SYNTHESIS AND CHARACTERIZATION OF NOVEL CYCLOPHANES FROM 5,5'-BI(ISOBENZOFURAN)

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Abstract

Isobenzofuran has since its discovery proven an important intermediate in the synthesis of novel organic compounds, due to its high reactivity in Diels-Alder reactions. This thesis details the synthesis, purification and characterization of cyclophane compounds derived from a novel analogue of isobenzofuran, 5,5'-bi(isobenzofuran). Because of the relative rarity of molecules containing multiple isobenzofuran units, 5,5'-bi(isobenzofuran) is an excellent candidate for study. Preliminary analysis of an additional novel analogue of isobenzofuran, 5,5'-bis(isobenzofuranyl)acetylene, is also presented.

Acknowledgements

To Elaine of course, for helping me prove that I can.

Special thanks go to Michelle Thibault, for moral and academic support. Also to Peter Dibble for accepting me as a grad student, and last but certainly not least, to my family for putting up with me for the past two and a half years.

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List of Abbreviations

Ar	Aryl
dipytet	3,6-di(2-pyridyl)-1,2,4,5-tetrazine
Et	Ethyl
FVP	Flash Vaccuum Pyrolysis
FVT	Flash Vaccuum Thermolysis
IBF	Isobenzofuran
LDA	Lithium diisopropylamide
Me	Methyl
NMR	Nuclear Magnetic Resonance
Ph	Phenyl
t-	tertiary
TMS	Tetramethylsilane
SN2	Substitution, Nucleophilic, Bimolecular
R	Organic chemical substituent
t-Bu	*Tertiary*-butyl
Bu	Butyl
ppm	Parts per million
IR	Infrared
λmax	Maximum wavelength of absorption

Chapter 1: Introduction

Isobenzofuran (IBF, **1**) is a particularly reactive Diels-Alder diene, first trapped as a transient intermediate in 1964[1](Fieser and Haddadin 1965). Since that time, IBF has proven useful in a variety of applications, including the synthesis of polymers[2], natural products[3] and polycyclic aromatic hydrocarbons[4]. The synthetic utility of isobenzofuran has led to a wide variety of analogues of IBF, ranging from simple substitutions to molecules containing two[5] or even three[6] isobenzofuran units. The purpose of this thesis is to present the synthesis and characterization of two novel analogues of IBF, 5,5'-bi(isobenzofuran) (bi-IBF, **2**) and 5,5'-bis(isobenzofuranyl) acetylene (acetylenedifuran, **3**), and their application towards the synthesis of cyclophanes.

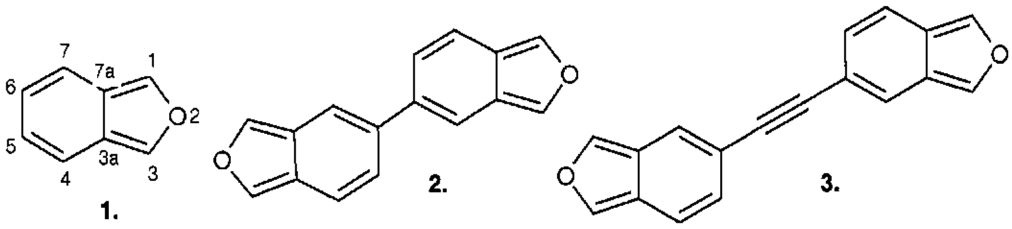

Figure 1-1: Isobenzofuran, 5,5'-bi(isobenzofuran) and 5,5'-bis(isobenzofuranyl)acetylene.

1.1: 5,5'-bi(isobenzofuran)

The primary goal of this project was to use bi(isobenzofuran) **2** as a "backbone" in the synthesis of cyclophanes. As research has shown, novel molecules from **2** may be synthesized from simple dienophiles such as methyl acrylate (adduct **4**), dimethyl fumarate (adduct **5**), and *N*-methylmaleimide (adduct **6**) without difficulty. When a double dienophile such as 1,5-bis(maleimido)pentane is used, however, reaction with

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[1] a) Fieser, L.F, Haddadin, M.J. *J. Am. Chem. Soc.* **1964**, *86*, 2081.
b) Fieser, L.F, Haddadin, M.J. *Can. J. Chem.* **1965**, *43*, 1599.

[2] Löffler, M, Packe, R, Schlüter. A. *Macromolecules.* **1992**, *25*, 4213.

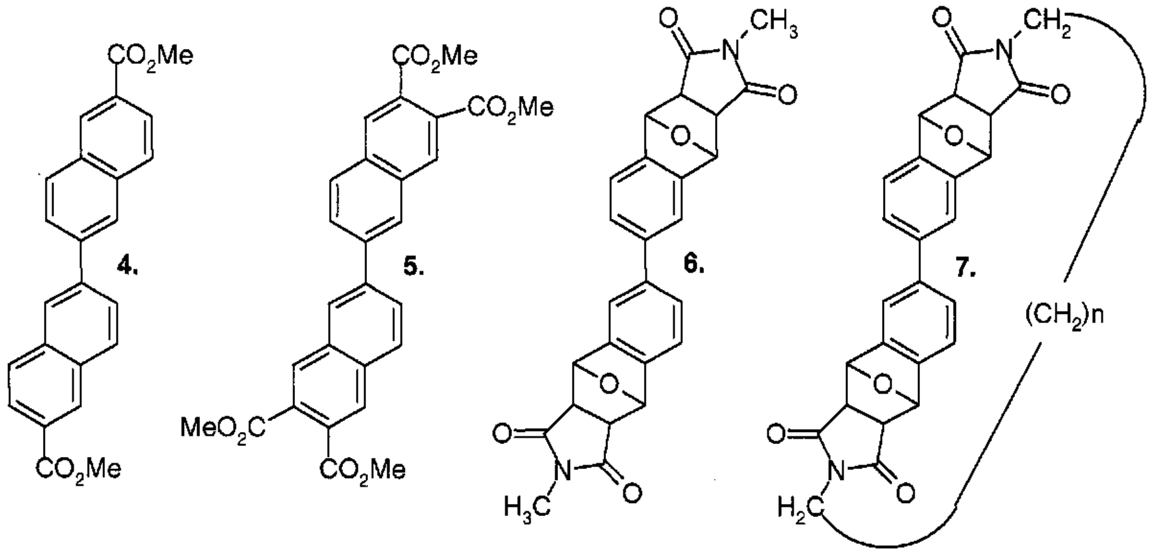
[3] Ross Kelly, T, Xu, D, Martinez, G, Wang, H. *Org. Let.*, **2002**, *4*, 1527.

[4] Moursounidis, J, Wege, D. *Aust. J. Chem.* **1988**, *41*, 235 (*note: correction on pg.1624, same journal*).

[5] Thibault, M.E, Closson, T.L.L, Manning, S.C, Dibble, P.W. *J. Org. Chem.* **2003**, *68*, 8373.

[6] Stringer, M.B, Wege, D. *Tet. Lett.* **1980**, *21*, 3831.

both isobenzofuran moieties occurs rapidly, leading to cyclophane **7** (n=5 for 1,5-bis(maleimido)pentane). Cyclophane **7** can also be obtained when a primary, terminal dibromide is reacted with the maleimide adduct of **2** using simple SN2 chemistry.

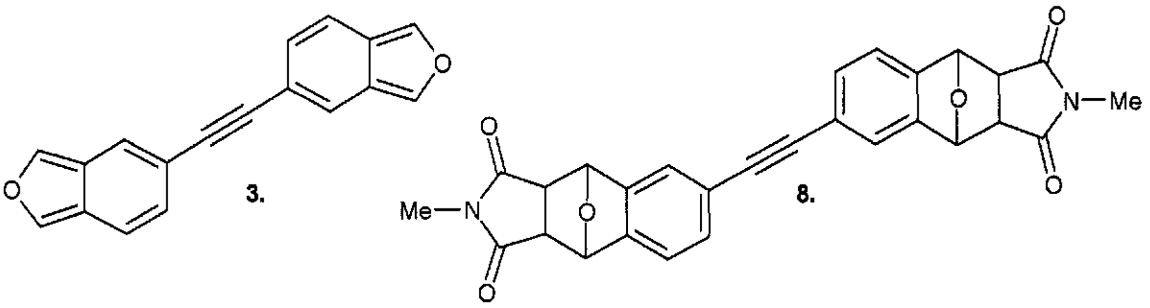


4. **5.** **6.** **7.**

Figure 1-2: Simple Adducts and a Cyclophane from bis(IBF)

1.2: 5,5'-bis(isobenzofuranyl)acetylene

5,5'-bis(isobenzofuranyl)acetylene may also be used for similar purposes, although it takes a secondary role in this thesis. Due to difficulty in the synthesis of starting materials, only small amounts of **3** were synthesized, allowing only for NMR characterization of **3** itself and its *N*-methylmaleimide cycloadduct (**8**).



