-C82	176.8(3)	C66-C67-C64-C64^{i}	–165(5)
C62A-C72-C82-N92	–177.3(2)	C67-C64-C64^{i}-C67^{i}	168(3)
C72-C82-N92-C932	–41.9(3)	C94^{i}-C95^{i}-C95-C94	11(7)
C82-N92-C932-C942	100.8(3)	C95^{i}-C95-C94-C93	23(5)
N92-C932-C942-C952	99(4)	C95-C94-C93-N9	26(2)
C932-C942-C952-C951	0(7)	C94-C93-N9-C8	94(1)
C942-C952-C951-C941	33(6)	C93-N9-C8-C7	–33(2)
C952-C951-C941-C931	–35(6)	N9-C8-C7-C6A	178(1)
C951-C941-C931-N91	132(3)	C8-C7-C6A-C6	–175(1)
C941-C931-N91-C81	103.1(3)	C7-C6A-C6-C61	0(2)
C931-N91-C81-C71	–40.7(4)	O10-C90-O85-C75	6(2)
N91-C81-C71-C61A	–176.9(3)	C8-N9-C90-O85	–174(1)
C81-C71-C61A-C61	177.5(3)	N9-C90-O85-C75	–177(1)
C71-C61A-C61-C611	3.1(4)	C90-O85-C75-C65	–163(1)
O101-C901-N91-C81	7.7(4)	O85-C75-C65-C15	–135(1)
O102-C902-N92-C82	3.9(4)		
C81-N91-C901-O851	–172.6(2)		
C82-N92-C902-O852	–176.7(2)		
C91-C901-O851-C751	–143.6(6)		
C92-C902-O852-C752	–143.3(4)		
C901-O851-C751-C651	–135.8(3)		
C902-O852-C752-C652	–96.2(3)		
O851-C751-C651-C151	–161.2(3)		
O852-C752-C652-C152	134.0(3)		

[a] Symmetry code: i) $-x$, y, $1/2-z$.

listed in Tables I, II and III. The conformations of 22- and 24-membered rings are illustrated in a polar diagram (Figure 10), which reveals an approximate C_2 symmetry of the molecule of **24** and exact of **26**. The noncrystallographic two-fold axis in **24** bisects the bonds C951-C952 and C631-C632 (Figure 8) whereas the crystallographic two-fold symmetry in **26** is between the bonds C95-C95^{i} and C64-C64^{i} (Figure 9). The ORTEP drawing of **26** with high thermal ellipsoids is related to disorder in octamethylene bridge; two

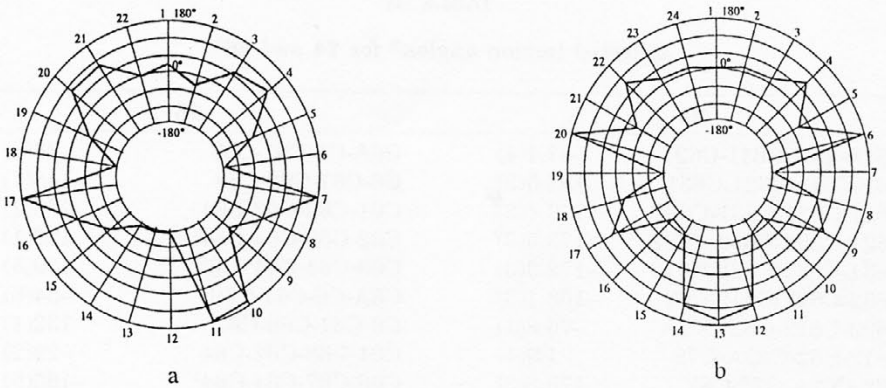


Figure 10. Polar diagrams of macrocyclic rings: a) in **24** with an approximate C_2 symmetry, b) in **26** where C_2 is preserved.

positions of methylene groups C62 and C66 as well as C63 and C67 were recorded but only one is shown. The phenanthridine units in **24** are nearly coplanar with the hexamethylene and hexadiyne bridge; the angles of the phenanthridine plane and terminal bonds of the hexamethylene bridge are 0.7(2) and 2.7(2)° whereas these angles with the hexadiyne bridge are 7.1(2) and 6.5(1)°. Both phenanthridine units in **24** deviate from planarity [<0.56(11)°>]. Analogous analysis for **26** cannot be reliable due to the disorder in the structure. The hexadiyne bridge in **24** and **26** as well as in seven crystal structures ($R \leq 0.07$) of macrocyclic compounds with an analogous moiety, extracted from the Cambridge Structural Database (version 5. 10, 1995),[22] are not linear (Figures 8 and 9). The bond angles involving carbon atoms in sp hybridization are smaller than 180°. The mean values of this angle in **24** and **26** are 174.8(3)° and 176(1)°, respectively. Data from CSD[22] revealed the minimum value of 164.9° and maximum value of 179.2° including 44 angles in sp hybridization.

Molecular Modelling Studies

The molecular structures of **24** and **26**, determined by the X-ray structural analysis revealed that the phenanthridine units are positioned away from each other in an *anti* arrangement with respect to the best plane of the macroring. However, the binding studies with **46–48** and nucleotides in water showed that complexes of 1 : 1 stoichiometry were formed and that both phenanthridinium units bound nucleic base cooperatively.[12b] It can be assumed that *anti* conformations of **24** and **26** result from the presence of bulky benzyloxycarbonyl protection groups on 8,8'-amino nitrogens which also introduce considerable strain into the macrocyclic system due to the

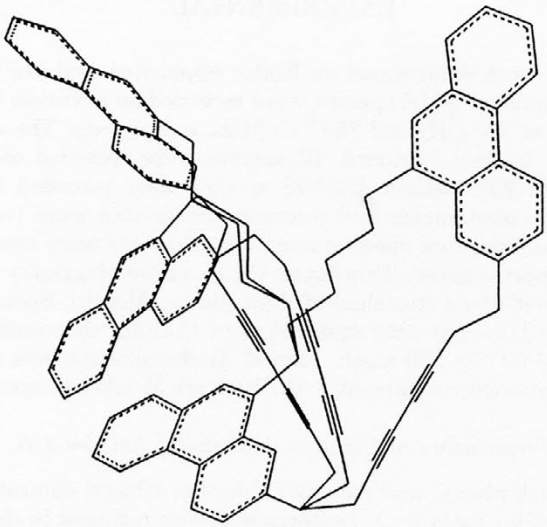


Figure 11. Selected minimized *syn*- and *anti*-conformations of unprotected **24** obtained by molecular dynamics calculations.

planarity of carbamate fragments. In this case, there should be a considerable energy difference between the *anti*- and *syn*-conformations of **24** and **26**. On the other hand, the energy difference between similar conformations of the corresponding 8,8'-amino unprotected bis-phenanthridine macrocycles should be much smaller. To check this assumption, molecular modelling studies were conducted on **24** and the corresponding unprotected macrocycle. Search of the conformational space was performed by molecular dynamics calculations using simulated annealing as a type of dynamics experiment. The calculations showed that the low energy *syn*-conformation of **24** is by 17 kcal/mol less stable than the *anti*-conformation. On the other hand, low energy *syn*- and *anti*-conformations of the unprotected macrocycle were close in energy (Figure 11), some *syn*- being even lower in energy than *anti*-. These results show that 8,8'-amino unprotected bis-phenanthridine macrocycles may adopt both conformations with approximately equal probability. Although the molecular modelling studies were not possible for cyclo-bis-intercaland **46** due to the lack of parametrization for quaternized phenanthridinium nitrogen, the above results may be taken as an additional support in favour of the *syn*-conformation of cyclo-bis-intercaland in a complex with a nucleotide.[12b] Such a complex structure results from a sort of induced fit between the monocyclic receptor and the substrate. On the other hand, the introduction of a third bridge, yielding bicyclo-bis-intercalands, would confer a higher degree of preorganization to the receptor entity.

EXPERIMENTAL

Melting points were determined on Kofler apparatus and are uncorrected. The one- and two-dimensional NMR spectra were recorded on a Varian Gemini-300 spectrometer operating at 300 (^{1}H) and 75 (^{13}C) MHz, respectively. The spectra were referenced to TMS as internal standard. IR spectra were recorded on a Perkin-Elmer 297 spectrometer in KBr pellets. UV/VIS spectra were recorded on a Philips PU-8700 UV/VIS spectrophotometer and fluorescence spectra were recorded on a Perkin-Elmer LS-50 luminiscence spectrometer. Mass spectra were recorded on a Extrel FTMS 2001 DD spectrometer. Thin-layer (TLC) chromatography and preparative TLC were carried out using Kieselgel 60 F_{254} plates (Merck). Spots were visualized by irradiation with UV light (254 and 365 nm). Column chromatography was performed on silica gel 60 (70–230 mesh, Merck). Hydrogenation was carried out using a Parr M 4561 minireactor equipped with the Parr M 4841 temperature controller.

Preparation of Bis-nitro-biphenylyl Amides ***1–3***

4'-Nitro-2-aminobiphenyl and suberoyl chloride, sebacyl chloride or *p*-phenylene diacetyl chloride, molar ratio 2 : 1, respectively, were refluxed in dry benzene for 24 hours. After cooling, the solid formed was collected by filtration. Small quantities of unreacted 4'-nitro-2-aminobiphenyl were removed by boiling the crude product in a EtOH/H_2O (1 : 1) mixture which dissolved the starting compound only. The product was recrystallized from the DMF/EtOH mixture.

N,N'-*Bis[(4'-nitro)-2-biphenylyl]-suberamide* (***1***)

4'-Nitro-2-aminobiphenyl (4 g, 18.6 mmol) and suberoyl chloride (1.96 g, 9.3 mmol) in dry benzene (114 cm^3) gave **1** (4.5 g, 85%); m.p. = 230–232 °C; R_f = 0.69 (SiO_2, CH_2Cl_2/MeOH = 9 : 1).

IR (KBr), ν_{max}/cm^{-1}: 3270, 2930, 2860, 1650, 1515, 1348, 855, 771, 750 ; ^{1}H-NMR (DMSO-d_6) δ/ppm: 1.33 (m, CH_2, 4H), 1.54 (m, CH_2, 4H), 2.24 (t, CH_2N, J = 7.0 Hz, 4H), 7.44–8.05 (m, Ar-H, 16H), 9.23 (s-br, NH, 2H); ^{13}C-NMR (DMSO-d_6) δ/ppm: 24.49, 28.10, 35.27, 122.96, 125.29, 126.97, 128.61, 129.80, 134.93, 146.22, 146.39, 171.16.

Anal. Calcd. for $C_{32}H_{30}O_6N_4$ (M_r = 566.61): C 67.83, H 5.34, N 9.89 %; found: C 67.55, H 5.51, N 9.93%.

N,N'-*Bis[(4'-nitro)-2-biphenylyl]-sebacamide* (***2***)

4'-Nitro-2-aminobiphenyl (3.6 g, 16.6 mmol) and sebacoyl chloride (2 g, 8.3 mmol) in dry benzene (102 cm^3) gave **2** (4.1 g, 83%); m.p. = 213–214 °C; R_f = 0.67 (SiO_2, CH_2Cl_2/MeOH = 9 : 1).

IR (KBr), ν_{max}/cm^{-1}: 3250, 2920, 2840, 1650, 1600, 1510, 1100, 1000, 850, 765, 750, 735, 695; ^{1}H-NMR (DMSO-d_6) δ/ppm: 1.75 (s-br, CH_2, 8H), 2.25 (m, CH_2, 4H), 2.60 (m, CH_2, 4H), 7.53–8.38 (m, Ar-H, 16H), 9.53 (s, NH, 2H); ^{13}C-NMR (DMSO-d_6) δ/ppm: 24.72, 28.44, 35.38, 123.03, 125.90, 127.09, 128.73, 129.85, 135.11, 146.33, 171.22.

Anal. Calcd. for $C_{34}H_{34}N_4O_6$ (M_r = 594.67): C 68.67, H 5.76, N 9.42%; found: C 68.61, H 5.88, N 9.41%.

N,N'-*Bis[(4'-nitro)-2-biphenylyl]*-p-*phenylenediacetamide* (***3***)

4'-Nitro-2-aminobiphenyl (4 g, 18.6 mmol) and *p*-phenylene diacetyl chloride (2.2 g, 9.3 mmol) in dry benzene (102 cm^3) gave **3**. (4.7 g, 86%); m.p. = 285–287 °C; R_f = 0.71 (SiO_2, CH_2Cl_2/MeOH = 9 : 1).

IR (KBr), ν_{max}/cm^{-1}: 3390, 3260, 3020, 2910, 2840, 1665, 1600, 1510, 1445, 1410, 1345, 1280, 1190, 1110, 1010, 970, 850, 770, 760, 750, 720, 700; ^{1}H-NMR (DMSO-d_6) δ/ppm: 3.57 (s, CH_2, 4H), 7.15 (s, *p*-Ph, 4H), 7.48–8.25 (m, Ar-H, 16H), 9.64 (s-br, NH, 2H); ^{13}C-NMR (DMSO-d_6) δ/ppm: 13.88, 123.14, 126.13, 126.92, 128.84, 129.74, 133.64, 134.93, 145.94, 146.28, 169.08.

Anal. Calcd. for $C_{43}H_{26}N_4O_6$ (M_r = 694.70): C 69.62, H 4.47, N 9.55%; found: C 69.67, H 4.61, N 9.39%.

