Pergamon

Tetrahedron Vol. 50, No. 26, pp. 7815-7826, 1994

0040-4020/94 $7.00+0.00

0040-4020(94)00371-8

Synthesis and Structural Features of New [5,7] Orthocyclophanes, [7,7] Cyclophanes and Corresponding Macrobicyclic Cryptophanes.

Patrick Bauchat [a], Nathalie Le Bras [a], Luc Rigal [b], André Foucaud* [a]

[a] *Groupe de Chimie Structurale associé au CNRS, Université de Rennes, 35042 Rennes, France.*
[b] *Laboratoire de Chimie Agro-industrielle, Ecole Nationale Supérieure de Chimie, 118, Route de Narbonne, 31077 Toulouse, France.*

Abstract - The Baylis-Hillman reaction of dialdehydes with methyl acrylate, followed by acetylation of the resulting diols gave diacetates **3**, **14**, **16** and **20**. Treated with ammonia, these diacetates afforded new cyclophanes and the corresponding macrobicyclic cryptophanes. Conformational analysis of the cyclophanes was described.

Introduction

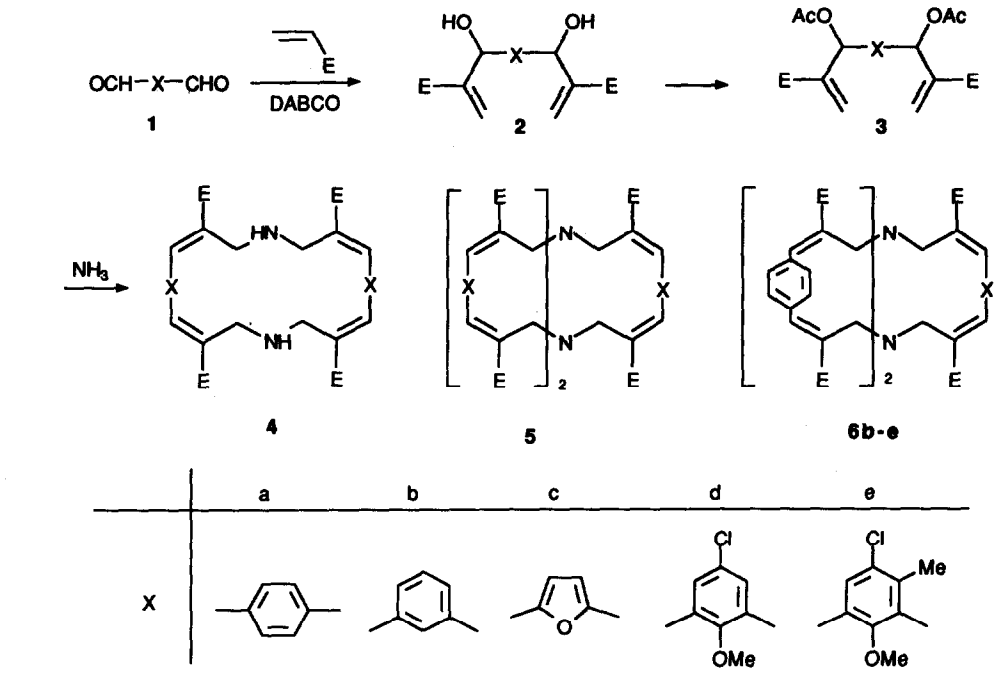
Much interest currently attaches to the synthesis and structural study of cyclophane molecules [1]. Cyclophanes with large cavities are well known [2,3], but the synthesis of macrobicyclic compounds presents a considerable challenge to the chemist. We report here a new synthesis and the conformational behavior of the [7,7] cyclophanes and the corresponding macrobicyclic cryptophanes and of the [5,7] orthocyclophanes.

Results and discussion

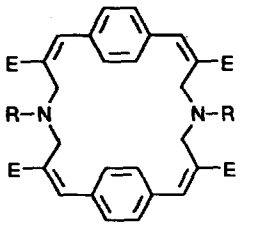
The strategy for the synthesis of cyclophanes is based on the Baylis-Hillman reaction [4,5]. Dialdehydes **1** were reacted with methyl acrylate in the presence of diazabicyclooctane (DABCO) or 3-quinuclidinol for 1-14 days, at room temperature to give one diastereomer **2**. Acetylation (AcCl-NEt_3) of the alcohols **2** afforded allylic acetates **3**. Treated with a solution of ammonia in methanol, the acetates **3** were submitted to a nucleophilic substitution with allylic rearrangement to give the cyclophanes **4**, the cryptophanes **5** and polymeric material. Compounds **4** and **5** were purified by crystallisation or by chromatography on silica gel (scheme 1).

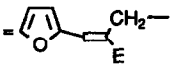
Thus, the acetate **3a** was converted to cyclophane **4a** (28 %). Treatment of **4a** with **3a**, in acetonitrile at high dilution at reflux temperature, afforded cryptophane **5a** in 95 % yield [6]. The high dilution reactions of **3b** and **3c** with ammonia gave the corresponding cryptophanes **5b** (15 %) and **5c** (23 %). The slow addition of ammonia into a dilute solution of **3d** in dichloromethane afforded the cyclophane **4d** (6 %) and the cryptophane **5d** (30 %), which can be separated by chromatography on silica gel. Spectral data support the structures **4** and **5**. The E configuration of the carbon-carbon double bond was confirmed by ^1H NMR spectra : the signal of the vinylic proton, deshielded by the neighbouring cis carbonyl group, was at δ 7.5-8.0 ppm, according to the literature [7]. The long range ^{13}C-H coupling constant between carbon of the carbonyl group and vinylic proton were about 5 Hz, according to the E-configuration [8]. The dissymetric cryptophanes **6b-6e** were prepared in 40-50 % yields by the reaction of cyclophane **4a** with the corresponding acetates **3b-3e** in acetonitrile at reflux temperature.

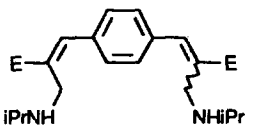
Scheme 1



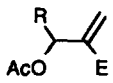
N-substituted paracyclophanes **7**, **8** and **9** can be prepared. The treatment of **3a** with isopropylamine, at room temperature, gave a mixture of **10EE** and **10EZ** in a ratio of 16:9. When the isomer **10EE**, purified by crystallization, was reacted with **3a**, in acetonitrile, the paracyclophane **7** was obtained in a yield of 50 %. When **4a** was reacted with acetate **11a** [9], the cyclophane **9** was obtained. The paracyclophane **8** was easily prepared by reaction of phenylisocyanate with **4a**.



7, R = iPr
8, R = PhNHCO
9, R = 



10 EE, EZ

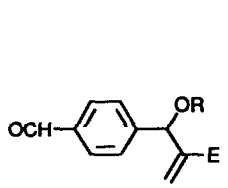


11a, R =
11b, R = Ph

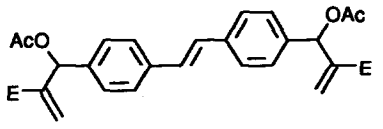
The syntheses of cyclophanes larger than **4** have been achieved by using acetate **13** as starting material. The reaction of terephthalaldehyde **1a** with methyl acrylate in the presence of DABCO for 90 min afforded essentially **12**. Acetylation of **12** using AcCl-NEt_3 gave the desired allylic acetate **13**. The reductive

coupling of **13** using $TiCl_4$-Zn in THF, at reflux temperature [10,11], gave **14E**. When the diacetate **14E**, in THF-methanol, was treated by an aqueous solution of ammonia, the paracyclophane **15** precipitated (13 %) (scheme 2).