3. **8.**

Figure 1-3: 5,5'-Bis(isobenzofuranyl)acetylene and adduct

Chapter 2: Existing Research on Isobenzofurans and Cyclophanes

2.1: Variations on the Isobenzofuran Theme

While isobenzofuran is considered the "parent" molecule for compounds of this type, 1,3-diphenylisobenzofuran (**9**) was the first IBF to be discovered in 1906[7]. Since that time, a wide variety of additional analogs of isobenzofuran have been synthesized. These include not only substitutions to the 1-and 3-positions as in **9**, but also substitutions to the six-membered back ring as in 5-methylisobenzofuran (**10**)[8]. Annulated compounds such as naptho-[2,3-*c*]furan (**11**)[9] contain extended π-systems throughout the molecule. Benzo(1,2-*c*,3,4-*c*,5,6-*c*)trifuran (**12**)[10] is unique in that it contains not one, but three reactive Diels-Alder diene sites. These four molecules illustrate different trends in isobenzofuran chemistry; a large number of additional isobenzofurans based on some combination or variation of these forms exist.[11,12]

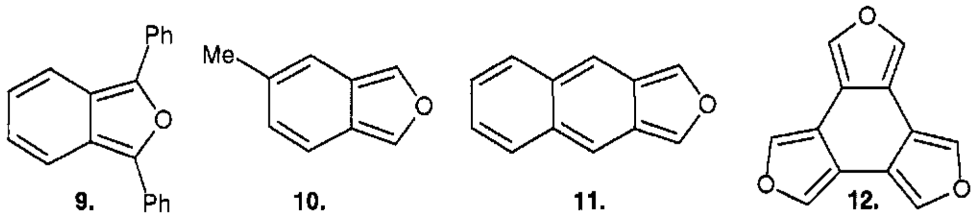


Figure 2-1: Analogues of Isobenzofuran

2.2: Synthesis of Isobenzofurans

It is possible to generate isobenzofurans using a variety of chemical techniques, but three routes in particular have established themselves as the primary means of preparing isobenzofurans. Depending on desired reaction conditions and precursors, any or all of these techniques may prove useful in the synthesis of novel isobenzofurans.

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[7] Guyot, A, Catel, J. *Bull. Soc. Chim. Fr.* **1906**, *35*, 1124.

[8] Hayakawa, K, Yamaguchi, Y, Kanematsu, K. *Tetrahedron Lett.* **1985**, 2689.

[9] Thibault, M.E, Closson, T.L.L, Manning, S.C, Dibble, P.W. *J. Org. Chem.* **2003**, *68*, 8373.

[10] Stringer, M.B, Wege, D. *Tetrahedron Lett.* **1980**, *21*, 3831.

[11] Rickborn, B. *Advances in Theoretically Interesting Molecules*. **1989**, *1*, 1.

[12] Friedrichsen, W. *Methoden der Organtschen Chemie.* **1994**, *E6b*, 163.

2.2.1: Isobenzofurans from Acetal Precursors

Isobenzofurans may be synthesized from precursors derived from *ortho*-substituted benzyl alcohols[13,14] such as 1,3-dihydro-1-methoxyisobenzofuran (Figure 2-2). Addition of excess strong base or catalytic weak acid leads to elimination of alcohol, yielding the isobenzofuran. The base-induced method allows for substitution of the furanoid protons with electrophiles, or for isolation of the IBF after aqueous workup. Acid-catalyzed techniques do not allow for isolation and require the presence of an *in situ* dienophile, but have the advantage of being simple, convenient and relatively mild. The greatest disadvantage of these techniques lies in the synthesis of the precursor, often requiring several synthetic steps of potentially low yield.

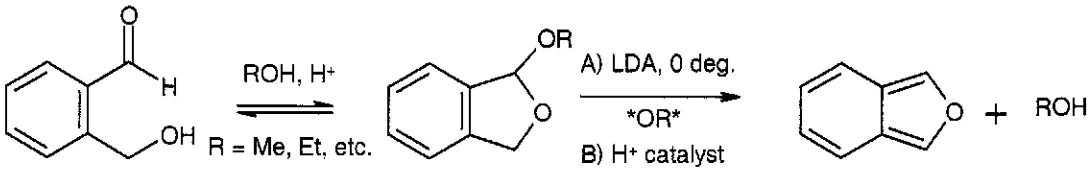

Figure 2-2: Alcohol Elimination Route to IBF

The next two synthetic routes to isobenzofurans both require an epoxide precursor, most often obtained from an appropriate aryl chloride or bromide. Generation of an aryne intermediate, followed by reaction with furan yields an epoxide[15], which is used in subsequent reactions. Several methodologies[16,17] may be employed to synthesize the aryne intermediate, most of which involve some sort of strong base and aryl halide. The method employed to synthesize the precursor of 5,5'-bis(isobenzofuran) involved the

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[13] Naito, K, Rickborn, B. *J. Org. Chem.* **1980**, *45*, 4061.
[14] Moss, R.J, Rickborn, B. *J. Org. Chem.* **1982**, *47*, 5391.
[15] Wittig, G, Pohmer, L. *Chem. Ber.* **1956**, *89*, 1334.
[16] Bertorello, M.M, Bertorello, H.E. *J. Organometal. Chem.* **1970**, *23*, 285.
[17] Apeloig, Y, Arad, D, Halton, B, Randall, C.J. *J. Am. Chem. Soc.* **1986**, *108*, 4932.

use of an aryl bromide and Caubere's[18] complex base in a dehydrohalogenation reaction (Figure 2-3).

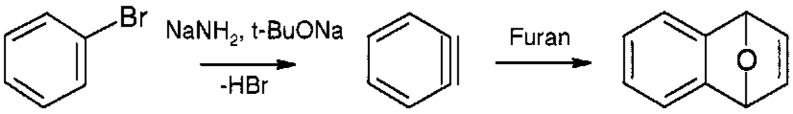

Figure 2-3: Epoxide Precursor Synthesis *via* Dehydrohalogenation

2.2.2: Multiple Diels-Alder Synthesis of Isobenzofurans

A mild, convenient method for the generation of isobenzofurans involves a number of successive Diels-Alder reactions. First, an electron-rich diene is mixed with an epoxide precursor. An inverse electron demand Diels-Alder reaction takes place, followed immediately by a retro Diels-Alder reaction to eliminate a molecule of relatively inert gas or other inert compound. A second retro Diels-Alder reaction yields the isobenzofuran, allowing for a normal electron demand Diels-Alder reaction to occur with a suitable dienophile. This method for generating IBFs requires no base, acid, or high temperatures, and isolation of pure solutions of IBF can be achieved through simple column chromatography. Note however that the presence of substituents on the 1- and 4- positions of the epoxide (1- and 3- positions of the IBF) hinders the initial Diels-Alder reaction, sometimes preventing the use of this technique. 3,6-Di(2-pyridyl)-1,2,4,5-tetrazine (Figure 2-4), or "dipytet" as it is commonly known, is often used as an electron-rich diene in this technique[19]. Other initial dienes include 1,2,3,4-tetraphenylcyclopentadienone[20] and α-pyrone[21], both of which have seen use since the early days of isobenzofuran research.

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[18] Carre, M.C, Gregoire, B, Caubere, P. *J. Org. Chem.* **1984**, *49*, 2050.
[19] Warrener, R.N. *J. Am. Chem. Soc.* **1971**, *93*, 2346.
[20] Fieser, L.F, Haddadin, M.J. *J. Am. Chem. Soc.* **1964**, *86*, 2081.
[21] Wege, D. *Tetrahedron Lett.* **1971**, 2337.

