

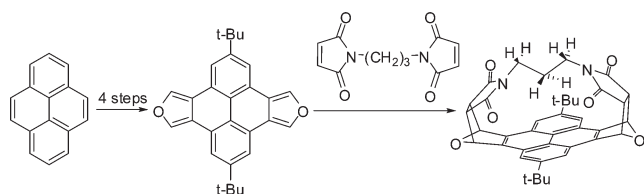
Synthesis and Characterization of 2,7-Di(*tert*-butyl)pyreno[4,5-*c*:9,10-*c'*]difuran and Derived Pyrenophanes

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Isobenzofurans (IBF) have seen widespread use in the synthesis of both natural products and polycyclic aromatic hydrocarbons. There are few examples that have two IBF entities linked in a fused aromatic ring system. Here we present the synthesis and characterization of a bis(IBF), 2,7-di(*tert*-butyl)pyreno[4,5-*c*:9,10-*c'*]difuran. Reaction with bis(maleimide) dienophiles gives pyrenophanes. The solid-state structures of the bis(IBF) and two cyclophanes are discussed.

Isobenzofuran (IBF, **1**, Figure 1) and its related compounds^{1–5} are highly reactive dienes in the Diels–Alder reaction and have proven to be useful intermediates in the

synthesis of medicinal natural products,^{6–9} polycyclic aromatic hydrocarbons,^{10–14} and fullerene derivatives.^{15,16}

There are only three previously known examples of bis(IBF) in which the two furan entities are part of a common aromatic ring system: benzodifuran **2** and naphthodifuran **3**, both prepared by Wege,¹⁷ and isomeric naphthodifuran **4**.^{18,19} A synthetic equivalent to bis(IBF) **5**, for which no stable classical valence bond structure can be drawn, was developed by Hart.²⁰ Collectively, these and related examples are very useful and have been used to prepare π -molecular switches,^{21,22} linear acenes,^{20,23} and cyclophanes.^{19,23} We now report the synthesis of 2,7-di(*tert*-butyl)pyreno[4,5-*c*:9,10-*c'*]difuran, **6**, an example in which the furans are fused to opposite faces of a pyrene ring system. Note that this molecule is an expanded analogue of **5** in which the additional rings enable one to draw a classical valence bond structure. As examples of the utility of **6**, two novel pyrenophanes have been prepared by its reaction with tethered bis(maleimide) dienophiles.

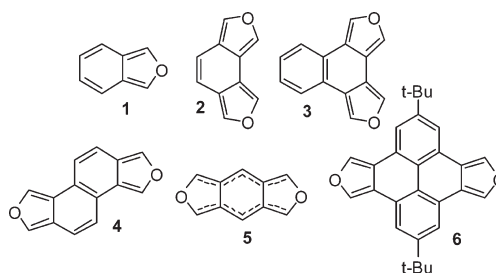


FIGURE 1. Examples of isobenzofuran and bis(isobenzofuran)s.

The synthesis of **6** (Scheme 1) started with the addition of *tert*-butyl groups²⁴ to positions 2 and 7 of pyrene; these groups direct subsequent bromination²⁵ to give the tetrabromide **7**. Reaction with *n*-BuLi forms arynes sequentially that were trapped with furan to produce bis(epoxide) **8**, as a mixture of *syn* and *anti* isomers. Reaction with dipyriddylenetrazine (dipyrtet)²⁶ gave difuran **6**. The relative reactivities of IBFs are easily predicted using the structure count ratio method developed by Herndon²⁷ and applied to IBFs by Wege.²⁸ On this basis, we expected **6** to be almost 300 times less reactive than **1** and probably isolable, whereas **1** is not.

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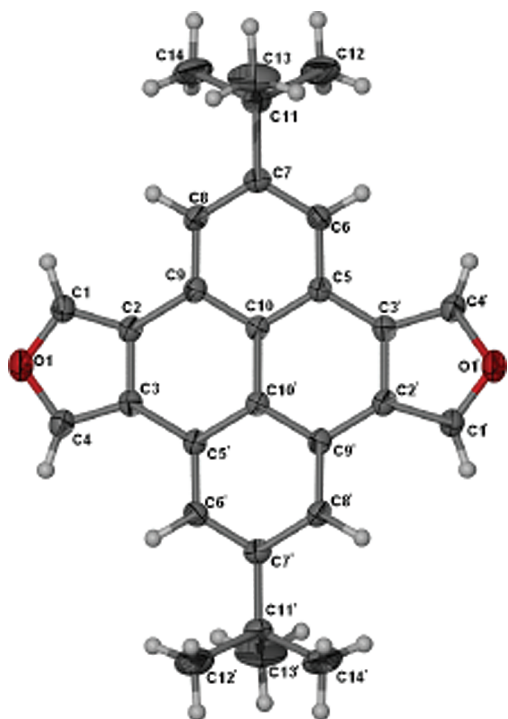


FIGURE 2. Solid-state structure of **6** showing the crystallographic inversion symmetry. Only one of the two independent molecules in the unit cell is shown. Ellipsoids drawn to 50% probability level, and hydrogens are drawn with arbitrary reduced radii using X-Seed (1999).