Preparation of Bis-aminobiphenylyl Amides ***4–6***

Nitro derivate **1**, **2** or **3** was dissolved in a mixture of DMF/EtOH (1 : 3), and hydrogenated 15 hours under the hydrogen pressure of 50 bar at a temperature of 70 °C in the presence of 10% Pd/C catalyst using the Parr hydrogenation apparatus. The product was obtained after removal of the catalyst and solvents.

N,N'-*Bis[(4'-amino)-2-biphenylyl]-suberamide* (***4***)

1 (4.3 g, 7.5 mmol) and Pd/C (852 mg) in DMF/EtOH (200 cm^3, 1 : 3) gave **4**, oil, (3.8 g, 100%), which was without further purification converted to **7**; R_f = 0.51 (SiO_2, CH_2Cl_2/MeOH = 9 : 1).

IR (KBr), ν_{max}/cm^{-1}: 3410, 3320, 3220, 3200, 1920, 1850, 1660, 1610, 1520, 1445, 1290, 1180, 830, 760; ^{1}H-NMR (DMSO-d_6) δ/ppm: 1.28 (s-br, CH_2, 4H), 1.55 (s-br, CH_2, 4H), 2.22 (s-br, CH_2, 4H), 5.15 (s-br, NH_2, 4H), 6.63–7.96 (m, Ar-H, 16H), 8.94 (s, NH, 2H); ^{13}C-NMR (DMSO-d_6) δ/ppm: 24.98, 28.47, 30.80, 113.79, 125.36, 125.95, 126.30, 129.39, 129.74, 134.75, 136.63, 147.93, 162.24, 171.45; MS: *m/z* 506.3 (M^+), 323.3, 305.2, 221.2, 211.2.

N,N'-*Bis[(4'-amino)-2-biphenylyl]-sebacamide* (***5***)

2 (4 g, 6.7 mmol) and Pd/C (759 mg) in DMF/EtOH (200 cm^3, 1 : 3) gave **5**, oil, (3.6 g, 100%), which was without further purification converted to **8**; R_f = 0.49 (SiO_2, CH_2Cl_2/MeOH = 9 : 1).

IR (KBr), ν_{max}/cm^{-1}: 3410, 3340, 3230, 3020, 2920, 2850, 1660, 1610, 1580, 1520, 1480, 1445, 1290, 1180, 830, 760; ^{1}H-NMR (DMSO-d_6) δ/ppm: 1.29 (s, CH_2, 8H), 1.56 (s-br, CH_2, 4H), 2.21 (m, CH_2, 4H), 5.15 (s-br, NH_2, 4H), 6.65–7.50 (m, Ar-H, 16H), 8.91 (s, NH, 2H); ^{13}C-NMR (DMSO-d_6) δ/ppm: 25.12, 28.72, 30.78, 35.76, 35.90, 113.73, 125.40, 125.93, 126.34, 129.45, 129.81, 134.75, 136.62, 148.01, 162.30, 171.53; MS: *m/z* 354 (M^+), 351.3, 333.3, 226.2, 211.2.

N,N'-*Bis[(4'-amino)-2-biphenylyl]*-p-*phenylenediacetamide* (***6***)

3 (4,4 g, 7.5 mmol) and Pd/C (846 mg) in DMF/EtOH (200 cm^3, 1 : 3) gave **6** (3.6 g, 91%), which was without further purification converted to **9**. m.p. = 198–201 °C; R_f = 0.44 (SiO_2, CH_2Cl_2/MeOH = 9 : 1)

IR (KBr), ν_{max}/cm^{-1}: 3460, 3230, 2920, 1665, 1610, 1585, 1520, 1445, 1300, 1180, 830, 760; ^{1}H-NMR (DMSO-d_6) δ/ppm: 3.68 (s, CH_2, 4H), 5.21 (s-br, NH_2, 4H), 6.62–7.76 (m, Ar-H, 20H), 9.08 (s-br, NH, 2H); ^{13}C-NMR (DMSO-d_6) δ/ppm: 42.63,

113.94, 125.54, 125.69, 126.24, 126.51, 129.30, 129.55, 129.96, 134.12, 134.58, 136.39, 148.20, 169.62.

Anal. Calcd. for $C_{34}H_{30}N_4O_2$ (M_r = 526.64): C 77.54, H 5.74, N 10.64%; found: C 77.52, H 5.95, N, 10.57%

Preparation of Bis-ethyloxycarbonylaminobiphenylyl Amides **7–9**

Bis-aminobiphenylyl amide **4**, **5**, or **6**, and *N,N'*-dimethylaniline were suspended in dry EtOH and warmed up to reflux. To this suspension, ethyl chloroformate was added dropwise during 10 minutes and the reaction mixture has refluxed for additional 6 hours. Solvent was evaporated and the residue was partitioned between water and EtOAc. The organic layer was washed with water, dried (Na_2SO_4) and evaporated. The oily residue crystallized from the MeOH/EtOH mixture.

N,N'-*Bis[(4'-ethyloxycarbonylamino)-2-biphenylyl]-suberamide* (**7**)

4 (3 g, 6 mmol), *N,N'*-dimethylaniline (5.9 cm^3, 46.5 mmol) and ethyl chloroformate (3.4 cm^3, 36 mmol) in EtOH (61 cm^3) gave **7** (3.3 g, 85%); m.p.= 96–98 °C; R_f = 0.60 (SiO_2, CH_2Cl_2/MeOH = 9 : 1).

IR (KBr), ν_{max}/cm^{-1}: 3300, 3100, 3050, 2980, 2940, 2860, 1705, 1680, 1580, 1533, 1450, 1410, 1320, 1235, 1170, 838, 765; ^{1}H-NMR (DMSO-d_6) δ/ppm: 1.36 (t, CH_3, J = 7.0 Hz, 6H), 1.52 (m, CH_2, 4H), 2.07 (m, CH_2, 4H), 3.33 (m, CH_2, 4H), 4.21 (q, OCH_2, J = 7.0 Hz, 4H), 7.37–7.68 (m, Ar-H, 16H), 8.09 (s-br, NH, 2H), 8.68 (s-br, NH, 2H); ^{13}C-NMR (DMSO-d_6) δ/ppm: 14.40, 24.88, 37.75, 60.10, 118.00, 125.62, 127.20, 128.06, 129.91, 132.79, 134.88, 136.23, 138.38, 153.50, 171.44.

Anal. Calcd. for $C_{38}H_{42}N_4O_6$ (M_r = 650.77): C 70.13, H 6.51, N 8.61%; found: C 69.86, H 6.71, N 8.73%.

N,N'-*Bis[(4'-ethyloxycarbonylamino)-2-biphenylyl]-sebacamide* (**8**)

5 (3.5 g, 6.6 mmol), *N,N'*-dimethylaniline (6.5 cm^3, 51.2 mmol) and ethyl chloroformate (3.7 cm^3, 38.8 mmol) in EtOH (67 cm^3) gave **8** (3.4 g, 76%); m.p. = 174–176 °C; R_f = 0.58 (SiO_2, CH_2Cl_2/MeOH = 9 : 1).

IR (KBr), ν_{max}/cm^{-1}: 3310, 3270, 2920, 2830, 1700, 1670, 1600, 1530, 1320, 1235, 1070, 830, 750; ^{1}H-NMR (DMSO-d_6) δ/ppm: 1.38 (m, CH_2, CH_3, 14H), 1.51 (m, CH_2, 4H), 1.60 (m, CH_2, 4H), 4.26 (q, OCH_2, J = 7.0 Hz, 4H), 7.34–7.70 (m, Ar-H, 16H), 9.09 (s, NH, 2H), 9.70 (s, NH, 2H); ^{13}C-NMR (DMSO-d_6) δ/ppm: 14.56, 25.169, 28.84, 35.78, 60.22, 125.850, 127.32, 129.18, 130.08, 132.85, 134.93, 136.40, 138.49, 153.56, 171.62.

Anal. Calcd. for $C_{40}H_{46}N_4O_6$ (M_r = 678.83): C 70.78, H 6.83, N 8.25%; found: C 70.80, H 6.81, N 8.42%.

N,N'-*Bis[(4'-ethyloxycarbonylamino)-2-biphenylyl]*-p-*phenylenediacetamide* (**9**)

6 (2.7 g, 5.1 mmol), *N,N'*-dimethylaniline (5 cm^3, 39.4 mmol) and ethyl chloroformate (2.9 cm^3, 30.4 mmol) in EtOH (58 cm^3) gave **9** (2.9 g, 85%); m.p. = 239–240 °C; R_f = 0.58 (SiO_2 CH_2Cl_2/MeOH = 9 : 1).

IR (KBr), ν_{max}/cm^{-1}: 3390, 3270, 3180, 3100, 3020, 2980, 2920, 1720, 1660, 1600, 1585, 1530, 1450, 1410, 1320, 1230, 1060, 830, 760, 715, 640; ^{1}H-NMR (DMSO-d_6) δ/ppm: 1.39 (t, CH_3, J = 7.0 Hz, 6H), 3.65 (s, CH_2, 4H), 4.26 (q, OCH_2, J = 7.0 Hz, 4H), 7.26–7.63 (m, Ar-H, 20H), 9.21 (s, NH, 2H), 9.69 (s, NH, 2H); ^{13}C-NMR (DMSO-d_6)

δ/ppm: 14.27, 42.33, 59.93, 118.17, 125.23, 125.51, 127.09, 128.84, 129.74, 132.23, 133.53, 134.65, 135.39, 138.27, 153.39, 169.08.

Anal. Calcd. for $C_{40}H_{38}N_4O_6$ (M_r = 670.76): C 71.63, H 5.71, N 8.35%; found: C 71.55, H 5.95, N 8.13%.

Preparation of Bis-ethyloxycarbonylaminophenanthridinyl Derivatives ***10–12***

Bis-biphenylyl derivate **7**, **8**, or **9** was heated with $POCl_3$ under reflux for 2 hours, poured on ice and made alkaline (pH = 8–9) by addition of conc. ammonia. Precipitated product was collected by filtration and recrystallized from the DMF/H_2O mixture.

*1,6-Bis[(8-ethyloxycarbonylamino)-6-phenanthridinyl]-hexane (**10**)*

7 (3.1 g, 4.7 mmol) and $POCl_3$ (13 cm^3, 142 mmol) gave **10** (2.2 g, 77%); m.p. = 230–232 °C; R_f = 0.54 (SiO_2, CH_2Cl_2/MeOH = 9 : 1).

IR (KBr), ν_{max}/cm^{-1}: 3340, 2980, 2940, 2860, 1700, 1620, 1590, 1520, 1480, 1410, 1240, 1090, 1070, 840, 760; ^{1}H-NMR (DMSO-d_6) δ/ppm: 1.38 (t, CH_3, J = 6.5 Hz, 6H), 1.73 (s-br, CH_2, 4H), 2.06 (s-br, CH_2, 4H), 3.26 (m, CH_2, 4H), 4.29 (q, OCH_2, J = 6.5 Hz, 4H), 7.75 (m, Phen-H3, -H2, 4H), 8.09 (m, Phen-H4, -H9, 4H), 8.63 (s, Phen-H7, 2H), 8.74 (d, Phen-H1, $J_{1,2}$ = 6.5 Hz, 2H), 8.85 (d, Phen-H10, $J_{9,10}$ = 6.5 Hz, 2H), 10.07 (s-br, NH, 2H); ^{13}C-NMR (DMSO-d_6) δ/ppm: 14.10, 27.76, 28.78, 34.98, 60.15, 113.09, 121.61, 122.23, 122.91, 123.14, 125.17, 126.01, 127.31, 128.83, 138.49, 142.38, 153.44, 160.78.

Anal. Calcd. for $C_{38}H_{38}N_4O_6$ (M_r = 646.74): C 74.25, H 6.23, N 9.11%; found: C, 74.02, H 6.27, N 9.23%.

*1,8-Bis[(8-ethyloxycarbonylamino)-6-phenanthridinyl)]-octane (**11**)*

8 (6.9 g, 10.2 mmol) and $POCl_3$ (37.4 cm^3, 408.5 mmol) gave **11** (6.2 g, 94%); m.p. = 208–210 °C; R_f = 0.54 (SiO_2, CH_2Cl_2/MeOH = 9 : 1).

IR (KBr), ν_{max}/cm^{-1}: 3320, 2980, 2920, 2850, 1700, 1620, 1590, 1550, 1520, 1480, 1240, 1070, 870, 840, 755, 720; ^{1}H-NMR (DMSO-d_6) δ/ppm: 1.28 (t, CH_3, J = 7.1 Hz, 6H), 1.45 (m, CH_2, 8H), 1.91 (m, CH_2, 4H), 3.25 (m, CH_2, 4H), 4.20(q, OCH_2, J = 7.0 Hz, 4H), 7.64 (m, Phen-H3, -H2, 4H), 8.00 (m, Phen-H4, -H9, 4H), 8.53 (s, Phen-H7, 2H), 8.63 (d, Phen-H1, $J_{1,2}$ = 7.4 Hz, 2H), 8.74 (d, Phen-H10, $J_{9,10}$ = 9.1 Hz, 2H); ^{13}C-NMR (DMSO-d_6) δ/ppm: 14.29, 28.04, 28.69, 29.07, 35.28, 60.37, 113.12, 122.04, 122.40, 123.25, 123.67, 124.41, 125.43, 126.44, 127.41, 127.79, 128.33, 128.65, 128.80, 128.93, 129.16, 138.86, 142.63, 153.81, 161.26.

Anal. Calcd. for $C_{40}H_{42}N_4O_4$ (M_r = 642.80): C 74.74, H 6.59, N 8.72%; found: C 74.67, H 6.69, N 8.80%.