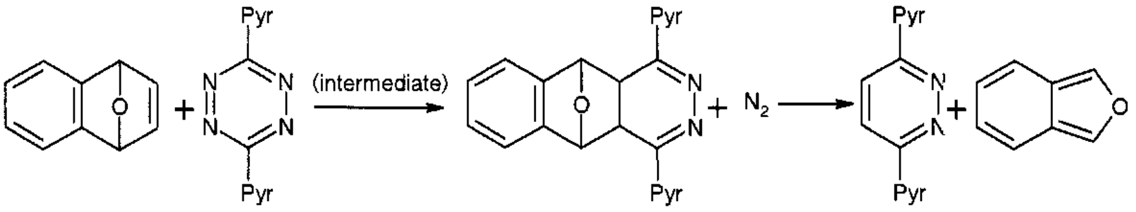

Figure 2-4: The Dipytet Route to Isobenzofuran

2.2.3: Flash Vacuum Thermolysis

The final technique for generating isobenzofurans is known as flash vacuum thermolysis (FVT)[22]. In this technique, a retro Diels-Alder reaction is performed at high temperature and low pressure on the vapour of an epoxide precursor, essentially "cracking" the molecule into the desired IBF and a molecule of ethylene (Figure 2-5). Precursors for this reaction are similar to those listed above, requiring only hydrogenation of the epoxide double bond. This method yields large amounts of IBF in high purity, but requires rather specialized equipment and a precursor capable of sublimation. Application of FVT towards isobenzofuran chemistry was pioneered by Wiersum and Mijs on 1,4-epoxy-1,2,3,4-tetrahydronaphthalene.

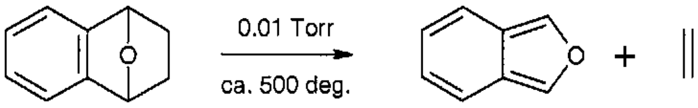

Figure 2-5: Isobenzofuran *via* FVT

2.2.4: Alternative Syntheses of IBFs

The three methods listed above represent the techniques most often used in the generation of novel isobenzofurans, but other methods certainly exist. Very recent work

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[22] Wiersum, U.E, Mijs, W.J. *J. Chem. Soc. Chem Commun.* **1972**, 347.

by Mikami and Ohmura[23] have shown that palladium (0) can be effective at catalyzing the breakdown of 1,3-dihydro-1-methoxyisobenzofuran *via* oxidative addition to produce isobenzofuran. Sambaiah and co-workers[24] have also found that $Ni(PPh_3)_2Cl_2$ in the presence of triphenylphosphine, zinc powder and an alkyne will catalyze a [2+2+2] trimerization, forming an aromatic by-product and isobenzofuran in a rather unusual reaction (Figure 2-6).

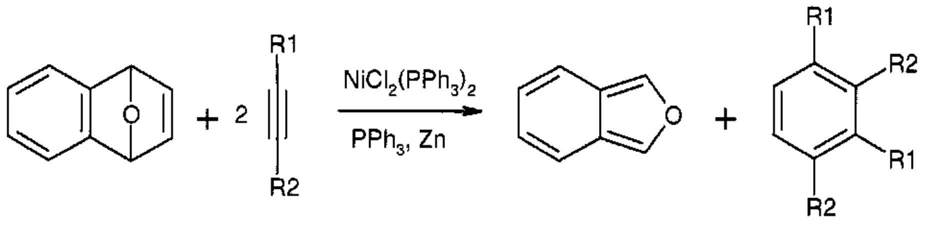

Figure 2-6: Nickel-Catalyzed Generation of IBF. R = any functional group.

2.3: Benzannulated Isobenzofurans

A large number of benzannulated isobenzofurans are described in two papers by Dieter Wege and colleagues[25,26]. Annulating furan with aryne precursors, Wege and his collaborators succeeded in synthesizing a number of benzannulated epoxides suitable for either FVT or multiple Diels-Alder generation of isobenzofurans. Wege tends to favor the latter technique, utilizing dipytet as an initial diene to generate examples **13**, **14** and **15** (Figure 2-7), among others not mentioned here. Interestingly, the vast majority of these compounds proved more stable than isobenzofuran, a property mentioned further in section 2.5: "*Reactivity of Isobenzofurans*".

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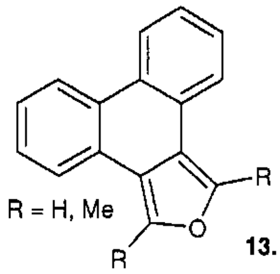
[23] Mikami, K, Ohmura, H. *Org. Lett.* **2002**, *4*, 3355

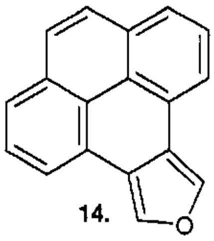
[24] Sambaiah, T, Huang, D, Cheng, C. *J. Chem. Soc., Perkin Trans. 1.* **2000**, 195.

[25] Stringer, M.B, Wege, D. *Tetrahedron Lett.* **1980**, *21*, 3831.

[26] Moursounidis, J, Wege, D. *Aust. J. Chem.* **1988**, *41*, 235 (*note: correction on pg.1624, same journal*).



13.



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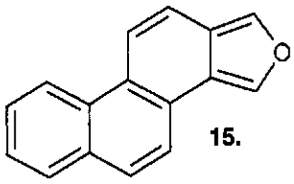

15.

Figure 2-7: Selected Benzannulated Isobenzofurans

2.4: Substituted Isobenzofurans

Substitutions to the furanoid positions (those next to oxygen) of IBF can be accomplished *in situ* through substitution chemistry. Removal of one or both furanoid protons with alkyllithium reagents leaves a nucleophilic carbon centre, which can then undergo reaction with a suitable substrate, such as methyl iodide[27]. (It should be noted that these reactions are usually performed on the IBF molecule itself, rather than any precursor molecules). Because of this fact, electrophiles are often selected based on ability to stabilize the IBF *via* steric hindrance. In addition to methyl iodide, trimethyl-[28] or triphenylsilyl[29] groups are also used, which sterically hinder homopolymerization of the IBF. Controlling the stoichiometry of the reaction allows for mono- or disubstitution.

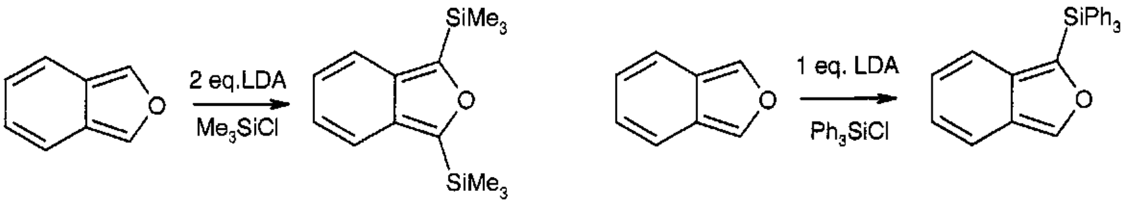

Figure 2-8: Silylation of Isobenzofuran

Isobenzofurans which are substituted on the carbocyclic region of the molecule are also known, and can be prepared by simply modifying the precursors, rather than the

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[27] Crump, S.L, Rickborn, B. *J. Org. Chem.* **1984**, *49*, 304.
[28] Tobia, D, Rickborn, B. *J. Org. Chem.* **1986**, *51*, 3849.
[29] Dibble, P.W, Masuda, J. Unpublished results.

IBF itself. For example, 4,7-dimethoxyisobenzofuran (Figure 2-9)[30,31] has been synthesized *via* the multiple Diels-Alder reaction methodology.