In the event, while chromatography of crude material led to substantial loss, it was possible to obtain large diffracting crystals of **6** from toluene in 2% yield.

From inspection of the Kekulé structure, one might expect the solid-state structure of **6**²⁹ (Figure 2) to resemble that of biphenyl with two bridging furans. Comparisons to related molecules (Table 1) show, however, that the bond lengths of the furan rings most closely resemble those of diphenylisobenzofuran and the bond lengths of the benzenoid rings in **6** are closer to those of pyrene than those of biphenyl. Furthermore the single bond (C2–C9) is shorter than a typical single bond, which when combined with the lengthening of the “interior aromatic bonds” (C2–C3 and C9–C10) suggests that π electrons are shared around the entire ring rather than in four separate moieties.

Cyclophanes **13** and **14** (Scheme 1) were prepared using bis(maleimide) dienophiles with methylene tethers **3** and **5** carbons in length. Reactions were carried out by stirring the bis(dienophile) with either **6** or with **6** generated in situ. Yields are poor (6% and 2%, respectively) but represent isolated yields of X-ray quality material and are not optimized. The proton NMR spectra of **13** and **14** exhibit signals upfield of TMS that are characteristic of these compounds.

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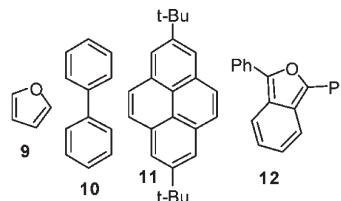
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TABLE 1. Comparison of Bond Lengths^a of **6** and Related Structures

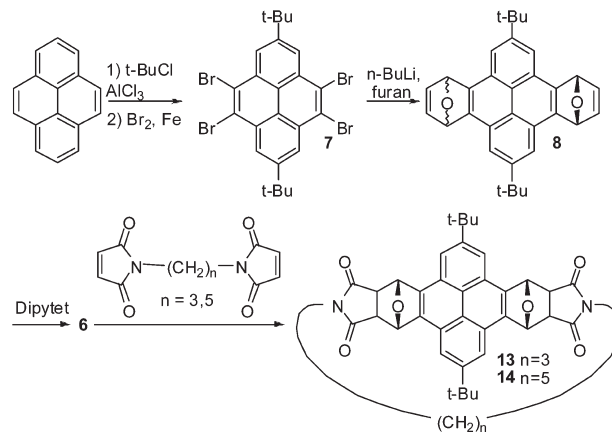
bond	6 ^b	9	10	11	12
C1–C2	1.373	1.322			1.373
C1–O1	1.372	1.369			1.368
C2–C3	1.431	1.425		1.345	1.434
C2–C9	1.454			1.434	1.426
C10–C10'	1.471		1.493	1.417	1.434
C5–C6	1.391		1.390	1.390	
C9–C10	1.412		1.396	1.415	1.349
C6–C7	1.392		1.387	1.392	
C7–C11	1.532			1.531	

^a Selected bond lengths in angstroms of **6** and reference structures: furan,³⁰ **9**; biphenyl,³¹ **10**; 2,7-di(*tert*-butyl)pyrene,³² **11**; and 1,3-diphenylisobenzofuran,³³ **12**, using the atom numbering introduced in Figure 2.



^b Due to disorder in one of the unique molecules in the crystal structure, bond lengths used are from “molecule 1”; see Supporting Information.

SCHEME 1. Synthesis of Bis(1,3-diphenylisobenzofuran) **6** and Cyclophanes **13** and **14**



Both compounds exhibit apparent C_{2v} symmetry in solution. In **13**, the central methylene is highly shielded by the pyrene π electrons and appears at -2.4 ppm. This cyclophane is closely comparable to naphthalenophane **15**^{19,34} in which the central methylene appears at -1.4 ppm. Cyclophane **14**, with the longer tether, exhibits two upfield signals: the central methylene appears at -2.1 ppm, and the adjacent methylenes (β to N) appear at -0.5 ppm.