*1,6-Bis[(8-ethyloxycarbonylamino)-6-phenanthridinyl]-p-xylene (**12**)*

9 (2.6 g, 3.9 mmol) and $POCl_3$ (11,3 cm^3, 123.4 mmol) gave **12** (2 g, 79%); m.p. = 289–291 °C; R_f = 0.46 (SiO_2, CH_2Cl_2/MeOH = 9 : 1).

IR (KBr), ν_{max}/cm^{-1}: 3320, 3060, 2980, 2930, 1730, 1700, 1620, 1590, 1580, 1550, 1530, 1480, 1465, 1415, 1385, 1330, 1240, 1170, 1100, 1070, 880, 870, 830, 760, 720; ^{1}H-NMR (DMSO-d_6) δ/ppm: 1.39 (t, CH_3, J = 7.0 Hz, 6H), 4.30 (q, OCH_2, J = 7.0 Hz, 4H), 4.67 (s, CH_2, 4H), 7.41 (s, p-Ph, 4H), 7.65–8.84 (m, Ar-H, 14H), 9.77 (s, NH, 2H);

^{13}C-NMR (DMSO-d_6) δ/ppm: 13.88, 37.19, 60.04, 113.55, 121.56, 122.80, 123.14, 124.89, 126.47, 127.55, 128.27, 136.06, 138.60, 153.21, 159.08.

Anal. Calcd. for $C_{40}H_{34}N_4O_4$ (M_r = 634.73): C 75.69, H 5.40, N 8.83%; found: C 75.48, H 5.58, N 8.72%.

Preparation of Bis-aminophenanthridinyl Derivatives ***13–15***

Bis-phenanthridine derivative **10**, **11**, or **12** was heated at 140 °C for 30 minutes in 70% H_2SO_4. Cooled reaction mixture was made alkaline (pH = 7–8) by addition of conc. ammonia. Precipitated product was collected by filtration and recrystallized from the DMF/H_2O mixture.

*1.6-Bis[(8-amino)-6-phenanthridinyl]-hexane (**13**)*

10 (6.55 g, 10.7 mmol) and 70% H_2SO_4 (227 cm^3) gave **13** (4.7 g, 93%); m.p. = 252–254 °C; R_f = 0.41(SiO_2 CH_2Cl_2/MeOH = 9 : 1).

IR (KBr), ν_{max}/cm^{-1}: 3380, 3290, 3180, 3050, 2940, 2920, 2850, 1620, 1570, 1530, 1480, 1460, 1380, 1350, 1330, 1300, 1260, 1250, 1230, 1210, 1150, 1030, 1000, 940, 870, 855, 835, 755, 750, 725; ^{1}H-NMR (DMSO-d_6) δ/ppm: 1.61 (s, CH_2, 4H), 1.93 (s-br, CH_2,4H), 3.22 (m, CH_2, 4H), 5.67 (s, NH_2, 4H), 7.27 (d, Phen-H9, $J_{9,10}$ = 8.9 Hz, 2H), 7.38 (s, Phen-H7, 2H), 7.53 (m, Phen-H3, -H2, 4H), 7.90 (m, Phen-H4, 2H), 8.47 (m, Phen-H1, -H10, 4H); ^{13}C-NMR (DMSO-d_6) δ/ppm: 28.00, 29.169, 35.18, 106.18, 120.15, 120.98, 122.58, 123.54, 123.99, 125.87, 125.91, 126.54, 128.88, 141.37, 148.45, 160.24.

Anal. Calcd. for $C_{32}H_{30}N_4$ (M_r = 470.62): C 81.67, H 6.43, N 11.9%; found: C 81.87, H 6.61, N 11.67%.

*1.8-Bis[(8-amino)-6-phenanthridinyl]-octane (**14**)*

11 (6.2 g, 9.6 mmol) and 70% H_2SO_4 (212 cm^3) gave **14** (3.7 g, 77%); m.p. = 273–276 °C; R_f = 0.48 (SiO_2 CH_2Cl_2/MeOH = 9 : 1).

IR (KBr), ν_{max}/cm^{-1}: 3460, 3280, 3160, 2920, 2840, 1620, 1570, 1530, 1480, 1460, 1375, 1350, 1325, 1300, 1260, 1225, 1205, 1045, 1035, 940, 850, 825, 755, 735, 720, 690, 660; ^{1}H-NMR (DMSO-d_6) δ/ppm: 1.44 (m, CH_2, 8H), 1.89 (m, CH_2, 4H), 3.18 (t, CH_2, J = 7.6 Hz, 4H), 5.67 (s-br, NH_2, 4H), 7.27 (d, Phen-H9, $J_{9,10}$ = 8.8 Hz, 2H), 7.36 (s, Phen-H7, 2H), 7.53 (m, Phen-H3, -H2, 4H), 7.91 (m, Phen-H4, 2H), 8.47 (m, Phen-H10, -H1); ^{13}C-NMR (DMSO-d_6) δ/ppm: 27.80, 28.78, 29.05, 35.01, 106.16, 120.04, 120.83, 122.55, 123.37, 123.87, 125.71, 125.77, 126.46, 128.77, 141.31, 148.29, 160.12.

Anal. Calcd. for $C_{34}H_{34}N_4$ (M_r = 498.67): C 81.89, H 6.87, N 11.24%; found: C 82.05, H 6.99, N 11.13%.

*1.6-Bis[(8-amino)-6-phenanthridinyl]-*p*-xylene (**15**)*

12 (3.7 g, 5.7mmol) and 70% H_2SO_4 (136 cm^3) gave **15** (2.6 g, 91%); m.p. = 223–225 °C; R_f = 0.44 (SiO_2, CH_2Cl_2/MeOH = 9 : 1).

IR (KBr), ν_{max}/cm^{-1}: 3460, 3360, 3230, 3180, 3060, 2920, 2840, 1660, 1620, 1570, 1535, 1510, 1485, 1460, 1380, 1350, 1290, 1260, 1230, 1210, 1150, 1090, 1020, 850, 820, 780, 760, 730, 710, 650; ^{1}H-NMR (DMSO-d_6) δ/ppm: 4.49 (s, CH_2, 4H), 5.63 (s, NH_2, 4H), 7.21 (m, Phen-H9, 2H), 7.24 (s, p-Ph, 4H), 7.33 (s, Phen-H7, 2H), 7.56 (m, Phen-H3, -H2, 4H), 7.94 (m, Phen-H4, 2H), 8.50 (m, Phen-H10, -H1); ^{13}C-NMR

(DMSO-d_6) δ/ppm: 106.78, 120.45, 121.18, 123.09, 123.69, 124.29, 126.61, 126.38, 126.76, 128.54, 129.16, 137.00, 148.57, 158.87, MS: m/z 491.3 (M^+), 474.3, 401.1, 355.2, 307.2, 282.2, 267.2, 207.2.

*Preparation of Bis-benzyloxycarbonylphenanthridinyl Derivatives **16–18**, **30***

Bis-phenanthridine derivatives **13–15** or 3,8-diamino-6-methyl-phenanthridine and $NaHCO_3$ were suspended in dry DMF and cooled at 0 °C. To this suspension benzyl chloroformate was added dropwise during 10 min. and the reaction mixture was stirred for additional 30 min. Evaporation of solvent under reduced pressure left an oily residue, which was triturated with EtOH. The crystalline product was collected by filtration and recrystallized from the DMF/EtOH mixture. Purification of compound **30** was carried out by chromatography (column, SiO_2) eluting with a gradient MeOH in CH_2Cl_2. Compound **18** was converted to compound **22** without further purification.

*1,6-Bis[(8-benzyloxycarbonylamino)-6-phenanthridinyl]-hexane (**16**)*

13 (4.4 g, 9.3 mmol), $NaHCO_3$ (3.5 g, 41.3 mmol) and benzyl chloroformate (11.7 cm^3, 50% solution in toluene, 41.1 mmol) in dry DMF (97 cm^3) gave **16** (6.0 g, 87%); m.p. = 220–222 °C; R_f = 0.63 (SiO_2, CH_2Cl_2/MeOH = 9 : 1).

IR (KBr), ν_{max}/cm^{-1}: 3310, 3060, 3030, 2920, 2850, 1700, 1620, 1590, 1575, 1550, 1520, 1480, 1460, 1405, 1360, 1325, 1310, 1250, 1230, 1080, 1070, 1025, 1000, 940, 910, 875, 860, 835, 760, 750, 740, 720, 696; ^{1}H-NMR (DMSO-d_6) δ/ppm: 1.62 (s-br, CH_2, 4H), 1.97 (s-br, CH_2, 4H), 3.29 (t, CH_2, J = 7.3 Hz, 4H), 5.22 (s, OCH_2, 4H), 7.44 (m, Ph, 10H), 7.63 (m, Phen-H3, -H2, 4H), 8.01 (m, Phen-H4, -H9, 4H), 8.52 (s, Phen-H7, 2H), 8.61 (d, Phen-H1, $J_{1,2}$ = 7.3 Hz, 2H), 8.73 (d, Phen-H10, $J_{9,10}$ = 8.8 Hz, 2H), 9.99 (s-br, NH, 2H).

Anal. Calcd. for $C_{48}H_{42}N_4O_4$ (M_r = 738.89): C 78.03, H 5.73, N 7.58%; found: C 77.95, H 5.97, N 7.71%.

*1,8-Bis[(8-benzyloxycarbonylamino)-6-phenanthridinyl]-octane (**17**)*

14 (3.4 g, 6.8 mmol), $NaHCO_3$ (1.9 g, 22.8 mmol) and benzyl chloroformate (6 cm^3, 50% solution in toluene, 20.7 mmol) in dry DMF (72 cm^3) gave **17** (3.8 g, 72%); m.p. = 118–120 °C; R_f = 0.59 (SiO_2, CH_2Cl_2/MeOH = 9 : 1).

IR (KBr), ν_{max}/cm^{-1}: 3200, 3050, 3020, 2920, 2840, 1710, 1620, 1580, 1560, 1525, 1480, 1450, 1380, 1320, 1220, 1145, 900, 820, 755, 690; ^{1}H-NMR (DMSO-d_6) δ/ppm: 1.43 (m, CH_2, 4H), 1.89 (m, CH_2, 4H), 3.21 (m, CH_2, 4H), 5.21 (s, OCH_2, 4H), 7.38 (m, Ph, 10H), 7.63 (m, Phen-H3, -H2, 4H), 7.97 (m, Phen-H4, -H9, 4H), 8.51 (s, Phen-H7, 2H), 8.63 (d, Phen-H1, $J_{1,2}$ = 9.1 Hz, 2H), 8.74 (d, Phen-H10, $J_{9,10}$ = 7.5 Hz, 2H), 10.16 (s, NH, 2H); ^{13}C-NMR (DMSO-d_6) δ/ppm: 28.12, 28.78, 29.15, 35.34, 65.99, 113.07, 121.96, 122.25, 123.11, 123.65, 125.30, 126.35, 127.40, 127.73, 128.01, 128.37, 129.04, 136.40, 138.55, 142.50, 153.47, 161.06.

Anal. Calcd. for $C_{50}H_{46}N_4O_4$ (M_r = 766.95): C 78.30, H 6.05, N 7.31%; found: C 78.10, H 6.33, N 7.46%.

*1,6-Bis[(8-benzyloxycarbonylamino)-6-phenanthridinyl]-*p*-xylene (**18**)*

15 (2.5 g, 5 mmol), $NaHCO_3$ (1.4 g, 16.7 mmol) and benzyl chloroformate (4.3 cm^3, 50% solution in toluene, 15 mmol) in dry DMF (52 cm^3) gave **18** (2.7 g, 70% crude product) which was without further purification converted to **22**.

*3,8-Bis(benzyloxycarbonylamino)-6-methyl-phenanthridine (**30**)*

3,8-Diamino-6-methyl-phenanthridine (1.3 g, 5.6 mmol), $NaHCO_3$ (1.6 g, 18.5 mmol) and benzyl chloroformate (4.9 cm^3, 50% solution in toluene, 16.8 mmol) in dry DMF (50 cm^3) gave **30** (1.5 g, 55%); m.p. = 230–232 °C; R_f = 0.24 (SiO_2, CH_2Cl_2/MeOH = 95 : 5).

IR (KBr), ν_{max}/cm^{-1}: 3340, 3060, 3040, 2960, 2920, 1750, 1720, 1630, 1590, 1570, 1525, 1450, 1340, 1320, 1290, 1240, 1220, 1180, 1070, 1050, 960, 940, 910, 875, 810, 760, 740, 695; ^{1}H-NMR (DMSO-d_6) δ/ppm: 2.87 (s, CH_3, 3H), 5.22 (s, OCH_2, 2H), 5.23 (s, OCH_2, 2H), 7.43 (m, Ph, 10H), 7.74 (d, Phen-H2, $J_{1,2}$ = 8.5 Hz, 1H), 7.93 (d, Phen-H9, $J_{9,10}$ = 8.8 Hz, 1H), 8.14 (s, Phen-H4, 1H), 8.44 (s, Phen-H7, 1H), 8.56 (d, Phen-H1, $J_{1,2}$ = 9.0 Hz, 1H), 8.66 (d, Phen-H10, $J_{9,10}$ = 9.2 Hz, 1H), 10.14 (s, NH, 1H), 10.24 (s, NH, 1H); ^{13}C-NMR (DMSO-d_6) δ/ppm: 23.15, 66.13, 113.63, 116.30, 118.38, 118.81, 122.83, 123.01, 123.46, 128.45, 128.53, 128.80, 136.80, 138.14, 139.17, 143.55, 153.75, 153.85, 158.81.