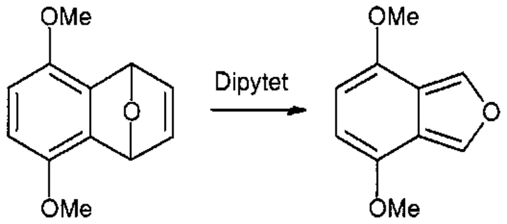

Figure 2-9: 4,7-dimethoxyisobenzofuran

Other substituents on isobenzofurans include alkyl groups and halides, with electron withdrawing groups being the least common. A variety of substituted IBFs have been synthesized, with a variety of substitents (Figure 2-10).[32,33,34,35]

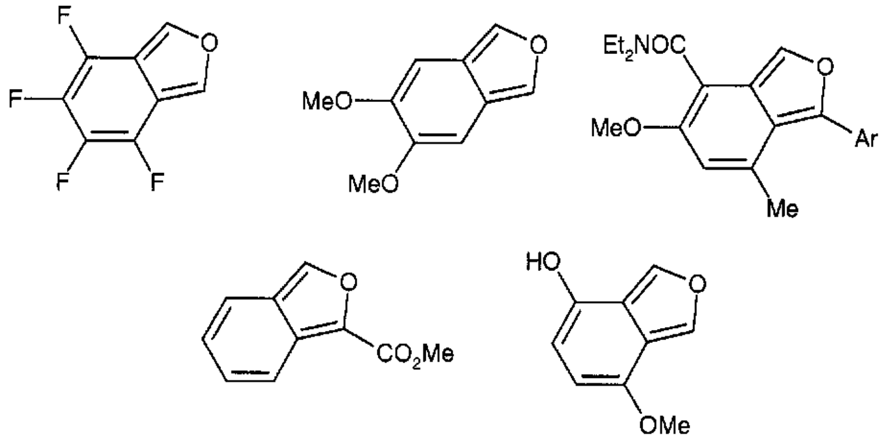

Figure 2-10: Substituted Isobenzofurans

2.5: Reactivity of Isobenzofurans

The reactivity of isobenzofuran in Diels-Alder reactions is approximately 1.4 million times greater than that of 1,3-butadiene. This reactivity can be modified by

---

[30] Keay, B.A, Rodrigo, R. *Can. J. Chem.* **1985**, *63*, 735

[31] Magnus, P, Eisenbeis, S.A, Magnus, N.A. *J. Chem. Soc., Chem. Commun.* **1994**, 1545.

[32] Heaney, H, Ley, S.V, Price, A.P, Sharna, R.P. *Tet. Lett.* **1972**, 3067

[33] Keay, B.A, Lee, D.K.W, Rodrigo, R. *Tet. Lett.* **1980**, 3663

[34] Keay, B.A, Rodrigo, R. *J. Am. Chem. Soc.* **1982**, *104*, 4725

[35] Warrener, R.N, Hammer, B.C, Russel, R.A. *J. Chem. Soc., Chem. Commun.* **1981**, 942.

substituents in the 1- and/or 3-positions on IBF[36], or by annulation to the benzo-ring. Substitution of the furanoid protons with electron-donating groups serve to destabilize the isobenzofuran, making the molecule more reactive. Electron-withdrawing groups have the opposite effect, stabilizing the IBF and making it less reactive. In either case, sterically bulky groups will serve to stabilize the IBF with respect to homopolymerization. Substituents on the benzo-ring of isobenzofuran tend to have little effect on IBF's reactivity in Diels-Alder reactions[37].

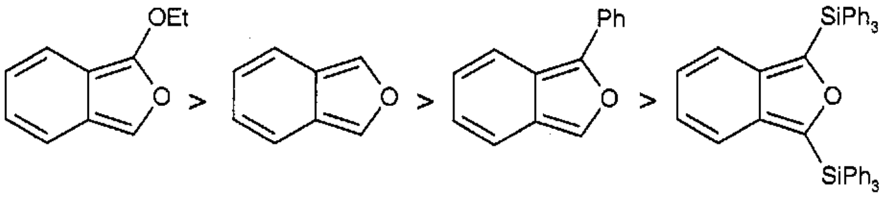

Figure 2-11: Reactivity of Substituted IBFs

Annulation of the benzo-ring of isobenzofuran can either increase or decrease the reactivity of the molecule, depending on the position of benzannulation[38,39]. Annulation on both the [4,5]- and [6,7]- positions serve to stabilize the IBF through resonance, while annulation on the [5,6]- position destabilizes the IBF by lack of resonance.

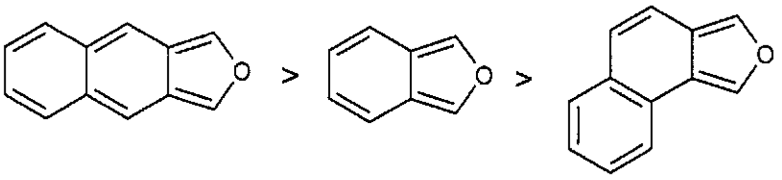

Figure 2-12: Reactivity of Benzannulated IBFs

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[36] Tobia, D, Rickborn, B. *J. Org. Chem.* **1987**, *52*, 2611.
[37] Rickborn, B. *Advances in Theoretically Interesting Molecules*. **1989**, *1*, 1. pp. 121-125.
[38] Moursounidis, J, Wege, D. *Aust. J. Chem.* **1988**, *41*, 235.
[39] Moursounidis, J, Wege, D. *Aust. J. Chem.* **1988**, *41*, 1624.

2.5.1: Dienophiles

Maleimides (Figure 2-13) are quite reactive dienophiles in normal demand Diels-Alder reactions, allowing for quantitative or near-quantitative yields. This is often an important consideration when initial starting materials may be available in milligram quantities. In addition to their reactivity, maleimides also possess extraordinary *endo*-selectivity with 1- and 3-substituted isobenzofurans, often exceeding 95%[40]. This selectivity not only simplifies the NMR spectrum of the final adduct mixture, but also suggests applications in which *endo*-selectivity is an asset. In particular, N-substitution[41,42] of various atoms or molecules or double Diels-Alder reactions with bis(IBF)s, in which reaction geometry is critical to cyclophane formation. For these reasons, maleimides have been a reagent of choice for the investigation of novel and/or unstable isobenzofurans[43].

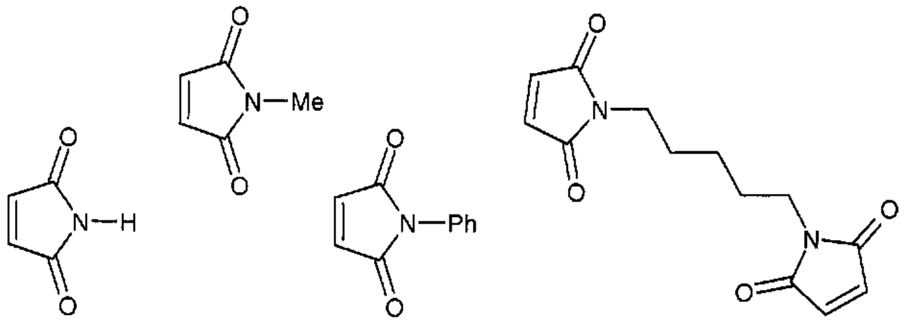

Figure 2-13: Selected Maleimide Dienophiles

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[40] Tobia, D, Rickborn, B. *J. Org. Chem.* **1987**, *52*, 2611.
[41] Walker, M.A. *J. Org. Chem.* **1995**, *60*, 5352.
[42] Wengrovius, J.H, Powell, V.M, Webb, J.L. *J. Org. Chem.* **1994**, *59*, 2813.
[43] Tobia, D, Harrison, R, Phillips, B, White, T.L, DiMare, M, Rickborn, B. *J. Org. Chem.* **1993**, *58*, 6701.

2.6: Molecules with Multiple Furan Moieties

Thus far, only molecules containing one isobenzofuran moiety have been discussed in any detail, but molecules containing multiple furan moieties are known. Two of the first examples of bis(isobenzofurans) (also called difurans) are molecules (**16**) and (**17**). Difurans **16** and **17**, along with trifuran **12** were all described in the same paper by Stringer and Wege in 1980.[44] Trifuran (**12**) is the only known molecule to contain three furan moieties. Other molecules with two furan units have since been discovered, although the number of known bis(isobenzofuran)s remain relatively few. With multiple Diels-Alder reaction sites, reaction with multiple dienophiles, or with molecules containing multiple dienophilic centers becomes possible. These molecules present potentially useful substrates for the synthesis of polymers and cyclophanes.

