Pergamon

SCIENCE DIRECT®

Tetrahedron 59 (2003) 1739–1747

TETRAHEDRON

Photochemical synthesis of [2.2](3,8)-pyridazinophane and quinolinophane-2(1*H*)-one as well as synthesis of [2](5,8)-quinolinophanes and fused spiro-pyranoindanoparacyclophanes

Ashraf A. Aly*

Department of Chemistry, Faculty of Science, El-Minia University, El-Minia, Egypt

Received 19 August 2002; revised 16 December 2002; accepted 16 January 2003

Abstract—Syntheses of various classes of unreported heterophanes derived from [2.2]paracyclophane are herein reported. The key to their successful synthesis depends on the photochemical synthesis of pyridazinophane and quinolinophane-2(1*H*)-one from freshly prepared 4-([2.2]paracyclophanyl)-azo-4′-[2.2]paracyclophane and 4-([2.2]paracyclophanyl)cinnnamanilide, respectively. Reactions of 4-amino-[2.2]paracyclophane with either acetyl- or benzoylacetone afforded condensed products. Then ring closure using polyphosphoric acid (PPA) at 120°C gave, in near quantitative yields, quinolinophanes. Reactions of [2](4,7)-indano-[2]paracyclophane-1-ylidene-propanedinitrile with active methylene compounds afforded fused spiro-pyranoindanoparacyclophane derivatives.

1. Introduction

More than 50 years after the first reported synthesis of [2.2]paracyclophane, its chemistry is still a field of ongoing research.[1,2] In the beginning, work was focused on the development of conventional synthetic methods yielding [2_n]cyclophanes and investigation of their physical properties. The importance of [2.2]paracyclophanes containing one or more condensed aromatic subunits comes from their stereochemical and electronic properties. The chemical behavior of [2_n]cyclophanes is determined, on the one hand, by interannular π-interaction between the benzene 'decks' and by the strain of the polycyclic systems, on the other, making them far more reactive as compared with the classical aromatic systems. [2_n]Cyclophanes are rigid molecules and have binding sites, which enable them to participate in specific aromatic binding interactions and serve as points of attachment functional groups for complexation and catalysis. Undoubtedly, research with future generations of cyclophanes will continue to contribute to some of the most fascinating developments in the field of supramolecular chemistry. One of the important applications of polycyclic [2_n]cyclophanes is their utility as precursors of topologically novel compounds such as circulenes, propellicences, paddlanes, and helicene-derived cyclophanes, to name but a few.[3] In light of the aforementioned, we previously prepared several phenanthrenoparacyclophanes and phenanthrenophanes via the reactions of benzyne with various divinyl[2.2]paracyclophanes.[4] The highlight of our synthetic program uses efficient, facile and elegant methods of preparation of novel heterophanes,[5] rather than those suffering from low yields due to the multiple steps described in their preparation.[6] Herein we report on our findings for the synthesis of various novel heterophanes, that can show increased binding interactions compared with the polycyclic cyclophanes, due to the incorporation of heteroatoms, which may be interesting from a biological perspective.

2. Results and discussion

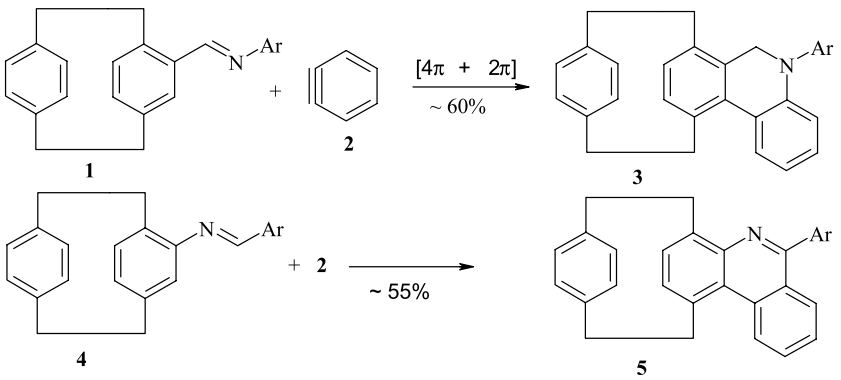
Recently, we have described the preparation of [2](1,4)-phenanthridinophane derivatives **3** and **5** by the reactions of azomethines containing [2.2]paracyclophane **1** and **4** with benzyne (**2**) (Scheme 1).[7]

The synthesis of these nitrogen-containing heterophanes led to the idea that the heterophane **11** could be obtained from the azoparacyclophane **10** by photocyclization. Consequently, the preparation of the azoxyparacyclophane **8** was required as a precursor for compound **11**. The synthesis of compound **8** can be achieved from the reported 4-nitro-[2.2]paracyclophane **7**.[8] However, using the reported procedure, compound **7** was isolated in low yield (20%).[8] Fortunately, compound **7** has recently been synthesized in about 65% yield by treatment of compound **6** with ytterbium(III) trifluoromethanesulfonate $(CF_3SO_3)_3Yb$ and

Keywords: photochemical synthesis of pyridazinophane; quinolinophanes; fused spiro-pyranoindanoparacyclophanes.

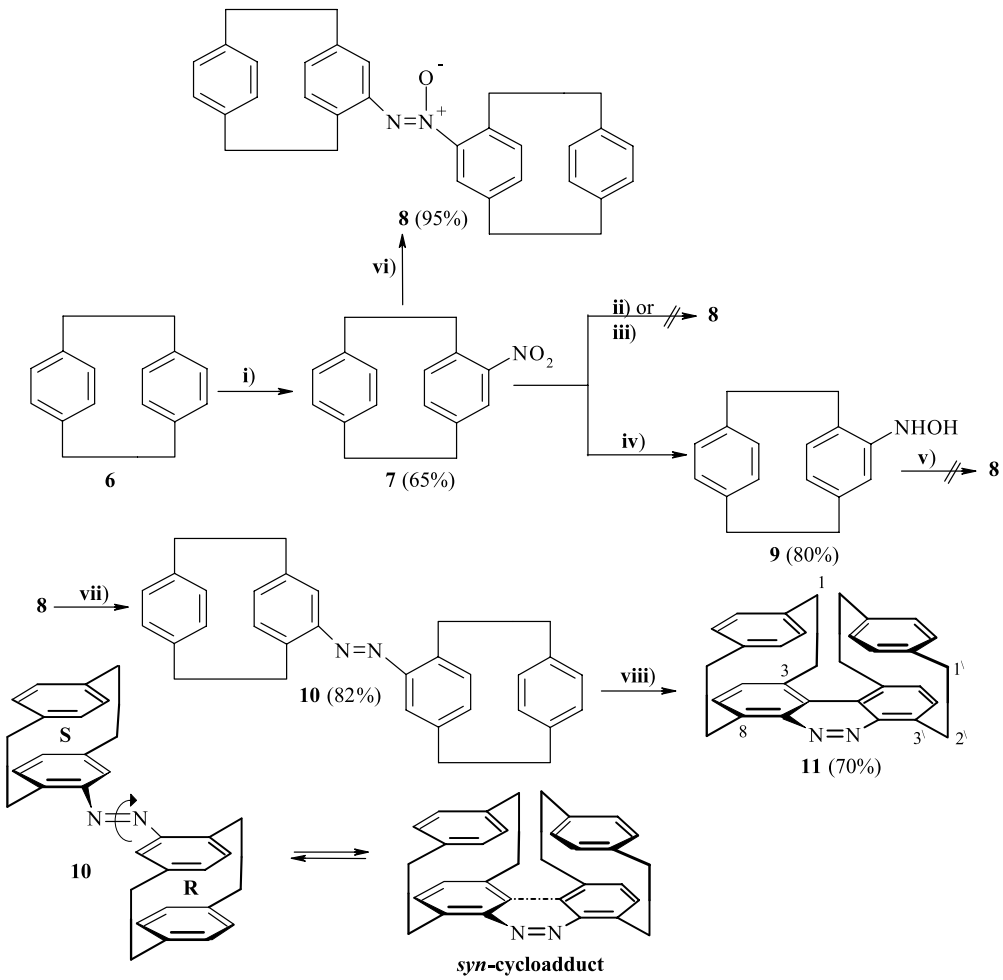
* E-mail: ashraf160@yahoo.com

0040–4020/03/$ - see front matter
doi:10.1016/S0040-4020(03)00112-1



Scheme 1. Synthesis of [2](1,4)phenanthridinophanes.