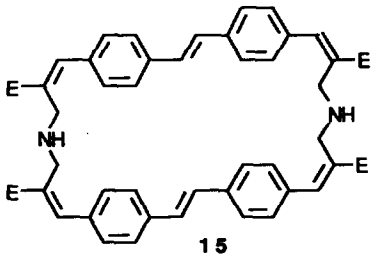
Scheme 2



12 R = H
13 , R = Ac



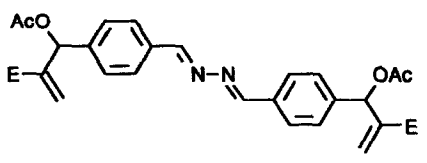
14



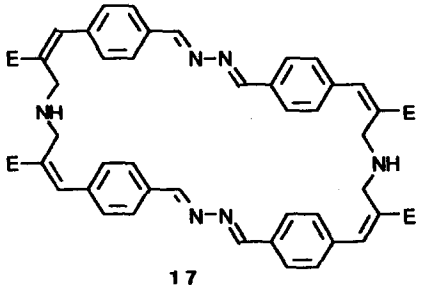
15

The treatment of **13** with hydrazine hydrate at room temperature gave the azine **16EE** (80 %). The reaction of **16** in THF with ammonia afforded the paracyclophane **17** as crystalline product (25 %) (scheme 3).

Scheme 3



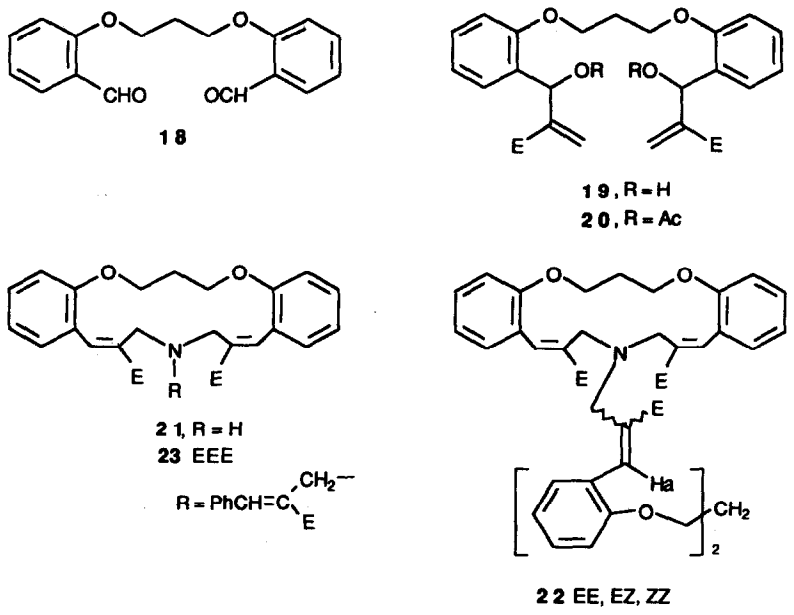
16



17

The dialdehyde **18** was formed by alkylation of 2-hydroxybenzaldehyde with 1,3-dibromopropane. Then, the dialdehyde **18** was reacted with methylacrylate and DABCO and the resulting diol **19** was acetylated to yield the allylic diacetate **20**. The high dilution reaction of **20** with ammonia gave a mixture of ortho cyclophanes **21** (14 %) and **22** (45 %) separated by column chromatography. ^1H NMR, ^{13}C NMR and mass spectra data are in conformity with the structures shown. ^1H NMR spectrum of **21** showed the signal of the vinylic protons at δ 7.72 according to the E-configuration of the carbon-carbon double bonds. ^1H NMR spectrum of **22** showed the presence of a EE/EZ/ZZ mixture. The Ha signals are at δ 7.75 for **22** EE, δ 6.82 for **22** ZZ and δ 7.00, δ 7.71 for **22** EZ. The formation of **22** can result from the reaction of the nucleophilic cyclophane **21** with the diacetate **20**. Indeed, when pure **21** was reacted with **20** in acetonitrile at reflux temperature, cyclophanes **22** were formed (scheme 4).

Scheme 4



18

19, R = H
20, R = Ac

21, R = H
23 EEE

R = PhCH=C(E)-CH$_2$-

22 EE, EZ, ZZ

The reaction of **21** with **13b** [9] afforded the ortho cyclophane **23** EEE.

Conformational analysis of cyclophanes

At room temperature, the magnetic equivalence of the aromatic protons of **4a** was observed, which suggests a free rotation about the axis passing through the 1,4-carbon atoms of the ring. Protonation at nitrogen atoms, with CF_3CO_2H in excess, leads to upfield shift of signal of aromatic protons (table I). It is postulated that the repulsion of positive nitrogen atoms is the cause of the conformational preference of the two aromatic rings, facing each other, which explains the shielding of the aromatic protons (**4a**, $2H^+$, scheme 5). The aromatic protons of **4a** are deshielded, probably on account of the conformational preference of the aromatic rings which are in the same plane.

The addition of one equivalent of maleic acid to cyclophane **4a** gave a crystalline salt. The ^1H NMR spectra of the salt shows that the aromatic protons have lost their magnetic equivalence (broad signal, δ 7.24 - 7.92). This salt probably adopts the conformation A (fig. 1), where the maleic anion is located between the benzene ring. However, the magnetic equivalence of the aromatic protons (δ 7.22) of the salt prepared by addition of two equivalents of maleic acid to **4a** is preserved (conformation B). The shielding of the aromatic protons of **4d** and the N-substituted paracyclophanes **7** and **9** suggests a conformational preference for the two benzene rings similar to that of (**4a**, $2H^+$) (scheme 5). The steric interactions between the nitrogen substituants and the macrocycle can explain this result. The protonation of **7** or **9** (table I) causes weak modifications of the chemical shift of the aromatic protons, and their magnetic equivalence is preserved. The structure of **5a** should be sufficiently rigid to avoid conformational modifications by protonation (scheme 5).

Three sets of signals are observed in the ^1H NMR and ^{13}C NMR spectra of cyclophane **6d** for NCH_2 groups and for ester groups, indicating the lack of free rotation of the substituted benzene ring ClC_6H_2OMe, the free rotation of the C_6H_4 groups being preserved. Likewise, ^1H NMR and ^{13}C NMR spectra

for **6e** exhibited 6 sets of peaks for esters groups and for NCH_2 groups. The free rotation of the aromatic groups of **5d** is impossible. However, the magnetic equivalence of the three OCH_3 methyl protons in the ^1H NMR spectrum suggests a conformation with a three fold rotation axis passing through the nitrogen atoms (scheme 5). The NCH_2 methylene protons of **4d, 5d, 5e, 6b, 6d** and **6e** gave AB systems in the ^1H NMR spectra at room temperature.

Scheme 5 - Aromatic ring positions of **4a**, (**4a**, $2H^+$), **4d, 5a, 5d, 6d, 7** and **9**, the molecules are viewed along the N,N axis.

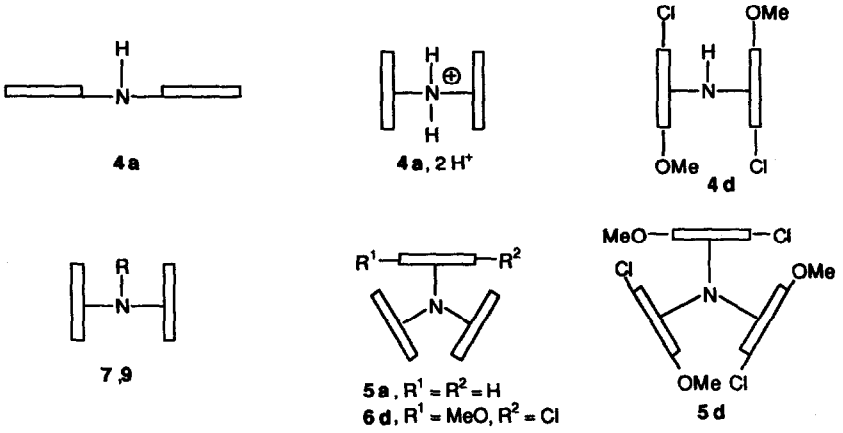


Table I - Shifts of ^1H NMR signals of **4a, 5a, 7, 9** and their protonated forms.