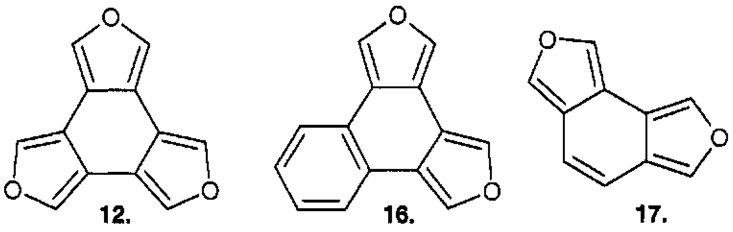

Figure 2-14: Early Di- and Trifurans

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[44] Stringer, M.B, Wege, D. *Tet. Lett.* **1980**, *21*, 3831.

Technically, the molecules presented in Figure 2-14 are not strictly isobenzofurans, but rather fused benzo(c)furans. As this implies, the initial reactivity of these molecules more closely resembles that of furan rather than IBF. These molecules are still generally considered analogues of isobenzofuran. After the first (or second) Diels-Alder reaction, the molecule does indeed become a benzologue of IBF, with the reactivity associated with isobenzofurans.

2.7: Introduction to Cyclophanes

The word "cyclophane" is a contraction of *cyclo-*, *phenyl,* and *alkane*. As the name implies, cyclophanes are cyclic molecules which contain both aromatic and aliphatic regions[45,46]. Cyclophanes vary greatly in size and structure, ranging from small, simple molecules to large cage structures. Indeed, a unique naming system has been developed to allow for description of different cyclophane structures[47].

[*n*]Cyclophanes are among the simplest possible cyclophane structures. The most common of these consist of a phenyl ring, to which is attached an aliphatic "tether" of length equal to *n* methylene units. As with any disubstituted benzene, [*n*]cyclophanes may be *meta-*, *para-* or *ortho-* (left to right, Figure 2-15), although [*n*]orthocyclophanes are often considered to be simple fused-ring systems rather than true cyclophanes.

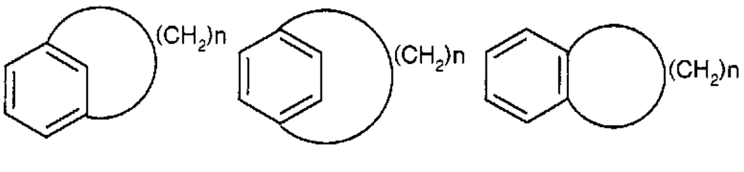

Figure 2-15: From left to right: *meta-*,*para-*, and *ortho-* [n]cyclophanes.

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[45] Schubert, W.M, Sweeney, W.A, Latourette, H.K. *J. Am. Chem. Soc.* **1954**, *76*, 5462.

[46] Cram, D.J, Abell, J. *J. Am. Chem. Soc.* **1955**, *77*, 1179.

[47] Smith, B.H. *Bridged Aromatic Compounds.* Academic Press, New York and London 1964. This text gives an extensive overview of basic cyclophane nomenclature.

More complicated are the [*m.n*]cyclophanes, molecules which contain two tethers with methylene chains of lengths *m* and *n*, respectively. Because of the added complexity of these molecules, many more permutations are possible than with the [*n*]cyclophanes. Once again, *meta-*, *para-*, and *ortho-* isomers are possible, in addition to adding the possibility of incorporating multiple tether and aromatic systems, as is the case with [*m*]para[*n*]metacyclophane **20**, [*m.n*]paracyclophane **21** and [*m.n*]metacyclophane **22** (Figure 2-16).

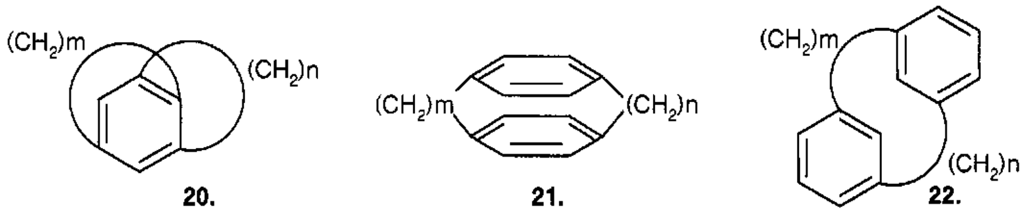

Figure 2-16: Some Examples of [m.n]cyclophanes

2.8: Extended Cyclophane Systems

All of the cyclophanes discussed so far have been based on the simplest possible aromatic region, namely benzene. Cyclophanes containing variations in their aromatic regions are also known. [8](2,7)pyrenophane **23** and [2]paracyclo[2](2,7) pyrenophane **24** (Figure 2-17) were synthesized by Bodwell and co-workers in 2000[48]. Interestingly enough, X-ray crystallography revealed that the pyrene moiety of both **23** and **24** proved to be significantly warped (as illustrated below). Even so the pyrene unit retains its aromatic character, an exception to the classic rules for aromaticity taught in undergraduate organic chemistry courses[49].

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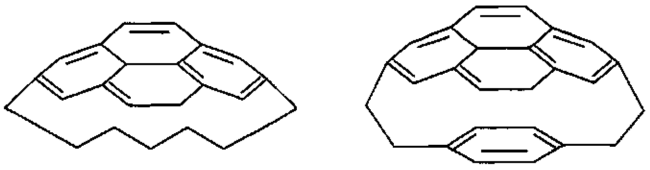
[48] Bodwell, G.J, Fleming, J.J, Mannion, M.R, Miller, D.O. *J. Org. Chem.* **2000**, *65*, 5360.

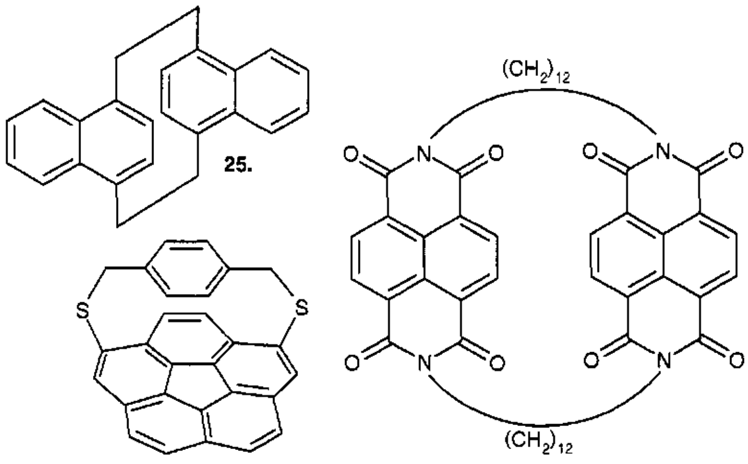
[49] Bodwell, G.J, Miller, D.O, Vermeij, R.J. *Org. Lett.* **2001**, *3*, 2093.



23. **24.**

Figure 2-17: Cyclophanes Synthesized by Bodwell & Colleagues

Other cyclophanes based on extended aromatic systems include [2.2]paracyclonaphthane **25** [50], and N,N'-[12.12]-naphthalene-bis(imide) cyclophane **26** [51], both of which are based on the naphthalene aromatic system (Figure 2-18). Molecule **27** represents the first cyclophane based on corrannulene to be synthesized[52], marking a significant step towards the synthesis of Buckminsterfullerenes.



25. **27.** **26.**

Figure 2-18: Assorted Complex Cyclophanes

2.9: Alicyclophanes

Although something of an oxymoron according to strict definitions, recent work by Warrener and co-workers has proven that synthesis of purely aliphatic cyclophane-like molecules are possible. Molecule **28** is an example of such a molecule, dubbed an "alicyclophane" due to both its solely aliphatic nature and structural resemblance to

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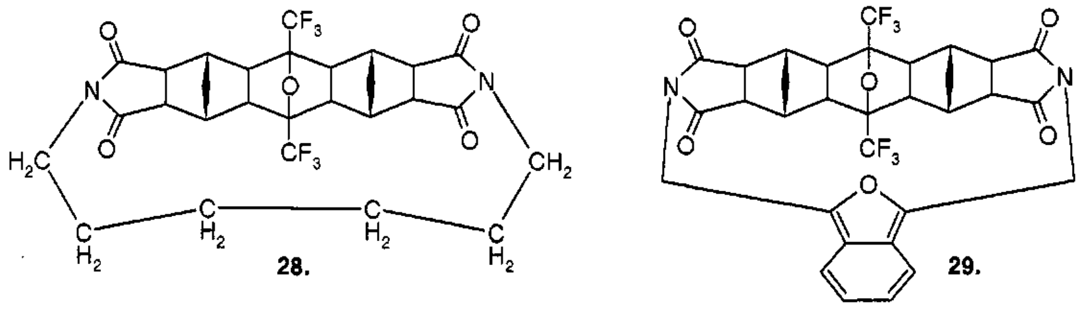
[50] Reich, H.J, Cram, D.J. *J. Am. Chem. Soc.* **1969**, *91*, 3527.