nitric acid in acetonitrile–water mixture (Scheme 2).[9] Reaction of **7** with thallium metal in ethanol, within three days, afforded compound **8** in 95% yield. It was reported that azoxybenzenes can be obtained by the action of $BiCl_3$–Zn[10] or $CdCl_2$–Zn[11] catalysts on nitrobenzenes. Unfortunately, on applying these methods to compound **7**, the reactions failed. Another method used to prepare azoxy compounds was established by reaction of $NaBH_4$–Sb in ethanol with nitrobenzenes to form the corresponding hydroxylamine derivatives, which on oxidation in sodium hydroxide provides the azoxy derivatives.[12] On applying the latter procedure to compound **7**, 4-([2.2]paracyclophanyl)-hydroxylamine (**9**) was produced in 80% yield, whereas oxidation of **9** in the presence of sodium hydroxide failed to



i) $Yb(OTf)_3$/ HNO_3, CH_3CN-H_2O; **ii)** $BiCl_3$-Zn, CH_3CN, reflux; **iii)** $CdCl_2$-Zn, CH_3CN, reflux; **iv)** $NaBH_4$-Sb, EtOH, reflux 2h; **v)** O_2/ NaOH, r.t.; **vi)** Tl/ EtOH, reflux 3d, N_2; **vii)** $LiAlH_4$/ THF, reflux 2h; **viii)** hν/ $AlCl_3$, Cl-CH_2-CH_2Cl.

Scheme 2. Photochemical synthesis of [2.2](3,8)-pyridazinophane **11**.

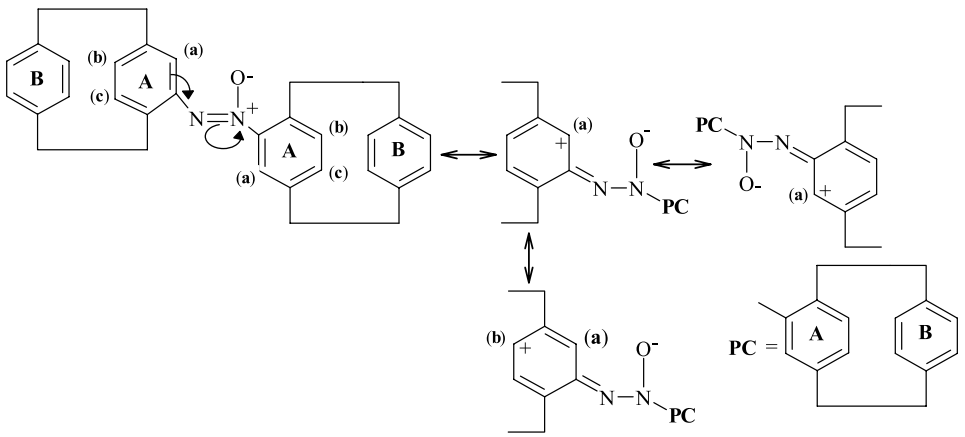


Figure 1. Resonance structures of compound **8**.

give compound **8** (Scheme 2). Transformation of **8** into **10** was accomplished in 82% yield, by reduction of **8** using lithium aluminumhydride in tetrahydrofuran (Scheme 2).

It was previously shown in the literature that polynuclear-azoxy derivatives are more stable at room temperature in their *trans*-configuration due to steric and electronic factors.[13] However, reduction of *trans*- and/or *cis*-azoxy compounds using $LiAlH_4$ gave only *trans*-azo derivatives.[13a,14] The latter conclusion is of importance in our case, since it can be deduced that the reduction step must involve the formation of an intermediate having a single bond between the two nitrogen-atoms. Such an intermediate has free rotation about the single bond and the most stable *trans*-form of the azo-compounds would naturally be formed. On the other hand, the *cis*-azo molecule is not coplanar, owing to steric effects and the departure from coplanarity has therefore led to a suppression of conjugation and produces a highly-strained molecule.[13a,15] Analogously, it is highly probable that compound **10** is found in its *trans*-form, which results in the reduction *trans*-azoxy compound **8**.

It is well-known that the azoxy group constitutes a dipole molecule.[16] Therefore, resonance stabilization between the functional group N=N(O) and the π-bonds of the aromatic rings **A** can cause a successive deshielding of the protons of ring **A** compared to the protons of ring **B** (Fig. 1). Consequently, the ^{1}H NMR spectrum of **8** revealed a singlet at δ_H 7.62 assigned to the two protons (**a**). The other four protons of the aromatic rings **A** appeared in the ^{1}H NMR spectrum of **8** as: a double of doublet at δ_H 7.06 (J=7.9, 1.8 Hz) for the two protons (**b**), and a doublet at δ_H 6.96 (J=7.9 Hz) for the two protons (**c**) (see Table 1). The remaining aromatic eight protons of rings **B** can be seen in Table 1.

Table 1. ^{1}H NMR and ^{13}C NMR spectral data for compounds **8**, **10** and **11**

Compound	δ_H ($CDCl_3$)	δ_C ($CDCl_3$)
8	2.80–2.85 (4H, m, CH_2–CH_2), 2.98–3.40 (8H, m, CH_2–CH_2), 3.60–3.72 (2H, m, CH_2–CH_2), 3.85–3.96 (2H, m, CH_2–CH_2), 6.38 (2H, dd, PC–H, J=7.9, 1.8 Hz, PC-**B**), 6.46–6.80 (6H, m, PC–H, PC-**B**), 6.96 [2H, d, J=7.9 Hz, PC-(**c**)], 7.06 [2H, dd, J=7.9, 1.8 Hz, PC-(**b**)], 7.62 [2H, s, PC–H, PC-(**a**)].	31.67, 31.90, 34.73, 34.97, 35.04, 35.10, 35.15, 35.26 (CH_2–CH_2), 127.61, 127.80, 127.90, 128.11, 131.12, 131.18, 132.10, 132.16, 132.20, 133.12 (PC–H), 130.20, 130.50 (PC–C), 130.74, 130.90, 131.86, 132.10 (PC–CH), 133.15, 133.40, 134.52, 134.70, 135.90, 136.22 (PC–C), 141.00 (PC–*C*–N), 149.50 (PC–*C*–N–O).
10	2.85–2.90 (2H, m, CH_2–CH_2), 3.10–3.25 (10H, m, CH_2–CH_2), 3.30–3.42 (2H, m, CH_2–CH_2), 4.20–4.25 (2H, m, CH_2–CH_2), 6.45 [2H, d, J=1.8 Hz, PC-(**d**)], 6.50 [2H, dd, J=7.9, 1.8 Hz, PC-(**e**)], 6.58–6.70 (8H, m, PC–H, PC-**B** and PC-**A**), 7.22 (2H, dd, J=7.8, 1.9 Hz, PC-**B**).	32.60, 33.00, 34.65, 34.82, 35.00, 35.22, 35.94, 35.96 (CH_2–CH_2), 128.90, 129.00, 130.00, 130.26, 131.14, 131.80, 132.00, 132.20, 132.37, 133.00 (PC–H), 133.15, 133.30 (PC–C), 133.40, 133.68, 133.70, 134.10 (PC–H), 136.10, 137.40, 137.50, 138.46, 138.80, 139.20 (PC–C), 143.22, 143.30 (PC–*C*–N).
11	2.76–2.80 (2H, m, CH_2–CH_2), 2.83–3.30 (10H, m, CH_2–CH_2), 3.75–3.84 (2H, m, CH_2–CH_2), 3.90–3.98 (2H, m, CH_2–CH_2), 6.10 [2H, d, J=8.0 Hz, PC-(**f**)], 6.45–6.80 (8H, m, PC–H), 7.25 [2H, dd, J=8.0, 2.00 Hz, PC-(**g**)].	29.88, 36.00, 36.78, 37.00 (CH_2–CH_2), 126.60, 129.66, 130.10, 131.45, 132.75, 133.00, 133.40 (PC–H), 134.90, 140.80, 141.12, 142.89 (PC–C), 155.28 (PC–*C*=N).

