JOC Article
pubs.acs.org/joc

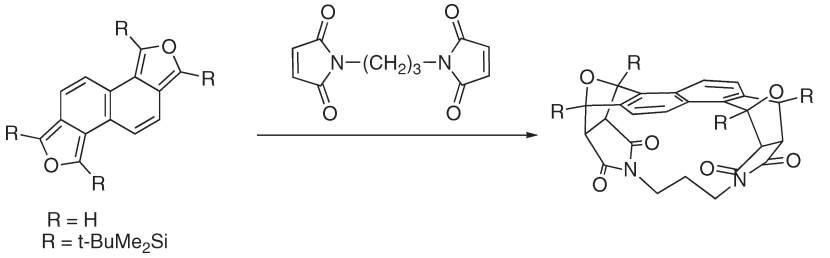
X-ray Structures of Cyclophanes Derived from Naphtho[1,2-*c*:5,6-*c*]-difuran and the Synthesis, Structure, and Reaction Kinetics of Its 1,3,6,8-Tetrasilylated Derivative

Steven J. Robbins, Michelle E. Thibault, Jason D. Masuda, David R. Ward, René T. Boeré, and Peter W. Dibble*

Department of Chemistry and Biochemistry, University of Lethbridge, Lethbridge AB, Canada, T1K 3M4

dibble@uleth.ca

Received August 18, 2008



A silylated derivative of naphtho[1,2-*c*:5,6-*c*]difuran, 1,3,6,8-tetrakis(*tert*-butyldimethylsilyl)naphtho-[1,2-*c*:5,6-*c*]difuran, has been isolated and its X-ray crystal structure determined. Bond localization confirms the polyene character of this isobenzofuran ring system. This molecule undergoes two successive Diels−Alder reactions with second-order rate constants differing by over 2 orders of magnitude, consistent with predictions based on their structure-count ratios and with the reactivity of the novel 1,3-bis(*tert*-butyldimethylsilyl)isobenzofuran. Crystal structures of two cyclophanes derived from the reaction of naphtho[1,2-*c*:5,6-*c*]difuran and bis(imide) or bis(ester) dienophiles show marked differences in the conformation of the aliphatic chain found in the solid state.

Introduction

Isobenzofuran (IBF) (**1**, Figure 1) is a fundamentally interesting molecule that has seen significant use in chemical synthesis[1−8] and has been of substantial theoretical interest.[9−11] IBFs undergo rapid Diels−Alder cycloaddition with a variety of dienophiles and have found use in a variety of fields from natural product synthesis[6] and polycyclic aromatic hydrocarbons[5] to the formation of open fullerenes.[12−14] There has also been interest in the relative reactivity of IBF and its benzologues such as naphtho[1,2-*c*]-furan **2**.[15] Recently we have become interested in the synthesis and use of bis(isobenzofuran)s, two reactive IBF entities coupled together, as linker molecules[16,17] and as cyclophane precursors. We have reported the synthesis of naphtho[1,2-*c*:5,6-*c*]difuran, **3a**, and described its use as a cyclophane precursor.[18] The X-ray structures of two cyclophanes based on ester and imide tethers have now been determined. In addition, we now report the synthesis, X-ray

(1) Friedrichsen, W. *Adv. Heterocycl. Chem.* **1980**, *26*, 135–241.
(2) Friedrichsen, W. In *Houben-Weyl, Methoden der Organischen Chemie*; Kreher, R., Ed.; Thieme Verlag: Stuttgart, Germany, 1994; Vol. E6b, pp 163−216.
(3) Friedrichsen, W. *Adv. Heterocycl. Chem.* **1999**, *73*, 1–96.
(4) Haddidin, M. J. *Heterocycles* **1978**, *9*, 865.
(5) Rickborn, B. In *Advances in Theoretically Interesting Molecules*; Thummel, R. P., Ed.; J.A.I. Press: Greenwich, CT, 1989; Vol. 1, p 1−134.
(6) Rodrigo, R. *Tetrahedron* **1988**, *44*, 2093–2135.
(7) Wege, D. In *Advances in Theoretically Interesting Molecules*; Thummel, R. P., Ed.; J.A.I. Press: Greenwich, CT, 1998; Vol. 4, p 1−52.
(8) Wiersum, U. E. *Aldrichim. Acta* **1981**, *14*, 53–59.
(9) Friedrichsen, W. *Struct. Chem.* **1999**, *10*, 47–52.
(10) Hess, B. A. Jr.; Schaad, L. J.; Holyoke, C. W. Jr. *Tetrahedron* **1972**, *28*, 3657–3667.
(11) Martinez, A.; Vazquez, M.-V.; Carreon-Macedo, J. L.; Sansores, L. E.; Salcedo, R. *Tetrahedron* **2003**, *59*, 6415–6422.
(12) Chuang, S.-C.; Sander, M.; Jarrosson, T.; James, S.; Rozumov, E.; Khan, S. I.; Rubin, Y. *J. Org. Chem.* **2007**, *72*, 2716–2723.
(13) Prato, M.; Suzuki, T.; Roroudian, H.; Li, Q.; Khemani, K.; Wudl, F.; Leonetti, J.; Little, R. D.; White, T. *J. Am. Chem. Soc.* **1993**, *115*, 1594–5.
(14) Sander, M.; Jarrosson, T.; Chuang, S.-C.; Khan, S. I.; Rubin, Y. *J. Org. Chem.* **2007**, *72*, 2724–2731.
(15) Moursounidis, J.; Wege, D. *Aust. J. Chem.* **1988**, *41*, 235–249.
(16) Leong-Neumann, S.; Derrick, S. D.; Dibble, P. W. *Tetrahedron Lett.* **1995**, *36*, 4181–4184.
(17) Mitchell, R. W.; Ward, T. R.; Wang, Y.; Dibble, P. W. *J. Am. Chem. Soc.* **1999**, *121*, 2601–2602.
(18) Thibault, M. E.; Closson, T. L. L.; Manning, S. C.; Dibble, P. W. *J. Org. Chem.* **2003**, *68*, 8373–8378.