Atom	4a	(4a,2H+)	(4a,maleic acid)	7	(7,2H+)	9	(9,2H+)	5a
H arom.	7.83 s	7.08 s	7.50 br	7.12 s	7.34 s	7.32 s	7.34 s	6.97 s
H vinyl.	7.83 s	8.07 s	7.85 s	7.53 s	8.14 s	7.72 s [a]	7.76 s [a]	7.75 s
CH_2	3.62 s	4.15 m	3.87 m	3.29 s	4.35 AB	3.50 s [a]	4.30 m [a]	2.90 s

[a] cyclophane ring.

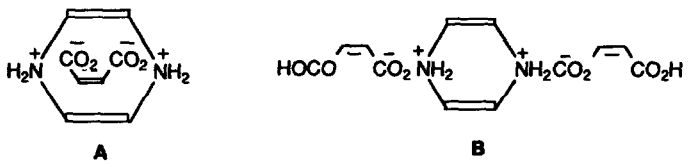


Figure 1 - Aromatic ring positions of **4a** - maleic acid salts.

It is known that cyclophanes can form π-complexes with soft metal ions as silver (I) [17]. In order to know if **5** are suitable to give complexes, we have examined the behaviour of the cryptophane **5a** in the presence of silver ion. Slow evaporation of a solution of **5a** and 1 equiv of silver triflate in chloroform-tetrahydrofurane gave a solid of mp = 260°C. The ^1H NMR spectrum of the solid showed downfield shifting of all signals from **5a**, especially those from aromatic and CH_2 protons. The signal of aromatic protons is

broad, which suggests a impeded rotation about the axis passing through the 1,4-carbon atoms of the rings (table II). These results suggest the formation of a complex **5a** - silver triflate.

Table II - ^{1}H NMR chemical shifts of **5a** - silver triflate complex and magnitudes of shifting relative to **5a**.

	-CH=	C_6H_4	CO_2Me	CH_2
5a/Ag^+ δ	7.96 s	7.83 br s	3.86 s	3.84 s
Δδ	+0.21	+0.86	+0.10	+0.94
4a/Ag^+ δ	7.85 s	7.13 s	3.90 s	3.88 m
Δδ	+0.01	-0.70	+0.03	+0.21

However, under the same conditions, no complexation was detected with the cryptophanes **5b** and **5c**. Indeed mixing equivalent amounts of **5b** or **5c** with silver triflate in $CDCl_3$ gave the same weak downfield shifting of all signals ($\Delta\delta \leq 0.1$ ppm) in the ^{1}H NMR spectra. With silver triflate, **4a** gave a high field shifting of aromatic protons ($\Delta\delta$ = -0.7 ppm), which suggests similar conformations for (**4a**, $AgSO_3CF_3$) and (**4a** , $2H^+$).

In conclusion, the Baylis Hillman reaction with dicarboxaldehydes followed by acetylation of the resulting dialcohols, gave diacetates. These compounds can lead to a series of cyclophanes by the reaction with ammonia or amines. Some of these cyclophanes are conformationally mobile.

Experimental

^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ with tetramethylsilane as internal reference on Bruker AC 300 spectrometer, at 300 MHz and 75 MHz respectively. Mass spectra were recorded under electron impact at 70 eV on a Varian MAT 311 instrument of the Centre de Mesures Physiques (Rennes) or under fast atom bombardement (FAB) on a JEOL JMS JX 102 spectrometer using a sample dissolved in a glycerol matrix. IR spectra were recorded using a Perkin Elmer 1420 spectrometer. Melting points were measured using a Kofler melting temperature apparatus and are uncorrected. Elemental analysis results were obtained from the Laboratoire Central de Microanalyse du CNRS.

Preparation of starting materials. 5-chloro-2-hydroxy-4-methyl-1,3-benzene dicarbox-aldehyde was prepared from 4-chloro 2-methylphenol by the literature method [12]. Dialdehyde **18** was prepared from 2-hydroxybenzaldehyde and 1,3-dibromopropane by a procedure similar to that used to prepare 4,4'-ethylenedioxy dibenzaldéhyde [13].

Dialdehydes 1d and 1e. Typical procedure. To a solution of 5-chloro-2-hydroxy-1,3-benzene dicarboxaldehyde or 5-chloro-2-hydroxy-4-methyl-1,3-benzene dicarboxaldehyde (10 mmol) and dimethylsulfate (30 mmol) in CH_2Cl_2 (30 mL) were added 1N sodium hydroxide (30 ml) and adogen 464 (0.25 g). The mixture was stirred at rt for 72 h. The organic phase was separated, washed successively with 1N ammonia, water and dried with magnesium sulfate. Removal of the solvent left dialdehyde.

5-chloro-2-methoxy-1,3-benzenedicarboxaldehyde **1d**, 86 %, mp 120°C (cyclohexane). ^{1} H NMR δ 4.11 (s, 3H), 8.01 (s, 2H), 10.35 (s, 2H).

5-chloro-4-methyl-2-methoxy-1,3-benzenedicarboxaldehyde **1e**, 88 %, mp 106°C (cyclohexane). ^{1}H NMR δ 2.65 (s, 3H), 4.01 (s, 3H), 8.00 (s, 1H), 10.29 (s, 1H), 10.51 (s, 1H).

Allylic alcohols **2**, **12** and **19** were prepared from corresponding dialdehydes and methylacrylate, according to literature procedure [4,9,14,15].

General procedure for the preparation of esters 2, 12 and 19. A mixture of dialdehyde (10 mmol), methylacrylate (2.58 g, 30 mmol) and DABCO (0.34 g, 3 mmol) or 3-quinuclidinol (0.38 g, 3 mmol) was kept at room temperature over a period indicated for each compound. Ethyl ether (80 mL) was added to the reaction mixture. The solution was washed with 1N aqueous hydrochloric acid solution (40 mL) and three times with water (40 mL), dried over sodium sulfate and concentrated in vacuum.

2a. Reaction time 14 days. Catalyseur DABCO. 95 %. mp 101°C (ether). ^{1}H NMR δ 3.55 (s, 2H), 3.62 (s, 6H), 5.45 (s, 2H), 5.82 (s, 2H), 6.25 (s, 2H), 7.27 (s, 4H). ^{13}C NMR δ 51.92 ; 72.62 ; 125.86 ; 126.79 ; 141.02 ; 142.06 ; 166.71. Anal. calcd for $C_{16}H_{18}O_6$ C, 62.74 ; H, 5.92. Found : C, 62.64 ; H, 5.87.

2b. Reaction time 6 days. Catalyseur DABCO. 87 %, mp 95°C (ether). ^{1}H NMR δ 3.37 (s, 2H), 3.61 (s, 6H), 5.45 (s, 2H), 5.79 (s, 2H), 6.25 (s, 2H), 7.26 (m, 4H). Anal. calcd for $C_{16}H_{18}O_6$ C, 62.74 ; H, 5.92. Found : C, 62.69 ; H, 5.90.

2c. Prepared from 2,5-furandicarboxaldehyde [16]. Reaction time 24 h in the dark and under nitrogen. 57 % ; oil purified by flash chromatography (silica gel, ether/petroleum ether 3 : 2). ^{1}H NMR δ 3.40 (s, 2H), 3.69 (s, 6H), 5.52 (s, 2H), 5.92 (s, 2H), 6.11 (s, 2H), 6.34 (s, 2H). Anal. calcd for $C_{14}H_{16}O_7$ C, 56.76 ; H, 5.40. Found : C, 56.81 ; H, 5.30.