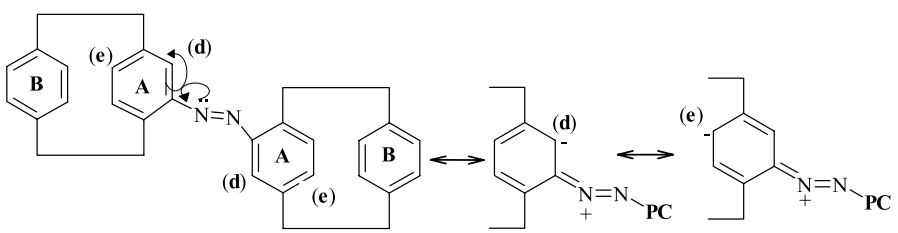


Figure 2. Resonance structures of compound **10**.

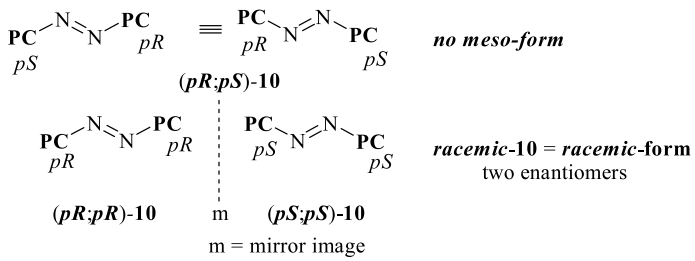


Figure 3. Possible stereoisomers of compound **10**.

From the above finding that **10** has to exist in its *trans*-unsymmetrical form, all protons and carbons of both paracyclophanyl moieties should appear in its NMR spectra. The resonance stabilization between the nitrogen lone-pair and the adjacent π-bond in the benzene rings **A** enhances the protons (**d**) (see Fig. 2) to be the most shielded aromatic protons. Consequently, the ^{1}H NMR spectrum of **10** revealed a doublet at δ_H 6.45 (J=1.8 Hz) for the two protons (**d**). The former resonance also enhances the shielding effect to protons (**e**) in rings **A** (Fig. 2), therefore these protons resonate as a double of doublet at δ_H 6.50 (J=7.9, 1.8 Hz). The observed ^{13}C NMR signals of **10** confirmed the ^{1}H NMR spectroscopy by the appearance of eight aliphatic and twenty four aromatic carbons (see Table 1). Similarly, the ^{13}C NMR spectrum of **8** revealed the same number of aliphatic and aromatic carbons as in **10**. The fact that the NMR spectra of either **8** or **10** is indeed for only one isomeric form is mainly related to their geometric isomerism rather than stereoisomerism.

According to semi-empirical calculations using the PM3 level of theory,[17] the bond length of the N=N is found to be ca 1.3 Å, in order to minimize the strain inflicted in compound **10**. On the other hand, the bond angle between N–N–C is ca 118.0°. The relative stereochemistry of the di-paracyclophanes **10** is of considerable interest, since it possesses two phane chiral elements, due to the presence of two paracyclophane residues, in that four stereoisomers possible. In the following, the residues are presented by $\mathbf{PC}_{pS}$ and $\mathbf{PC}_{pR}$. Accordingly, the number of isomers consists of two types of enantiomers (*racemic*-mixture) and/or *RS* (*SR*). The latter two isomers do not constitute the *meso*-form of **10**, due to the lack of a plane of symmetry in its *trans*-form (Fig. 3).

2.1. Synthesis of [2.2]paracyclophanyl-[5′,4′-c]-[2.2](3,8)-pyridazinophane (11)

[2.2]Paracyclophane derivatives have demonstrated a diverse range of biological activities, when compared with similar analogues of some classic aromatic systems.[5c] Pyridazines are of chemical and biological interest because they have been reported to have antihypertensive activity.[18] In addition, they display analgesic and anti-inflammatory activities.[19] Our aim is now extended to the synthesis of pyridazinophane **11** (Scheme 2) starting from compound **10**. It is noteworthy to mention that the presence of **10** as a mixture of stereoisomer structures does not affect any subsequent reaction. Irradiation of **10** in the presence of anhydrous $AlCl_3$ using 1,2-dichloroethane as a solvent afforded the pyridazinophane **11** in 70% yield (Scheme 2). Mass spectrometry and elemental analysis of **11** confirmed its molecular formula as $C_{32}H_{28}N_2$. The ^{1}H NMR and ^{13}C NMR spectra (see Table 1) of **11** clearly indicated that cyclization of **10** had occurred to give **11**. Moreover, the stereoview of the preferred conformation of **11**, determined by the PM3 program,[17] confirmed the preferred existence of the *syn*-cycloadduct rather than the *anti*-one and this is in accord with the *RS* configuration of compound **10** as shown in Scheme 2. Although, molecular modeling[17] of compound **11** also indicated that protons (**f**) of the paracyclophanyl molecule are some distance away from the shielding effect of the azo group, one can expect a type of transannular electronic interaction, which enhances the shielding effect of protons (**f**) compared with the other aromatic protons (Fig. 4). On the other site, this type of transannular electronic interaction stimulates the deshielding effect of protons (**g**) compared with the other aromatic protons (Fig. 4). The latter was indicated by the appearance a doublet for the two protons (**f**) at δ_H 6.10 (J=8.0 Hz) and a double of doublet for the two protons (**g**) at δ_H 7.25 (J=8.0, 2.0 Hz) in the ^{1}H NMR spectrum of **11** (see Table 1). It was also concluded that compound **11** has a symmetrical structure assignment based on its NMR spectra (Table 1). For example, the ^{13}C NMR spectrum of **11** revealed only four carbon signals from δ_C 29.88–37.00 for the ethano-bridges and the aromatic carbons appeared as twelve signals from δ_C 126.60–155.28 (see Table 1).

2.2. Synthesis of [2](5,8)quinolinophane derivatives

Fused heterocycloquinolines are a large group of poly-heterocycles with diverse interesting biological activities.[20–24] They also constitute an important class of natural products, so that many synthetic methods for them have been developed.[25] With the aim to prepare the quinolinophane-2(1*H*)-one

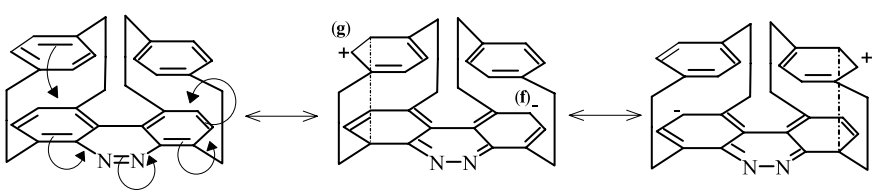
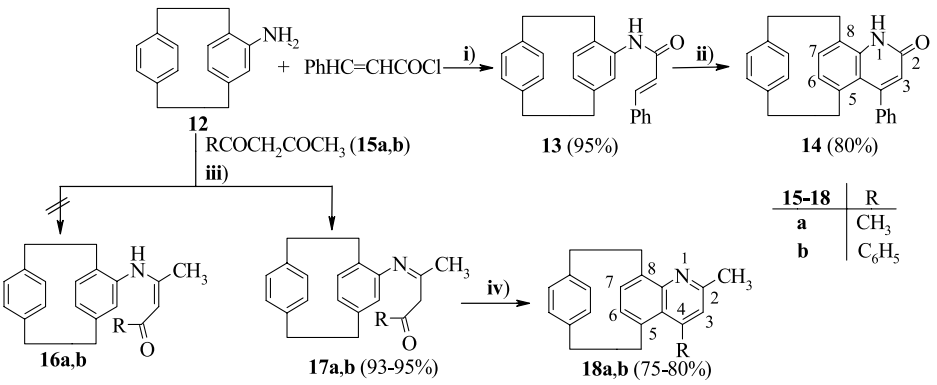


Figure 4. Resonance structures of compound **11**.



Scheme 3. Synthesis of various quinolinophanes.