Published on Web 06/19/2009 DOI: 10.1021/jo900582r

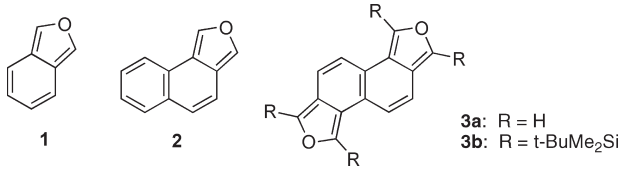


FIGURE 1. Isobenzofurans.

structure, reaction kinetics, and cyclophane-forming utility of a sterically stabilized derivative of **3a**: 1,3,6,8-tetrakis (*tert*-butyldimethylsilyl)naphtho[1,2-*c*:5,6-*c*]difuran, **3b**.

Results and Discussion

There are several problems associated with the high reactivity of IBF and its reactive benzologues. The parent compound is stable only in solution at room temperature.[19,20] It is unstable in the presence of acid and must be trapped in situ when generated under conditions of acid catalysis.[20,21] This makes stoichiometric control of reactions difficult, a problem that is compounded in Diels–Alder reactions in which the dienophile is also highly reactive. In our work preparing cyclophanes, high reactivity results in substantial competing polymerization. Finally, the lack of thermal stability and homopolymerization in the solid state[19] have made the structural characterization of IBFs by X-ray crystallography difficult.

Synthesis and Structure of 3b. In an attempt to circumvent these problems with the naphtho[1,2-*c*:5,6-*c*]difuran system, we adopted the technique developed by Rickborn[22−25] of stabilizing IBFs by incorporating silyl substituents in the 1,3-positions. We prepared **3b** by the addition of LDA to acetal **4** (Scheme 1). Base-induced elimination of methanol forms **3a** in situ. Each of the 1, 3, 6, and 8 positions undergoes stepwise deprotonation and silylation to generate difuran **3b**. This product is crystalline and can be stored for several months under cool, dark conditions. An X-ray crystal structure[26] of **3b** was obtained (Figure 2). It is the first crystal structure of a bis-IBF, and only the sixth of an IBF to be analyzed.

Selected bond lengths for **3b** are presented in Table 1 along with previously published data for four other IBFs. While **3b** is a planar delocalized 18 π-electron system that formally fits Huckel's criteria for aromaticity, it exhibits polyene character

SCHEME 1. Synthesis of 3b

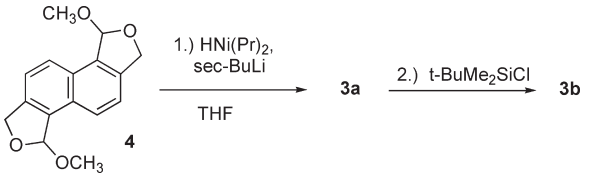
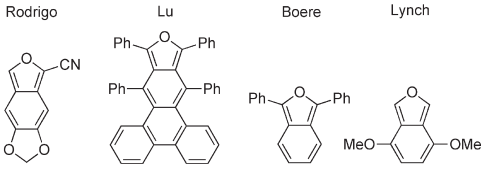


TABLE 1. Select Bond Lengths for IBF-Containing Compounds[a]

bond	difuran **3b**	Rodrigo[27]	Lu[28]	Boeré[29]	Lynch[30]
C1−C2	1.368(3)	1.355	1.388(3)	1.373(3)	1.358(3)
C2−C3	1.442(2)	1.436	1.444(3)	1.435(3)	1.441(2)
C3−C4	1.387(3)	1.372	1.389(3)	1.372(3)	1.360(3)
O1−C4	1.387(2)	1.355	1.376(3)	1.369(2)	1.362(3)
O1−C1	1.374(2)	1.374	1.374(3)	1.366(2)	1.364(2)
C2−C7A	1.426(3)	1.431	1.434(3)	1.425(3)	1.431(3)
C6A-C7A	1.345(3)	1.353	1.381(3)	1.351(3)	1.350(3)
C6A-C5A	1.439(3)	1.454	1.470(3)	1.435(3)	1.445(3)
C5−C5A	1.393(4)	1.353	1.386(3)	1.346(3)	1.349(3)
C3−C5	1.443(2)	1.462	1.438(3)	1.427(3)	1.432(3)

[a] Atom labels correspond to those in Figure 2.



with alternating short and long bonds and little evidence of bond-averaging. Peri-interactions widen the C2−C1−Si1 bond angle to 137.95°, significantly greater than the expected 126° for an sp^2 center about a five-membered ring. Steric interactions in the bay-region make the corresponding angle (C3−C4−Si2) of the other silyl groups wider still at 143.19°. This interaction also accounts for the increased C3−C4 bond length.

Kinetic Studies of 3b. The reactivity of IBF and its benzologues was examined by Wege in 1990.[15] Second-order rate constants were determined for a series of IBFs in reaction with maleic anhydride (MA). The results were rationalized by using the structure-count ratio (SC_{ratio}) theory developed by Herndon.[31] Higher structure-count ratios represent increasing resonance energy during reaction, which is reflected in higher reaction rates. The Herndon relationship can be used to predict that difuran **3b**, with a SC_{ratio} of 3, should be more reactive than monoadduct **5** (Scheme 2), which has a SC_{ratio} of only 2.5. This has been demonstrated qualitatively for the parent system.[18] With **3b** in hand, we were in a position to make quantitative measurements of the relative reaction rates of **3b** and **5** to establish that they were consistent with their structure-count ratios.