Solid-state structures of **13**³⁵ and **14**³⁶ were obtained. The structure of **13** provides a useful comparison to that of naphthalenophane **15**.^{34,37} Both exhibit an antistaggered

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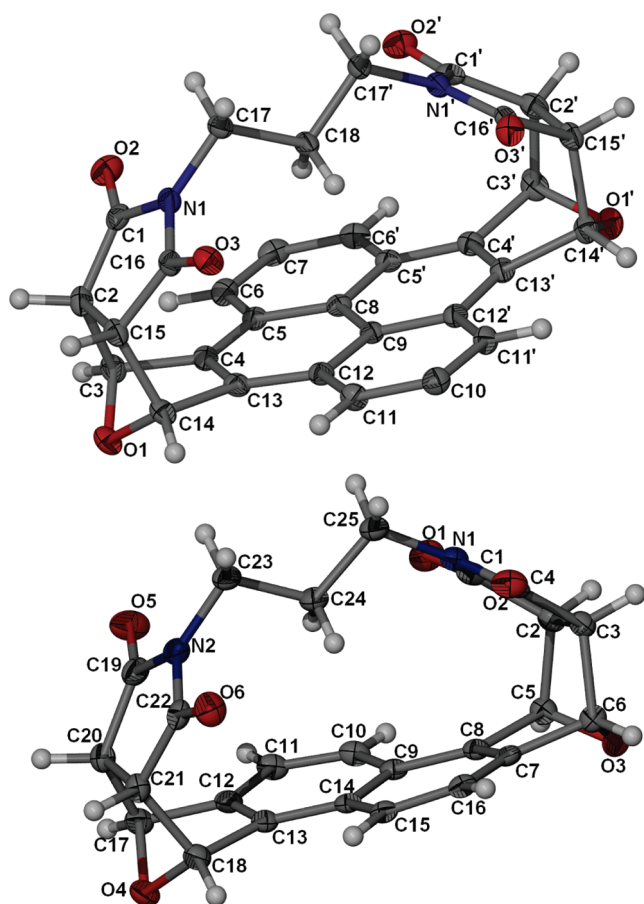


FIGURE 3. Structures of **13** and **15** as found in the crystals; **13** is located on a crystallographic mirror plane that bisects C(7)–C(10) and C(18). *tert*-Butyl groups are omitted for clarity. Ellipsoids drawn to 50% probability level, and hydrogens are drawn with arbitrary reduced radii using X-Seed (1999).

chain between the two N atoms. Distances between the N atoms in **13** and **15** are very similar: 4.83 and 4.89 Å, respectively. The distances from the central methylene carbons to the centroids of the carbon–carbon bonds below (C8–C9 in **13**, C9–C14 in **15**) are nearly identical: 3.37 versus 3.35 Å. There is a marked difference in the geminal angles found in the different methylene tethers. In **15**, the geminal angles along the tether are 108°–115°–108°. On the basis of this and other structural data, our conclusion was that the geminal angle about the central methylene of **15** was widened because it was being pushed out by the π electrons and not because the tether was being stretched between the two N atoms. In contrast, the geminal angles along the tether of **13** are similar to each other and closer to normal angles: 110.4(2)°, 112.6(2)°, 110.4(2)°. There is clear evidence that in **13** there is some strain associated with the N atoms being tugged together. Although the pyrene ring is still planar, all four bridgehead carbons (such as C14) are pulled approximately 0.4 Å out of the pyrene plane. In addition, the geminal angles about the bridgehead carbons (such as C13–C14–C15) are slightly narrower (107.3(1)–107.5(1)°) than in **15** (108–111°).

Pyrenophane **14** has a tether that is too long to easily adopt an antistaggered conformation between the N atoms. In this structure (Figure 4) the N atoms are much further apart (6.09 Å). The “slack” in the tether is taken up with a series

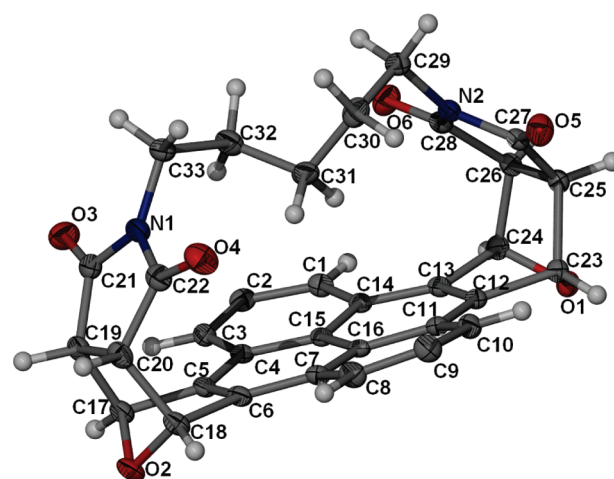


FIGURE 4. Structure of **14** as found in the crystal. *tert*-Butyl groups are omitted for clarity. Ellipsoids drawn to 50% probability level, and hydrogens are drawn with arbitrary reduced radii using X-Seed (1999).