2d. Reaction time 12 days. Catalyseur 3-quinuclidinol. 86 %. Oil purified by flash chromatography (silica gel, ether/petroleum ether 3 : 2). ^{1}H NMR δ 3.55 (br s, 2H), 3.70 (s, 6H), 3.85 (s, 3H), 5.87 (s, 2H), 5.90 (s, 2H), 6.39 (s, 2H), 7.27 (s, 2H).

2e. Reaction time 22 days. Catalyseur 3-quinuclidinol. 10 %. Oil purified by flash chromatography (silica gel, ether/petroleum ether 3 : 2). ^{1}H NMR δ 2.36 (s, 3H), 3.52 (br s, 2H), 3.71 (s, 3H), 3.76 (s, 3H), 5.51 (s, 1H), 5.81 (s, 1H), 5.84 (s, 1H), 6.06 (s, 1H), 6.24 (s, 1H), 6.36 (s, 1H), 7.34 (s, 1H).

12. Reaction time 90 min. Catalyseur DABCO. 86 %. Oil, bp 130-132°C (0.02 mm Hg). ^{1}H NMR δ 3.69 (s, 3H), 3.72 (br s, 1H), 5.61 (s, 1H), 5.90 (s, 1H), 6.35 (s, 1H), 7.5 - 7.8 (m, 4H), 9.92 (s, 1H).

19. Reaction time 21 days. Catalyseur 3-quinuclidinol. 94 %. Oil purified by flash chromatography (silica gel, ether/petroleum ether 3 : 2). ^{1}H NMR δ 2.20 (m, 2H), 3.50 (br s, 2H), 3.60 (s, 6H), 4.10 (t, 4H, J = 6 Hz), 5.65 (s, 2H), 5.87 (s, 2H), 6.17 (s, 2H), 6.90 (t, 4H, J = 8 Hz), 7.10 - 7.40 (m, 4H).

General procedure for the preparation of acetates 3a-e, 13 and 20. To a stirred solution of esters **2**, **12** or **19** (10 mmol) and triethylamine (1.5 g, 15 mmol) in anhydrous THF (50 mL) under nitrogen at 0°C was added dropwise a solution of 3 equivalents (for **2a**, **2b**) or 5 equivalents (for **2c-e**, **19**) of acetylchloride in anhydrous diethylether (25 mL). The reaction mixture was stirred 5 h at room temperature, then filtered. The organic solution was concentrated under reduced pressure. The residue was dissolved in diethylether (40 mL). This solution was washed three times with water (15 mL) dried (Na_2SO_4). The solvent was removed at reduced pressure. The acetates were purified by crystallization or by flash chromatography.

3a, 97 %, mp 134-135°C (diethylether). ^{1}H NMR δ 2.07 (s, 6H), 3.67 (s, 6H), 5.85 (s, 2H), 6.37 (s, 2H), 6.67 (s, 2H), 7.32 (s, 4H). Anal. calcd for $C_{20}H_{22}O_8$ C, 61.53 ; H, 5.68. Found : C, 61.62 ; H, 5.55.

3b, purified by chromatography (silica gel, ether/petroleum ether 1 : 1), 97 %, oil. ^{1}H NMR δ 2.06 (s, 6H), 3.66 (s, 6H), 5.82 (s, 2H), 6.36 (s, 2H), 6.55 (s, 2H), 7.32 (m, 4H). Anal. calcd for $C_{20}H_{22}O_8$ C, 61.53 ; H, 5.68. Found : C, 61.49 ; H, 5.91.

3c, purified by chromatography (silica gel, ether/petroleum ether 3 : 2), 32 %, mp 111°C (diethyl ether). ^{1}H NMR δ 2.07 (s, 6H), 3.68 (s, 6H), 5.92 (s, 2H), 6.24 (s, 2H), 6.42 (s, 2H), 6.67 (s, 2H). Anal. calcd for $C_{18}H_{20}O_9$ C, 56.85 ; H, 5.27. Found : C, 56.91 ; H, 5.38.

3d, purified by chromatography (silica gel, ether/petroleum ether 3 : 2), 25 %, oil. ^{1}H NMR δ 2.09 (s, 6H), 3.72 (s, 6H), 3.91 (s, 3H), 5.66 (d, J = 4 Hz, 2H), 6.42 (d, J = 3.2 Hz, 2H), 6.98 (s, 2H), 7.26 (s, 2H).

3e, purified by chromatography (silica gel, ether/petroleum ether 3 : 1), 30 %, oil. ^{1}H NMR δ 2.07 (s, 6H), 2.39 (s, 3H), 3.71 (s, 6H), 3.81 (s, 3H), 5.39 (d, 1H, J = 2.4 Hz), 5.48 (d, 1H, J = 3 Hz), 6.59 (d, 1H, J = 2.4 Hz), 6.31 (d, 1H, J = 3 Hz), 6.40 (s, 1H), 6.94 (s, 1H), 7.28 (s, 1H).

13, 80 %, bp 130-135°C (0.02 mm Hg). ^{1}H NMR δ 2.12 (s, 3H), 3.65 (s, 3H), 5.92 (s, 1H), 6.42 (s, 1H), 6.71 (s, 1H), 7.85 - 7.55 (m, 4H), 9.97 (s, 1H).

20, 90 %, oil purified by chromatography (silica ge., ether/petroleum ether 3 : 2). ^{1}H NMR δ 1.91 (s, 6H), 2.20 (m, 2H), 3.55 (s, 6H), 4.11 (t, 4H, J = 5.6 Hz), 5.58 (s, 2H), 6.28 (s, 2H), 6.86 (m, 2H), 6.95 (s, 2H), 7.16 (m, 4H), 7.26 (m, 2H).

(E)-di-p [2-methoxycarbonyl-1-acetylprop-2-enyl] stilbene 14. To a stirred solution of aldehyde **13** (0.79 g, 3 mmol) and $TiCl_4$ (0.86 g, 4.5 mmol) in THF (20 mL) at -10°C, under nitrogen, was added a suspension of zinc powder (0.59 g, 9 mmol) in THF (10 ml). After reflux for 4 h, the reaction mixture was poured in 0.1 M aqueous sodium carbonate solution (30 mL). The mixture was extracted with diethyl ether (100 mL). The organic phase was washed with 0.1 M aqueous sodium carbonate solution and two times with water. The solvent was removed and the residue was dissolved in diethyl ether. The organic phase was dried (Na_2SO_4) and evaporated. The residue was purified by chromatography (silica gel, ether/petroleum ether 1 : 1) to afford the diester **14** (86 %), mp 110-111°C. ^{1}H NMR δ 2.07 (s, 6H), 3.69 (s, 6H), 5.87 (m, 2H), 6.39 (m, 2H), 6.66 (m, 2H), 7.05 (s, 2H), 7.46-7.32 (m, 8H). Anal. calcd for $C_{28}H_{28}O_8$ C, 68.29 ; H, 5.29. Found : C, 68.20 ; H, 5.60.

1,4-di [p(2'-methoxycarbonyl-1'-acetylprop-2'-enyl) phenyl]-2,3-diazabutadiene 16. To a stirred solution of aldehyde **13** (1.31 g, 5 mmol) in diethyl ether (10 mL) was added hydrazine monohydrate (0.125 g, 2.5 mmol). After 1 h 30 stirring at room temperature, the solution was washed with water (2 x 10 mL), dried (Na_2SO_4) and concentrated in vacuo. Azine **16** was purified by chromatography (silica gel, ether/petroleum ether 9 : 1) ; oil, 80 %. ^{1}H NMR δ 2.09 (s, 6H), 3.67 (s, 6H), 5.89 (m, 2H), 6.40 (m, 2H), 6.70 (m, 2H), 7.8 - 7.45 (m, 8H), 8.59 (s, 2H).

