[2.2](4,7)Isobenzofuranophanes – Synthesis, Characterisation, and Reactivity

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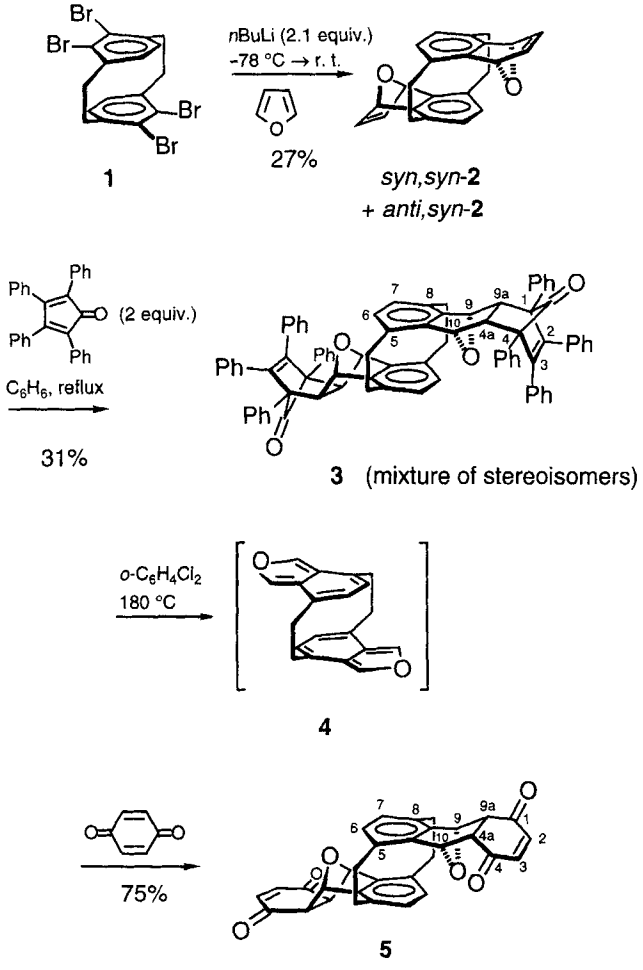
The isomeric Diels-Alder adducts **3**, obtained by cycloaddition of tetraphenylcyclopentadienone to the 4,5:12,13-bis(oxanorbornadieno)[2.2]paracyclophanes *syn,syn-* and *anti,syn-***2**[*], yield the unstable isobenzofuranophane **4** by consecutive extrusion of carbon monoxide and tetraphenylbenzene when heated to 180°C. The molecular ion of **4** was observed in the EI mass spectrum. The stable tetraphenyl-substituted analogue **10** was synthesized independently from the previously unknown 4,5,12,13-tetrabenzoyl[2.2]paracyclophane (**9**). UV/Vis as well as fluorescence spectra and an X-ray crystal structure analysis of **9** are reported.

[2.2]Furanophane[1] has been used in cycloaddition reactions yielding bridged Diels-Alder adducts. Isobenzofuran[2] is a much more reactive diene for cycloadditions than furan due to the rearomatisation upon addition of the dienophile. A variety of methods have been developed to generate the unstable isobenzofuran and to trap it in situ as well as to observe it at low temperature or in highly diluted solutions[3]. While engaged in designing new approaches to stair-like multilayered [2.2]paracyclophanes[4,5], we have generated and characterised [2.2](4,7)isobenzofuranophane (**4**) and also prepared its stable tetraphenyl-substituted derivative **10**.

4,5,12,13-Tetrabromo[2.2]paracyclophane (**1**), easily prepared from commercially available [2.2]paracyclophane, can be applied as a new bis-aryne equivalent[4]. The in situ-trapping of the corresponding bis-aryne with furan yields the two products *syn,syn-***2**[*] and *anti,syn-***2** (ratio 1:1)[4]. This mixture of isomeric compounds **2** reacts with two equivalents of tetraphenylcyclopentadienone in refluxing benzene to yield the insoluble Diels-Alder adducts **3**[5] as a mixture of four diastereomers. When heated in *o*-dichlorobenzene solution or neat to 180°C, extrusion of carbon monoxide occurs, and isobenzofuran moieties are formed on both decks of the molecule by retro-Diels-Alder reaction to yield [2.2](4,7)isobenzofuranophane (**4**). The molecular ion of **4** was observed in the mass spectrum (EI and FD) of **3**, and the molecular formula was confirmed by high-resolution mass spectrometry. The highly reactive **4** can be trapped in situ when **3** is heated in *o*-dichlorobenzene solution in the presence of *p*-benzoquinone to yield the two diastereomeric Diels-Alder adducts *syn,syn-***5** and *anti,syn-***5** (ratio undetermined).