The second-order rate constants for the reaction of both **3b** and **5** with *N*-methylmaleimide (NMM) (Scheme 2) were measured by fluorescence spectroscopy and proton NMR, respectively (Table 2). These can be compared to those of naphtho[1,2-*c*]furan (**2**, Figure 1) and IBF[15] since both pairs of molecules have the same structure-count ratios. The ratio of the rate constants **3b**:**5** is 3.4 times larger than the corresponding ratio observed for **2**:**1**. Taking into account

(19) Wiersum, U. E.; Mijs, W. J. *J. Chem. Soc., Chem. Commun.* **1972**, 347–348.
(20) Keay, B. A.; Lee, D. K. W.; Rodrigo, R. *Tetrahedron Lett.* **1980**, *21*, 3663–3666.
(21) Contreras, L.; MacLean, D. B.; Faggiani, R.; Lock, C. J. L. *Can. J. Chem.* **1981**, *59*, 1247–1256.
(22) Crump, S. L.; Netka, J.; Rickborn, B. *J. Org. Chem.* **1985**, *50*, 2746–2750.
(23) Camenzind, R.; Rickborn, B. *J. Org. Chem.* **1986**, *51*, 1914–1916.
(24) Netka, J.; Crump, S. L.; Rickborn, B. *J. Org. Chem.* **1986**, *51*, 1189–1199.
(25) Pollart, D. J.; Rickborn, B. *J. Org. Chem.* **1986**, *51*, 3155–3161.
(26) CCDC 696904 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
(27) Rodrigo, R.; Knabe, S. M.; Taylor, N. J.; Rajapaksa, D.; Chernishenko, M. J. *J. Org. Chem.* **1986**, *51*, 3973–3978.
(28) Lu, J.; Ho, D. M.; Vogelaar, N. J.; Kraml, C. M.; Bernhard, S.; Byrne, N.; Kim, L. R.; Pascal, R. A. *J. Am. Chem. Soc.* **2006**, *128*, 17043–17050.
(29) Boeré, R. T.; Dibble, P. W.; Fischer, K. E. *Acta Crystallogr.* **2008**, *E64*, o686.
(30) Lynch, V. M.; Fairhurst, R. A.; Magnus, P.; Davis, B. E. *Acta Crystallogr.* **1995**, *C51*, 780–782.
(31) Herndon, W. C. *J. Chem. Educ.* **1974**, *51*, 10–15.

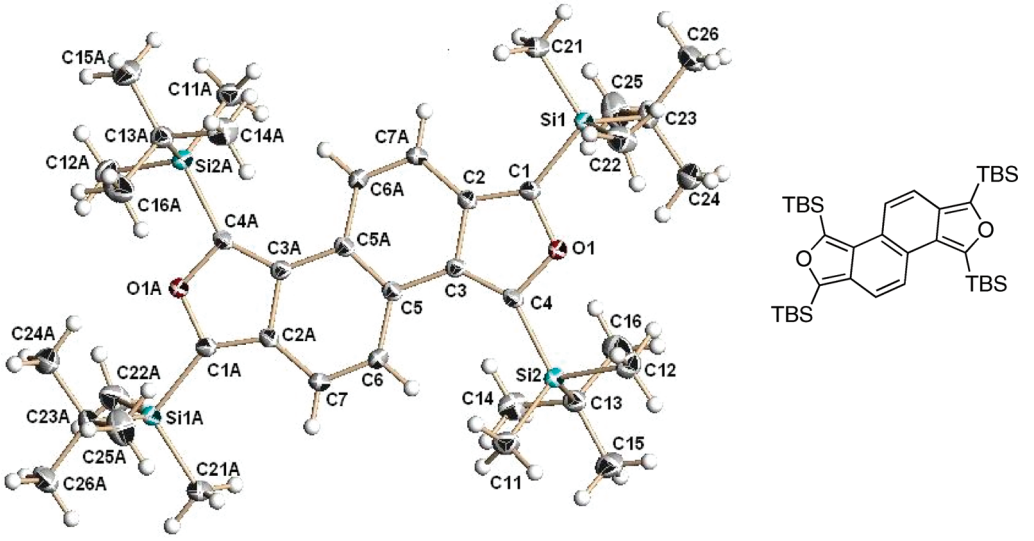
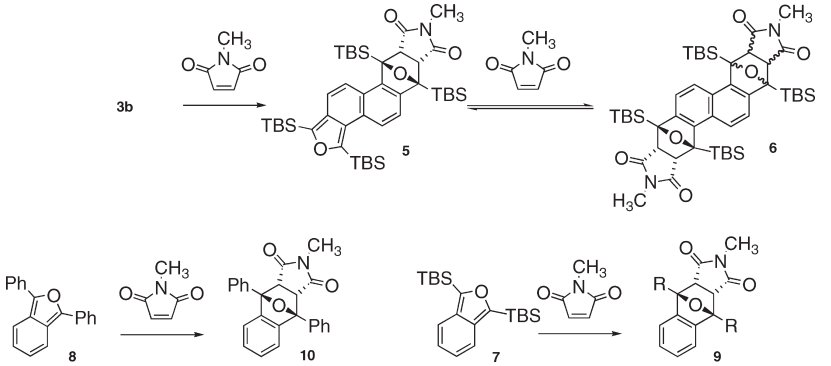


FIGURE 2. Structure of difuran **3b** as found in the crystal including the atom numbers. Thermal ellipsoids (50% probability) are drawn in SHELXTL, 6.14. Molecules are located at an inversion center; related atoms are designated with an "A".

SCHEME 2. Reaction Kinetics



the presence of two reaction sites in **3b**, this ratio is reduced to 1.7. This is well within the range of discrepancy found with compounds having the same structure-count ratio.

In the kinetic studies, we were surprised to note that the reaction of **5** and NMM to form **6** does not go to completion but reaches equilibrium with $K_{eq} = 25$ (based on the NMR integration of the N-Me signals). Our experience has been that the Diels–Alder cycloadditions of IBF derivatives are not appreciably reversible. It was still possible to crystallize bis-adduct **6** from the reaction solution as an equal mixture of *syn-endo,endo-* and *anti-endo,endo*-isomers. In $CDCl_3$ solution, however, a sample of the *syn,endo,endo*-isomer[32] produced a mixture of **5**, **6**, and NMM over several hours. Interestingly, *exo*-isomers were never observed, even at equilibrium. *Exo-* and *endo*-isomers can be differentiated in proton NMR spectra by the shielding observed for N-Me or ring-junction protons trans to the epoxide oxygen. No such signals for *exo*-NMM adducts were observed. Steric interactions between the SiMe groups and the carbonyls in the *exo*-NMM adducts may be responsible for destabilizing this stereoisomer so that it is no longer the thermodynamically more stable product.