Diamine 10. To a solution of diester **2a** (1 g, 3.2 mmol) in THF (25 mL) was added isopropylamine (0.74 g, 12.5 mmol). The mixture was stirred for 3 h. The solvent was removed under vacuum and the residue was dissolved in ether (50 mL). The organic phase was dried ($MgSO_4$), then concentrated. Diamine **10** EE crystallized from ether.

1,4-di (3'-isopropylamino-2'-methoxycarbonylprop-1'-enyl) benzene 10 EE. 59 %, mp 95°C (EtOAc). ^{1}H NMR δ 1.04 (d, 12H, J = 6.4 Hz), 1.71 (br s, 2H), 2.82 (m, 2H), 3.56 (s, 4H), 3.80 (s, 6H), 7.56 (s, 4H), 7.76 (s, 2H). MS HR calcd for $C_{22}H_{32}N_2O_4$ (M^+) 388.2361, found 388.2357.

10EZ oil not purified, 33 %. ^{1}H NMR δ 1.02 (d, 6H, J = 6.4 Hz), 1.05 (d, 6H, J = 6.4 Hz), 1.66 (br s, 2H), 2.82 (m, 2H), 3.56 (br s, 4H), 3.65 (s, 3H), 3.80 (s, 3H), 6.82 (s, 1H), 7.25 - 7.50 (m, 4H), 7.74 (s, 1H).

Reaction of ammonia with diacetates 3, 14, 16

Tetramethyl 5,16-diazatricyclo [18.2.2.2^{9,12}] hexacosa-2,7,9,11,13,18,20,22,23,25-decaene-3,7,14,18-tetracarboxylate 4a. To a solution of diacetate **3a** (0.76 g, 2.5 mmol) in THF (5 mL) and MeOH (10 mL) was added dropwise a 8M ammonia solution in MeOH (20 mL) over a period of 40 min. The paracyclophane **4a** that precipitated was filtered : 28 %, mp 260°C (CH_2Cl_2). ^{1}H NMR δ 2.05 (s, 2H), 3.67 (s, 8H), 3.87 (s, 12H), 7.83 (s, 8H), 7.84 (s, 4H). ^{13}C NMR δ 40.03, 52.23, 130.18, 130.51, 136.00, 141.54, 168.30. MSHR calcd for $C_{32}H_{34}N_2O_8$ (M^+) 574.2315, found : 574.2318. Anal. calcd for $C_{32}H_{34}N_2O_8$ C, 66.89 ; H, 5.92 ; N, 4.87. Found : C, 66.86 ; H, 6.10 ; N, 5.06.

Hexamethyl 1,12-diazapentacyclo [10.10.10.2^{5,8}.2^{16,19}.2^{26,29}] octatriaconta 3,5,7,33(34),9,14,16,18,37(38),20,24,26,28,35(36),30-pentadecaene-3,10,14,21,24,31-hexa-carboxylate 5a. To a suspension of **4a** (0.8 g, 1.4 mmol) in acetonitrile (200 mL) was added **3a** (0.4 g, 1.4 mmol) and NEt_3 (0.27 g, 2.7 mmol). The mixture was stirred at reflux for 90 h. After being cooled to room temperature, **5a** was filtered : 95 %, mp 265°C ($CHCl_3$). ^{1}H NMR δ 2.90 (s, 12H), 3.76 (s, 18H), 6.97 (s, 12H), 7.75 (s, 6H). ^{13}C NMR δ 50.43, 51.89, 128.79, 133.02, 135.72, 141.22, 168.90. MSHR

calcd for $C_{48}H_{48}N_2O_{12}$ (M^+) 844.3207. Found 844.3182. Anal. calcd for $C_{48}H_{48}N_2O_{12}$ C, 68.23 ; H, 5.73 ; N, 3.32. Found : C, 68.35 ; H, 5.50 ; N, 3.12.

General procedure for the preparation of 5b-d. To a solution of diacetate **3** (2.5 mmol) in CH_2Cl_2 (100 mL) was added dropwise a 0.26 M ammonia solution in MeOH (60 mL). The mixture was stirred at room temperature for 24 h. The solvent was removed and the residue was dissolved in CH_2Cl_2 (60 mL). This solution was washed with water (3 x 40 mL), dried (Na_2SO_4), then concentrated. The residue, washed with acetone, furnished **5**.

Hexamethyl 1,13-diazapentacyclo [11.11.11.1^{5,9}.1^{17,21}.1^{28,32}] octatriaconta-3,5,7,9(36),10, 15,17,19,21(37),22,26,28,30,32(38),33-pentadecaene-3,11,15,23,26,34-hexacarboxylate 5b. 14 %, mp 265°C (CH_2Cl_2). ^{1}H NMR δ 3.09 (s, 12H), 3.69 (s, 18H), 7.01 (s, 3H), 7.45-7.36 (m, 9H), 7.88 (s, 6H). ^{13}C NMR δ 47.09, 51.89, 128.52, 129.28, 130.41, 130.96, 135.07, 140.63, 168.16. IR (Nujol, ν 1710 cm^{-1}. MS (FAB) m/z (rel. inten) 845 (M^++1, 45), 787 (3), 729 (8), 575 (30), 442 (19), 309 (10), 271 (26), 211 (77), 153 (74). Anal. calcd for $C_{48}H_{48}N_2O_{12}$ C, 68.25 ; H, 5.69. Found : C, 68.01 ; H, 5.46.

Hexamethyl 33,34,35-trioxa-1,12 diazapentacyclo [10.10.10.1^{5,8}.1^{16,19}.1^{26,29}]pentatriaconta-3,5,7,9,14,16,18,20,24,26,28,30-dodecaene-3,10,14,21,24,31 hexacarboxylate 5c. 23 %, mp 270°C (CH_2Cl_2). ^{1}H NMR δ 3.65 (s, 18H), 3.95 (br s, 12H), 6.65 (s, 6H), 7.41 (s, 6H). ^{13}C NMR δ 49.85, 51.91, 120.08, 126.5, 128.25, 153.17, 168.75. IR (Nujol), ν 1700 cm^{-1}. MS m/z (rel. inten) 814 (M^+, 15), 785 (2), 755 (1), 619 (7), 552 (4), 370 (5), 357 (11), 355 (14), 341 (14), 277 (24), 263 (21), 262 (61), 203 (16), 115 (13). MSHR calcd for $C_{42}H_{42}N_2O_{15}$ 814.2584. Found : 814.2569. Anal. calcd for $C_{42}H_{42}N_2O_{15}$, 1.5 CH_2Cl_2 C, 55.44 ; H, 4.78 ; N 2.97. Found : C, 55.02 ; H, 4.56 ; N, 3.02.

The reaction of **3d** with NH_3 gave a mixture of **4d** and **5d** which was chromatographed (silica gel, ether/petroleum ether 4 : 1) to obtain **4d** (6 %) and **5d** (30 %).

Tetramethyl 11,23-dichloro-25,26-dimethoxy-5,17-diazatricyclo [19.3.1.1^{9,13}] hexacosa-2,7,9,11,14,19,21,23,25,26-decaene-3,7,15,19-tetracarboxylate 4d. mp 215°C (ether). ^{1}H NMR d 2.41 (br s, 2H), 3.29 (br s, 8H), 3.39 (s, 6H), 3.83 (s, 12H), 7.17 (s, 4H), 7.72 (s, 4H). MS m/z (rel inten) 706 (3), 704 (16), 702 (25), 675 (13), 673 (31), 672 (16), 671 (38), 670 (15), 643 (5), 614 (5), 670 (5), 351 (17), 349 (16), 335 (17), 334 (17), 332 (23), 321 (12), 320 (12), 319 (58), 318 (53), 317 (60), 316 (24), 300 (30), 276 (30), 274 (23), 261 (28), 260 (21), 259 (100). MSHR calcd for $C_{34}H_{36}N_2O_{10}{}^{35}Cl_2$ 702.1746. Found 702.1773.