[+] X-Ray crystal structure analysis.

[*] The stereochemical descriptors *syn* and *anti* refer to the orientation of the oxygen bridge in the oxabicyclo[2.2.1]heptadiene subunits with respect to the [2.2]paracyclophane skeleton.

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The stability of the reactive isobenzofuran is increased by phenyl substituents, e.g. in 1,3-diphenylisobenzofuran[6]. Accordingly, 1,1',3,3'-tetraphenyl[2.2](4,7)isobenzofuranophane (**10**) was expected to be a stable compound. The logical precursor of **10**, 4,5,12,13-tetrabenzoyl[2.2]paracyclophane (**9**), was prepared in 64% yield from dibenzoylacetylene (**7**) and 1,2,4,5-hexatetraene (biallene) (**6**) by adaption of the procedure of Hopf et al.[7] for the preparation of [2.2]paracyclophane-4,5,12,13-tetracarboxylate.

Suitable crystals for X-ray structure analysis of **9** (see Figure 1) were obtained by slow concentration of its dichloromethane solution. The molecule of **9** possesses a crystallographic inversion centre. The torsional angles between the carbonyl and phenyl groups are −21.1° for O1−C9−C10−C15 and 163.6° for O2−C16−C17−C18. The values for the corresponding angles between the carbonyl groups and the phane benzene rings are 120.2° for O1−C9−C3−C4 and −46.5° for O2−C16−C4−C3.

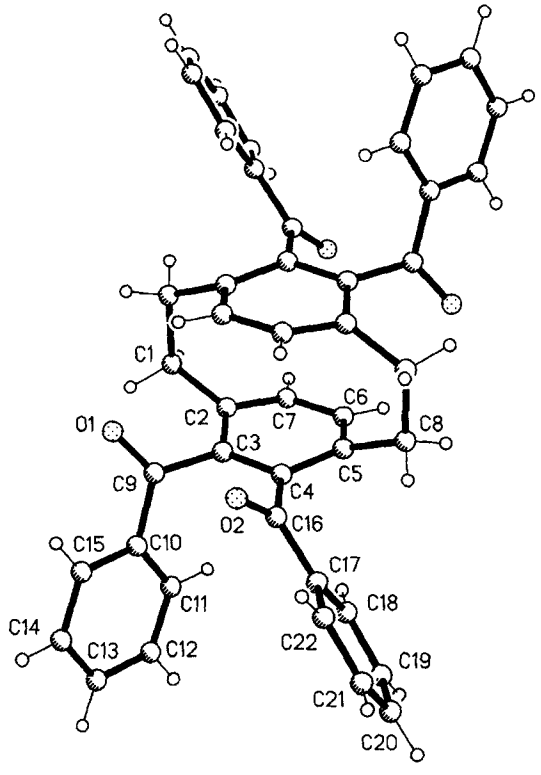
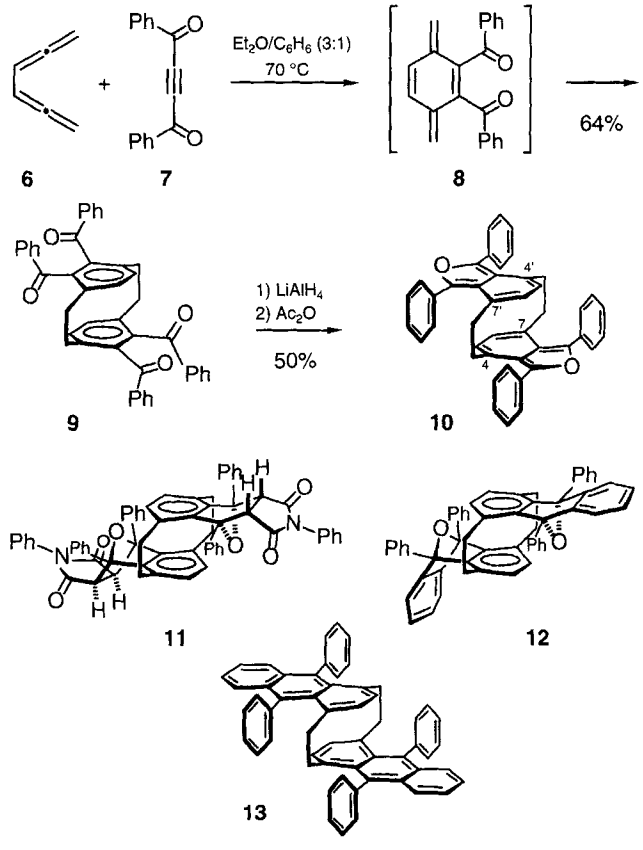