Anal. Calcd. for $C_{30}H_{25}N_3O_4$ (M_r = 491.55): C 73.31, H 5.13, N 8.55%; found: C 73.49, H 4.92, N 8.46%.

*Preparation of Bis-propargyl Derivatives **19–23**, **31***

Ethyloxycarbonyl or benzyloxycarbonyl derivatives of bis-phenanthridine **10**, **12**, **16–18** or **30**, K_2CO_3 and propargyl bromide were suspended in dry DMF. Reaction mixture was stirred for additional 48 hours in the dark at 45 °C in an Ar atmosphere. Evaporation of the solvent left a residue which was chromatographed (column, SiO_2) eluting with a gradient $(CH_3)_2CO$ or MeOH in CH_2Cl_2 to afford the main fraction. Pure products were obtained by recrystallization from the CH_2Cl_2 /diethyl ether mixture.

*1,6-Bis[(8-propargylbenzyloxycarbonylamino)-6-phenanthridinyl]-hexane (**19**)*

16 (1.8 g, 2.5 mmol), K_2CO_3 (3.4 g, 25 mmol) and propargyl bromide (2.1 cm^3, 80% solution in toluene, 19.6 mmol) in dry DMF (94 cm^3) gave **19** (1.3 g, 65%); m.p. = 150–152 °C; R_f = 0.47 (SiO_2, CH_2Cl_2/$(CH_3)_2CO$ = 9 : 1);

IR (KBr), ν_{max}/cm^{-1}: 3260, 3060, 3020, 2930, 2840, 2110, 1710, 1610, 1580, 1570, 1530, 1480, 1440, 1390, 1350, 1290, 1260, 1230, 1210, 1180, 1120, 1050, 990, 935, 910, 895, 865, 835, 760, 740, 720, 690, 670, 650; ^{1}H-NMR ($CDCl_3$) δ/ppm: 1.60 (s-br, CH_2, 4H), 1.95 (s-br, CH_2, 4H), 2.37 (t, CH, J = 2.3 Hz, 2H), 3.31 (t, CH_2, J = 7.9 Hz, 4H), 4.56 (d, CH_2, J = 2.4 Hz, 4H), 5.22 (s, OCH_2, 4H), 7.29 (s, Ph, 10H), 7.61 (m, Phen-H2, 2H), 7.70 (m, Phen-H3, 2H), 7.80 (d, Phen-H9, $J_{9,10}$ = 8.3 Hz, 2H), 8.09 (d, Phen-H4, $J_{3,4}$ = 8.1 Hz, 2H), 8.25 (s-br, Phen-H7), 8.49 (d, Phen-H1, $J_{1,2}$ = 7.0 Hz, 2H), 8.69 (d, Phen-H10, $J_{9,10}$ = 8.9 Hz, 2H); ^{13}C-NMR ($CDCl_3$) δ/ppm: 29.14, 29.73, 36.20, 40.16, 67.85, 72.85, 79.23, 121.81, 123.06, 123.28, 125.48, 126.38, 127.71, 128.04, 128.38, 128.61, 128.92, 129.52, 131.33, 135.87, 140.08, 143.68, 154.66, 161.69.

Anal. Calcd. for $C_{54}H_{46}N_4O_4$ (M_r = 814.45): C 79.57, H 5.69, N 6.88%; found: C 79.58, H 5.70, N 6.86%.

*1,6-Bis[(8-propargylethyloxycarbonylamino)-6-phenanthridinyl]-hexane (**20**)*

10 (1 g, 1.6 mmol), K_2CO_3 (2.3 g, 16.3 mmol) and propargyl bromide (1.4 cm^3, 80% solution in toluene, 1.3 mmol) in dry DMF (83 cm^3) gave **20** (0.92 g, 81%); m.p. = 128–129 °C; R_f = 0.48 (SiO_2, CH_2Cl_2/$(CH_3)_2CO$ = 9 : 1).

IR (KBr), ν_{max}/cm^{-1}: 3300, 3250, 2990, 2950, 2910, 2860, 2120, 1710, 1620, 1580, 1545, 1485, 1470, 1445, 1380, 1350, 1250, 1240, 1155, 1130, 1060, 1030, 870, 845, 835, 770, 730, 705, 675; ^{1}H-NMR ($CDCl_3$) δ/ppm: 1.24 (t, CH_3, J = 6.9 Hz, 6H), 1.64 (s-br, CH_2, 4H), 1.98 (m, CH_2, 4H), 2.37 (t, CH, J = 2.3 Hz, 2H), 3.32 (t, CH_2, J = 7.8 Hz, 4H), 4.24 (q, OCH_2, J = 7.0 Hz, 4H), 4.55 (d, CH_2, J = 2.3 Hz, 4H), 7.61 (m, Phen-H2, 2H), 7.70 (m, Phen-H3, 2H), 7.81 (d, Phen-H9, $J_{9,10}$ = 7.4 Hz, 2H), 8.10 (d, Phen-H4, $J_{3,4}$ = 7.4 Hz, 2H), 8.25 (s, Phen-H7, 2H), 8.49 (d, Phen-H1, $J_{1,2}$ = 7.9 Hz, 2H), 8.61 (d, Phen-H10, $J_{9,10}$ = 8.8 Hz, 2H); ^{13}C-NMR ($CDCl_3$) δ/ppm: 14.38, 29.25, 29.75, 36.28, 39.95, 62.32, 72.61, 79.34, 121.76, 123.17, 125.42, 126.36, 128.54, 128.92, 129.44, 131.164, 140.23, 143.58, 154.81, 161.69.

Anal. Calcd. for $C_{44}H_{42}N_4O_4$ (M_r = 690.85): C 76.50, H 6.13, N 8.11%; found: C 76.75, H 6.04, N 7.96%.

*1,8-Bis[(8-propargylbenzyloxycarbonylamino)-6-phenanthridinyl]-octane (**21**)*

17 (1.5 g, 1.9 mmol), K_2CO_3(2.6 g, 19 mmol) and propargyl bromide (1.6 cm^3, 80% solution in toluene, 15.2 mmol) in dry DMF (75 cm^3) gave **21** (1.13 g, 70%); m.p. = 117–118 °C; R_f = 0.41 (SiO_2, CH_2Cl_2/$(CH_3)_2CO$ = 9 : 1).

IR (KBr), ν_{max}/cm^{-1}: 3300, 3250, 2920, 2850, 2010, 1710, 1651, 1570, 1530, 1480, 1450, 1435, 1390, 1350, 1285, 1260, 1230, 1120, 1050, 980, 865, 830, 760, 720, 690; ^{1}H-NMR ($CDCl_3$) δ/ppm: 1.39 (m, CH_2, 4H), 1.51 (m, CH_2, 4H), 1.89 (m, CH_2, 4H), 2.35 (t, CH, J = 2.3 Hz, 2H), 3.29 (t, CH_2, J = 7.9 Hz, 4H), 4.56 (d, CH_2, J = 2.4, 4H), 5,22 (s, OCH_2, 4H), 7.25 (s, Ph, 10H), 7.61 (m, Phen-H2, 2H), 7.70 (m, Phen-H3, 2H), 7.80 (d, Phen-H9, $J_{9,10}$ = 8.7 Hz, 2H), 8.11 (d, Phen-H4, $J_{3,4}$ = 8.1 Hz, 2H), 8.24 (s, Phen-H7, 2H), 8.49 (d, Phen-H1, $J_{1,2}$ = 8.1 Hz, 2H), 8.61 (d, Phen-H10, $J_{9,10}$ = 8.9 Hz, 2H); ^{13}C-NMR ($CDCl_3$) δ/ppm: 29.44, 29.49, 29.93, 36.28, 40.28, 67.98, 72.88, 79.33, 121.92, 123.18, 123.40, 125.54, 127.82, 128.15, 128.32, 128.34, 128.49, 128.78, 129.00, 129.01, 131.48, 135.95, 140.22, 143.54, 154.77, 161.98.

Anal. Calcd. for $C_{56}H_{50}N_4O_4$ (M_r = 843.05): C 79.80, H 5.98, N 6.55%; found: C 79.68, H 5.78, N 6.55%.

*1,6-Bis[(8-propargylbenzyloxycarbonylamino)-6-phenanthridinyl]-*p*-xylene (**22**)*

18 (1 g, 1.3 mmol), K_2CO_3(1.8 g, 13 mmol) and propargyl bromide (1.14 cm^3, 80% solution in toluene, 10.6 mmol) in dry DMF (50 cm^3) gave **22** (0.56 g, 52%); m.p. = 185–187 °C; R_f = 0.58 (SiO_2, CH_2Cl_2/$(CH_3)_2CO$ = 9 : 1).

IR (KBr), ν_{max}/cm^{-1}: 3260, 3050, 3020, 2920, 2840, 1710, 1610, 1570, 1530, 1510, 1480, 1435, 1390, 1350, 1280, 1260, 1230, 1210, 1120, 1505, 980, 760, 740, 720, 690; ^{1}H-NMR ($CDCl_3$) δ/ppm: 2.12 (s, CH, 2H), 4.33 (d, CH_2, J = 2.2 Hz, 4H), 4.58 (s, CH_2, 4H), 5.14 (s, OCH_2, 2H), 7.18 (s, p-Ph, 4H), 7.28 (s, Ph, 10H), 7.62 (m, Phen-H2, 2H), 7.71 (m, Phen-H3, -H9, 4H), 8.14 (m, Phen-H7, -H4, 4H), 8.47 (d, Phen-H1, $J_{1,2}$ = 7.4 Hz, 2H), 8.54 (d, Phen-H10, $J_{9,10}$ = 8.9 Hz, 2H); ^{13}C-NMR ($CDCl_3$) δ/ppm: 40.02, 42.31, 67.79, 72.86, 78.95, 121.84, 123.15, 123.29, 125.45, 125.48, 126.74, 127.77, 128.04, 128.36, 128.67, 128.74, 129.73, 131.47, 135.84, 136.73, 140.06, 143.59, 154.49, 159.60.

Anal. Calcd. for $C_{56}H_{42}N_4O_4$ (M_r = 834.98): C 80.56, H 5.07, N 6.71%; found: C 80.35, H 5.03, N 6.66%.

*1,6-Bis[(8-propargylethyloxycarbonylamino)-6-phenanthridinyl]-p-xylene (**23**)*

12 (0.9 g, 1.4 mmol), K_2CO_3(2 g, 14.3 mmol) and propargyl bromide (1.2 cm^3, 80% solution in toluene, 13 mmol) in dry DMF (75 cm^3) gave **23** (0.80 g, 78%); m.p. = 190–192 °C; R_f = 0.40 (SiO_2, CH_2Cl_2/$(CH_3)_2CO$ = 9 : 1).

IR (KBr), ν_{max}/cm^{-1}: 3200, 2960, 2910, 2100, 1700, 1610, 1570, 1530, 1510, 1480, 1430, 1375, 1340, 1270, 1235, 1220, 1135, 1045, 1020, 945, 925, 880, 865, 830, 780, 753, 720, 705, 660; ^{1}H-NMR ($CDCl_3$) δ/ppm: 1.15 (s-br, CH_3, 6H), 2.14 (t, CH, J = 2.3 Hz, 2H), 4.15 (q, OCH_2, J = 6.8 Hz, 4H), 4.35 (d, CH_2, J = 2.3 Hz, 4H), 4.63 (s, CH_2, 4H), 7.23 (s, p-Ph, 4H), 7.62 (m, Phen-H2, 2H), 7.71 (m, Phen-H3, 2H), 7.77 (s-br, Phen-H9, 2H), 8.15 (m, Phen-H4, -H7, 4H), 8.49 (d, Phen-H1, $J_{1,2}$ = 7.1 Hz, 2H), 8.57 (d, Phen-H10, $J_{9,10}$ = 9.0 Hz, 2H), ^{13}C-NMR ($CDCl_3$) δ/ppm: 14.33, 39.87, 42.34, 62.31, 72.65, 77.13, 88.36, 121.82, 123.08, 123.26, 123.33, 125.51, 126.76, 128.64, 128.74, 129.00, 129.72, 131.38, 136.76, 140.32, 143.57, 154.68, 159.61.

Anal. Calcd. for $C_{46}H_{38}N_4O_4$ (M_r = 710.84): C 77.73, H 5.39, N 7.88%; found: C 77.60, H 5.29, N 7.95%.

*3,8-Bis(propargylbenzyloxycarbonylamino)-6-methyl-phenanthridine (**31**)*

30 (1.2 g, 2.4 mmol), K_2CO_3 (6.6 g, 48 mmol) and propargyl bromide (4.1 cm^3, 80% solution in toluene, 38.4 mmol) in dry DMF (102 cm^3) gave **31** (1 g, 73%); m.p. = 44–47 °C; R_f = 0.58 (SiO_2, CH_2Cl_2/MeOH = 95 : 5).

IR (KBr), ν_{max}/cm^{-1}: 3300, 3060, 3040, 2960, 2120, 1710, 1620, 1590, 1580, 1540, 1490, 1440, 1390, 1360, 1280, 1240, 1220, 1130, 1050, 1000, 970, 930, 910, 820, 770, 730, 700; ^{1}H-NMR ($CDCl_3$) δ/ppm: 2.32 (s, CH, 1H), 2.38 (s, CH, 1H), 2.92 (s, CH_3, 3H), 4.57 (s, CH_2, 4H), 4.66 (s, OCH_2, 4H), 7.30 (s-br, Ph, 10H), 7.61 (d, Phen-H2, $J_{1,2}$ = 8.3 Hz, 1H), 7.78 (d, Phen-H9, $J_{9,10}$ = 8.6 Hz, 1H), 8.06 (s, Phen-H4, 1H), 8.16 (s, Phen-H7, 1H), 8.38 (d, Phen-H1, $J_{1,2}$ = 9.0 Hz, 1H), 8.47 (d, Phen-H10, $J_{9,10}$ = 8.9 Hz, 1H); ^{13}C-NMR ($CDCl_3$) δ/ppm: 22.87, 39.92, 40.02, 64.54, 67.56, 67.74, 72.56, 72.77, 79.02, 121.51, 122.29, 123.01, 123.15, 125.29, 125.88, 126.55, 126.99, 127.44, 127.60, 127.72, 127.93, 128.06, 128.14, 128.23, 129.06, 130.29, 135.60, 135.82, 139.99, 141.40, 143.71, 154.41, 154.47, 158.95.