TABLE 2. Diels–Alder Second-Order Rate Constants

furan	$\lambda_{excitation}$ (nm)	$\lambda_{emission}$ (nm)	k (M^{-1} s^{-1})	k_{rel}	k_{rel}
3b	258	426	37.5	129	
5			0.292	1	
8	417	460	1280	4380	8.9
7	343	395	144	493	1

Rickborn has published rate data for a variety of substituted IBFs.[33] In part to check our data, we prepared 1,3-bis(*tert*-butyldimethylsilyl)IBF **7** and compared its reaction rate with NMM to that of diphenylIBF **8** (Table 2). We found **8** to be 8.9 times more reactive than **7** while Rickborn found **8** to be only 3.8 times more reactive than 1,3-bis (trimethylsilyl)isobenzofuran. This is consistent with the presence of slightly smaller silyl substituents in the latter case. The stabilizing influence of the silyl groups is clearly steric in nature. Electron-donating substituents are known to activate IBFs by raising the HOMO energy[5] so there may be

(32) Crystals of the syn,endo,endo isomer were obtained from a reaction mixture containing excess NMM. The crystals did not diffract well so a high-resolution structure was not obtained though the stereochemistry of the product was determined. CCDC 711249 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

(33) Tobia, D.; Rickborn, B. *J. Org. Chem.* **1987**, *52*, 2611–2615.

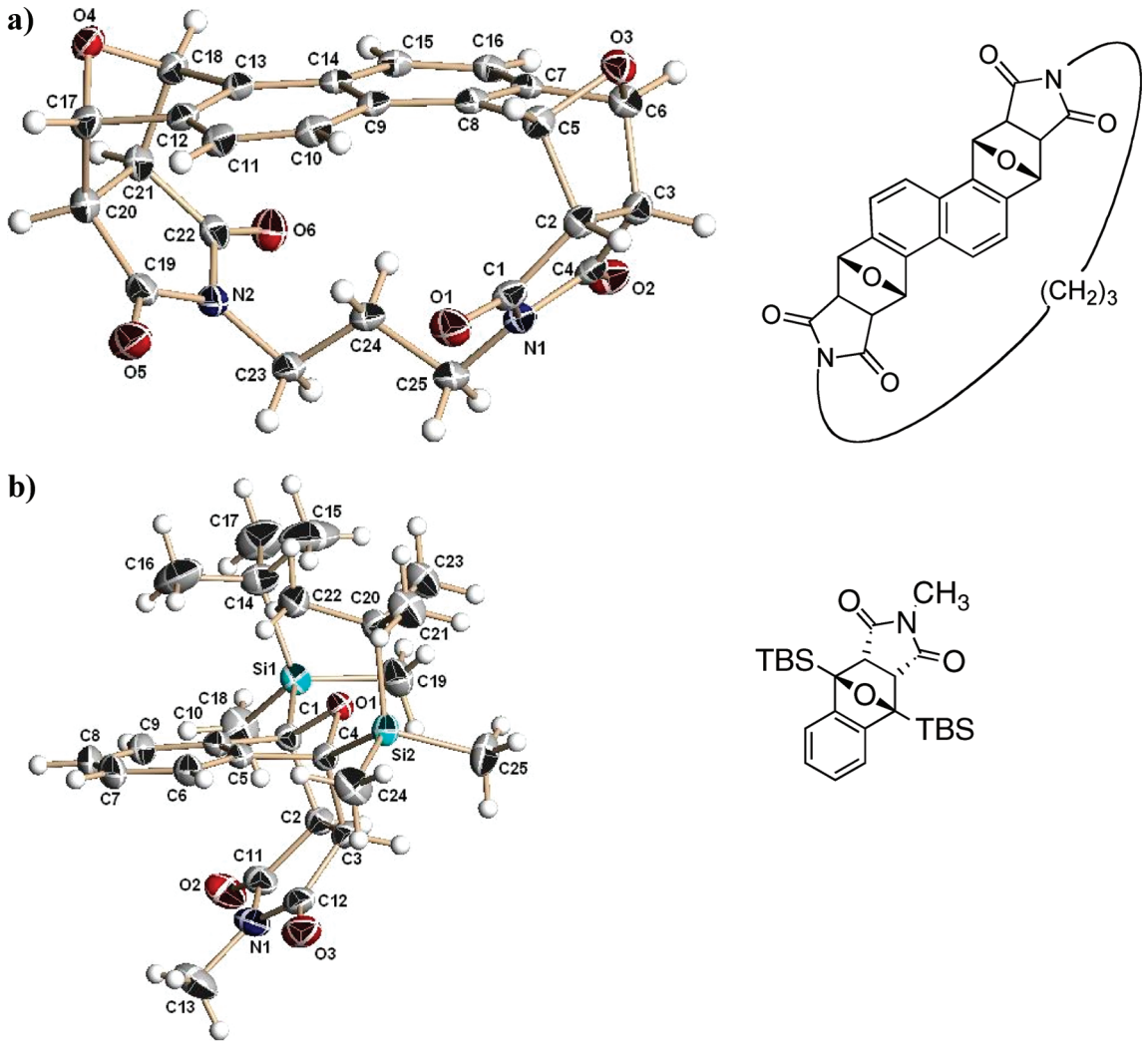


FIGURE 3. Structures of (a) cyclophane **11a** and (b) **9** as found in the crystals. Thermal ellipsoids (50% probability) drawn in SHELXTL, 6.14.

a relatively small electronic component that increases reactivity. Consistent with this, the UV spectrum of **7** shows a slight red-shift of 12 nm compared to **1**.