14, we reacted 4-amino-[2.2]paracyclophane (**12**)[8] with cinnamoyl chloride in the presence of sodium hydroxide to give 4-([2.2]-paracyclophanyl)cinnnamanilide (**13**) in 95% yield (Scheme 3). Photolysis of **13** using iodine as the oxidizing agent in 1,2-dichloroethane afforded the desired compound **14** in 80% yield (Scheme 3). The mass spectrum and elemental analysis of **14** confirmed its molecular formula as $C_{25}H_{21}NO$. The ^{1}H NMR spectrum of **14** (see Table 2) gave strong evidence for its formation and showed two doublets at δ_H 6.20 (J=7.9 Hz) and at δ_H 6.44 (J=7.9 Hz) corresponding to the *ortho*-coupled protons (H-6 and H-7) of the paracyclophanyl moiety (Table 2). In addition, the ^{1}H NMR spectrum of **14** revealed that the vinylic H-3 was amongst the paracyclophanyl aromatic protons at δ_H 6.50–6.58 (see Fig. 5 and Table 2) and this is in accordance with the ^{1}H NMR spectra of electron-donating-4-substituted-quinoline-2(1*H*)-ones.[26] The ^{13}C NMR spectrum of **14** supports the ^{1}H NMR spectroscopy data, by the appearance of the C-3 and C-4 carbons at δ_H 116.78 and 145.98, respectively, (see Table 2). The chemical shifts (δ_H and δ_C) of some distinctive protons and carbons of compound **14** are shown in Figure 5.

Interestingly, we have also investigated the synthesis of the quinolinophane derivatives **17a**,**b** as a general method for preparing this class of compounds, so as to facilitate their future synthesis. Accordingly, treatment of compound **12** with acetyl- and benzoylacetone (**15a**,**b**) in ethanol gave compounds **17a**,**b**. The NMR spectra data of compounds **17a**,**b** proved unambiguously their monomeric forms rather than the other form **16a**,**b**. The latter was elucidated by the ^{1}H NMR spectra of compounds **17a**,**b**, which indicated the presence of one excess CH_2 superimposed on the para-cyclophane-CH_2 protons. In addition, the ^{13}C NMR spectrum of compound **17a** showed the methylene carbon of the $CH_2C{=}O$ group at δ_C 29.09 and the azomethine carbon of the $CH_3C{=}N$ group at δ_C 160.92, whereas the carbonyl group appeared at δ_C 190.96. Furthermore, the

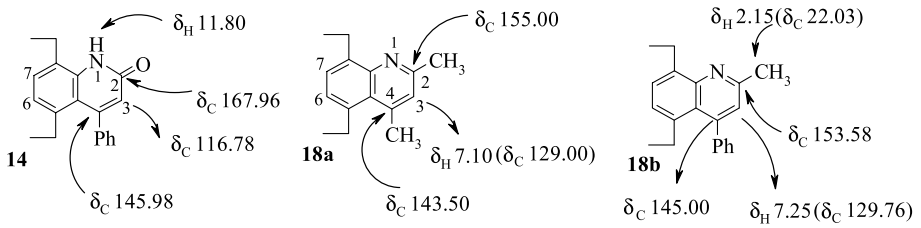
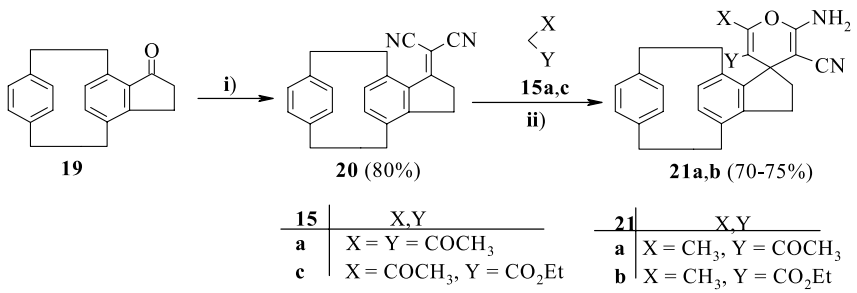


Figure 5.

Table 2. ^{1}H NMR and ^{13}C NMR spectral data for compounds **14** and **18a**,**b**

Compound	δ_H ($CDCl_3$)	δ_C ($CDCl_3$)
14	2.55–2.72 (6H, m, CH_2–CH_2), 2.75–2.77 (2H, m, CH_2–CH_2), 6.20 (1H, d, J=7.9 Hz, H-7), 6.44 (1H, d, J=7.9 Hz, PC–H), 6.50–6.58 (4H, m, vinylic H-3 and PC–H), 6.90–7.34 (6H, m, PC–H, Ph–H), 11.80 (IH, br, s, NH).	33.00, 33.20, 34.72, 35.28 (CH_2–CH_2), 116.78 (CH-3), 121.00, 125.80, 128.54, 129.00, 130.12, 130.34, 130.70 (–CH), 131.34, 132.08, 133.48 (–C), 134.20, 134.76 (–CH), 134.80 (–C), 135.66 (–CH), 135.90 (–C), 136.08 (–CH), 136.80, 139.00 (–C), 145.98 (C-4), 167.96 (CO).
18a	2.10 (3H, s, CH_3), 2.15 (3H, s, CH_3), 2.70–2.73 (1H, m, CH_2–CH_2), 2.83–3.25 (7H, m, CH_2–CH_2), 5.50 (1H, d, PC–H, J=7.8 Hz, H-6), 5.70 (1H, d, PC–H, J=7.8 Hz, H-7), 6.30–6.65 (4H, m, PC–H), 7.10 (1H, s, H-3).	20.80, 21.03 (2CH_3), 33.00, 35.80, 36.40, 37.20 (CH_2–CH_2), 126.68, 127.12, 127.45, 128.00, 128.10, 128.40 (PC–CH), 129.00 (CH-3), 133.49, 134.55, 135.00, 136.20, 137.50, 138.01 (PC–C), 143.50 (C-4), 155.00 (C-2).
18b	2.15 (3H, s, CH_3), 2.60–2.62 (1H, m, CH_2–CH_2), 2.85–3.20 (7H, m, CH_2–CH_2), 5.60 (1H, d, PC–H, J=7.9 Hz), 5.82 (1H, d, PC–H, J=7.8 Hz), 6.54–6.84 (4H, m, PC–H), 7.25 (1H, s, H-3), 7.40–7.65 (5H, m, Ph–H).	22.03 (CH_3), 32.90, 34.75, 35.90, 36.12 (CH_2–CH_2), 126.14, 128.40, 128.90 (–CH), 129.76 (CH-3), 131.40, 132.22, 132.40, 132.48, 133.43, 133.98 (–CH), 134.05, 134.65 (–C), 135.28 (–CH), 136.20 (–C), 136.67 (–CH), 137.42, 137.64, 138.01, 139.52 (–C), 145.00 (C-4), 153.58 (C-2).



i) $CH_2(CN)_2$/ Et_3N, EtOH, reflux 10h; **ii**) EtOH/ Et_3N, reflux 6-8h.

Scheme 4. Synthesis of spiro-pyranoindanoparacyclophanes.

disappearance of the NH-proton and the deshielding effect of the quaternary azo-carbon in the $CH_3C{=}N$ group confirmed the suggested structure of **17a**,**b**.

Treatment of **17a**,**b** with polyphosphoric acid (PPA) at 120°C afforded the desired 2-methyl-4-substituted-[2]paracyclo-[2](5,8)-quinolinophanes **18a**,**b** (Scheme 3). For example, the ^{1}H NMR spectrum of compound **18a** (Table 2) exhibited H-3 as a singlet at δ_H 7.10, which is in accord with to the region of lower field of ^{1}H NMR spectra of electron-donating-4-substituted-quinolines.[26] The two inner hydrogen protons of the *para*-phenylene ring that lie over the heterocyclic quinoline ring (H-6 and H-7) appear in the ^{1}H NMR spectrum as a doublet at δ_H 5.50 and 5.70 (J=7.8 Hz). The ^{13}C NMR spectrum of **18a** revealed the CH-3 and C-2 carbons at δ_C 129.00 and 155.00, respectively. The H–H-COSY spectrum of **18a** showed long-range coupling (J=1.0 Hz) between H-3 (δ_H 7.10) and both methyl protons (δ_H 2.10 and 2.15). Furthermore, NOEs saturated with H-3 at δ_H 7.10 enhanced the signals of the two methyl protons. The complete spectral data is in good agreement with these cyclized structures of either **18a** or **18b**. A comparative study of some distinguished chemical shifts (δ_H and δ_C) between compounds **18a** and **18b** are shown in Figure 5, whereas the NMR spectra data of both compounds are given in Table 2.