Anal. Calcd. for $C_{36}H_{29}N_3O_4$ (M_r = 567.65): C 76.17, H 5.15, N 7.40%; found: C 76.38, H 5.15, N 7.28%.

*Preparation of Cyclo-bis-phenanthridines **24–29**, **32**, **33***

A solution of $Cu(OAc)_2 \times H_2O$ (9 equiv.) in CH_3CN, pyridine or in a mixture of pyridine/CH_3CN (5 : 1) was heated at 60 °C in an Ar atmosphere. To this reaction mixture, a solution of bis-propargyl derivates **19–23** or **31** in CH_3CN or in pyridine was added using a syringe pump during 48 hours, and the reaction mixture was stirred for additional 24 hours. Additional 4 equiv. of $Cu(OAc)_2 \times H_2O$ was added in two portions during the last 48 hours. Evaporation of the solvent left a residue which was chromatographed (column, SiO_2) eluting with a gradient $(CH_3)_2CO$ in CH_2Cl_2 to afford the main fraction. Separation of compounds **32** and **33** was achieved by chromatography (preparative TLC, SiO_2, sixfold developed) eluting with a gradient EtOH and EtOAc in CH_2Cl_2. Additional purification of all products was carried out by recrystallization from CH_2Cl_2 /diethyl ether.

Cyclo-bis-phenanthridine ***24***

19 (0.5 g, 0.6 mmol) and $Cu(OAc)_2 \times H_2O$ (1.6 g, 7.8 mmol) in pyridine/CH_3CN mixture (320 cm^3, 5 : 1) gave **24** (0.24 g, 49%); m.p. = 237–238 °C; R_f = 0.34 (SiO_2, $CH_2Cl_2/(CH_3)_2CO$ = 9 : 1).

IR (KBr), ν_{max}/cm^{-1}: 3420, 3060, 3020, 2920, 2850, 1950, 1710, 1620, 1575, 1530, 1500, 1485, 1460, 1450, 1440, 1390, 1360, 1290, 1225, 1140, 1055, 1025, 1000, 975, 930, 920, 905, 875, 865, 840, 760, 725, 705, 695; ^{1}H-NMR ($CDCl_3$) δ/ppm: 1.70 (s-br, CH_2, 4H), 1.96 (m, CH_2, 4H), 3.67 (m, CH_2, 4H), 4.68 (s, CH_2, 4H), 5.28 (s, OCH_2, 4H), 7.35 (s-br, Ph, 10H), 7.62 (m, Phen-H2, 2H), 7.72 (m, Phen-H3, 4H), 7.74 (m, Phen-H9, 2H), 8.11 (d, Phen-H4, $J_{3,4}$ = 7.1 Hz, 2H), 8.28 (s, Phen-H7, 2H), 8.49 (d, Phen-H1, $J_{1,2}$ = 7.3 Hz, 2H), 8.58 (d, Phen-H10, $J_{9,10}$ = 9.0 Hz, 2H); ^{13}C-NMR ($CDCl_3$) δ/ppm: 30.06, 30.34, 37.02, 41.21, 68.23, 68.54, 74.79, 121.97, 123.24, 123.29, 125.44, 126.59, 128.03, 128.30, 128.40, 128.600, 128.80, 128.94, 129.23, 129.61, 131.32, 135.83, 143.83, 154.49, 162.03; MS: *m/z* 813.4 (M^+), 613.3, 461.3, 460.1, 443.2, 439.2, 329.1, 289.6, 202.2.

Cyclo-bis-phenanthridine ***25***

20 (0.8 g, 1.6 mmol) and $Cu(OAc)_2 \times H_2O$ (3.0 g, 15.2 mmol) in pyridine (600 cm^3) gave **25** (0.39 g, 47%); m.p. = 212–214 °C; R_f = 0.39 (SiO_2, $CH_2Cl_2/(CH_3)_2CO$ = 9 : 1).

IR (KBr), ν_{max}/cm^{-1}: 2980, 2920, 2830, 1710, 1620, 1575, 1530, 1480, 1440, 1380, 1340, 1295, 1260, 1220, 1170, 1130, 1060, 830, 725, 705; ^{1}H-NMR ($CDCl_3$) δ/ppm: 1.31 (t, CH_3, J = 6.7 Hz, 6H), 1.72 (s-br, CH_2, 4H), 1.98 (s-br, CH_2, 4H), 3.40 (t, CH_2, J = 8.1 Hz, 4H), 4.30 (q, OCH_2, J = 7.1 Hz, 4H), 4.66 (s, CH_2, 4H), 7.62 (m, Phen-H2, 2H), 7.71 (m, Phen-H3, 2H), 7.79 (d, phen-H9, $J_{9,10}$ = 6.6 Hz, 2H), 8.11 (d, Phen-H4, $J_{3.4}$ = 7.3 Hz, 2H), 8.29 (s, Phen-H7, 2H), 8.49 (d, Phen-H1, $J_{1,2}$ = 7.9 Hz, 2H), 8.58 (d, Phen-H10, $J_{9,10}$ = 9.1 Hz, 2H); ^{13}C-NMR ($CDCl_3$) δ/ppm: 14.55, 30.06, 30.26, 36.97, 41.09, 62.71, 68.44, 74.92, 121.01, 121.94, 123.21, 125.53, 126.56, 128.72, 129.27, 129.70, 131.25, 140.95, 143.94, 154.69, 162.00.

Anal. Calcd. for $C_{44}H_{40}N_4O_4$ (M_r = 688.83): C 76.72, H 5.86, N 8.13%; found: C 76.57, H 6.06, N 8.05%.

Cyclo-bis-phenanthridine ***26***

21 (0.4 g, 0.5 mmol) and $Cu(OAc)_2 \times H_2O$ (1.3 g, 6.5 mmol) in pyridine/CH_3CN mixture (245 cm^3, 5 : 1) gave **26** (0.23 g, 57%); m.p. = 209–210 °C; R_f = 0.27 (SiO_2, $CH_2Cl_2/(CH_3)_2CO$ = 9 : 1).

IR (KBr), ν_{max}/cm^{-1}: 3060, 2920, 2840, 1720, 1620, 1570, 1530, 1480, 1460, 1435, 1390, 1350, 1220, 1140, 1060, 870, 760, 730, 700; ^{1}H-NMR ($CDCl_3$) δ/ppm: 1.39 (m, CH_2, 4H), 1.50 (m, CH_2, 4H), 1.89 (m, CH_2, 4H), 3.33 (t, CH_2, J = 7.8 Hz, 4H), 4.69 (s, CH_2, 4H), 5.24 (s, OCH_2, 4H), 7.32 (s, Ph, 10H), 7.61 (m, Phen-H2, 2H), 7.71 (m, Phen-H3, 2H), 7.63 (s-br, Phen-H9, 2H), 8.11 (d, Phen-H4, $J_{3,4}$ = 8.1 Hz, 2H), 8.23 (s, Phen-H7, 2H), 8.48 (d, Phen-H1, $J_{1,2}$ = 8.1 Hz, 2H), 8.57 (d, Phen-H10, $J_{9,10}$ = 9.0 Hz, 2H); ^{13}C-NMR ($CDCl_3$) δ/ppm: 28.75, 29.34, 29.75, 36.20, 40.82, 68.06, 68.59, 74.39, 121.82, 123.04, 123.20, 125.38, 126.43, 127.82, 128.12, 128.42, 128.67, 129.35, 131.29, 135.65, 140.01, 143.60, 154.38, 162.12; MS: *m/z* 841.4 (M^+), 705.3, 613.2, 460.2, 349.2, 329.1, 307.2, 289.1, 208.2.

Cyclo-bis-phenanthridine ***27***

22 (0.32 g, 0.4 mmol) and $Cu(OAc)_2 \times H_2O$ (1.04 g, 5.2 mmol) in pyridine/CH_3CN mixture (200 cm^3, 5 : 1) gave **27** (0.17 g, 52%); m.p. = 265–267 °C; R_f = 0.21 (SiO_2, $CH_2Cl_2/(CH_3)_2CO$ = 9 : 1).

IR (KBr), ν_{max}/cm^{-1}: 3060, 3020, 2930, 1720, 1610, 1570, 1530, 1510, 1490, 1480, 1460, 1440, 1380, 1350, 1330, 1290, 1240, 1220, 1030, 880, 840, 825, 760, 725, 710, 680; ^{1}H-NMR (DMSO-d_6) δ/ppm: 4.59 (s, CH_2, 4H), 4.96 (s, CH_2,4H), 5.19 (s, OCH_2, 4H), 7.35 (m, Ph, p-Ph, 14H), 7.65 (m, Phen-H2, 2H), 7.73 (m, Phen-H3, 2H), 7.94 (d, Phen-H9, $J_{10,9}$ = 7.3 Hz, 2H), 8.04 (d, Phen-H4, $J_{3,4}$ = 8.1 Hz, 2H), 8.39 (s, Phen-H7, 2H), 8.68 (d, Phen-H1, $J_{1,2}$ = 8.1 Hz, 2H), 8.79 (d, Phen-H10, $J_{9,10}$ = 9.2 Hz, 2H); ^{13}C-NMR (DMSO-d_6) δ/ppm: 67.54, 67.61, 75.22, 121.78, 122.71, 122.87, 123.67, 124.80, 127.00, 127.80, 128.09, 128.46, 128.74, 128.88, 129.27, 129.40, 130.61, 136.12, 136.97, 139.83, 143.23, 153.87, 160.08; MS: *m/z* 833.4 (M^+); 613.3, 482.3, 460.2, 357.3, 329.2, 307.1, 289.2, 203.2.

Cyclo-bis-phenanthridine ***28***

23 (0.8 g, 1.1 mmol) and $Cu(OAc)_2 \times H_2O$ (2.9 g, 14.3 mmol) in pyridine (570 cm^3) gave **28** (0.44 g, 55%); m.p. = 259–261 °C; R_f = 0.30 (SiO_2, $CH_2Cl_2/(CH_3)_2CO$ = 9 : 1).

IR (KBr), ν_{max}/cm^{-1}: 2980, 2930, 2850, 1710, 1620, 1570, 1530, 1510, 1480, 1460, 1440, 1370, 1340, 1290. 1250, 1220, 1170, 1130, 1060. 1020, 930, 870, 830, 760, 720, 700; ^{1}H-NMR ($CDCl_3$) δ/ppm: 1.26 (t, CH_3, J = 6.8 Hz, 6H), 4.23(q, OCH_2, J = 7.0 Hz, 4H), 4.61 (s, CH_2, 4H), 4.65 (s, CH_2, 4H), 7.36 (s, p-Ph, 4H), 7.59 (m, Phen-H2, 2H), 7.69 (m, Phen-H3, 2H), 7.74 (s, Phen-H9, 2H), 8.12 (d, Phen-H4, $J_{3,4}$ = 8.0Hz, 2H), 8.27 (s, Phen-H7, 2H); 8.45 (d, Phen-H1, $J_{1,2}$ = 8.2 Hz, 2H), 8.54 (d, Phen-H10, $J_{9,10}$ = 9.0 Hz, 2H); ^{13}C-NMR ($CDCl_3$) δ/ppm: 14.36, 40.22, 42.24, 62.54, 68.34, 73.93, 121.78, 122.04, 122.125, 123.150, 125.51, 126.86, 128.62, 128.88, 129.17, 129.70, 131.45, 136.58, 139.94, 143.71, 154.50, 159.77.

Anal. Calcd. for $C_{46}H_{36}N_4O_4$ (M_r = 708.82): C 77.95, H 5.12, N 7.90%; found: C 77.69, H 5.32, N 7.98%.

Cyclo-bis-phenanthridine ***29***

To the suspension of **23** (0.5 g, 0.84 mmol) in dry DMF (57 cm^3) K_2CO_3 (1.17 g, 8.45 mmol) was added and the mixture was stirred for 30 min at room temperature until the starting compound **23** was completely dissolved. Then, the temperature of the reaction mixture was raised to 70–80 °C and a solution of α,α'-dibromo-*p*-xylene (0.22 g, 0.84 mmol) in DMF (7 cm^3) was added during two days. After 7 days of additional stirring, DMF was evaporated, the residue mixed with CH_2Cl_2 (20 cm^3) and the solid filtered off. Evaporation of CH_2Cl_2 left a residue which was chromatographed (column, SiO_2) eluting with a gradient of petrolether in EtOAc to afford the main fraction. Evaporation of solvents gave **29** (56 mg, 9%); m.p. = 245–247 °C; R_f = 0.48(SiO_2, EtOAc/petrol ether = 2 : 1).