Figure 1. Molecular structure of compound **9** in the crystal[8]. Radii are arbitrary. Only the asymmetric unit is numbered. Selected bond lengths [pm]: C(1)−C(8') 157.9(3), C(1)−C(2) 151.5(3), C(3)−C(9) 150.0(3), C(9)−C(10) 149.4(3), C(9)−O(1) 121.8(3); bond angles [°]: C(3)−C(9)−C(10) 118.1(2), C(3)−C(9)−O(1) 121.2(2), C(5)−C(8)−C(1') 112.3(2); dihedral angles [°]: C(1)−C(2)−C(8')−C(5') 4.9, C(10)−C(9)−C(3)−C(4) −64.9, C(17)−C(16)−C(4)−C(3) 132.7; bending of *para*-bridged benzene rings: angle between axis C(1)−C(2) [C(5)−C(8)] and plane C(3)−C(7)−C(4)−C(6) 20 [25], angle between plane C(2)−C(3)−C(7) [C(4)−C(5)−C(6)] and plane C(3)−C(7)−C(4)−C(6) 12 [13]

The nearly orthogonal orientation of the benzoyl substituents with respect to the cyclophane unit in **9** is reflected in the UV spectrum [λ_{max} (lg ε) = 253 nm (4.56), 280 (4.16, sh), 320 (3.56) in tetrahydrofuran, 251 (4.54), 280 (4.17, sh), 318 (3.58) in acetonitrile] which shows mainly the absorption of a carbonyl-substituted benzene like acetophenone [λ_{max} (lg ε) = 243 nm (4.11), 279 (3.08), 315 (1.74)] or benzaldehyde [λ_{max} (lg ε) = 242 nm (4.15), 280 (3.15), 328 (1.74)]. The considerable increase in intensity for the n → π* transition near 320 nm most probably results from better overlap between the n orbitals of the twisted carbonyl groups and the paracyclophane π system, thus facilitating the electronic transition. Excitation of **9** in acetonitrile at 250 nm to only very weak fluorescence near 340 nm ([2.2]paracyclophane: 351 nm), probably due to reabsorption of photons from the $S_1 \rightarrow S_0$ transition by the relatively strong and broad n → π* band of **9**.

Reduction of **9** with $LiAlH_4$ in tetrahydrofuran and subsequent treatment of the resulting tetrol with acetic anhydride[9] gave **10** in 50% yield. The diphenylisobenzofuran moieties in **10** both readily cycloadd dienophiles like *N*-phenylmaleinimide and in situ generated dehydrobenzene to give the double Diels-Alder adducts **11** and **12**[10], respectively, as mixtures of the *syn,syn* and *anti,syn* isomers.



Both isobenzofuranophanes **4** and **10** can be envisaged as starting materials for extended [2.2]bisarenophanes like **13**[4] and even multilayered [2.2]paracyclophanes with a stair-like structure.

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Experimental

^{1}H NMR: Bruker WM 270 and AM 400; δ = 0 for tetramethylsilane as internal standard, δ = 7.26 for chloroform. – ^{13}C NMR: Bruker WM 270 and AM 400; δ = 77 for [D$_1$]chloroform; the multiplicity of the signals was determined by the DEPT technique and quoted as (+) for CH_3 and CH groups, (–) for CH_2 and (C_{quat}) for quaternary carbons. – IR: Nicolet 320 FT-IR. – MS: Finnigan MAT 8430. – UV/Vis and fluorescence: Cary 219 (Varian) and Perkin-Elmer MPF-44A. – Melting points: Hot-plate microscope, uncorrected. – Column chromatography (CC): Merck silica gel 60, 70–230 mesh; PE (60/70) stands for petroleum ether with a boiling range of 60–70°C. – TLC was carried out on silica gel-coated aluminium sheets (Merck F_{254}).