2.3. Synthesis of fused spiro-pyranoindano-paracyclophanes

In order to explore the above mode of synthesis for another class of heterocycles, the ylidene **20** was prepared in 80% yield from the reaction of [2](4,7)-indano-[2]paracyclophane-5-one (**19**)[27] with malononitrile (Scheme 4). Mass spectrum and elemental analysis confirmed the molecular formula of **20** as $C_{22}H_{18}N_2$. The ^{13}C NMR spectrum showed the $C{=}C(CN)_2$ carbon at δ_C 176.00, whereas the $={C}(CN)_2$ carbon appeared at δ_C 70.92 (see Section 3). The preparation of compound **20** in good yield gives us the opportunity for preparing various spiro-heterocyclic compounds. Avoiding repetition, we choose only two examples. Thus, reaction of compound **19** with the active methylene derivatives **15a**,**c** yielded spiro-(4,7)-indano-[2]-paracyclophanyl-4′-pyran derivatives **21a**,**b** in high yields (Scheme 4). Besides, the ^{13}C NMR spectra revealed the spiro-carbons of compounds **21a** and **21b** at δ_C 40.00 and 45.00, respectively (see Section 3).

In conclusion, our results are in continuation of our annulation strategy which has demonstrated for the first time, a general methodology for the construction of a wide variety of heterophanes derived from [2.2]paracyclophane that have not previously been synthesized. Further studies in our laboratory are aimed to synthesizing new heterophanes derived from tetrasubstituted-[2.2]paracyclophanes. These studies will be reported in due course.

3. Experimental

3.1. General

Melting points are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ and measured on Bruker AM 400 (400.134 and 100.60 MHz) instrument. The chemical shifts (δ's) were measured relative to the internal standard TMS. Coupling constants were expressed in Hz. Elemental analyses were performed by the Microanalysis Center of the Institut für Anorganische Chemie, Technische Universität Braunschweig. Mass spectra were performed using Finnigan MAT 8430 spectrometer at 70 eV. The IR spectra were obtained by Nicolet 320 FT-IR using KBr pellets. UV spectra were recorded on Beckman UV 5230 spectrophotometer. For preparative layer chromatography (TLC), glass plates (20×48 cm) were covered by a slurry of silica gel PF_{254} (Merck) and air-dried using the solvents listed for development. Column chromatography was coated by silica gel 7714 (Merck) and alumina. Zones were detected by quenching of indicator fluorescence upon exposure to 254 nm light. Photochemical reactor was established using Philips HPK 250 W mercury-quartz lamp in a water-cooled quartz apparatus of 250 mL capacity under nitrogen. **PC** stands for [2.2]paracyclophane.

3.1.1. 4-([2.2]Paracyclophanyl)hydroxylamine (9). To a cooled (−15°C) solution of **7**[8] (0.51 g, 2.28 mmol) in absolute ethanol (200 mL), antimony powder (0.24 g, 1.97 mmol) and $NaBH_4$ (0.29 g, 7.67 mmol) were gradually added with vigorous stirring under N_2 for 10 min. The reaction mixture was refluxed for 2 h until most of **7** was consumed. Under bubbling of N_2, the cooled mixture (0°C) was acidified with 1N hydrochloric acid to pH 6, and immediately extracted with $CHCl_3$. The organic layer was washed several times with water and dried over $MgSO_4$. After the evaporation of the solvent in vacuo, the residue was purified by column chromatography using CH_2Cl_2 as eluent (R_f 0.65, CH_2Cl_2) to give the *title* compound **9** (0.46 g, 80%) as red crystals, mp 130–132°C (acetone);

[Found: C, 80.45; H, 7.12; N, 5.82. $C_{16}H_{17}NO$ (239.316) requires C, 80.30; H, 7.16; N, 5.85%]; ν (KBr) 3500 (OH), 3230 (NH), 3010–3000 (Ar–CH), 2880–2865 (ali.-CH) cm^{-1}; δ_H ($CDCl_3$): 2.79–3.20 (7H, m, CH_2–CH_2), 3.60–3.62 (1H, m, CH_2–CH_2), 5.92 (1H, s, PC–H), 6.14 (1H, br, s, OH), 6.42–6.78 (6H, m, PC–H), 11.20 (1H, br, s, NH); δ_C ($CDCl_3$): 35.32, 35.42, 36.78, 36.92 (CH_2–CH_2), 127.45, 130.18, 131.90 (PC–CH), 132.16 (PC–C), 133.40, 133.60, 134.00, 134.23 (PC–CH), 134.64, 135.60, 136.08 (PC–C), 145.34 (PC–*C*–NHOH); *m/z*(%) 239 [M^+] (100), 221 (22), 206 (14), 136 (32), 104 (18), 57 (16).

3.1.2. 4-([2.2]Paracyclophanyl)-azoxy-4′-[2.2]paracyclophane (8). A mixture of **7** (0.51 g, 2 mmol) and thallium (0.61 g, 3 mmol) in absolute ethanol (250 mL) was stirred under reflux for 3 h. The reaction progress was followed by TLC reaction. The precipitate of compound **8** and the excess thallium of the cooled solution was collected by filtration and then washed several times with hot ethanol (150 mL). To the filtrate and these solutions, potassium iodide (1 g) was added, and the mixture was stirred at room temperature for 1 h. The precipitated thallium(I) iodide was then removed by filtration and the filtrate was evaporated to dryness in vacuo. The residue was dissolved in CH_2Cl_2 and the solution was filtered through short column packing with silica gel to give a second crop of the title compound **8** (0.88 g, 95%) as yellow crystals, mp 180–182°C (acetonitrile); [Found: C, 83.65; H, 6.56; N, 6.12. $C_{32}H_{30}N_2O$ (458.602) requires C, 83.81; H, 6.59; N, 6.11%]; ν (KBr) 3018–3000 (Ar–CH), 2888–2849 (ali.-CH), 1195 (N–O) cm^{-1}; UV (CH_3CN): λ_{max} 362 nm; δ_H and δ_C ($CDCl_3$): see Table 1; *m/z*(%) 459 (M+1, 20), 458 [M^+] (50), 442 (100), 414 (10), 354 (M^+-104, 60), 337 (24), 325 (22), 310 (8), 235 (30), 221 (40), 220 (60), 191 (16), 178 (10), 105 (22), 104 (50), 91 (20), 77 (18), 57 (12), 43 (8).

3.1.3. 4-([2.2]Paracyclophanyl)-azo-4′-[2.2]paracyclophane (10). A mixture of **8** (0.46 g, 1 mmol) and $LiAlH_4$ (0.61 g, 3 mmol) in absolute THF (200 mL) was refluxed under N_2 for 2 h. The reaction mixture was then cooled to −15°C and then an ice diluted hydrochloric acid (250 mL) was added. The mixture was then stirred at room temperature for 1 h. The organic layer was extracted with CH_2Cl_2, and then washed several times with $NaHCO_3$ solution and water. The organic layer was dried over $MgSO_4$. After the solvent was evaporated, the residue was purified by column chromatography using toluene–cyclohexane (1:1) [R_f 0.55, toluene–cyclohexane (1:1)] as eluent to give the *title* compound **10** (0.36 g, 82%) as pale red crystals, mp 206–208 °C (benzene); [Found: C, 86.75; H, 6.80; N, 6.32. $C_{32}H_{30}N_2$ (442.603) requires C, 86.84; H, 6.83; N, 6.33%]; ν (KBr) 3009–2925 (Ar–CH), 2894–2852 (ali.-CH), 1179 (N=N) cm^{-1}; UV (CH_3CN): λ_{max} 418, 320 nm; δ_H and δ_C ($CDCl_3$): see Table 1; *m/z* 443 (M+1, 12), 442 [M^+] (40), 339 (24), 338 (M^+-104, 100), 337 (54), 234 (38), 233 (40), 219 (20), 105 (10), 104 (12), 77 (14), 44 (16).