Hexamethyl 7,19,30-trichloro-3,6,37,38-trimethoxy-1,13-diazapentacyclo [11.11.11.1^{5,9}.1^{17,21}.1^{28,32}] octatriaconta-3,5,7,9(38),10,15,17,19,21(37), 22,26,28,30,32(36), 33-pentadecaene-3,11,15,23,26,34-hexa carboxylate 5d. 28 %, mp 265°C ($CHCl_3$). ^{1}H NMR δ 2.14 (d, 6H, J = 12.4 Hz), 2.82 (d, 6H, J = 12.4 Hz), 3.25 (s, 9H), 3.70 (s, 18H), 7.12 (s, 6H), 7.60 (s, 6H). ^{13}C NMR δ 50.30, 51.88, 61.50, 128.41, 129.79, 131.24, 134.10, 135.13, 152.49, 167.71. MS m/z (rel inten) 1042 (12), 1040 (45), 1038 (100), 1036 (86), 1007 (22), 1005 (17), 701 (26), 699 (14), 671 (11), 669 (19), 620 (28), 318 (68). MSHR calcd for $C_{51}H_{51}N_2O_{15}{}^{35}Cl_3$ 1036.2354. Found : 1036.2364.

General procedure for the preparation of 6b-e. To a solution of paracyclophane **4a** (150 mg, 0.26 mmol) in MeCN (150 mL) was added the corresponding diacetate **3** (0.26 mmol) and NEt_3 (53 mg, 0.52 mmol). The mixture was stirred at reflux for 25 h. The solvent was removed under vacuo. The residue was dissolved in CH_2Cl_2 (30 mL) and washed with water (2 x 20 mL). The organic phase was dried (Na_2SO_4). The product was isolated by concentration of the organic phase followed by chromatography.

Hexamethyl 1,12-diazapentacyclo [10.10.11.2^{5,8}.2^{16,19}.1^{26,30}] octatriaconta-3,5,7,34(35),9, 14,16,18,36(37),20,24,26,28,38(30),31-pentadecaene-3,10,14,21,24,32-hexacarboxylate 6b. Purified by chromatography (silica gel, ether/petroleum ether 9 : 1). 41 %, mp 228°C ^{1}H NMR δ 2.63 (s, 4H), 2.55 (d, 4H, J = 12.8 Hz), 2.77 (d, 4H, J = 12.8 Hz), 3.70 (s, 6H), 3.75 (s, 12H), 6.60 (s, 1H), 6.92 (s, 8H), 7.25 (m, 3H), 7.68 (s, 2H), 7.87 (s, 4H). MS m/z (rel inten) 844 (M^+, 3), 242 (54), 210 (99), 182 (100), 154 (46), 128 (41), 115 (78). MSHR calcd for $C_{48}H_{48}N_2O_{12}$ 844.3207. Found 844.3264.

Hexamethyl 33-oxa-1,12-diazapentacyclo [10.10.10.1^{5,8}.2^{13,16}.2^{26,29}] heptatriaconta-3,5,7, 9,14,16,18,34(35),20,24,26,28,36(37),30-tetradecaene-3,10,14,21,24,31 hexa carboxylate 6c. Purified by chromatography (silica gel, ether/petroleum ether 4 : 1). 42 %, mp 230°C ^{1}H NMR δ 2.84 (s, 8H), 2.92 (s, 4H), 3.66 (s, 6H), 3.74 (s, 12H), 6.46 (s, 2H), 7.10 (s, 10H), 8.02 (s, 4H). ^{13}C NMR δ 49.32, 50.04, 51.81, 52.02, 120.69, 125.76, 128.03, 128.47, 128.78, 136.05, 142.20, 153.23, 167.72, 169.11. MS m/z (rel inten) 834 (M^+, 77), 819 (6), 803 (10), 571 (25), 242 (54), 211 (74), 153 (55), 129 (47), 115 (100), 28 (80). MSHR calcd for $C_{46}H_{46}N_2O_{13}$ 834.2999. Found 834.2965.

Hexamethyl 7-chloro-34-methoxy-1,13-diazapentacyclo [11.10.10.1^{5,9}.2^{17,20}.2^{27,30}] octatriaconta-3,5,7,9(34),10,15,17,19,35(36),21,25,27,29,37(38),31-pentadecaene-3,11,15,22,25,32-hexacarboxylate 6d. Purified by chromatography (silica gel, ether/petroleum ether 85 : 15). 50 %, mp 231°C (ether) ^{1}H NMR δ 1.64 (d, 2H, J = 12 Hz), 1.86 (d, 2H, J = 12 Hz), 2.14 (d, 2H, J = 12 Hz), 3.10 (d, 2H, J = 12 Hz), 3.20 (d, 2H, J = 12 Hz), 3.28 (d, 2H, J = 12 Hz), 3.30 (s, 3H), 3.76 (s, 6H), 3.78 (s, 6H), 3.80 (s, 6H), 6.88 (s, 4H), 7.00 (s, 4H), 7.07 (s, 2H), 7.47 (s, 2H), 7.85 (s, 2H), 7.92 (s, 2H). ^{13}C NMR δ 48.26, 50.83, 51.19, 51.65, 51.75, 51.95, 60.93, 127.73, 127.89, 128.27, 129.04, 131.18, 133.78, 134.23, 134.30, 135.31, 135.58, 135.85, 141.29, 141.73, 152.33, 167.54, 167.64, 167.70. MS m/z (rel inten) 910 (M^+, 11), 909 (11), 908 (M^+, 21), 644 (5), 622 (7), 504 (6), 502 (8), 465 (7), 414 (5), 340 (5), 337 (10), 319 (24), 307 (34), 306 (29), 291 (20), 277 (28), 275 (67), 274 (12), 271 (15), 263 (41), 262 (14), 261 (13), 260 (34), 243 (20), 242 (41). MSHR calcd for $C_{49}H_{49}N_2O_3{}^{35}Cl$: 908.2922. Found 908.2948.

Hexamethyl 7-chloro-34-methoxy-8-methyl-1,13-diazapentacyclo [11.10.10.1^{5,9}.2^{17,20}. 2^{27,30}] octatriaconta-3,5,7,9(34),10,15,17,19,35(36),21,25,27, 29,37(38),31-penta-decaene-3,11,15, 22,25,32-hexacarboxylate 6e. Purified by chromatography (silica gel, ether), 40 %, oil. ^{1}H NMR δ 1.58 (d, 1H, J = 12 Hz), 1.70 (d, 1H, J = 12 Hz), 1.90 (d, 1H, J = 12 Hz), 1.91 (d, 1H, J = 12 Hz), 2.16 (d, 1H, J = 13 Hz), 2.19 (d, 1H, J = 13 Hz), 2.28 (s, 3H), 3.06 (d, 1H, J = 12 Hz), 3.07 (d, 1H, J = 12 Hz), 3.13 (d, 1H, J = 13 Hz), 3.22 (d, 1H, J = 12 Hz), 3.30 (d, 1H, J = 13 Hz), 3.31 (d, 1H, J = 12 Hz), 3.27 (s, 3H), 3.76 (s, 3H), 3.77 (s, 3H), 3.775 (s, 3H), 3.78 (s, 3H), 3.79 (s, 3H), 3.81 (s, 3H), 6.77 (d, 2H, J = 8 Hz), 6.89 (d, 2H, J = 8 Hz), 7.01 (s, 4H), 7.15 (s, 1H), 7.45 (s, 1H), 7.49 (s, 1H), 7.78 (s, 1H), 7.86 (s, 1H), 7.93 (s, 1H), 7.94 (s, 1H). ^{13}C NMR δ 17.76, 48.08, 48.56, 50.60, 50.72, 51.00, 51.11, 51.63, 51.68, 51.71, 51.77, 51.94, 60.83, 127.56, 127.90, 127.94, 128.17, 129.22, 133.54, 133.64, 133.70, 133.79, 134.28, 134.67, 135.30, 135.48, 135.53, 135.69, 135.75, 135.84, 141.34, 141.77, 167.72, 167.75. MS m/z (rel inten) 924 (M^+, 15), 923 (17), 922 (M^+, 29), 891 (6), 651 (12), 274 (19), 242 (20), 226 (8), 214 (14), 212 (20), 211 (13), 208 (11), 183 (8), 182 (9), 155 (16), 154 (22), 153 (38), 152 (11). MSHR calcd for $C_{50}H_{51}N_2O_{13}{}^{35}Cl$ 922.3079. Found 922.3116.