Our examination of the substituent kinetic data leads us to wonder about the influence of phenyl substituents, particularly in **8**. The popular wisdom has been that phenyl groups stabilize IBF sterically but that conjugation effects are also important.[7] The data actually suggest that these two effects work in *opposite* directions and that phenyl substituents are electronically activating. Phenylbutadiene, for example, is actually more reactive (with maleic anhydride) than butadiene itself.[34] Consistent with this, 1-phenylIBF is almost as reactive as IBF itself in spite of the steric demands of the substituent.[33] Activation by phenyl substituents would also explain the apparent anomaly in the reactions of **1** and **8** with singlet oxygen. In reaction with NMM, **1** is 12 times more reactive than **8** whereas with singlet oxygen, the reactivity is reversed with **8** being 10 times more reactive than **1**.[33] It is hard to imagine a less sterically demanding dienophile than singlet oxygen, so it would appear that when the steric influence of the phenyl substituents is not a factor, **8** is indeed more reactive than **1**. None of this should be too surprising, since phenyl substituents would be expected to raise the HOMO of IBF.

Synthesis and Structures of Cyclophanes Derived from 3a. The preparation of cyclophane **11a** from **3a** (Scheme 3) has been reported previously[18] and we have since determined its X-ray crystal structure (Figure 3).[35] An X-ray structure of noncyclophane adduct **6**[36] (Scheme 2) has also been obtained. Comparison of these allows us to see the impact of the cyclophane tether on the naphthalene ring and the oxabicyclo rings of **11a**.

In the solid-state structure of **11a**, the central methylene protons of the chain were found to point toward the naphthalenic π-system. These protons appear at -1.41 ppm in the proton NMR spectrum suggesting that the solution state structure is similar to that found in the solid-state structure. There is a slight warp associated with the naphthalene ring such that C11 is found 0.591 Å above the plane defined by C8−C7−C16 of the opposite ring. The C23−C24−C25 bond angle (about the central methylene) is widened to 115.17°. The

(34) Sauer, J.; Sustmann, R. *Angew. Chem., Int. Ed. Engl.* **1980**, *19*, 772–807.

(35) Thibault, M. E.; Parvez, M.; Dibble, P. W. *Acta Crystallogr.* **2008**, *E64*, o1837.

(36) CCDC 711248 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

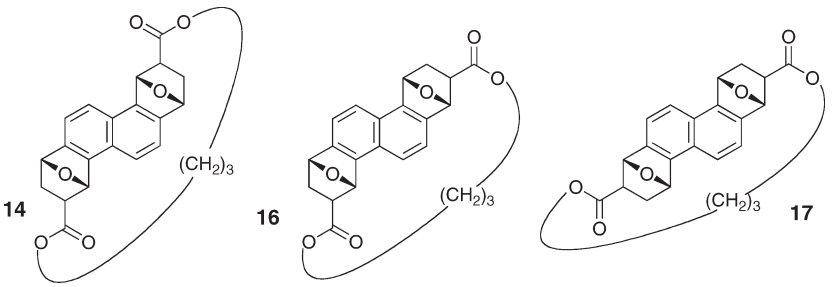
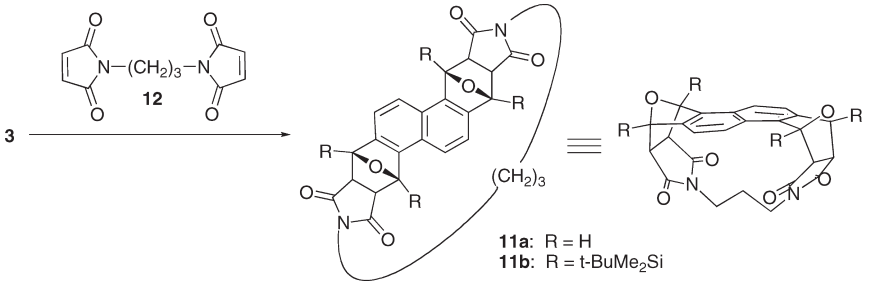


FIGURE 4. Regioisomers of cyclophane **14**.

SCHEME 3. Imide Cyclophanes Derived from 3



calculated N−N distance of 1,3-diaminopropane (4.96 Å) is longer than the N−N distance of 4.86 Å found in **11a**. This indicates that the chain is not being stretched, but that the π-system of the naphthalene is pushing down on the aliphatic chain, particularly on the central atom, to produce this wide geminal angle. Commensurate with this is the observation that the angle about the bridgehead of the oxabicyclo rings of **11a** (C8−C5−C2) is 108.5° and only 104° in **9**. The warp found in the naphthalene ring of **11a** is therefore due to the steric interaction with the central methylene and not due to the N atoms being pulled together. Tsuzuki et al. have performed calculations on the interaction between the naphthalene π-system and a molecule of methane.[37] They found that methane with two hydrogens facing the aromatic system has a C−π equilibrium distance between 3.4 and 3.5 Å depending on where the methane interacts with the aromatic system. If this distance is significantly reduced the interaction quickly becomes destabilizing. In cyclophane **11a** the orientation of the central methylene is analogous to the methane orientation of Tsuzuki et al., but the distance from C24 to the aromatic plane is only 3.337 Å.

Reaction of difuran **3b** with tethered imide **12** gave cyclophane **11b**, which, based on its spectral data, appears to be completely analogous to **11a**. A significant difference is that this reaction appears to be much cleaner than its nonsilyl counterpart with approximately 80% of the crude reaction mixture being cyclophane, twice that observed in the formation of **11a**. This is an important consequence if we hope to elaborate these cyclophanes to prepare strained nonplanar aromatic compounds by aromatization of the oxabicyclo-rings.

We have found that imide-based cyclophanes of **3a** do not crystallize readily (suitable crystals of cyclophane **11a** took many months to grow). It is for this reason that the use of an ester-based tether, 1,3-propanediol diacrylate **13**, was investigated (Scheme 4). Crystals of cyclophane **14** were isolated in our first attempt.

We recognized several disadvantages of using the diester **13**. Endo selectivity, necessary for the formation of cyclophanes, is not as great for acrylates as it is for maleimides.[38] The possibility of regioisomers (Figure 4) was a major concern particularly since regioselectivity in the first Diels−Alder reaction (to form **15**, for example) was not expected based on earlier experience. It was a pleasant surprise, then, to find preferential formation of only one of the three possible cyclophane products.

The proton NMR spectrum of the crude reaction mixture shows that **14** represents approximately 75% of all products. Pure material was obtained by column chromatography and crystallization from chloroform/ethyl acetate. The proton NMR spectrum exhibited signals that could only be due to **14** or **17** based on their *C*2 symmetry. An X-ray crystal structure was ultimately necessary to identify the structure of this compound as **14**.