3.1.4. [2.2]Paracyclophanyl-[5′,4′-c]-[2.2](3,8)-pyridazinophane (11). A solution of anhydrous $AlCl_3$ (1.0 g) in absolute 1,2-dichloroethane (150 mL) was refluxed for 3 h under N_2 to render it free from hydrogen chloride gas. After addition of **10** (0.44 g, 1 mmol), the solution was irradiated under N_2 at ambient temperature for 3 d (the reaction was followed up by TLC). The reaction was quenched by the addition of water (100 mL) and then 1,2-dichloroethane was removed by distillation in vacuo. The aqueous solution was neutralized with sodium bicarbonate (3 g) followed by extraction of the organic layer with CH_2Cl_2. The organic layer was then dried over $MgSO_4$. The solvent was evaporated in vacuo and the residue was applied on column packing with alumina using toluene–cyclohexane (1:1) as eluent [R_f 0.65, toluene–cyclohexane (1:1)] to give the *title* compound **11** (0.31 g, 70%) as orange crystals, mp 150°C (ethanol); $C_{32}H_{28}N_2$ (440.587); [Found: C, 87.35; H, 6.39; N, 6.32 requires C, 87.24; H, 6.41; N, 6.36%]; ν (KBr) 3045–2950 (Ar–CH), 2900–2880 (ali.-CH), 1181 (N=N) cm^{-1}; UV (CH_3CN): λ_{max} 440, 345 nm; δ_H and δ_C ($CDCl_3$): see Table 1; *m/z*(%) 440 [M^+] (100), 412 (40), 336 (18), 308 (32), 220 (56), 132 (22), 104 (42).

3.1.5. 4-([2.2]-Paracyclophanyl)cinnnamanilide (13). To a cooled (0°C) stirred solution of **12**[8] (0.45 g, 2 mmol) with sodium hydroxide (0.20 g, 5 mmol) in acetone–water (150:30 mL), cinnamoyl chloride (0.41 g, 2.5 mmol) was gradually added. The mixture was stirred at this ambient temperature for 1 h and at room temperature for 2 h and then poured into ice water (100 mL). The resulting precipitate was collected to give the title compound **13** (0.67 g, 95%) as buff crystals, mp 230–232°C (ethanol); [Found: C, 84.85; H, 6.55; N, 3.92 requires $C_{25}H_{23}NO$ (353.463): C, 84.95; H, 6.56; N, 3.96%]; ν (KBr) 3270 (NH), 3045–3008 (Ar-CH), 2960–2890 (ali.-CH), 1695 (CO), 1582 (C=C) cm^{-1}; UV (CH_3CN): λ_{max} 362 nm; δ_H ($CDCl_3$): 2.60–2.90 (7H, m, CH_2–CH_2), 3.70–3.72 (1H, m, CH_2–CH_2), 5.40 (1H, s, PC–H), 6.45–6.70 (5H, m, PC–H, vinylic-H), 6.82–7.42 (7H, m, PC–H, Ph–H), 7.60 (1H, d, *J*=15.6 Hz, vinylic-H), 10.30 (1H, br, s, NH); δ_C ($CDCl_3$): 32.80, 33.44, 34.96, 35.48 (CH_2–CH_2), 118.00 (vinylic-CH), 120.44, 124.29, 126.34, 127.44, 128.54, 128.60, 128.90 (–CH), 129.12 (–C), 129.56, 129.90, 130.48, 131.24 (–CH), 132.66, 133.46 (–C), 134.56 (–CH), 135.00 (–C), 135.88 (–CH), 136.12, 138.50 (–C), 164.96 (CO); *m/z*(%) 353 [M^+] (50), 310 (30), 275 (22), 249 (M^+-104, 100), 223 (28), 158 (22), 145 (12), 131 (32), 119 (10), 103 (32), 91 (34), 77 (18).

3.1.6. [2]Paracyclophanyl-4-phenyl-[2](5,8)-quinolinophane-2(1*H*)-one (14). To a solution of **13** (0.71 g, 2 mmol) in absolute 1,2-dichloroethane (200 mL) and under N_2, few crystals of iodine crystals were added. The mixture was irradiated at ambient temperature for 20 h (the reaction was monitored with TLC reaction). The reaction was quenched by the addition of 1N of $NaHSO_3$ solution (100 mL) and then stirred for 1 h. The organic layer was extracted with CH_2Cl_2 and washed several times with water. The organic layer was dried over $MgSO_4$. After removal of the solvent, the residue was dissolved in acetone and the residue was subjected to thin-layer chromatography using toluene as eluent (R_f 0.35, toluene) to afford red crystals of the *title* compound **14** (0.56 g, 80%), mp >300°C (ethanol); [Found: C, 85.25; H, 6.00; N, 3.98. $C_{25}H_{21}NO$ (351.447) requires C, 85.44; H, 6.02; N, 3.99%]; ν (KBr) 3265 (NH), 3065–3020 (Ar-CH), 2956–2896 (ali.-CH), 1690 (CO), 1590 (C=C) cm^{-1}; UV (CH_3CN): λ_{max} 395 nm; δ_H and δ_C ($CDCl_3$): see Table 2; *m/z*(%) 351 [M^+] (40), 308 (18), 247

(M^+-104, 100), 221 (34), 156 (20), 142 (18), 129 (54), 118 (60), 101 (18), 91 (16), 77 (20).

3.2. Synthesis of compounds 17a,b

To a stirred solution of **12** (0.45 g, 2 mmol) in absolute ethanol (100 mL), a solution of either **15a** or **15b** (2 mmol) was added over 30 min. The reaction mixture was refluxed with stirring for 2–4 h (the reaction was followed by TLC progress). The mixture was then cooled and poured into ice water (150 mL). The resulting precipitate of either **17a** or **17b** was collected by filtration. The analytical and physical data for compounds **17a** and **17b** are as follows.

3.2.1. 4′-([2.2]Paracyclophanylamino)-pent-3-en-2-one (17a). (0.57 g, 93%) as buff crystals, mp 115–117°C (acetonitrile); [Found: C, 82.45; H, 7.50; N, 4.59. $C_{21}H_{23}NO$ (305.419) requires C, 82.58; H, 7.59; N, 4.59%]; ν (KBr) 3250 (NH), 3020–3000 (Ar-CH), 2940–2895 (ali.-CH), 1690 (CO), 1580 (C=C) cm^{-1}; δ_H ($CDCl_3$): 1.65 (3H, s, CH_3), 2.10, (3H, s, CH_3), 2.63–2.68 (2H, m, CH_2–), 2.80–3.20 (8H, m, CH_2), 6.05 (1H, s, H-5, PC–H), 6.35–6.47 (5H, m, PC–H), 7.11 (1H, dd, J=7.8, 2.0 Hz, PC–H); δ_C ($CDCl_3$): 19.59 (CH_3C=N), 26.88 (CH_3–CO), 29.09 (CH_2C=O), 32.67, 33.97, 34.83, 35.23 (CH_2–CH_2), 128.30, 130.00, 130.60, 131.90, 131.96 (PC–CH), 133.49 (PC–C), 134.24 (PC–CH), 135.00, 137.48, 138.98, 139.57 (PC–C), 146.07 (PC–C–N), 160.92 (CH_3–C=N), 190.96 (CO); m/z 306 (M+1, 22), 305 [M^+] (100), 262 (38), 248 (18), 236 (14), 201 (24), 200 (46), 158 (50), 143 (54), 119 (40), 104 (14), 91 (10).