[51] Ozser, M.E, Uzun, D, Elci, I, Icil, H, Demuth, M. *Photochem. Photobiol. Sci.* **2003**, *2*, 218.

[52] Seiders, T.J, Baldridge, K.K, Siegel, J.S. *J. Am. Chem. Soc.* **1996**, *118*, 2754.

classical cyclophanes[53]. In a rather interestingly synergistic application, isobenzofuran has been stabilized[54] through incorporation into alicyclophane **29**. Because of the bulk of the alicyclophane backbone, the isobenzofuran suspended in the tether of **29** does not polymerize, but remains reactive with small, dienophiles. Research by Warrener *et al*[55] has provided the inspiration for much of the work presented in this thesis.



28.

29.

Figure 2-19: Alicyclophanes

2.10: Isobenzofurans and Cyclophanes

Isobenzofurans have also found a niche in the synthesis of cyclophanes. 1,1',4,4'-tetrahydro-1,4,1',4'-diepoxy-[*2.2*](1,4)-naphthalenophane **30** has been studied as a potential precursor to isobenzofuranophane **33** through two retro Diels-Alder reactions. In the event however, **33** was not formed, the highly reactive IBF moiety of intermediate **31** reacting with the epoxide *pi*-bond to form cyclophane **32** after expulsion of one equivalent of acetylene but before the second equivalent could be expelled[56].

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[53] Butler, D.N, Shang, M, Warrener, R.N. *Tet. Lett.* **2000**, *41*, 5985.

[54] Warrener, R.N, Shang, M, Butler, D.N. *Chem. Commun.* **2001**, *17*, 1550.

[55] See refs. 53 and 54.

[56] Halverson, A, Keehn, P.M. *J. Am. Chem. Soc.* **1982**, *104*, 6125.

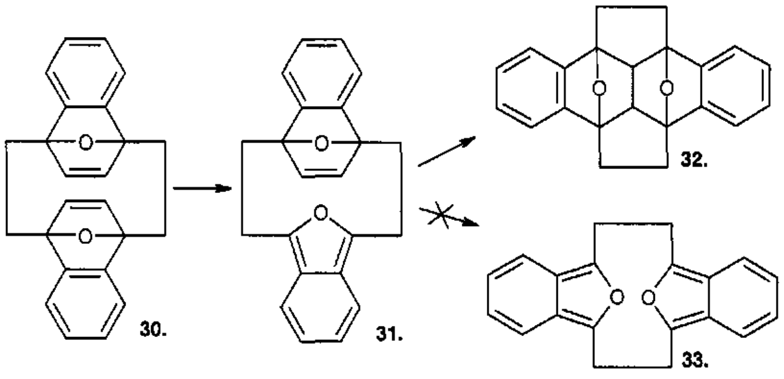

Figure 2-20: Isobenzofuranophanes

Directly related to the work presented in this thesis is a molecule synthesized by Thibault *et al*[57], naphtho[1,2-c:5,6-c]difuran **18**. In addition to standard Diels-Alder chemistry, **18** can be reacted with one equivalent of a “double-barreled” dienophile containing two reactive sites, such as bis(maleimido)propane. At low concentrations (approximately 200mg/L), one molecule of difuran will react with only one molecule of bis-dienophile, resulting in the generation of cyclophane **19**. Higher concentrations of the reaction mixture lead to polymeric products, which have not been investigated. Cyclophane **19** is very similar to structures presented later in this thesis.

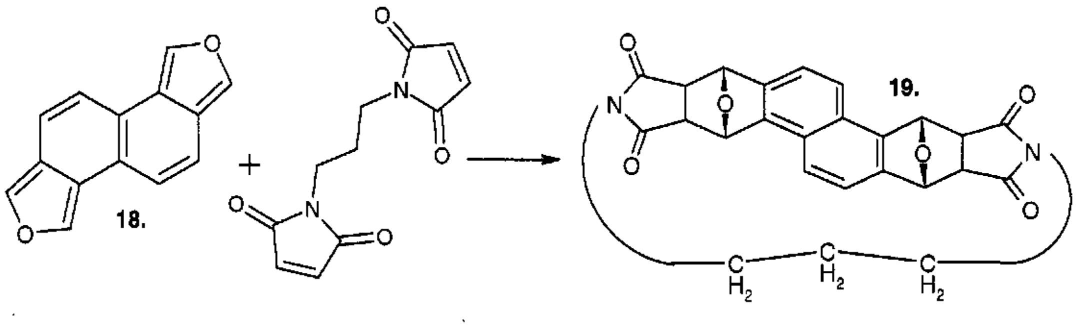

Figure 2-21: Naphtho[1,2-*c*:5,6-c]difuran and Derived Cyclophane

2.11: Unusual NMR Spectra of Cyclophanes

The aromatic regions of cyclophanes often cause unusual proton NMR behaviour. Protons on the tether portion of the molecule can be forced into close proximity to the

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[57] Thibault, M.E, Closson, T.L.L. Manning, S.C, Dibble, P.W. *J. Org. Chem.* **2003**, *68*, 8373.

shielding region of the aromatic ring, resulting in a pronounced shift in frequency. Indeed, methylene protons in aliphatic tethers are often at an NMR frequency less than TMS itself. Molecule **19** can be used to illustrate the proton shielding effect of aromatic rings. Protons in bold (Figure 2-22) show unusual shielding; a multiplet at δ -1.5 from TMS in the proton spectrum results from the central methylene protons[58]. Similar investigations into cyclophanes synthesized by Bodwell and co-workers also exhibit this NMR behavior; some of Bodwell's cyclophanes[59] exhibit aliphatic tether proton resonances as low as δ -2.06ppm.

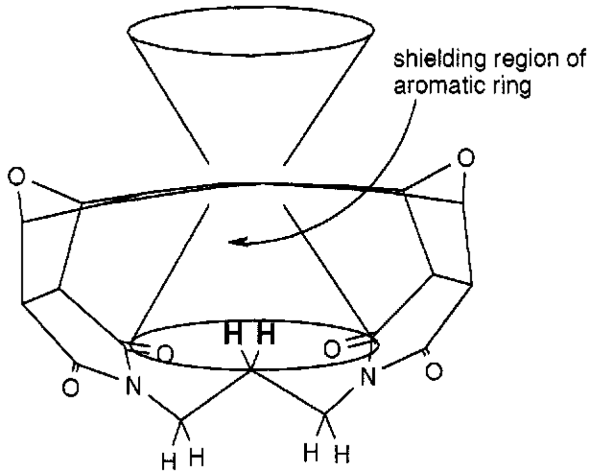

Figure 2-22: Shielding of Tether Protons of Molecule 19.

2.12: Some Applications of Cyclophanes

A number of applications for cyclophanes have been developed. [2.2]Paracyclophanes have been used as precursors in chemical vapor deposition processes, such as thin-film polymers and electronic coatings. These coatings are used as inert barriers in such applications, very similar to the oiling of steel objects to prevent

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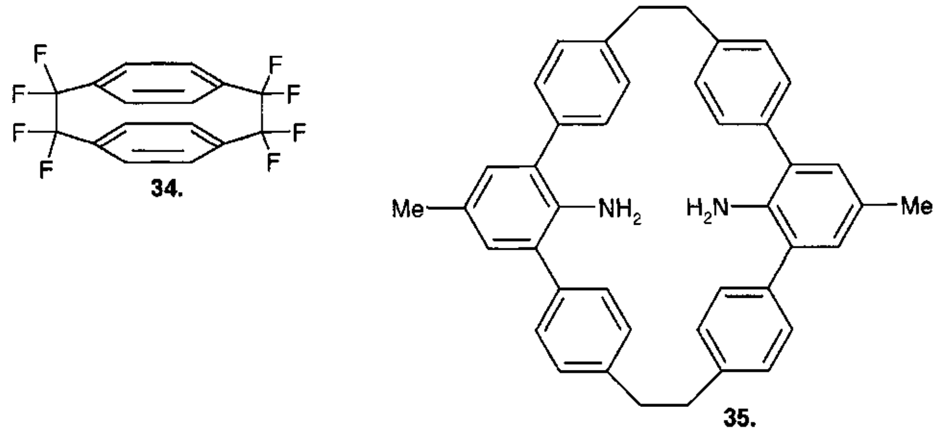
[58] Thibault, M.E, Closson, T.L.L, Manning, S.C, Dibble, P.W. *J. Org. Chem.* **2003**, *68*, 8373.