1,4,4a,9,9a,10,1',4',4a',9',9a',10'-Dodecahydro-1,2,3,4,1',2',3',4'-octaphenyl-9,10,9',10'-diepoxy-1,4,1',4'-bis(oxomethano)[2.2](5,8)anthracenophane (**3**): 500 mg (1.47 mmol) of *syn,syn-/anti,syn*-**2** and 1.13 g (2.94 mmol) of tetraphenylcyclopentadienone were refluxed in 100 ml of benzene for 2 d, during which time the colourless product precipitated. The reaction mixture was concentrated in vacuo to 30 ml, the precipitate was collected on a filter, washed with 50 ml of hot ethanol and dried in vacuo to yield 500 mg (31%) of **3** as a colourless solid, m.p. 185°C (dec.). – IR (KBr): $\tilde{\nu}$ = 3055 cm^{-1}, 1775, 1604, 1078. – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 3.00 (s, 4H), 3.30 (m, 8H), 5.62 (s, 4H), 6.35 (s, 4H), 6.90–7.40 (m, 40H). – MS (70 eV), *m/z* (%): 382 (100) [tetraphenylbenzene], 288 (38) [**4**]. – MS (FD), *m/z* (%): 698 (10), 382 (100), 288 (30). – $C_{20}H_{16}O_2$: calcd. for [M$^+$] of **4** 288.1150; found 288.1143 (MS).

anti-1,4,4a,9,9a,10,1',4',4a',9',9a',10'-Dodecahydro-1,4,1',4'-tetraoxo-9,10,9',10'-diepoxy[2.2](5,8]anthracenophane (**5**): A mixture of 30 mg (0.027 mmol) of **3** and 50 mg (0.46 mmol) of *p*-benzoquinone in 10 ml of dichlorobenzene was heated under nitrogen at 180°C for 5 min. After cooling to room temp. 20 ml of PE (60/70) was added, the precipitated crystals were filtered off and dried in vacuo yielding 10 mg (75%) of **5**. – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.80–3.30 (m, 10H), 3.52 (m, 2H), 5.45 (s, 2H), 5.60 (m, 2H), 5.92 (s, 2H), 6.20 (s, 2H), 6.35 (s, 2H), 6.85 (s, 2H).

4,5,12,13-Tetrabenzoyl[2.2]paracyclophane (**9**): A mixture of 180 ml (108 mmol, approx. 0.6 M of 1,2,4,5-hexatetraene (**6**) in diethyl ether and 18 g (77 mmol) of dibenzoylacetylene (**7**) in 60 ml of benzene was heated in a distillation apparatus with a 40-cm Vigreux column for 5 h at 45°C and for 20 h at 70°C. The cold reaction mixture was filtered, the solid residue recrystallized from toluene and dried in vacuo to yield 15.3 g (64%) of **9** as a colourless solid, m.p. >280°C. – IR (KBr) $\tilde{\nu}$ = 1671 cm^{-1}, 1594, 1448, 1269, 692. – UV (THF): λ_{max} (lg ε) = 253 nm (4.564), 280 (4.16, sh), 320 (3.556); (acetonitrile): λ_{max} (lg ε) = 251 (4.538), 280 (4.17, sh), 318 (3.580). – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.90 (m, 8H), 7.10–7.55 (m, 24H). – ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 33.82 (–), 127.96 (+), 129.20 (+), 132.67 (+), 134.74 (+), 137.02 (C_{quat}), 138.32 (C_{quat}), 139.91 (C_{quat}), 196.72 (C_{quat}). – MS (70 eV), *m/z* (%): 624 (100) [M$^+$]. – $C_{44}H_{32}O_4$ (624.7): calcd. C 84.59, H 5.16; found C 84.42, H 5.22.

X-Ray Structure Determination of Compound **9**[8]: $C_{44}H_{32}O_4$, M = 624.70, triclinic, space group $P\bar{1}$, a = 91.4(4), b = 983.1(4), c = 1040.3(5) pm, α = 94.01(2), β = 116.10(2), γ = 106.32(2)°, V = 0.7879(6) nm^3, Z = 1, λ(Mo-K_α) = 0.71073 Å, μ = 0.083 mm^{-1}, D_x = 1.314 Mg m^{-3}, F(000) = 328, T = 143 K. A colourless prism (ca. 0.65 × 0.30 × 0.25 mm) was mounted on a glass fibre in inert oil (type RS3000, donated by Fa. Riedel de Haën) and transferred to the cold gas stream of a Stoe STADI-4 diffractometer with a Siemens LT-2 low-temperature attachment. Cell constants were refined from ±ω values of 52 reflections in the 2Θ range 20–23°. A total of 2980 intensities (2792 unique, R_{int} = 0.0197) were measured to 2Θ ≤ 50°. The structure was solved by direct methods and refined anisotropically on F^2 (program SHELXL-93, G. M. Sheldrick, University of Göttingen). Hydrogen atoms were included with a riding model. The final $wR(F^2)$ for all reflections was 0.123, with a conventional $R(F)$ of 0.0487, for 217 parameters.