3.2.2. 4′-([2.2]-Paracyclophanylamino)-1-phenyl-but-2-en-1-one (17b). (0.66 g, 95%) as brown crystals, mp 225–227°C (ethanol); [Found: C, 84.85; H, 6.75; N, 3.72. $C_{26}H_{25}NO$ (367.490) requires C, 84.98; H, 6.86; N, 3.81%]; ν (KBr) 3238 (NH), 3040–3008 (Ar-CH), 2960–2900 (ali.-CH), 1692 (CO), 1585 (C=C) cm^{-1}; δ_H ($CDCl_3$): 2.20 (3H, s, CH_3), 2.60–2.73 (2H, m, CH_2–), 2.83–3.25 (8H, m, CH_2–), 6.18 (1H, s, H-5, PC–H), 6.30–6.45 (5H, m, PC–H), 7.20 (1H, dd, J=7.8, 2.0 Hz, PC–H), 7.50–7.70 (5H, m, Ph–H); δ_C ($CDCl_3$): 18.00 (CH_3C=N), 30.00 (CH_2–CO), 32.79, 33.90, 35.02, 35.30 (CH_2–CH_2), 128.00, 128.42, 129.05, 129.65, 130.18, 131.56 (–CH), 131.00 (–C), 131.12, 131.75, 132.90 (–CH), 133.00 (–C), 133.34, 133.78, 134.84 (–CH), 135.88, 137.54, 139.65, 141.70 (–C), 162.00 (=CCH$_3$), 193.00 (CO); m/z(%) 367 [M^+] (100), 342 (26), 262 (18), 246 (14), 200 (20), 158 (38), 142 (50), 104 (60), 77 (24).

3.3. Synthesis of compounds 18a,b

To 89% phosphoric acid (20 mL), 40 g of P_2O_5 was added. The mixture was left to stand over 30 min. The mixture was then heated to 120°C, and then 1 mmol of either **17a** or **17b** was gradually added over 30 min. The mixture was stirred at ambient temperature for 2 h. The reaction temperature was then cooled to 50°C and ice water (500 mL) was added. The formed precipitate was filtered and washed several times with water. The filtrate was extracted with CH_2Cl_2 and the organic layer was washed with water several times. The organic layer was dried over $MgSO_4$. The solvent was removed in vacuo and the residue was purified by column chromatography using CH_2Cl_2 as eluent to give compounds **18a** and **18b**. The analytical and physical data of the products obtained are as follows.

3.3.1. 2,4-Dimethyl-[2]paracyclophanyl-[2](5,8)-quinolinophane (18a). (R_f 0.65, toluene), (0.22 g, 75%) as pale yellow crystals, mp 250°C (benzene); [Found: C, 87.65; H, 7.32; N, 4.80. $C_{21}H_{21}N$ (287.404) requires C, 87.76; H, 7.36; N, 4.87%]; ν (KBr) 3050–3019 (Ar-CH), 2965–2900 (ali.-CH), 1610 (C=N) cm^{-1}; δ_H and δ_C ($CDCl_3$): see Table 2; m/z(%) 287 [M^+] (100), 272 (66), 256 (48), 183 (22), 168 (42), 152 (28), 143 (54), 119 (40), 104 (34), 80 (16).

3.3.2. 2-Methyl-4-phenyl-[2]paracyclophanyl-[2](5,8)-quinolinophane (18b). (R_f 0.70, toluene); (0.28 g, 80%) as yellow crystals, mp 280–282°C (ethanol); [Found: C, 89.45; H, 6.64; N, 4.00. $C_{26}H_{23}N$ (349.475) requires C, 89.36; H, 6.63; N, 4.01%]; ν (KBr) 3065–3025 (Ar-CH), 2970–2860 (ali.-CH), 1612 (C=N) cm^{-1}; δ_H and δ_C ($CDCl_3$): see Table 2; m/z(%) 349 [M^+] (100), 334 (48), 256 (48), 245 (26), 230 (18), 216 (40), 183 (22), 168 (42), 152 (28), 119 (22), 104 (26), 77 (20).

3.3.3. [2](4,7)-Indano-[2]-paracyclophane-1-ylidene-propanedinitrile (20). A mixture of **19**[27] (0.52 g, 2 mmol), malononitrile (0.20 g, 3 mmol) and two drops of Et_3N in absolute ethanol (200 mL) was refluxed for 10 h. The solvent was removed and the residue was neutralized with diluted hydrochloric acid. The organic layer was extracted with CH_2Cl_2 and washed several times with water. The organic layer was dried over $MgSO_4$. The solvent was removed and the residue was applied on column chromatography using $CHCl_3$ as eluent (R_f 0.50) to give the *title* compound **20** (0.50 g, 80%) as colorless crystals, mp 240°C (ethanol); [Found: C, 85.05; H, 5.80; N, 9.00. $C_{22}H_{18}N_2$ (310.398) requires C, 85.13; H, 5.85; N, 9.03%]; ν (KBr) 3040–3000 (Ar-CH), 2980–2850 (ali.-CH), 2220 (CN) cm^{-1}; δ_H ($CDCl_3$) 2.00–2.22 (2H, m, CH_2–CH_2), 2.80–3.20 (8H, m, CH_2–CH_2), 3.45–3.60 (2H, m, CH_2–CH_2), 6.18 (1H, d, J=7.9 Hz, PC–H), 6.50–7.10 (5H, m, PC–H); δ_C ($CDCl_3$) 28.90, 29.68, 33.80, 34.95, 35.60, 37.20 (CH_2–CH_2), 70.92 (=C(CN)$_2$), 115.90, 117.80 (CN), 129.10, 129.70, 130.60, 131.40 (PC–CH), 132.80, 133.00 (PC–C), 133.45, 133.60 (PC–CH), 134.32, 135.00, 136.30, 137.00 (PC–C), 176.00 (C=C(CN)$_2$); m/z(%) 310 [M^+] (24), 262 (100), 246 (24), 234 (12), 219 (10), 205 (14), 191 (8), 158 (30), 129 (20), 115 (22), 105 (32), 104 (60), 91 (10).

3.4. Synthesis of spiro-pyranoindanoparacyclophanes

A mixture of **20** (0.31 g, 1 mmol) and either **15a** or **15c** (1 mmol) with two drops of Et_3N in absolute ethanol (100 mL) was refluxed for 6–8 h. The mixture was neutralized with dilute hydrochloric acid. The precipitates formed were then filtered off and washed several times with water. Recrystallization of the formed products afforded the pure products of **21a** and **21b**. The analytical and physical data are as follows:

3.4.1. 5′-Acetyl-2′-amino-6′-methyl-spiro-[(4,7)-indano-[2]-paracyclophanyl-4′-pyran]-3′-carbonitrile (21a). (0.29 g, 70%) as pale yellow crystals, mp 268–270°C

(methanol); [Found: C, 79.12; H, 6.30; N, 6.80. $C_{27}H_{26}N_2O_2$ (410.514) requires C, 79.00; H, 6.38; N, 6.82%]; ν (KBr) 3320 (NH_2), 3055–3010 (Ar-CH), 2980–2850 (ali.-CH), 2225 (CN), 1700 (CO), 1110 (C–O) cm^{-1}; δ_H ($CDCl_3$): 1.95 (3H, s, CH_3), 2.10–2.20 (2H, m, CH_2–CH_2), 2.30 (3H, s, CH_3), 2.32–2.65 (4H, m, CH_2–CH_2), 2.80–3.35 (6H, m, CH_2–CH_2), 4.80 (2H, br, s, NH_2), 6.20 (1H, d, J=7.9 Hz, PC–H), 6.45–6.75 (5H, m, PC–H); δ_C ($CDCl_3$): 12.92, 24.80 ($2CH_3$), 28.60, 29.00, 34.18, 35.70, 35.92, 36.80 (CH_2–CH_2), 40.00 (spiro-C), 62.70 (C-3), 117.40 (CN), 118.20 (C-5), 129.10, 129.70, 130.85, 131.20, 131.66 (PC–CH), 133.00, 133.66 (PC–C), 133.92 (PC–CH), 134.00, 135.75, 136.00, 146.46 (PC–C), 154.00 (C-6), 165.00 (C-2), 195.00 (CO); m/z(%) 410 [M^+] (100), 394 (18), 368 (16), 350 (14), 336 (32), 306 (40), 280 (16), 219 (10), 205 (14), 191 16), 158 (30), 129 (34), 115 (22), 105 (32), 104 (60), 91 (10).