Unlike **11a**, the crystal structure of **14**[39] (Figure 5) shows the presence of an ordered major component (78% refined occupancy) and a disordered minor component (22%). Analysis of the minor component indicates that it probably has the same basic conformation as that of the major but is disordered due to out-of-register packing in the lattice that leads to unfavorable packing contacts.[40] Most likely the tether of cyclophane **14** is more flexible than the imide tether of cyclophane **11a** because rotation of the carbonyl is now possible. Given the success of B3LYP/6-31G(d) theory at predicting the geometry of cyclophane **11a** and difuran **3b**, a

(37) Tsuzuki, S.; Honda, K.; Fujii, A.; Uchimaru, T.; Mikami, M. *Phys. Chem. Chem. Phys.* **2008**, *10*, 2860–2865.

(38) Tobia, D.; Harrison, R.; Phillips, B.; White, T. L.; DiMare, M.; Rickborn, B. *J. Org. Chem.* **1993**, *58*, 6701–6706.

(39) CCDC 696905 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

(40) A description of this disorder in the crystal structure of **14** appears in the Supporting Information.

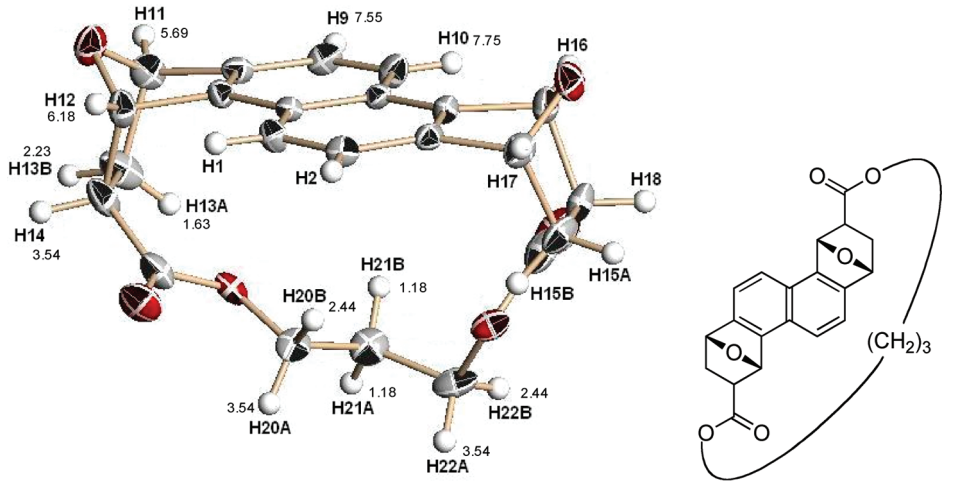
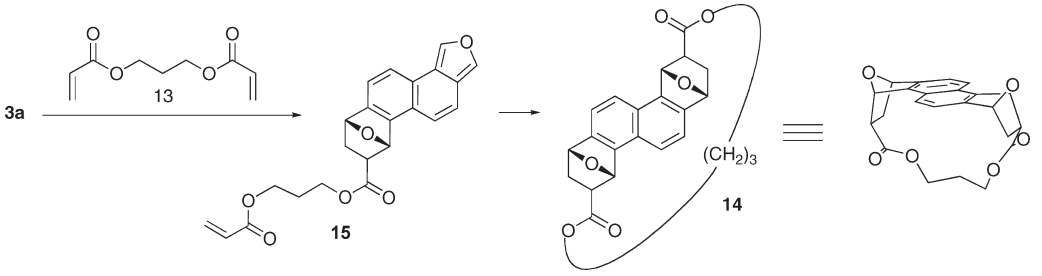


FIGURE 5. Structure of cyclophane **14** as found in the crystal showing the ordered major (78% refined occupancy) component of the tether chain. Thermal ellipsoids (50% probability) drawn in SHELXTL, 6.14. Assigned proton NMR chemical shifts are shown in ppm.

SCHEME 4. Ester Cyclophane



calculated model was used for the analysis of cyclophane **14**. A conformational search[41] was performed to determine the best geometry for the tether. The low-energy conformation corresponded well with the X-ray structures' ordered tether conformation shown in Figure 5. On the basis of the proton NMR evidence, we believe that this corresponds well with the conformation of the ordered major component of the tether in the X-ray structure as shown in Figure 5.

A proton−proton COSY of the product allowed us to assign the proton positions and these are shown in Figure 5. The increased flexibility associated with this molecule means that the homotopic central methylene protons can rotate away from the π-system and do not experience the same shielding effect as those in cyclophane **11a**. Diastereotopic protons H20A and H2OB (on the methylene group attached to the ester oxygen) are found at 3.54 and 2.44 ppm, respectively. This is a significant difference in shift for geminal protons and is consistent with the structure shown in Figure 5.

In cyclophane **11a**, the plane defined by the tether carbons is perpendicular to the plane of the naphthalene ring and the tether is perfectly antistaggered. In contrast, the tether of **14** includes a gauche interaction and has part of the chain lying parallel to the naphthalene ring. This parallel type of tether orientation is observed in the cyclophanes made by Warrener[42] and Bodwell,[43] who also used flexible hydrocarbon tethers. The experimental bond angles O6−C22−C21, C22−C21−C20, and C21−C20−O4 are 112.22°, 113.60°, and 106.28°, respectively. The extra flexibility in the tether allows a different orientation for the central methylene such that it does not point toward the naphthalene ring, therefore the π-system is relatively planar compared to **11a**.

Conclusions

The structure of **3b** confirms isobenzofuran as being more polyene in character than aromatic. It undergoes two Diels−Alder cycloadditions and their relative rates are consistent with what has been observed for IBFs with the same structure-count ratios. Several advantages to using silylated IBFs have been demonstrated including better yields of cyclophane products in reaction with bis(dienophiles). The structures of two cyclophanes derived from naphtho[1,2-*c*:5,6-*c*]difuran incorporating imide or ester-based tethers have been shown to have markedly different tether orientations in the solid state.