of gauche interactions between the methylenes. Torsional angles along the chain are not optimally staggered: 61.8(3)°, 78.3(3)°, 94.0(3)°, and 71.8(3)°. Geminal angles fall in a narrow range (111.8(2)–114.1(2)°). Surprisingly, the central methylene adopts a position similar to the other examples (pointing into the aromatic ring) and its carbon lies 3.26 Å away from the centroid of the C15–C16 bond, slightly closer than in **13** and **15**.

For cyclophanes **13** and **15**, complexity in the proton NMR methylene signals are consistent with a solution-state structure that is conformationally rigid. In contrast, the tether signals of **14** suggest that there is significant conformational averaging in solution. Nevertheless, the high upfield shift of the central methylene and the results of a conformational search³⁸ suggest that the conformation adopted by **14** in the solid state is also important in solution.

The most surprising feature in the solid-state structure of **14** is the distortion in the pyrene backbone. It is warped inward with the carbon atoms bearing the *tert*-butyl groups (C2 and C9) lying 0.4 Å out of the plane defined by the central 10 carbon atoms. The ring exhibits an overall bend angle³⁹ of 18.5°. We were tempted to attribute this to the tether forcing the N atoms apart since in physical models this induces the observed warp. Analysis of the crystal packing, computational modeling, and the similarity of the UV spectrum to that of pyrene indicates that this distortion is due to intermolecular interactions in the solid state (see Supporting Information).

In summary, we have developed the synthesis of a novel bis(IBF) based on pyrene and have characterized two cyclophane derivatives. In addition to being a cyclophane precursor, we believe that **6** can be applied to the synthesis of an aromatic molecular belt or cyclacene,^{40,41} and we are exploring those possibilities. Other potential applications are to

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the preparation of graphitic materials,⁴² Diels–Alder polymers,^{43,44} and polyacene ribbon polymers.^{45,46}

Experimental Section

***syn-* and *anti*-2,9-Di(*tert*-butyl)-4,7,11,14-diepoxy-4,7,11,14-tetrahydrodibenzo[*e,f*]pyrene (8).** To a solution of **7** (4.87 g, 7.73 mmol) and furan (20 mL, 0.28 mol) cooled to $-70\text{ }^{\circ}\text{C}$ were added two aliquots of 1.6 M *n*-BuLi (5 mL, 8.0 mmol) 1 h apart. The solution was cooled for an additional 1 h and left overnight. The solution was quenched with water, extracted with CHCl_3 , dried (MgSO_4), and concentrated. It was used in the next step without further purification. ^1H NMR (CDCl_3 , 300 MHz) δ 1.63 (s, 18H), 6.57 (s, 4H) 7.36 and 7.40 (s, 4H), 8.20 (s, 4H) ppm; ^{13}C NMR (CDCl_3 , 75 MHz) δ 32.0, 35.4, 82.2, 116.9, 119.75, 119.78, 126.69, 126.76, 144.21, 144.25, 148.22, 148.27 ppm.

2,7-Di(*tert*-butyl)pyreno[4,5-*c*:9,10-*c'*]difuran (6). A solution of crude **8** (~3.9 mmol) in CHCl_3 was charged with dipyriddyltetrazine (1.97 g, 8.35 mmol) and refluxed for 18.5 h. The solution was then washed with 1 M HCl and dried (MgSO_4). Crystals (116.7 mg, 0.2958 mmol, 2.0%) were found after an extended period in toluene: mp = $240\text{ }^{\circ}\text{C}$ (dec); IR (ATR, neat) 647, 770, 1043, 1547, 1608 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ 1.51 (s, 18H), 8.02 (s, 4H) 8.36 (s, 4H) ppm; ^{13}C NMR (CDCl_3 , 75 MHz) δ 31.5, 34.9, 119.2, 121.7, 122.5, 125.7, 136.4, 149.8 ppm; UV–vis (CH_2Cl_2) λ_{max} (nm) [$\log \epsilon$ ($\text{mol}^{-1}\text{ cm}^{-1}\text{ L}$)] 255 (4.65), 299 (4.35), 273 (4.61), 312 (4.27), 327 (4.18); HRMS calcd for $\text{C}_{28}\text{H}_{26}\text{N}_2\text{O}_2^+$ 394.19273, found m/z 394.19294.