^{1}H-NMR ($CDCl_3$) δ/ppm: 1.22 (t, CH_3, J = 7.1 Hz, 6H), 4.21 (q, OCH_2, J = 7.0 Hz, 4H), 4.60 (s, CH_2, 4H), 4.91 (s, NCH_2, 4H), 6.90 (s, p-Ph, 4H), 7.13 (s, p-Ph, 4H), 7.58 (m, Phen-H2, 2H), 7.68 (m, Phen-H3, -H9, 4H), 8.10 (m, Phen-H7, -H4, 4H), 8.27 (d, Phen-H1, $J_{1,2}$ = 8.1 Hz, 2H), 8.52 (d, Phen-H10, $J_{9,10}$ = 8.8 Hz, 2H); ^{13}C-NMR ($CDCl_3$) δ/ppm: 14.31, 41.77, 52.60, 62.03, 121.82, 123.43, 124.30, 125.51, 126.79, 127.55, 128.51, 128.67, 129.20, 129.82, 131.17, 136.18, 137.01, 140.63, 143.73, 155.54, 159.58; MS: *m/z* 736 (M^+), 662, 592, 295, 267, 205, 190.

*Cyclo-bis-phenanthridines **32**, **33***

31 (400 mg, 0.7 mmol) and $Cu(OAc)_2 \times H_2O$ (2.5 g, 12.7 mmol) in CH_3CN (350 cm^3) gave **32** (55 mg, 14%); m.p. = 215–217 °C; R_f = 0.67 (SiO_2, CH_2Cl_2/EtOH/EtOAc = 48 : 1 : 1) and **33** (48 mg, 12%); m.p. = 127–129 °C; R_f = 0.63 (SiO_2, CH_2Cl_2/EtOH/EtOAc = 48 : 1 : 1).

*Cyclo-bis-phenanthridine **32***

IR (KBr), ν_{max}/cm^{-1}: 3060, 3030, 2950, 1710, 1620, 1590. 1575, 1190, 1440, 1400, 1360, 1310, 1270, 1230, 1140, 1045, 970, 930, 910, 810, 760, 730, 700; ^{1}H-NMR ($CDCl_3$) δ/ppm: 2.85 (s, CH_3, 6H), 4.67 (s, CH_2, 8H), 5.22 (s, OCH_2, 8H), 7.30 (s, Ph, 20H), 7.57 (d, Phen-H2, $J_{1,2}$ = 5.9 Hz, 2H), 7.81 (d, Phen-H9, $J_{9,10}$ = 7.7 Hz, 2H), 8.12 (d, Phen-H4, $J_{2,4}$ = 1.8 Hz, 2H), 8.29 (s, Phen-H7, 2H), 8.44 (d, Phen-H1, $J_{1,2}$ = 9.0 Hz, 2H), 8.59 (d, Phen-H10, $J_{9,10}$ = 9.0 Hz, 2H); ^{13}C-NMR ($CDCl_3$) δ/ppm: 23.25, 40.63, 40.72, 67.91, 68.07, 68.33, 69.31, 74.11, 74.72, 121.87, 122.60, 123.35, 125.43, 126.23, 127.66, 127.77, 127.97, 128.13, 128.37, 128.43, 129.88, 130.77, 135.70, 135.86, 139.80, 141.30, 144.00, 154.63, 159.48.

Anal. Calcd. for $C_{72}H_{54}N_6O_8$ (M_r = 1131.27): C 76.45, H 4.81, N 7.43%; found: C 76.34, H 4.98, N 7.45%.

*Cyclo-bis phenanthridine **33***

IR (KBr), ν_{max}/cm^{-1}: 3060, 3030, 2940, 2840, 1710, 1620, 1590, 1575, 1485, 1435, 1400, 1360, 1270, 1230, 1140, 1045, 100, 930, 910, 815, 765, 730, 695; ^{1}H-NMR ($CDCl_3$) δ/ppm: 2.87 (s, CH_3, 6H), 4.67 (s, CH_2, 4H), 4.68 (s, CH_2, 4H), 5.21 (s, OCH_2, 8H), 7.67 (d, Phen-H2, $J_{1,2}$ = 7.1 Hz, 2H), 7.75 (d, Phen-H9, $J_{9,10}$ = 8.8 Hz, 2H), 8.12 (s, Phen-H4, 2H), 8.15 (s, Phen-H7, 2H), 8.51 (m, Phen-H1, -H10, 4H); ^{13}C-NMR ($CDCl_3$) δ/ppm: 22.73, 40.55, 40.69, 67.91, 68.12, 68.81, 68.99, 74.16, 121.87, 122.64, 123.50, 123.93, 124.04, 124.09, 125.99, 126.20, 126.32, 127.64, 127.83, 127.94, 128.21, 128.36, 128.46, 129.77, 130.94, 135.59, 135.86, 139.67, 141.41, 154.54, 154.60, 159.00.

Anal. Calcd. for $C_{72}H_{54}N_6O_8$ (M_r = 1131.27): C 76.45, H 4.81, N 7.43%; found: C 76.27, H 4.82, N 7.51%.

*Preparation of Bis-triflate Salts **34–38**, **41–45** and **49**, **51***

Acyclic- **16**, **17**, **19**, **20**, **23** or cyclic-bis-phenanthridine derivatives **24–28**, **32**, **33** and $CF_3SO_2OCH_3$ were refluxed in dry 1,2-dichloro ethane for 24 hours under an Ar atmosphere. Then the reaction mixture was cooled to 40 °C and CF_3SO_3H was added. The reaction mixture was stirred additional for 24 hours. After solvent removal, a pure bis-triflate product was obtained by precipitation with diethyl ether and recrystallization from CH_3CN/diethyl ether. Melting points were not determined since all the triflate salts melted in a wide temperature range.

*Bis-triflate **34***

20 (0.21 g, 0.3 mmol) and $CF_3SO_2OCH_3$ (100 ml, 0.91 mmol) in dry 1,2-dichloro ethane (133 cm^3) gave **34** (0.27 g, 88%).

^{1}H-NMR (CD_3CN) δ/ppm: 1.42 (t, CH_3, J = 7.0 Hz, 6H), 2.24 (s-br, CH_2, 4H), 2.67 (t, CH, J = 1.7 Hz, 2H), 3.77 (m, CH_2, 4H), 4.22 (q, OCH_2, J = 7.0 Hz, 4H), 4.59 (s, NCH_3, 6H), 4.69(d, CH_2, J = 2.3 Hz, 4H), 8.07 (m, Phen-H3, -H2, 4H), 8.28 (s-br, Phen-H9, 2H), 8.38 (m, Phen-H4, 2H), 8.65 (s-br, Phen-H7, 2H), 8.92 (s-br,

Phen-H1, 2H), 9.01 (s-br, Phen-H10, 2H); ^{13}C-NMR (CD_3CN) δ/ppm: 14.84, 29.46, 30.08, 32.68, 40.29, 42.27, 63.77, 74.61, 80.36, 121.05, 124.83, 125.40, 125.51, 125.95, 126.47, 131.21, 133.08, 136.63, 144.30.

Anal. Calcd. for $C_{48}H_{48}N_4O_{10}S_2F_6$ (M_r = 1019.04): C 56.58, H 4.75, N 5.50 %; found: C 56.43, H 4.73, N 5.61%.

Bis-triflate ***35***

23 (0.3 g, 0.42 mmol) and $CF_3SO_2OCH_3$ (102 ml, 0.93 mmol) in dry 1,2-dichloro ethane (180 cm^3) gave **35** (262 mg, 60%).

^{1}H-NMR (CD_3CN) δ/ppm: 1.17 (t, CH_3, J = 7.2 Hz, 6H), 2.47 (s, CH, 2H), 4.17 (q, OCH_2, J = 7.3 Hz, 4H), 4.54 (s, CH_2, NCH_3, 10H), 5.21 (s, CH_2, 4H), 7.21 (s, p-Ph, 4H), 8.04–9.04 (m, Ar-H, 14H); ^{13}C-NMR (CD_3CN) δ/ppm: 26.91, 28.93, 29.54, 30.18, 31.65, 33.05, 33.61, 121.23, 125.62, 125.79, 130.59, 131.15, 131.89, 133.47, 133.98, 134.99, 137.02, 137.25, 144.93, 155.47.

Anal. Calcd. for $C_{50}H_{44}N_4O_{10}S_2F_6$ (M_r = 1039.03): C 57.80, H 4.27, N 5.39%; found: C 57.56, H 4.21, N 5.56%.

Bis-triflate ***41***

25 (83 mg, 0.12 mmol) and $CF_3SO_2OCH_3$ (44 ml, 0.4 mmol) in dry 1,2-dichloro ethane (53 cm^3) gave **41** (91 mg, 75%).

^{1}H-NMR (CD_3CN) δ/ppm: 1.32 (t, CH_3, J = 7.1 Hz, 6H), 3.83 (m, CH_2, 4H), 4.31 (q, OCH_2, J = 7.1 Hz, 4H), 4.63 (s, NCH_3, 6H), 4.85 (s, CH_2, 4H), 8.13 (m, Phen-H3, -H2, 4H), 8.42 (d, Phen-H9, $J_{9,10}$ = 9.0 Hz, 2H), 8.51 (m, Phen-H4, -H7, 4H), 8.96 (s, Phen-H1, 2H), 8.99 (s, Phen-H10, 2H); ^{13}C-NMR (CD_3CN) δ/ppm: 15.69, 30.53, 31.15, 33.64, 41.93, 43.06, 64.96, 69.75, 77.26, 121.90, 124.38, 126.017, 126.36, 126.47, 126.75, 132.11, 133.92, 137.42, 137.81, 145.38, 168.74.

Anal. Calcd. for $C_{48}H_{46}N_4O_{10}S_2F_6$ (M_r = 1017.04): C 56.69, H 4.56, N 5.51%; found: C 56.53, H 4.32, N 5.48%.

Bis-triflate ***42***

28 (0.14 g, 0.2 mmol) and $CF_3SO_2OCH_3$ (75 ml, 0.68 mmol) in dry 1,2-dichloro ethane (89 cm^3) gave **42** (0.19 g, 88%).

^{1}H-NMR (CD_3CN) δ/ppm: 1.25 (t, CH_3, J = 7.1 Hz, 6H), 4.23 (q, OCH_2, J = 7.1 Hz, 4H), 4.55 (s, NCH_3, 6H), 4.74 (s, CH_2, 4H), 5.19 (s, CH_2, 4H), 7.29 (s, p-Ph, 4H), 8.08–8.96 (m, Ar-H, 14H); ^{13}C-NMR (CD_3CN) δ/ppm: 14.23, 37.53, 40.69, 42.22, 64.11, 75.74, 121.05, 124.04, 125.23, 125.57, 126.30, 126.68, 130.42, 130.87, 131.61, 113.24, 133.64, 134.54, 136.68, 137.14, 164.73.

Anal. Calcd. for $C_{50}H_{42}N_4O_{10}S_2F_6$ (M_r = 1037.01): C 57.91, H 4.08, N 5.40%; found: C 57.80, H 4.35, N 5.46%.

Bis-triflate ***36***

19 (100 mg, 0.12 mmol) and $CF_3SO_2OCH_3$ (50 ml, 0.49 mmol), then CF_3SO_3H (43 ml, 0.49 mmol) in dry 1,2-dichloro ethane (96 cm^3) gave **36** (105 mg, 100%).

^{1}H-NMR (CD_3CN) δ/ppm: 1.97 (s-br, CH_2, 4H), 2.61 (s-br, CH_2, 4H), 2.95 (m, CH, 2H), 3.76 (d, CH_2, J = 8.2 Hz, 4H), 4.24 (d, CH_2, J = 2.3 Hz, 4H), 4.58 (s, NCH_3, 6H), 7.60 (s, Phen-H7, 2H), 7.77 (d, Phen-H9, $J_{9,10}$ = 9.0 Hz, 2H), 7.99 (m, Phen-H1, -H3, 4H), 8.42 (m, Phen-H4, 2H), 8.81 (m, Phen-H2, -H10, 4H); ^{13}C-NMR (CD_3CN)

δ/ppm: 29.51, 29.95, 32.87, 42.47, 43.10, 73.37, 80.95, 121.19, 125.45, 125.59, 125.85, 126.23, 127.33, 131.59, 132.175, 134.02, 136.07, 136.28, 137.06, 168.58.

Bis-triflate ***37***

16 (150 mg, 0.2 mmol) and $CF_3SO_2OCH_3$ (63 ml, 0.6 mmol), then CF_3SO_3H (35 ml, 0.4 mmol) in dry 1,2-dichloro ethane (100 cm^3) gave **37** (160 mg, 100%).

^{1}H-NMR (CD_3CN) δ/ppm: 1.97 (m, CH_2, 4H), 2.07 (m, CH_2, 4H), 3.86 (m, CH_2, 4H), 4.66 (s, NCH_3, 6H), 6.13 (s-br, NH_2, 4H), 8.16 (m, Phen-H3, -H2, 4H), 8.32 (d, Phen-H9, $J_{9,10}$ = 9.1 Hz, 2H), 8.55 (d, Phen-H4, $J_{3,4}$ = 8.8 Hz, 4H), 8.34 (s, Phen-H7, 2H), 8.99 (d, Phen-H1, $J_{1,2}$ = 8.0 Hz, 2H), 9.12 (d, Phen-H10, $J_{9,10}$ = 9.1 Hz,2H); ^{13}C-NMR (CD_3CN) δ/ppm: 29.41, 29.95, 32.84, 42.38, 121.11, 125.35, 125.61, 125.68, 126.88, 131.44, 132.51, 133.61, 135.03, 136.81, 168.42.

Bis-triflate ***38***

17 (100 mg, 0.13 mmol) and $CF_3SO_2OCH_3$ (30 ml, 0.3 mmol), then CF_3SO_3H (35 ml, 0.4 mmol) in dry 1,2-dichloro ethane (34 cm^3) gave **38** (75 mg, 85%).