Experimental Section

1,3,6,8-Tetrakis(*tert*-butyldimethylsilyl)naphtho[1,2-*c*:5,6-*c*]-difuran, 3b. In 100 mL of dry THF was stirred acetal **4**[18] (0.20 g, 0.83 mmol). Under N_2 the solution was cooled to −60 °C. A catalytic amount of LDA (0.40 mL, 2.0 M, 0.80 mmol) and 6 mL of *sec*-butyllithium (1.4 M, 8.4 mmol) were added. This solution was stirred for 10 min before the addition of *tert*-butyldimethylsilyl chloride (0.63 g, 4.2 mmol). The mixture was warmed to

(41) Random torsion variation conformational search with Hyperchem Release 7.52 for Windows.
(42) Butler, D. N.; Shang, M.; Warrener, R. N. *Tetrahedron Lett.* **2000**, *41*, 5985–5989.
(43) Bodwell, G. J.; Bridson, J. N.; Houghton, T. J.; Kennedy, J. W. J.; Mannion, M. R. *Chem.—Eur. J.* **1999**, *5*, 1823–1827.

20 °C and stirred for 5 h. The reaction was quenched with 100 mL of water and the aqueous phase extracted with three 30 mL portions of methylene chloride. The solvent was dried with $MgSO_4$ and filtered. The resulting solid was suspended in 10 mL of hexanes and placed atop a column of silica. The column was eluted with hexanes and removal of the eluant gave 0.27 g of a yellow solid (48%), **3b**: mp 231−233 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.47 (12H, s), 0.56 (12H, s), 0.97 (18H, s), 1.03 (18H, s), 7.56, (2H, d, J = 9.0 Hz), 7.74 (2H, d, J = 9.0 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ −5.7, −3.8, 17.8, 18.6, 26.5, 26.9, 118.9, 123.5, 123.7, 132.6, 133.3, 156.7, 156.9; IR (KBr) 1470, 1462, 1360, 833, 820, 806, 772, 674, 417 cm^{-1}; UV−vis (c 1.052 × 10^{-5}, n-hexane) λ_{max} 256, 266, 276, 291, 349, 369, 389, 411 nm; MS (EI) m/z calcd for $C_{38}H_{64}O_2Si_4$ 664.39834, found 664.39771; 665 (M^+,12), 664 (21), 607 (15), 147 (15), 91 (15), 73 (70), 57 (22), 55 (100). Anal. Calcd for $C_{38}H_{64}O_2Si_4$: C, 68.61; H, 9.70. Found: C, 69.00; H, 9.68.

1,3-Bis(*tert*-butyldimethylsilyl)isobenzofuran, 7. To 125 mL of dry THF was added 500 mg (3.33 mmol) of 1,3-dihydro-1-methoxyisobenzofuran.[44] The solution was stirred under N_2 and cooled to −70 °C. A catalytic amount of LDA (1.25 mmol) was added followed by 14.1 mL of 1.4 M *sec*-butyllithium (19.7 mmol). This mixture was stirred for 15 min and 1.25 g (8.30 mmol) of *tert*-butyldimethylsilylchloride was added. The dark solution was warmed to room temperature and stirred for 1 h. The mixture was quenched with water and extracted with hexanes, then the organic phase was dried over $MgSO_4$. After removal of the solvent, the crude product was placed on a short column of silica and eluted with hexanes. Removal of the solvent gave 0.396 g (36%) of product as a yellow oil: ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.41 (s, 12H), 0.94 (s, 18H), 6.85 and 7.55 (AA′BB′, 4H); ^{13}C NMR (60 MHz, $CDCl_3$) δ 18.0, 26.7, 120.8, 123.3, 123.3, 134.0, 157.0; IR (neat) 773, 807, 821, 836, 2928, 2953 cm^{-1}; UV/vis (MeOH) 231 (3.5), 339 (3.3).

4,9-Bis(*tert*-butyldimethylsilyl-4,9-epoxy-3a,4,9,9a-tetrahydro-2-methyl-2*H*-benzo[*f*]isoindole-1,3-dione, 9. In 25 mL of $CHCl_3$ was dissolved 50 mg (0.14 mmol) of **7**. To this was added 16 mg (0.14 mmol) of *N*-methylmaleimide and the solution was stirred for 2 h before removal of the solvent. The crude product was placed atop a column of silica and eluted with CH_2Cl_2. The product was recrystallized from MeOH to give 32 mg of white crystals (48%): mp 163−167 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 0.36 (s, 6H), 0.42 (s, 6H), 0.97 (s, 18H), 2.17 (s, 3H), 3.60 (s, 2H), 7.08 and 7.16 (AA′BB′, 4H); ^{13}C NMR (60 MHz, $CDCl_3$) δ 18.5, 24, 28, 53, 85.7, 121.5, 121.6, 126.8, 126.8, 145.4, 175.0; IR (KBr) 774, 803, 824, 837, 1251, 1698, 1768, 2858, 2928, 2960 cm^{-1}; MS (EI) m/z calcd for $C_{25}H_{39}NO_3Si_2$ 457.24686, found 457.24529; 457 (M^+, 1), 346 (39), 290 (31), 289 (100), 111 (9), 83 (12), 73 (59), 69 (23), 57 (33). Anal. Calcd for $C_{25}H_{39}NO_3Si_2$: C, 65.60; H, 8.59, 8.42; N, 3.06. Found: C, 65.72; H, 8.59; N, 3.11.