[59] Bodwell, G.J, Bridson, J.N, Chen, S, Poirier, R.A. *J. Am. Chem. Soc.* **2001**, *123*, 4704.

rust. 1,1,2,2,9,9,10,10-octafluoro [2.2]paracyclophane **34** [60] has seen use as a chemical vapor deposition polymer precursor, and is used in the microchip industry[61] as a protective barrier, similar to Teflon, for printed circuit boards. Cyclophanes containing internal chelating sites such as the amine functional groups of compound **35** have potential applications as ligands for single-site catalysts[62].



34.

35.

Figure 2-23: Industrially Significant Cyclophanes

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[60] Chow, S.W, Pilato, L.A, Wheelwright, W.L. *J. Org. Chem.* **1970**, *35*, 20.
[61] Dolbier, W.R, Duan, J-X, Roche, A.J. *Org. Lett.* **2000**, *2*, 1867.
[62] Camacho, D.H, Salo, E.V, Guan, Z. *Org. Lett.* **2004**, *6*, 865.

Chapter 3: Results and Discussion

3.1: Isolation of 5,5'-bi(isobenzofuran)

5,5'-Bi(isobenzofuran) was synthesized *via* a methodology developed by Warrener[61] for the synthesis of isobenzofuran. Dehydrobromination of 4,4'-dibromobiphenyl by sodium amide / sodium t-butoxide (Caubère's base)[62] in the presence of furan served to give 6,6'-bis(1,4-epoxy-1,4-dihydronaphthalene) **38** (Figure 3-1) in 75% yield. Using the multiple Diels-Alder route described in section 2.2, two equivalents of dipytet reacted with diepoxide **38** to form the initial adduct **39**, rapidly evolving nitrogen. This intermediate adduct readily underwent another reverse Diels-Alder reaction at room temperature, forming 5,5'-bis(isobenzofuran) **2** in unknown yield along with yellow 3,6-di(2-pyridyl)-1,2-pyridazine. The difuran was then isolated by filtration through a short (ca. 1cm) pad of silica gel to remove any reaction by-products and unreacted reagents.

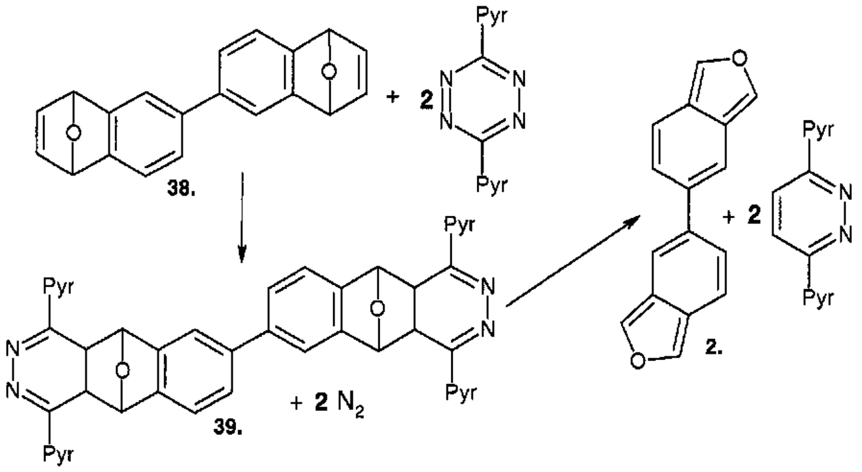

Figure 3-1: Synthesis of 5,5'-bis(isobenzofuran)

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[61] Warrener, R.N. *J. Am. Chem. Soc.* **1971**, *93*, 2346.
[62] Carre, M.C, Gregoire, B, Caubere, P. *J. Org. Chem.* **1984**, *49*, 2050.

The structure of **2** is that of two isobenzofuran molecules linked by a carbon-carbon single bond. As such, the lack of any functional groups in the 1- and 3- positions suggests reactivity nearly identical to isobenzofuran itself, for both IBF moieties. Timed NMR analysis confirm that **2** is qualitatively very similar in stability to IBF, with dilute solutions of **2** surviving at room temperature for a matter of hours, and with some unreacted difuran lasting up to two days at -20°C. In the latter case, significant polymer formation was observed after the first day. If one works carefully, sufficient unreacted **2** will survive column chromatography and solvent evaporation to obtain a proton NMR spectrum (figure 3.2). An NMR sample left standing for two hours at room temperature showed no signals save those of polymeric bi(IBF).

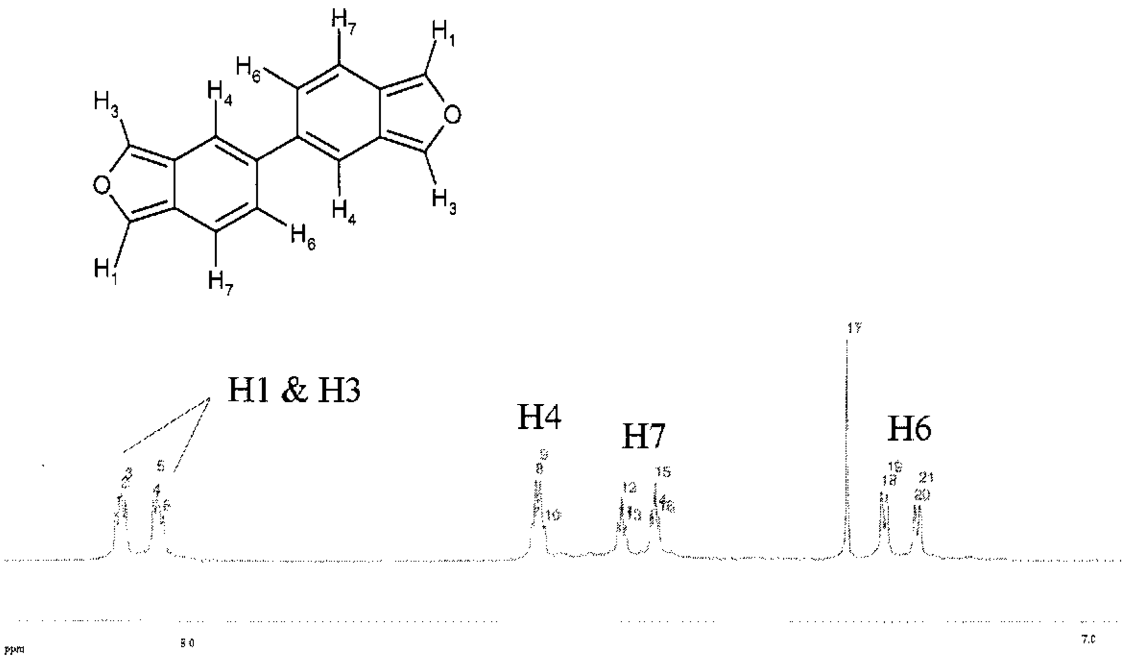

Figure 3-2: Proton NMR Spectrum and Assignment of Peaks for 5,5'-bi(IBF) at 250MHz in $CDCl_3$

The proton NMR spectrum of bi(IBF) shows some interesting long-range coupling patterns. The furanoid protons H1 and H3 show coupling to each other, as well as coupling to protons H7 and H4, respectively. Presumably, H1 is the upfield and H3 the downfield signal, but this is difficult to confirm without a COSY or NOE NMR spectrum, which was not acquired because of a lack of a conveniently available spectrometer capable of such experiments. H4 shows coupling to H3 and H6, H6 exhibits coupling to H4 and H7, and H7 couples to H1 and H6. This coupling pattern is consistent with known IBF coupling patterns[63,64].