^{1}H-NMR (DMSO-d_6) δ/ppm: 1.60 (m, CH_2, 4H), 1.82 (m, CH_2, 8H), 3.61 (m, CH_2, 4H), 4.55 (s, NCH_3, 6H), 7.68–8.94 (m, Ar-H, 14H); MS: FAB$^+$, *m/z* 677.26861 + 149 (bis-phenanthridine^{2+}, $CF_3SO_3^-$)$^+$.

Bis-triflate ***43***

24 (100 mg, 0.12 mmol) and $CF_3SO_2OCH_3$ (34 ml, 0.3 mmol), then CF_3SO_3H (53 ml, 0.6 mmol) in dry 1,2-dichloro ethane (33 cm^3) gave **43** (91 mg, 89%).

^{1}H-NMR (CD_3CN) δ/ppm: 1.87 (s-br, CH_2, 4H), 3.80 (t, CH_2, J = 8.0 Hz, 4H), 4.32 (d, CH_2, J = 6.2 Hz, 4H), 4.60 (s, NCH_3, 6H), 6.01 (m, NH, 2H), 7.46 (s, Phen-H7, 2H), 7.71 (d, Phen-H9, $J_{9,10}$ = 9.0 Hz, 2H), 8.00 (m, Phen-H3, -H1, 4H), 8.42 (m, Phen-H4, 2H), 8.75 (d, Phen-H10, $J_{9,10}$ = 9.2 Hz, 2H), 8.83 (m, Phen-H2, 2H).

Bis-triflate ***44***

26 (100 mg, 0.12 mmol) and $CF_3SO_2OCH_3$ (49 ml, 0.45 mmol), then CF_3SO_3H (53 ml, 0.6 mmol) in dry 1.2-dichloro ethane (64 cm^3) gave 44 (92 mg, 85%); ^{1}H-NMR (DMSO-d_6) δ: 1.58 (s-br, CH_2, 4H), 1.76 (s-br, CH_2, 4H), 1.93 (s-br, CH_2, 4H), 3.75 (s-br, CH_2, 4H), 4.36 (s, NCH_3, 6H), 7.31 (m, NH, 2H), 7.45 (s, Phen-H7, 2H), 7.66 (d, Phen-H9, $J_{9,10}$ = 9.1 Hz, 2H), 7.95 (m, Phen-H3, -H1, 4H), 8.54 (m, Phen-H4, 2H), 8.86 (d, Phen-H10, $J_{9,10}$ = 9.4 Hz, 2H), 8.91 (m, Phen-H2, 2H); ^{13}C-NMR (DMSO-d_6) δ/ppm: 27.48; 27.99; 28.89; 65.86; 76.35; 105.14; 119.98; 123.09; 124.21; 125.00; 125.123; 125.51; 127.20; 129.79; 129.52; 133.53; 148.37; 165.35.

Bis-triflate ***45***

27 (98 mg, 0.12 mmol) and $CF_3SO_2OCH_3$ (50 ml, 0.49 mmol), then CF_3SO_3H (53 ml, 0.6 mmol) in dry 1,2-dichloro ethane (92 cm^3) gave **45** (107 mg, 100%).

^{1}H-NMR (DMSO-d_6) δ/ppm: 4.63 (m, NCH_3, CH_2, 10H), 5.10 (s-br, CH_2, 4H), 5.81 (s-br, NH, 2H), 7.50 (s, p-Ph, 4H), 7.71–9.03 (m, Ar-H, 14H).

Bis-triflate ***49***

32 (57 mg, 0.05 mmol) and $CF_3SO_2OCH_3$ (14 ml, 0.13 mmol), then CF_3SO_3H (44 ml, 0.5 mmol) in dry 1,2-dichloro ethane (27 cm^3) gave **49** (36 mg, 78%).

^{1}H-NMR (DMSO-d_6) δ/ppm: 3.13 (m, CH_3, 6H), 4.23 (s-br, NCH_3, 6H), 4.32 (m, CH_2, 4H), 4.70 (m, CH_2, 4H), 7.18–7.56 (m, NH, Phen-H2, -H4, -H7, -H9, 12H), 8.53 (s-br, Phen-H1, -H10, 4H).

Bis-triflate ***51***

33 (35 mg, 0.03 mmol) and $CF_3SO_2OCH_3$ (9 ml, 0.08 mmol), then CF_3SO_3H (27 ml, 0.3 mmol) in dry 1,2-dichloro ethane (15 cm^3) gave **51** (19 mg, 69%).

^{1}H-NMR (DMSO-d_6) δ/ppm: 3.11 (m, CH_3, 6H), 4.24 (s-br, NCH_3, 6H), 4.34 (m, CH_2, 4H), 4.72 (m, CH_2, 4H), 7.14–7.53 (m, NH, Phen-H2, -H4, -H7, -H9, 12H), 8.51 (s-br, Phen-H1, -H10, 4H).

Preparation of Bis-hydrogensulphates ***39, 40, 46–48, 50, 52***

In solution of acyclic **36**, **37** or cyclic bis triflate derivatives **43–45** or **49**, **51** in dry CH_3CN, a solution of tetrabutylammonium hydrogensulphate (20 equiv.) in dry CH_3CN was added. Precipitated product was collected by filtration, and recrystallized from DMSO/CH_2Cl_2. Melting points were not determined since all the hydrogen sulphate salts melted in a wide temperature range.

Bis-hydrogensulphate ***39***

36 (74 mg, 0.085 mmol) and tetrabutylammonium hydrogensulphate (570 mg, 1.7 mmol) in dry CH_3CN (2 × 10 cm^3) gave **39** (57 mg, 81%).

^{1}H-NMR (DMSO-d_6) δ/ppm: 1.83 (s.br, CH_2, 4H), 1.92 (s-br, CH_2, 4H), 3.23 (s, CH, 2H), 3.77 (s-br, CH_2, 4H), 4.23 (d, CH_2, J = 3.2 Hz, 4H), 4.59 (s, NCH_3, 6H), 7.32 (t, NH, J = 5.8 Hz, 2H), 7.57 (s, Phen-H7, 2H), 7.73 (d, Phen-H9, $J_{9,10}$ = 9.2 ,2H), 7.95 (m, Phen-H3, -H1, 4H), 8.56 (m, Phen-H4, 2H), 8.90 (m, Phen-H2, -H10, 4H).

Anal. Calcd. for $C_{40}H_{42}N_4O_8S_2 \times 3H_2O$ (M_r = 824.98): C 58.23, H 5.86, N 6.79%; found: C 58.20, H 5.68, N 6.79%.

Bis-hydrogensulphate ***40***

37 (31 mg, 0.04 mmol) and tetrabutylammonium hydrogensulphate (272 mg, 0.78 mmol) in dry CH_3CN (2 × 5 cm^3) gave **40** (25 mg, 73%).

^{1}H-NMR (DMSO-d_6) δ/ppm: 1.83 (s-br, CH_2, 8H), 3.68 (s-br, CH_2, 4H), 4.50 (s-br, NH_2, 4H), 7.64 (d, Phen-H9, $J_{9,10}$ = 8.9 Hz, 2H), 7.71 (s, Phen-H7, 2H), 7.92 (m, Phen-H1, -H3, 4H), 8.51 (d, Phen-H4, $J_{3,4}$ = 8.1 Hz, 2H), 8.83 (m, Phen-H10, $J_{9,10}$ = 8.8 Hz, 2H), 8.88 (m, Phen-H2, 2H).

Anal. Calcd. for $C_{34}H_{38}N_4O_8S_2 \times 9H_2O$ (M_r = 856.97): C 47.65, H 6.59, N 6.54%; found: C 47.55, H 6.46, N 6.54%.

Bis-hydrogensulphate ***46***

43 (72 mg, 0.074 mmol) and tetrabutylammonium hydrogensulphate (509 mg, 1.5 mmol) in dry CH_3CN (2 × 10 cm^3) gave **46** (47 mg, 76%).

^{1}H-NMR (DMSO-d_6) δ/ppm: 1.96 (s-br, CH_2, 4H), 1.87 (s-br, CH_2, 4H), 4.40 (s-br, CH_2, 4H), 4.58 (s, NCH_3, 6H), 7.40 (s-br, NH, 2H), 7.45 (s-br, Phen-H7, 2H), 7.66 (d, Phen-H9, $J_{9,10}$ = 8.2 Hz, 2H), 7.39 (m, Phen-H1, -H3, 4H), 8.54 (m, Phen-H4, 2H), 8.87 (m, Phen-H2, -H10, 4H).

Anal. Calcd. for $C_{40}H_{40}N_4O_8S_2 \times 4H_2O$ (M_r = 840.97): C 57.13, H 5.75, N 6.66%; found: C 57.23, H 5.54, N 6.85%.

Bis-hydrogensulphate ***47***

44 (76 mg, 0.084 mmol) and tetrabutylammonium hydrogensulphate (577 mg, 1.7 mmol) in dry CH_3CN (2 × 11 cm^3) gave **47** (57 mg, 80%).

^{1}H-NMR (DMSO-d_6/D_2O = 1 : 1) δ/ppm: 1.59 (s-br, CH_2, 4H), 1.77 (s-br, CH_2, 4H), 1.93 (s-br, CH_2, 4H), 3.76 (s-br, CH_2, 4H), 4.38 (d, CH_2, J = 5.7 Hz, 4H), 4.59 (s-br, NCH_3, 6H), 7.34 (m, NH, J = 5.9 Hz, 2H), 7.46 (s, Phen-H7, 2H), 7.68 (d, Phen-H9, $J_{9,10}$ = 9.2 Hz, 2H), 7.96 (m, Phen-H1, -H3, 4H), 8.55 (m, Phen-H4, 2H), 8.88 (d, Phen-H10, $J_{9,10}$ = 9.2, 2H), 8.93 (m, Phen-H2, 2H).

Anal. Calcd. for $C_{42}H_{44}N_4O_8S_2 \times 3\ H_2O$ (M_r = 851.02): C 59.29, H 5.92, N 6.58%; found: C 59.52, H 5.69, N 6.70%.

Bis-hydrogensulphate ***48***

45 (100 mg, 0.12 mmol) and tetrabutylammonium hydrogensulphate (760 mg, 2.24 mmol) in dry CH_3CN (2 × 15 cm^3) gave **48** (82 mg, 79%).

^{1}H-NMR (DMSO-d_6) δ/ppm: 4.56 (m, CH_2, NCH_3, 10H), 5.00 (s-br, CH_2, 4H), 5.71 (s-br, NH, 2H), 7.40 (s, p-Ph, 4H), 7.62–8.94 (m, Ar-H, 14H).

Anal. Calcd. for $C_{42}H_{36}N_4O_8S_2 \times 4H_2O$ (M_r = 860.97): C 58.59, H 5.15, N 6.51%; found: C 58.58, H 5.10, N 6.52%.

Bis-hydrogensulphate ***50***

49 (36 mg, 0.04 mmol) and tetrabutylammonium hydrogensulphate (265 mg, 0.8 mmol) in dry CH_3CN (2 × 5 cm^3) gave **50** (27 mg, 77%).

^{1}H-NMR (DMSO-d_6) δ/ppm: 3.13 (s, CH_3, 6H), 4.25 (s, NCH_3, 6H), 4.35 (s, CH_2, 8H), 6.95 (m, NH, 4H), 7.17 (s, Phen-H4, 2H), 7.22 (m, Phen-H2, 2H), 7.36 (s, Phen-H7, 2H), 7.51 (m, Phen-H9, 2H), 8.51 (m, Phen-H1, -H10, 4H).

Anal. Calcd. for $C_{42}H_{38}N_6O_8S_2 \times 3H_2O$ (M_r = 872.99): C 57.79, H 5.08, N 9.63%; found: C 57.76, H 4.89, N 9.57%.

Bis-hydrogensulphate ***52***

51 (19 mg, 0.02 mmol) and tetrabutylammonium hydrogensulphate (140 mg, 0.4 mmol) in dry CH_3CN (2 × 3 cm^3) gave **52** (15 mg, 86%).

^{1}H-NMR (DMSO-d_6) δ/ppm: 3.13 (s, CH_3, 6H), 4.26 (s, NCH_3, 6H), 4.35 (s, CH_2, 8H), 6.95 (m, NH, 4H), 7.18 (s, Phen-H4, 2H), 7.23 (m, Phen-H2, 2H), 7.35 (s, Phen-H7, 2H), 7.52 (m, Phen-H9, 2H), 8.51 (m, Phen-H1, -H10, 4H).

Anal. Calcd. for $C_{42}H_{38}N_6O_8S_2 \times 3H_2O$ (M_r = 872.99): C 57.79, H 5.08, N 9.63%; found: C 57.63, H 5.11, N 9.55%.