anti-1,1',3,3'-Tetraphenyl[2.2](4,7)isobenzofuranophane (**10**): To 200 mg (0.32 mmol) of **9** suspended in 110 ml of anhydrous THF was added 40 mg (1.05 mmol) of $LiAlH_4$ at room temp., the mixture was stirred for an additional 10 min, then evaporated to dryness in vacuo, 60 ml of acetic anhydride was added to the residue, and the mixture was refluxed under nitrogen for 30 min. After cooling to room temp. the precipitated solid was collected by filtration, washed with water (3 × 20 ml) and dried in vacuo to yield 95 mg (50%) of **10** as a green solid. m.p. >280°C. – IR (KBr): $\tilde{\nu}$ = 2937 cm^{-1}, 956, 760. – UV (dichloromethane): λ_{max} (lg ε) = 252 nm (3.980), 343 (3.997), 439 (3.801). – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.05 and 3.10 (m, 8H), 5.72 (s, 4H), 7.10–7.80 (m, 20H). – MS (70 eV), *m/z* (%): 592 (38) [M$^+$], 296 (100) [M^{2+}].

Diels-Alder Reaction of **10** *with N-Phenylmaleinimide:* 20 mg (0.034 mmol) of **10** and 24 mg (0.14 mmol) of *N*-phenylmaleinimide were refluxed in 20 ml of toluene for 30 min, during this time the green fluorescence disappeared. The solvent was removed in vacuo, the solid residue washed with 20 ml of dichloromethane and dried in vacuo to yield 19.5 mg (61%) of compound **11** (mixture of *syn,syn* and *anti,syn* isomers, most probably with a ratio of 1:1). – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.70 and 2.22 (m, 8H), 3.95 (s, 4H), 6.35 (s, 4H), 6.48 (m, 4H), 7.26, 7.50 and 8.35 (m, 26H). – ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 30.89 (–), 56.76 (+), 91.02 (C_{quat}), 126.53, 127.29, 127.78, 128.46, 128.72 and 128.83 (+), 131.14 and 132.69 (C_{quat}), 135.50 (+), 138.02, 140.66 and 173.14 (C_{quat}). – MS (70 eV), *m/z* (%): 592 (28), 173 (100).

Diels-Alder Reaction of **10** *with Dehydrobenzene:* To a mixture of 50 mg (0.084 mmol) of **10** and 400 mg (1.70 mmol) of 1,2-dibromobenzene in 60 ml of anhydrous THF was added dropwise at –40°C 1.2 ml (1.8 mmol) of *n*-butyllithium (1.5 M solution in hexane) in 10 ml of hexane. The mixture was stirred for 20 min and then allowed to warm up to room temp., 2 ml of methanol and 100 ml of dichloromethane were added, and the organic phase was washed with water (3 × 50 ml), dried with $MgSO_4$, and evaporated to dryness in vacuo. Chromatography of the residue on 50 g of silica gel (dichloromethane) yielded four fractions: I (R_f = 0.9) 1,2-dibromobenzene, not isolated. – II (R_f = 0.64): 15 mg (24%) of *9,9',10,10'-tetrahydro-9,9',10,10'-tetraphenyl-anti,syn-9,10:9',10'-diepoxy-anti[2.2](1,4)anthracenophane*[10] (*anti,syn*-**12**). – III (R_f = 0.46): 6 mg (10%) of *9,9',10,10'-tetrahydro-9,9',10,10'-tetraphenyl-syn,syn-9,10:9',10'-diepoxy-anti-[2.2](1,4)anthracenophane*[10] (*syn,syn*-**12**). – IV (R_f = 0.36): 15 mg (28%) of **9**.

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[8] Full details of the structure determination have been deposited at the Fachinformationszentrum Karlsruhe, Gesellschaft für wissenschaftlich-technische Information mbH, D-76344 Eggenstein-Leopoldshafen, Germany, from where this material may be obtained on quoting the full literature citation and the reference number CSD-58420.
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[10] Compound **12** has previously been prepared by cycloaddition of diphenylisobenzofuran to in situ generated 4,5:12,13-bis-(dehydro[2.2]paracyclo)phane[4] followed by deoxygenation. Spectroscopic data for the two samples were identical.

[167/94]