Tetramethyl 5,22-diazapentacyclo [30.2.2.2^{9,12}.2^{15,18}.2^{26,29}] dotetraconta-2,7,9,11,13,15, 17,19,24,26,28,30,32,34,35,37,39,41-octadecaene-3,7,20,24-tetracar-boxylate 15. To a solution of diacetate **14** (0.9 g, 1.8 mmol) in THF/MeOH 3 : 10 (13 ml) was added dropwise a 4M ammonia solution in MeOH (15 ml) over a period of 5 min. The mixture was stirred for 1 h. The paracyclophane **15** that precipitated was filtered and washed with THF. 13 %, mp 260°C. ^{1}H NMR ($CDCl_3$/CF_3CO_2H) δ 3.95 (s, 12H), 4.20 (br s, 8H), 7.02 (s, 4H), 7.13 - 7.42 (m, 16H), 8.05 (s, 4H), 8.80 (br s, 2H). MS (FAB) m/z (rel inten) 779 (M^++1,31), 380 (12), 374 (10), 341 (25), 324 (12), 307 (12), 277 (24). Anal. calcd for $C_{48}H_{46}O_8N_2$, H_2O C, 72.36 ; H, 6.03 ; N, 3.51. Found : C, 72.07 ; H, 5.89 ; N, 3.29.

Tetramethyl 3,4,13,22,23,32-hexaazapentacyclo [34.2.2.2^{6,9}.2^{17,20}.2^{25,28}] hexatetraconta-2,4,6,8,10,15,17,19,21,23,25,27,29,34,36,38,39,41,43,45-eicosaene-11,15,30,34-tetracarboxylate 17. To a solution of diacetate **16** (0.75 g, 1.5 mmol) in THF/MeOH 1 : 4 (15 mL) was added dropwise a 1.2 M ammonia solution in MeOH (20 mL). The mixture was stirred for 1 h. The paracyclophane **17** that precipitated was filtered and washed with THF.25 %, mp 270°C (MeOH). ^{1}H NMR ($CDCl_3$ - CF_3CO_2H) δ 4.03 (s, 12H), 4.22 (m, 8H), 7.99 - 7.33 (m, 8H), 8.21 (s, 4H), 8.50 (s, 2H), 8.90 (s, 4H). Anal. calcd for $C_{48}H_{46}O_8N_6$, MeOH C, 67.89 ; H, 5.77 ; N, 9.69. Found, C, 68.06 ; H, 5.66 ; N, 9.78. MS (FAB) m/z 835 (M^++1).

Tetramethyl 5,16-di isopropyl-5,16-diazatricyclo [18.2.2.2^{9,12}] hexacosa-2,7,9,11,13, 18,20,22,23,25-decaene-3,7,14,18-tetracarboxylate 7. To a solution of diamine **10** EE (0.77 g, 2 mmol) and NEt_3

(0.41 g, 4 mmol), stirred and heated to reflux, was added dropwise a solution of diacetate **3a** in MeCN (100 mL). The reaction mixture was stirred for two days. The solvent was removed under vacuum and the residue was dissolved in ether (60 mL). The solution was washed with water (3 x 40 mL), dried ($MgSO_4$) and concentrated. The residue was washed with THF to give **7** (50 %). mp 228°C (ether). ^1H NMR δ 0.84 (d, 12H, J = 6.4 Hz), 2.97 (m, 2H), 3.29 (s, 8H), 3.78 (s, 12H), 7.12 (s, 8H), 7.53 (s, 4H). MS m/z (rel inten) 658 (M^+, 60), 643 (61), 615 (75), 386 (70), 329 (100), 211 (68), 153 (76). MSHR calcd for $C_{38}H_{46}N_2O_8$ 658.3253. Found 658.3237.

Tetramethyl 5,16-di(phenylaminocarbonyl)-5,16-diaza tricyclo [18.2.2.2^{9,12}] hexacosa-2,7,9,11,13,18,20,22,23,25-decaene-3,7,14,18-tetracarboxylate 8. To a solution of **4a** (0.57 g, 1 mmol) in anhydrous CH_2Cl_2 (70 mL) was added phenylisocyanate (0.23 g, 2 mmol) in CH_2Cl_2 (10 mL). The reaction mixture was stirred at room temperature for 17 h then concentrated in vacuo to afford **8** as a white solid (94 %). mp 257°C (CH_2Cl_2/ether). ^1H NMR δ 3.76 (s, 12H), 4.41 (s, 8H), 7.10 (s, 8H), 7.28 - 7.41 (m, 10H), 7.50 (s, 4H), 8.84 (br s, 2H). IR (Nujol) ν 1675, 1700, 3320 cm^{-1}. Anal. calcd for $C_{46}H_{44}N_4O_{10}$ C, 67.98 ; H, 5.42. Found C, 67.80 ; H, 5.53.

Tetramethyl 5,16-di (3'-furyl-2'-methoxycarbonyl allyl)-5,16-diaza tricyclo [18.2.2.2^{9,12}] hexacosa-2,7,9,11,13,18,20,22,23,25-decaene-3,7,14,18-tetracarboxylate 9. A solution of cyclophane **4a** (0.34 g, 0.6 mmol) and ester **11a** (0.28 g, 1.22 mmol) in acetonitrile (50 mL) was stirred at reflux for 90 h. The solvent was removed under vacuo. The residue was dissolved in CH_2Cl_2 (30 mL) and washed with water (2 x 30 mL). The organic phase was dried (Na_2SO_4). The product was isolated by concentration of the organic phase. mp 180°C (75 %). ^1H NMR δ 3.50 (s, 8H), 3.62 (s, 4H), 3.74 (s, 18H), 6.42 (m, 2H), 6.71 (d, 2H, J = 3 Hz), 7.32 (s, 8H), 7.55 (d, 2H, J = 1 Hz), 7.57 (s, 2H), 7.72 (s, 4H). Anal. calcd for $C_{50}H_{50}N_2O_{14}$ C, 66.52 ; H, 5.54 ; N, 3.10. Found : C, 66.48 ; H, 5.32 ; N, 3.22.

Preparation of cyclophanes 21 and 22. To a solution of diacetate **20** (945 mg, 1.83 mmol) in CH_2Cl_2 (80 mL) was added dropwise a 0.8 M ammonia solution in MeOH (60 mL). The mixture was stirred at room temperature for 24 h. The solvent was removed under vacuo and the residue was dissolved in CH_2Cl_2 (80 mL). The solution was washed with water (3 x 50 mL), dried (Na_2SO_4) then concentrated. The residue was chromatographed (silica gel, ether/petroleum ether : 90/10).