3.4.2. Ethyl 6′-amino-5′-cyano-2′-methyl-spiro-[(4,7)-indano-[2]paracyclophanyl-4′-pyran]-3′-carboxylate (21b). (0.32 g, 75%) as yellow crystals, mp 274–276°C (methanol); [Found: C, 76.20; H, 6.40; N, 6.42. $C_{28}H_{28}N_2O_3$ (440.537) requires C, 76.34; H, 6.41; N, 6.36%]; ν (KBr) 3330 (NH_2), 3060–3015 (Ar-CH), 2985–2840 (ali.-CH), 2225 (CN), 1710 (CO), 1115 (C–O) cm^{-1}; δ_H ($CDCl_3$): 1.50 (3H, t, CH_3-ester, J=7.5 Hz), 2.35 (3H, s, CH_3), 2.34–2.38 (2H, m, CH_2–CH_2), 2.40–2.65 (4H, m, CH_2–CH_2), 2.75–3.30 (6H, m, CH_2–CH_2), 3.95 (2H, q, CH_2-ester, J=7.6 Hz), 5.12 (2H, br, s, NH_2), 6.18 (1H, d, J=7.9 Hz, PC–H), 6.40–6.68 (m, 5H, PC–H); δ_C ($CDCl_3$): 10.70, 28.60 ($2CH_3$), 28.90, 29.18, 33.22, 34.56, 35.66, 35.90, 40.48 (CH_2), 45.00 (spiro-C), 63.34 (C-3), 115.20 (CN), 119.84 (C-5), 128.96, 129.14, 130.65, 131.34, 132.00 (PC–CH), 132.88 (PC–C), 133.76 (PC–CH), 133.90, 134.48, 135.98, 136.56, 145.16 (PC–C), 153.22 (C-6), 168.16 (C-2), 176.80 (CO); m/z(%) 440 [M^+] (20), 424 (100), 410 (16), 380 (24), 365 (18), 320 (26), 234 (44), 219 (20), 206 (28), 191 (14), 158 (30), 129 (34), 115 (22), 104 (48), 91 (16).

References

1. Brown, C. J.; Farthing, A. C. *Nature* **1949**, *164*, 915–921.
2. (a) Vögtle, F. *Cyclophane Chemistry*; Wiley: New York, 1993. (b) Diederich, F. *Cyclophanes*; Royal Society of Chemistry: Cambridge, 1991. For recent reviews on cyclophane chemistry see (c) Bodwell, G. I. *Angew. Chem.* **1996**, *108*, 2221–2225, *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 2085–2089. (d) de Meijere, A.; König, B. *Synlett* **1997**, 1221–1227. (e) König, B. Carbon Rich Cyclophanes with Unusual Properties—An Update, Topics in Current Chemistry. *Synthesis*; Springer: Berlin, 1998; Vol. 196, pp 91–136.
3. Keehn, P. M.; Rosenfeld, S. M. *Cyclophanes I and II*; Academic: New York, 1983; Chapter 7, pp 443–484.
4. Aly, A. A.; Hopf, H.; Ernst, L. *Eur. J. Org. Chem.* **2000**, 3021–3029.
5. (a) Aly A. A. PhD Thesis, Faculty of Science, Chemistry Department, El-Minia University, El-Minia, Egypt, 1994. (b) Aly, A. A.; Hassan, A. A.; Mourad, A. E. *Can. J. Chem.* **1993**, *71*, 1845–1849. (c) Aly, A. A.; Hassan, A. A.; Mourad, A. E.; Hopf, H. *Arch. Pharm.* **1992**, *325*, 625–628. (d) Aly, A. A.; Hassan, A. A.; Mourad, A. E. *Bull. Chem. Fr.* **1994**, *131*, 45–47. (e) Aly, A. A.; Mourad, A. E. *Tetrahedron* **1993**, *49*, 7325–7336.
6. (a) Chan, C. W.; Wong, H. N. C. *J. Am. Chem. Soc.* **1988**, *110*, 462–469. (b) Chan, C. W.; Wong, H. N. C. *J. Am. Chem. Soc.* **1985**, *107*, 4790–4791. (c) Reiser, O.; Reichow, S.; de Meijere, A. *Angew. Chem.* **1987**, *99*, 1285–1292, *Angew. Chem. Int. Ed. Engl.* **1987**, *26*, 1277–1284. (d) Ashton, P. R.; Isaacs, N. S.; Kohnke, F. H.; Mathias, J. P.; Stoddart, J. F. *Angew. Chem.* **1989**, *101*, 1266–1272; *Angew. Chem. Int. Ed. Engl.* **1989**, *28*, 1258–1262. (e) Blatter, K.; Schülter, A. D. *Macromolecules* **1989**, *22*, 3506–3508. (f) Blatter, K.; Schülter, A. D. *Chem. Ber.* **1989**, *122*, 1351–1356.
7. Aly, A. A.; Mourad, A. E.; El-Shaieb, K. M.; Hopf, H. *Synth. Commun.* **2001**, 637–642.
8. Cram, D. J.; Dalto, C. K.; Knox, G. R. *J. Am. Chem. Soc.* **1963**, *85*, 1088–1093.
9. Hopf, H.; Sankararaman, S.; Dix, I.; Jones, P. G. *Eur. J. Org. Chem.* **2000**, 2711–2716.
10. Borah, H. N.; Prajapati, D.; Sandhu, J. C.; Ghosh, A. C. *Tetrahedron* **1994**, *35*, 3167–3172.
11. Tang, R.; Qian, X.; Tai, Z. T. *J. Chem. Lett.* **1996**, 351–352.
12. Ren, P.; Dong, T.; Wu, S. *Synth. Commun.* **1997**, *27*(9), 1547–1552.
13. (a) Badger, G. M.; Jamieson, N. C.; Lewis, G. E. *Aust. J. Chem.* **1965**, *18*, 190–198. (b) Badger, G. M.; Lewis, G. E. *Aust. J. Chem.* **1963**, *16*, 285–288. (c) Badger, G. M.; Lewis, G. E. *Aust. J. Chem.* **1964**, *17*, 371–374.
14. Nystorm, R. F.; Brown, W. G. *J. Chem. Soc., Chem. Commun.* **1944**, 3739–3742.
15. Blackstock, S. C.; Kochi, J. K. *J. Am. Chem. Soc.* **1987**, *109*, 2484–2490.
16. (a) Huisgen, R. *Angew. Chem.* **1963**, *75*, 604–634; *Angew. Chem. Int. Ed.* **1963**, *2*, 565–595. (b) Huisgen, R. *Angew. Chem.* **1963**, *75*, 742–746; *Angew. Chem. Int. Ed.* **1963**, *2*, 633–637.
17. Allinger N. L. MM2 (91) force field Program, obtained from Quantum Chemistry Program, Indiana University; Molecular Mechanics PM3 Program (ACD/3D), Advanced Chemical Development Inc., Toronto, Canada, 1988.
18. Curran, M. V. *J. Med. Chem.* **1974**, *17*, 273–280.
19. Nannini, G.; Biasoli, G.; Perrone, E.; Forgione, A.; Buttinoni, A.; Ferrari, M. *J. Med. Chem.-Chim. Ther.* **1979**, *14*, 53–58.
20. Katner, S. A. US Patent 3890324, 1975; *Chem. Abstr.* **1975**, *83*, 164169h.
21. Skotnicki, S. J.; Gilman, C. S.; Steinbaugh, A. B.; Musser, H. J. US Patent 4248246, 1988; *Chem. Abstr.* **1988**, *109*, 110425u.
22. Afonso, A.; Kelly, J. M.; Chackalamannil, S. US Patent 5608067, 1997; *Chem. Abstr.* **1997**, *126*, 225297x.
23. Wentland, M. P.; Aldous, S. C.; Gruett, D. M.; Perni, R. B.; Powles, R. G.; Danz, D. W.; Klingbeil, K. M.; Perverly, A. D.; Robinson, R. G. *Bioorg. Med. Chem. Lett.* **1995**, *5*, 405–409.
24. Chu, D. T. W. *J. Heterocycl. Chem.* **1990**, *27*, 839–843.
25. Makioka, Y.; Shindo, T.; Taniguchi, Y.; Takaki, K.; Fujiwara, Y. *Synthesis* **1995**, 801–804.
26. Woersdoerfer, U.; Vögtle, F. *J. Prakt. Chem.* **1999**, *341*, 445–448.
27. Hopf, H.; Raulfs, F.-W. *Isr. J. Chem.* **1985**, *25*, 210–216.