X-ray Structure Determination of ***24*** *and* ***26***

The crystals suitable for X-ray analysis were grown from CH_2Cl_2/$(CH_3)_2CO$ over seven days at 4 °C. Crystal data and experimental details are listed in Table IV. Data were collected on an Enraf-Nonius CAD4 diffractometer with graphite-monochromated Cu-Kα radiation for **24** and Mo-Kα for **26** and rescaled for decay on the basis of the intensity reduction of standard reflections; the maximum reduction was 10.3% for **24** and 0.5% for **26**. Lorentz and polarization corrections were applied using an Enraf-Nonius SDP package.[23] Structures were solved by direct methods using the programme SHELX86[24] and refined by SHELX76[25] with a full-matrix least-squares procedure minimizing $\Sigma w(|F_o| - |F_c|)^2$ on F values. Scattering factors were

TABLE IV

Crystal data and refinement details for **24** and **26**

	24	**26**
Molecular formula	$C_{54}H_{44}N_4O_4$	$C_{56}H_{48}N_4O_4$
M_r	812.97	841.03
Crystal size/mm	0.20 × 0.18 × 0.15	0.30 × 0.25 × 0.15
a/Å	9.072(2)	15.400(5)
b/Å	9.619(2)	11.376(1)
c/Å	26.182(4)	25.392(5)
α/°	86.01(2)	90.0
β/°	86.66(2)	103.52(3)
γ/°	65.28(2)	90.0
V/Å^3	2069.4(8)	4325(2)
Crystal system	triclinic	monoclinic
Space group	$P\bar{1}$	$C2/c$
D_x/g cm^{-3}	1.305	1.292
Z	2	4
μ(Mo-Kα)/cm^{-1}		7.61
μ(Cu-Kα)/cm^{-1}	6.20	
F(000)	856	1776
T/K	295(3)	295(3)
No. of reflections used for cell parameters and θ range/°	25 14–42	24 8–20
θ/° range for intensity measurement	2–74	2–25
hkl range	(–11, 11; –12, 12; 0, 32)	(–18, 18; –13, 0; 0, 29)
Scan	$\omega/2\theta$	$\omega/2\theta$
$\Delta\omega$	0.79 + 0.26 tanθ	0.50 + 0.52 tanθ
No. of measured reflections	8614	3950
No. of symm. independent refl.	4812 $I > 3\ \sigma(I)$	1405 $I > 2\ \sigma(I)$
No. of variables	620	259
R	0.047	0.125
R_w, $w^{-1} = k/(\sigma^2(F_o) + gF_o^2)$	0.050	0.133
Final shift/error	< 0.05	6.886 (C66, x)*
S	0.71	5.26
Residual electron density $(\Delta\rho)_{max}$, $(\Delta\rho)_{min}$/e Å^{-3}	0.21, –0.19	1.14, –0.51

*Atom in disorder

TABLE V

Final atomic coordinates and equivalent isotropic thermal parameters for **24**

Atom	x	y	z	$U_{eq}/Å^{2}$ [a]
O101	0.9761(3)	0.4108(3)	0.40180(8)	0.0764(8)
O102	0.0457(2)	0.8208(2)	0.10378(7)	0.0572(7)
O851	0.8204(3)	0.3500(3)	0.35112(8)	0.0778(8)
O852	0.2191(2)	0.5999(2)	0.14282(7)	0.0540(7)
N51	0.5651(3)	1.2244(3)	0.43754(9)	0.0587(8)
N52	0.4274(3)	1.3338(2)	0.05833(8)	0.0439(7)
N91	0.7054(3)	0.5635(3)	0.39348(8)	0.0520(8)
N92	0.3204(3)	0.7500(2)	0.10034(7)	0.0408(7)
C11	0.8385(4)	1.0169(4)	0.54376(11)	0.0596(11)
C11A	0.7254(3)	0.9171(3)	0.47727(9)	0.0476(9)
C11B	0.7423(3)	1.0394(3)	0.50130(10)	0.0498(9)
C12	0.1409(3)	1.3824(3)	–0.04435(9)	0.0425(9)
C12A	0.2726(3)	1.1625(3)	0.01945(9)	0.0372(8)
C12B	0.2467(3)	1.3110(3)	–0.00384(9)	0.0373(8)
C21	0.8576(4)	1.1369(4)	0.56327(13)	0.0659(11)
C22	0.1135(3)	1.5284(3)	–0.06247(10)	0.0459(9)
C31	0.7826(4)	1.2845(4)	0.54081(13)	0.0667(11)
C32	0.1921(3)	1.6075(3)	–0.04182(10)	0.0480(10)
C41	0.6868(4)	1.3101(4)	0.49962(12)	0.0640(11)
C41A	0.6640(3)	1.1899(3)	0.47933(10)	0.0537(10)
C42	0.2954(3)	1.5408(3)	–0.00264(10)	0.0449(9)
C42A	0.3241(3)	1.3922(3)	0.01749(9)	0.0398(8)
C61	0.5477(3)	1.1141(3)	0.41597(10)	0.0533(10)
C61A	0.6308(3)	0.9536(3)	0.43331(10)	0.0478(9)
C62	0.4503(3)	1.2001(3)	0.07967(9)	0.0421(9)
C62A	0.3724(3)	1.1075(3)	0.06224(9)	0.0382(8)
C71	0.6235(3)	0.8343(3)	0.40657(10)	0.0501(10)
C72	0.3888(3)	0.9689(3)	0.08801(10)	0.0411(8)
C81	0.7075(3)	0.6837(3)	0.42247(10)	0.0488(9)
C82	0.3080(3)	0.8876(3)	0.07238(9)	0.0391(8)
C91	0.7947(3)	0.6480(3)	0.46780(10)	0.0535(10)
C92	0.2147(3)	0.9387(3)	0.02861(10)	0.0437(9)
C101	0.8018(3)	0.7618(3)	0.49426(11)	0.0533(10)
C102	0.1979(3)	1.0723(3)	0.00259(10)	0.0427(9)
C151	1.0634(3)	0.04172(19)	0.26570(8)	0.0873(16)
C152	–0.1100(2)	0.7058(3)	0.23618(9)	0.0808(16)
C251	1.0786(3)	0.01361(19)	0.21367(8)	0.0988(17)
C252	–0.1437(2)	0.7448(3)	0.28722(9)	0.1012(19)
C351	0.9993(3)	0.13264(19)	0.17790(8)	0.0876(16)
C352	–0.0179(2)	0.6974(3)	0.32157(9)	0.0972(19)
C451	0.9047(3)	0.27977(19)	0.19416(8)	0.0803(16)
C452	0.1416(2)	0.6110(3)	0.30488(9)	0.0885(16)
C551	0.8895(3)	0.30788(19)	0.24619(8)	0.0738(12)

TABLE V

(continued)

Atom	*x*	*y*	*z*	U_{eq}/Å^2 [a]
C552	0.1753(2)	0.5720(3)	0.25384(9)	0.0703(11)
C611	0.4435(4)	1.1586(4)	0.36997(12)	0.0625(11)
C612	0.5567(4)	1.1471(4)	0.12559(11)	0.0523(10)
C621	0.5432(4)	1.1533(4)	0.32039(10)	0.0656(11)
C622	0.4571(4)	1.1712(4)	0.17592(11)	0.0673(11)
C631	0.4557(4)	1.1551(4)	0.27268(12)	0.0643(11)
C632	0.5522(4)	1.1515(4)	0.22322(11)	0.0667(11)
C651	0.9688(3)	0.18885(19)	0.28196(8)	0.0652(11)
C652	0.0495(2)	0.6194(3)	0.21949(9)	0.0519(10)
C751	0.9584(6)	0.2117(4)	0.33788(14)	0.1170(19)
C752	0.0825(4)	0.5723(4)	0.16554(11)	0.0607(11)
C901	0.8472(4)	0.4377(3)	0.38357(11)	0.0597(10)
C902	0.1814(3)	0.7322(3)	0.11479(9)	0.0440(9)
C931	0.5535(4)	0.5808(4)	0.37137(11)	0.0571(11)
C932	0.4783(3)	0.6408(3)	0.11902(10)	0.0457(9)
C941	0.5401(3)	0.6200(3)	0.31621(11)	0.0570(11)
C942	0.4985(3)	0.6513(3)	0.17342(11)	0.0485(9)
C951	0.5250(3)	0.6421(3)	0.27117(11)	0.0572(11)
C952	0.5125(3)	0.6525(3)	0.21801(11)	0.0538(10)

[a] $U_{eq} = 1/3\ \Sigma_i\ \Sigma_j\ \boldsymbol{U}_{ij}\ a_i^* a_j^* \boldsymbol{a_i}\ \boldsymbol{a_j}$

those included in SHELX76.[25] The hydrogen atoms were calculated on stereochemical grounds and refined riding on their respective C atoms with an overall temperature factor for the chemically analogous groups, *e.g.* methyl, phenanthridine, phenyl. Only for those clearly resolved in the difference Fourier maps, the experimental values were used. The phenyl rings of benzyloxycarbonyl groups were treated as geometrically ideal groups during the refinement. In the structure of **26**, a disorder of four methylene groups was observed; each carbon atom (C62 and C66, C63 and C67) was treated with a population parameter of 0.5. Molecular geometry was calculated by the programme package EUCLID.[26] Drawings were prepared by ORTEP II.[21] The final atomic coordinates and equivalent isotropic thermal parameters are listed in Tables V and VI. Calculations were performed on Micro-VAXII and INDIGO2 computers of the X-ray laboratory, Ruđer Bošković Institute, Zagreb, Croatia.

Molecular Modeling

Molecular modeling studies were conducted using the Sybyl software (Version 6.2, Tripos force field) running on a Silicon Graphics Indy workstation. The molecule was built using its X-ray structure of **24** and modified by removal of N-protecting groups. Simulated annealing was used as a type of molecular dynamics experiment. The number of cycles to run was 20, the initial temperature for annealing was 700 K. The system was kept at this temperature for 1000 fs. Then the temperature was re-

TABLE VI

Final atomic coordinates and equivalent isotropic thermal parameters for **26**

Atom	*x*	*y*	*z*	U_{eq}/Å^{2} [a]
O10	0.0053(7)	0.4958(9)	0.4154(4)	0.082(4)
O85	0.1072(6)	0.4564(7)	0.3676(4)	0.072(4)
N5	–0.1917(9)	–0.0831(11)	0.4477(5)	0.091(6)
N9	0.0550(6)	0.3098(10)	0.4076(4)	0.053(4)
C1	–0.2087(12)	0.1149(14)	0.5593(7)	0.107(8)
C2	–0.2666(12)	0.0539(16)	0.5824(7)	0.103(8)
C3	–0.3003(10)	–0.0541(15)	0.5597(6)	0.072(7)
C4	–0.2758(9)	–0.0955(13)	0.5141(5)	0.064(6)
C4A	–0.2155(9)	–0.0347(12)	0.4924(5)	0.054(5)
C6	–0.13636	–0.02972	0.42557	0.109(8)
C6A	–0.1002(10)	0.0836(12)	0.4422(5)	0.063(5)
C7	–0.0452(9)	0.1449(14)	0.4163(5)	0.070(6)
C8	–0.0051(9)	0.2516(11)	0.4353(5)	0.051(5)
C9	–0.0255(9)	0.3023(13)	0.4795(5)	0.072(6)
C10	–0.0811(10)	0.2460(13)	0.5068(6)	0.081(7)
C11A	–0.1199(8)	0.1363(12)	0.4885(5)	0.057(5)
C11B	–0.1802(9)	0.0716(13)	0.5143(5)	0.057(5)
C15	0.2238(6)	0.6744(9)	0.3118(5)	0.094(8)
C25	0.2621(6)	0.6888(9)	0.2676(5)	0.131(10)
C35	0.2326(6)	0.6208(9)	0.2211(5)	0.132(11)
C45	0.1648(6)	0.5384(9)	0.2189(5)	0.106(8)
C55	0.1264(6)	0.5240(9)	0.2631(5)	0.098(7)
C61	–0.11228	–0.08497	0.37726	0.200(11)
C62*	–0.0428(11)	–0.134(2)	0.3756(12)	0.083(9)
C63*	–0.023(5)	–0.109(7)	0.3283(14)	0.37(4)
C64	0.00181	–0.12919	0.28205	0.182(10)
C65	0.1559(6)	0.5920(9)	0.3095(5)	0.082(7)
C66*	–0.103(3)	–0.097(4)	0.3315(7)	0.147(15)
C67*	–0.0702(12)	–0.119(3)	0.2934(11)	0.108(11)
C75	0.1142(12)	0.5813(12)	0.3569(7)	0.098(8)
C90	0.0500(9)	0.4283(13)	0.3992(5)	0.056(6)
C93	0.1105(9)	0.2362(12)	0.3811(5)	0.061(6)
C94	0.0648(9)	0.2213(11)	0.3241(7)	0.060(6)
C95	0.0233(10)	0.2166(13)	0.2765(6)	0.065(6)

*Atoms with population parameter 0.5.

[a] $U_{eq} = 1/3\ \Sigma_i\ \Sigma_j\ \boldsymbol{U}_{ij}\ a_i{}^{*}a_j{}^{*}\boldsymbol{a_i}\ \boldsymbol{a_j}$

duced during 1000 fs until 50 K was reached. The annealing function (temperature *vs* time) was exponential. Two resulting *syn*-conformations were selected from 20 low energy conformations. Selected conformers were used as the starting points for energy minimizations setting the convergence criteria RMS displacement 0.001 kcal/mol Å and using 1000 steps of Powel minimization until the energy gradient of 0.05 kcal/mol Å was reached. Atomic partial charges were computed by the Gasteiger-Hückel method.

Supplementary Materials. – List of structure factors, anisotropic displacement parameters, H-atom coordinates, have been desposited with IUCr.
Copies can be obtained through the Managing Editor, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, UK.

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SAŽETAK

Sinteza ciklo-bis-interkalandnih receptorskih molekula s fenantridinijevim jedinicama

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Sintetizirani su makrociklički ciklo-bis-interkalandni molekulski receptori s fenantridinijevim jedinicama i proučena su njihova spektroskopska svojstva (NMR, UV i fluorescencija). Određene su molekulske strukture dvaju makrocikličkih bis-fenantridinskih prekursora metodom rentgenske strukturne analize.