Dimethyl 8,9,18,19-tetrahydro-7H, 17H dibenzo [f,o] [14,20,8] dioxaaza-cyclohexadecine-6,10-dicarboxylate 21. 14 %, mp 144°C (ether). ^1H NMR δ 1.72 (s, 1H), 2.15 (m, 2H), 3.20 (s, 4H), 3.55 (s, 6H), 4.13 (t, 4H, J = 6 Hz), 6.99 (m, 6H), 7.25 (m, 2H), 7.72 (s, 2H). ^{13}C NMR δ 28.90 ; 43.33 ; 51.97 ; 64.60 ; 113.99 ; 121.33 ; 125.02 ; 129.83 ; 130.04 ; 130.63 ; 140.32 ; 155.49 ; 167.16. MS, m/z, (rel inten) 437 (M^+, 42), 378 (43), 214 (50), 187 (64), 160 (74), 156 (79), 131 (100), 128 (54). MSHR calcd for $C_{25}H_{27}NO_6$ 437.1838. Found : 437.1835.

Cyclophane **22**. oil (43 %). ^1H NMR δ : 2.12 (m, 6H), 3.02 (s, 8H), 3.16 (s, 4H), 3.47 (s, 12H), 3.70 (s, 6H), 4.11 (m, 12H), 6.92 (m, 18H), 7.24 (m, 6H), 7.67 (s, 4H), 7.81 (s, 2H). ^{13}C NMR δ 29.24 ; 29.48 ; 49.38 ; 51.56 ; 51.75 ; 64.57 ; 65.59 ; 111.26 ; 114.61 ; 120.45 ; 120.84 ; 124.48 ; 125.02 ; 129.29 ; 130.05 ; 130.55 ; 130.60 ; 131.06 ; 131.09 ; 139.76 ; 140.04 ; 155.72 ; 156.74 ; 168.12 ; 169.08. MS (FAB) m/z 1295 (M^++1).

Preparation of 22 from orthocyclophane 21. To a solution of cyclophane **21** (100 mg, 0.23 mmol) and diacetate **20** (65 mg, 0.115 mmol) in MeCN (15 mL) was added NEt_3 (24 mg, 0.23 mmol). The mixture was stirred at reflux for 48 h. The solvent was removed and the residue was dissolved in CH_2Cl_2 (20 mL). This solution was washed with water (2 x 10 mL), dried (Na_2SO_4) then concentrated to give **22** purified by chromatography.

Dimethyl 8,9,18,19-tetrahydro-8-(2'-methoxycarbonyl-3'-phenylprop-2'-enyl)-7H, 17H dibenzo [f,o] [14,20,8] dioxaazacyclohexadecine-6,10-dicarboxylate 23. To a solution of cyclophane **21** (87 mg, 0.2 mmol) in MeCN (15 mL) was added NEt_3 (20 mg, 0.2 mmol) and **11b** (47 mg, 0.2 mmol). The mixture was stirred at reflux for 48 h. The solvent was removed under vacuo and the residue was dissolved in Et_2O (20 mL). This solution was washed with water (2 x 10 mL), dried (Na_2SO_4) and evaporated in vacuo. Flash chromatography on silica gel afforded the pure product **23** EEE as a colorless oil (90 %). ^1H NMR δ 2.16 (m, 2H), 3.17 (s, 4H), 3.37 (s, 2H), 3.55 (s, 6H), 3.80 (s, 3H), 4.17 (t, 4H, J = 5.6 Hz), 6.96 (m,

6H), 7.25 (m, 2H), 7.37 (s, 5H), 7.66 (s, 1H), 7.70 (s, 2H). MS m/z (rel inten) 611 (M^+, 14), 552 (11), 436 (42), 188 (50), 160 (47), 149 (100), 131 (67). MSHR calcd for $C_{36}H_{37}NO_8$ 611.2519. Found : 611.2514.

1 : 1 Cyclophane 4a - maleic acid salt. To a solution of paracyclophane **4a** (50 mg, 0.087 mmol) in $CHCl_3$ (5 ml) was added a solution of maleic acid (7.3 mg, 0.087 mmol) in acetone (1 mL). The resulting precipitate was filtered off. mp 234°C. ^1H NMR δ 3.87 (s, 20H), 6.09 (s, 2H), 7.60 (br s, 8H), 7.85 (s, 4H). Anal. calcd for $C_{32}H_{34}N_2O_8$, $C_4H_4O_4$: C, 62.61 ; H, 5.51 ; N, 4.06. Found C, 62.70 ; H, 5.50 ; N, 4.05.

1 : 2 Cyclophane 4a - maleic acid salt. To a solution of **4a** (0.05 g, 0.087 mmol) in $CHCl_3$ (5 ml) was added a solution of maleic acid (14.6 mg, 0.174 mmol) in acetone (2 mL). The salt did not precipitate. The solvent was removed under vacuo to afford the salt, mp 243°C. ^1H NMR δ 3.90 (s, 12H), 4.45 (s, 8H), 6.11 (s, 4H), 7.22 (s, 8H), 7.88 (s, 4H). Anal. calcd for $C_{32}H_{34}N_2O_8$, 2 $C_4H_4O_4$ C, 59.55 ; H, 5.21 ; N, 3.47. Found : C, 59.49 ; H, 5.33 ; N, 3.35.

References

1 Diederich, F. in Cyclophanes, The Royal Society of Chemistry, Cambridge, 1991.

2 Seel, C. ; Vögtle, F. *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 528.

3 Odashima, K. ; Itai, A. ; Iitaka, Y. ; Koga, K. *J. Am. Chem. Soc.* **1980**, *102* , 2504.
Odashima, K. ; Itai, A. ; Iitaka, Y. ; Koga, K. *J. Org. Chem.* **1985**, *50* , 4478.

4 Baylis, A.B. ; Hillman, M.E. German Patent 1972, 2155113.

5 Drewes, S.E., Roos, G.H.P. *Tetrahedron*, **1988**, *44*, 4653.

6 Bauchat, P. ; Foucaud, A. *Tetrahedron Lett.* **1989**, *30*, 6337.

7 Pascual, C. ; Meier, J. ; Simon, W. *Helv. Chim. Acta*, **1966**, *49*, 164.
Matter, U.E. ; Pascual, C. ; Pretsch, E. ; Pross, A. ; Simon, W. ; Sternhell, S. *Tetrahedron*, **1969**, *25*, *691*, 2023.

8 Vogeli, V. ; Von Philipsborn, W. *Org. Magn. Res.* **1975**, *7*, 617.

9 Foucaud, A. ; El Guemmout, F. *Bull. Soc. Chim. Fr.* **1989**, 403.

10 Mukaiyama, T. ; Sato, T. ; Hanna, *J. Chem. Lett.* **1973**, 1041.

11 Mc Murry, J.E., *Acc. Chem. Res.* **1983**, *16*, 405.

12 Hu, Y. ; Hu, H. *Synthesis*, **1991**, 325.

13 Shiraishi, K. ; Kato, K. ; Sugiyama, K. *Bull. Chem. Soc. Jpn* **1990**, *63*, 1848.

14 Rabe, J. ; Hoffmann, H.M.R. *Angew. Chem. Int. Ed. Engl.* **1983**, *22*, 795.

15 Hoffmann, H.M.R. ; Rabe, J. *J. Org. Chem.* **1985**, *50*, 3849.

16 Gaset, A. ; Rigal, L. ; Paillasa, G. ; Salome, J.P. French Patent 8 314 646 (1983). *Chem. Abst.* **1985**, *103*, 215715.

17 Kang, H.C. ; Hanson, A.W. ; Eaton, B. ; Boekelheide, V. *J. Am. Chem. Soc.* **1985**, *107*, 1979.
Pierre, J.L. ; Barret, P. ; Chautemps, P. ; Armand, P. *J. Am. Chem. Soc.* **1981**, *103*, 2986.
Heirtzler, F.R. ; Hopf, H. ; Jones, P.G. ; Bubenitschek, P. ; Lehne, V. *J. Org. Chem.* **1993**, *58*, 2781.

(*Received in Belgium* 30 *January* 1994; *accepted* 14 *April* 1994)