***syn*- and *anti*-4,7,11,14-Tetrakis(*tert*-butyldimethylsilyl)-4,7,-14,11-diepoxy-3a,4,7,7a,10a,11,14,14a-octahydro-2,9-dimethylnaphtho[1,2-*f*:5,6-*f*′]diisoindole-1,3,8,10-tetrone, 6.** To 25 mL of chloroform was added 0.075 mg (0.11 mmol) of **3b** and 0.038 mg (0.34 mmol) of NMM. The solution was stirred for 4 h and the solvent was removed. The crude extract was recrystallized from ethyl acetate to give 25 mg of white crystals as a mixture of syn and anti products (yield 26%): mp 111.7−114.3 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ, syn product 0.45 (6H, s), 0.48 (6H, s), 0.51 (6H, s), 0.64 (6H, s), 0.90 (18H, s), 1.02 (18H, s), 1.78 (6H, s), 3.67 (2H, d, J = 8 Hz), 3.68 (2H, d, J = 8 Hz), 7.40 (2H, d, J = 8 Hz), 7.82 (2H, d, J = 8 Hz), anti product 0.53 (6H, s), 0.54 (6H, s), 0.56 (6H, s), 0.59 (6H, s), 0.93 (18H, s), 1.00 (18H, s), 2.08 (6H, s), 3.70 (2H, d, J = 8 Hz), 3.72 (2H, d, J = 8 Hz), 7.34 (2H, d, J = 8 Hz), 7.79 (2H, d, J = 8 Hz); IR (crystalline) 422, 771, 806, 821, 1252, 1702, 2857, 2930 cm^{-1}. Attempts to dry this compound led to reversion to **3b**. Retro-Diels−Alder reaction in solution made further characterization impossible.

Synthesis of the 3C Maleimide Tether Cyclophane 11b: 4,14:7,11-Diepoxy-4,7,11,14-tetrakis(*tert*-butyldimethylsilyl)-2,9-propanonaphtho[1,2-*f*:5,6-*f*′]diisoindole-1,3,8,10-tetrone, 11b. To 50 mL of $CHCl_3$ was added 103 mg (0.155 mmol) of **3b** and 37 mg (0.158 mmol) of maleimide tether **12**. This mixture was stirred for 30 min and the solvent was removed. The crude product was placed atop a column of silica and was eluted with 80% ethyl acetate in $CHCl_3$. The collected product was recrystallized from a 3:1 mixture of ethyl acetate and $CHCl_3$ to give 98 mg of white crystals (70%): mp 164.5−166.3 °C dec; ^{1}H NMR (300 MHz, $CDCl_3$) δ −1.49 (2H, p, J = 4.2 Hz), 0.432, (6H, s), 0.464 (6H, s), 0.489 (6H, s), 0.654 (6H, s), 0.810 (18H, s), 1.029 (18H, s), 2.52 (2H, m), 2.72 (2H, m), 3.63 (2H, d, J = 7.5 Hz), 3.74 (2H, d, J = 7.5 Hz), 7.38 (2H, d, J = 8.4 Hz), 7.74 (2H, d, J = 8.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ −6.4, −6.2, −5.5, −4.4, 18.1, 18.4, 25.7, 25.9, 27.5, 34.4, 50.7, 53.4, 86.0, 87.9, 119.7, 126.1, 128.5, 143.1, 144.5, 173.5, 173.6; IR (KBr) 416, 548, 583, 653, 672, 771, 822, 985, 1124, 1219, 1250, 1390, 1700, 2857 cm^{-1}; MS (ESI) m/z calcd for $C_{49}H_{74}N_2O_6Si_4$ 899.46239, found 899.47048; 899.5 (M^+, 19), 665.4 (42), 257.1 (100). Anal. Calcd for $C_{49}H_{74}N_2O_6Si_4$: C, 65.44; H, 8.29; N, 3.11. Found: 65.65; H, 8.45; N, 2.95.

Synthesis of 3C Ester Tether Cyclophane: 1^1,1^4,1^7,1^{10}-Diepoxy-1^1,1^2,1^3,1^4,1^7,1^8,1^9,1^{10}-octahydro-1(2,9)chrysena-3,7-dioxa-2,8-dionacyclooctaphane, 14. Acetal **4**[18] (100 mg, 3.7 mmol) was dissolved in 30 mL of dry diethyl ether and the solution was cooled to 0 °C under nitrogen. LDA (4.0 mL of a 2.0 M solution, 8 mmol) was added via syringe and the mixture was stirred for 30 min. The reaction was quenched with water and extracted several times with ether. The combined extracts were washed once with brine, dried with $MgSO_4$, and filtered. Meanwhile, 91 mg (0.50 mmol) of diacrylate **13** was dissolved in 50 mL of $CHCl_3$. The two solutions, ether and $CHCl_3$, were added dropwise over 3 h to a flask containing 500 mL of refluxing $CHCl_3$. This mixture was refluxed overnight before removing the solvent by evaporation. The resulting crude product was placed on top of a column of silica and eluted with a 1:9 ethyl acetate/hexanes mixture. The product was recrystallized from a mixture of $CHCl_3$ and ethyl acetate to give 14 mg of white crystals (yield 8.5%): mp 400 °C dec; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.18 (2H, m), 1.63 (2H, dd, J = 3.9, 12 Hz), 2.32 (2H, m), 2.44 (2H, m), 3.54 (4H, m), 5.69 (2H, d, J = 5 Hz), 6.18 (2H, d, J = 5 Hz), 7.55 (2H, d, J = 8 Hz), 7.75 (2H, d, J = 8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 28.4, 31.3, 45.7, 51.9, 80.2, 81.0, 119.5, 125.1, 127.1, 139.9, 143.8, 171.8; IR (crystalline) 540, 775, 802, 1043, 1252, 1714, 2960 cm^{-1}; MS (EI) m/z calcd for $C_{23}H_{20}O_6$ 392.12599, found 392.12598; 393 (M^{+1}, 13), 392 (M^+, 45), 209 (46), 208 (100), 152 (9), 55 (25). Anal. Calcd for $C_{23}H_{20}O_6$: C, 70.40; H, 5.14. Found: C, 70.16, H, 5.23.

Acknowledgment. The authors thank the University of Lethbridge and the Natural Sciences and Engineering Council of Canada for operating funds, recent equipment support (NMR and XRD), an NSERC PGS (Thibault), USRA (Ward), and the Keith and Hope Ferguson Memorial Scholarship fund (Robbins).

Supporting Information Available: Crystallographic information files for reported crystal structures, Cartesian coordinates for geometrically optimized structures, and proton NMR spectra for novel compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

(44) Smith, J. G.; Dibble, P. W. *J. Org. Chem.* **1983**, *48*, 5361–5362.