6,14-Di(*tert*-butyl)-4,16:8,12-diepoxy-3a,4,8,8a,11a,12,16,16a-octahydro-2,10-propanopyreno[4,5-*f*:9,10-*f'*]diisoindole-1,3,9,11-tetrone (13). To a solution of crude **8** (0.73 mmol) in CHCl_3 was added dipyriddyltetrazine (0.36 g, 1.5 mmol), and the solution was refluxed overnight. *N,N'*-1,5-bis(maleimido)propane (0.18 g, 0.75 mmol) was added, and the solution stirred for 1 h. The solution was washed with 1 M HCl and dried (MgSO_4). The solvent was removed, and the residue was subjected to flash

chromatography eluting with ethyl acetate/hexanes. Crystals (27 mg, 0.042 mmol, 5.8%) were obtained from CHCl_3 : mp $340\text{ }^{\circ}\text{C}$ (dec); IR (ATR, neat) 874, 1218, 1698 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ -2.46 (m, 2H), 1.64 (s, 18H), 2.23 (m, 4H), 3.91 (m, 4H), 6.57 (m, 4H), 8.25 (s, 4H) ppm; ^{13}C NMR (CDCl_3 , 75 MHz) δ 24.2, 31.8 34.1, 35.5, 48.36, 80.5, 121.0, 123.7, 124.9, 138.0, 150.0, 172.2 ppm; UV–vis (CH_2Cl_2) λ_{max} (nm) [$\log \epsilon$ ($\text{mol}^{-1}\text{ cm}^{-1}\text{ L}$)] 246 (4.71), 254 (4.74), 280 (4.48), 293 (4.64), 330 (4.00), 346 (4.32), 363 (4.51); HRMS calcd for $\text{C}_{39}\text{H}_{36}\text{N}_2\text{O}_6\text{Na}^+$ 651.24656, found m/z 651.24693.

6,14-Di(*tert*-butyl)-4,16:8,12-diepoxy-3a,4,8,8a,11a,12,16,16a-octahydro-2,10-pentanopyreno[4,5-*f*:9,10-*f'*]diisoindole-1,3,9,11-tetrone (14). To a solution of crude **8** (1.0 mmol) in CHCl_3 were added dipyriddyltetrazine (0.51 g, 2.2 mmol) and *N,N'*-1,5-bis(maleimido)pentane (0.27 g, 1.0 mmol), and the mixture was refluxed overnight. The solution was washed with 1 M HCl and dried (MgSO_4). The solvent was removed, and the residue was subjected to flash chromatography eluting with ethyl acetate/hexanes. Crystals (11.3 mg, 0.0172 mmol, 1.65%) were formed from a mixture of CHCl_3 and hexanes: mp = $340\text{ }^{\circ}\text{C}$ (dec); IR (ATR, neat) 752, 853, 1393, 1692 cm^{-1} ; ^1H NMR (CDCl_3 , 300 MHz) δ -2.1 (m, 2), -0.46 (p, $J = 5.9\text{ Hz}$, 4H), 1.63 (s, 18H), 2.61 (t, $J = 6.2\text{ Hz}$, 4H), 4.06 (d, $J = 3.6\text{ Hz}$, 4H), 6.48 (d, $J = 2.9\text{ Hz}$, 4H), 8.27 (s, 4H); ^{13}C NMR (CDCl_3 , 75 MHz) δ 17.6, 24.6, 31.8, 35.6, 37.3, 48.5, 80.3, 120.1, 123.3, 125.0, 139.0, 149.9, 173.9 ppm; UV–vis (CH_2Cl_2) λ_{max} (nm) [$\log \epsilon$ ($\text{mol}^{-1}\text{ cm}^{-1}\text{ L}$)] 246 (4.93), 254 (4.99), 280 (4.68), 292 (4.90), 330 (4.26), 345 (4.59), 363 (4.81); HRMS calcd for $\text{C}_{41}\text{H}_{40}\text{N}_2\text{O}_6^+$ 656.28809, found m/z 656.28847.

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Supporting Information Available: Compound characterization data, including copies of ^1H and ^{13}C NMR spectra of **6**, **8**, **13** and **14**, details of our preparation of **7**, and both crystallization information files (CIF format) and UV–vis spectra of compounds **6**, **13**, and **14**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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