3.2: 2:1 Adducts of 5,5'-bi(isobenzofuran)

Synthesis of simple adducts took place through one of two methodologies. In the first of these techniques, the difuran was isolated by chromatography. A dienophile was then added directly to the resulting bi(IBF) solution and allowed to react at room temperature. Solvent was removed *in vacuo*, and the final product purified as necessary through either silica gel column chromatography or recrystallization.

The second, simpler methodology involved adding epoxide, dipytet and dienophile to a reaction vessel containing chloroform or methylene chloride, and allowing the mixture to react at room temperature. Extraction of the reaction mixture with 1M HCl served to protonate unwanted dipytet and its byproducts, making them water-soluble and allowing for the isolation of chloroform-soluble adducts.

Both methods outlined above differ mechanically from each other, giving practical uses in the synthesis of 2:1 adducts. The first method allows for isolation of a relatively concentrated solution of difuran, which can be reacted with dienophiles quickly and cleanly. The second method yields a gradual increase in difuran concentration, which can be exploited by having a dienophile *in situ*. As the difuran is generated, it reacts

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[63] Thibault, M.E, Pacarynuk, L.A, Closson, T.L.L, Dibble, P.W. *Tet. Lett.* **2001**, *42*, 789.

[64] Warrener, R.N. *J. Am. Chem. Soc.* **1971**, *93*, 2346.

immediately with available dienophiles, maintaining a constant, low concentration and minimizing problems with polymer formation. The second method is particularly valuable in the synthesis of cyclophanes, where polymer formation with a bis(dienophile) is a significant problem.

Once the methodology for generating and reacting bis(IBF) had been developed, addition of typical Diels-Alder dienophiles such as methyl acrylate or maleimide resulted in the expected adducts. Complex mixtures of isomers resulted due to the formation of diastereomers and regioisomers. Stereoisomerism is associated with endo/exo selectivity, and is dependant on the dienophile being used. Methyl acrylate, for example, showed no stereoselectivity, while maleimide-based dienophiles all yielded exclusively endo-adducts. Stereoisomerism is also associated with the molecular symmetry of the adduct; in all cases, dienophiles can react in a syn- fashion, yielding Cs symmetry, or in an anti-fashion, yielding products with C2 symmetry. In all cases, 2:1 adducts showed no clear syn- or anti- selectivity. Thus, the methyl acrylate adduct can form no less than thirty-two separate isomers, each isomer being some combination of endo/exo, syn/anti, and regioisomeric products with substituents in the 6- and/or 7- positions (Figure 3-3).

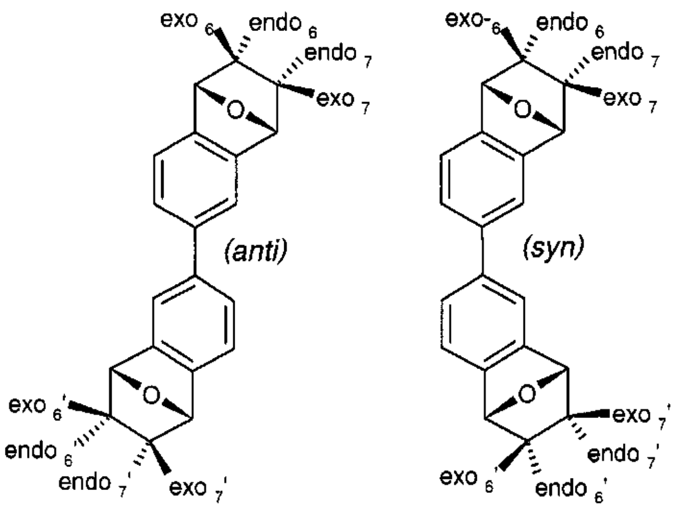


Figure 3-3: Possible Adduct Isomers.

The use of dimethyl fumarate simplified the reaction mixture by eliminating issues associated with *endo/exo* selectivity and substitution to the 6- and 7- positions, but diastereoisomers were still observed. To simplify the product mixtures, compounds **4** and **5** were synthesized from adducts by dehydration with methanesulfonic acid, giving simplified NMR spectra at the expense of yield. Due to the endo- selectivity and symmetry of maleimide and *N*-methylmaleimide, no aromatization of their adducts was necessary. This proved fortunate, as all attempts to aromatize maleimide-based adducts have failed thus far. Although only one adduct was apparent in the NMR spectra of non-cyclophanic adducts **6** and **41** (Figure 3-4), *syn*- and *anti*- diastereomers were probably formed, with coincidentally identical NMR spectra. When cyclophanes from **41** were synthesized *via* SN2 chemistry, different NMR spectra for each of the two diastereomeric cyclophanes became apparent, confirming this hypothesis.

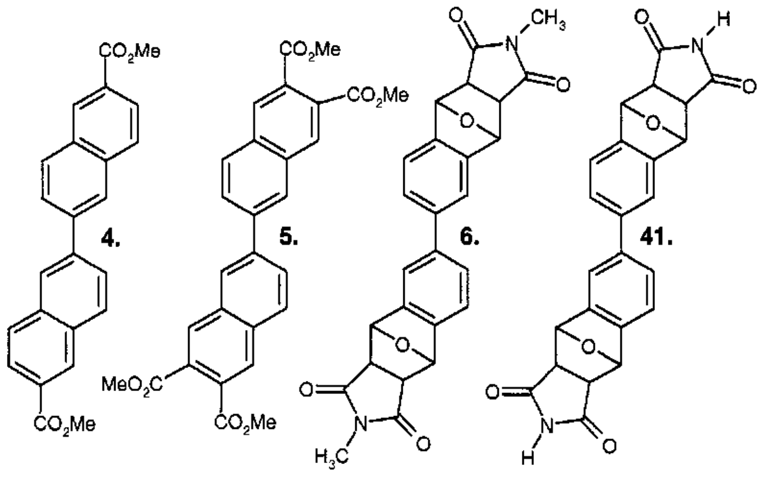


Figure 3-4: 2:1 Adducts of 5,5'-bis(IBF), both Aromatized and non-.

3.3: Nomenclature of Cyclophane Targets

We have developed our own, "in-house" system of nomenclature for the cycloadducts mentioned below. Using this system, the rigid aromatic/bicyclic system arising from the Diels-Alder reaction is collectively referred to as the "backbone" of the molecule. Atoms suspended between the two imide nitrogens constitute the "tether". Once the double Diels-Alder reaction is complete, the cyclophanic products are described primarily by their tethers; in this thesis the backbone is in all cases identical. Thus, the term "7 carbon cyclophane" refers to cyclophane **7** (Figure 3-5), with n = 7 methylene units. "*para*-xylyl cyclophane" refers to molecule **42**, the tether in this case being a *para*-xylylene moiety suspended between the two backbone nitrogen atoms.

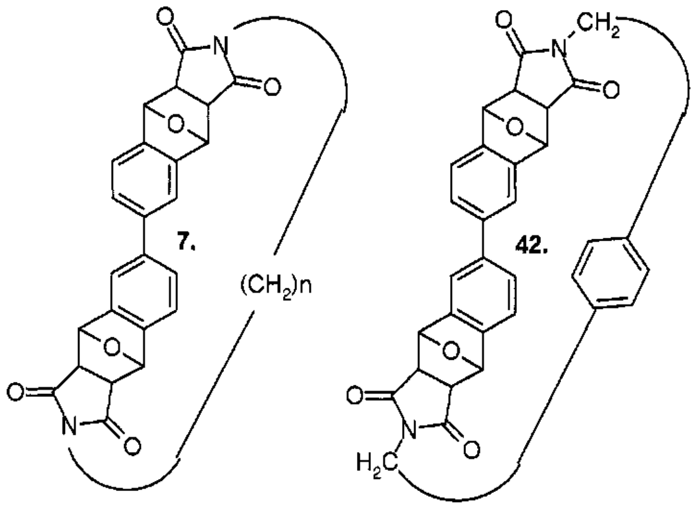

7.
42.

Figure 3-5: n-carbon and *para*-xylyl cyclophanes

Protons in the tether region of cyclophanes have also been given their own naming system. Methylene protons next to nitrogen have been dubbed α-protons, followed by β-, γ-, and so on as one moves away from the imide nitrogens (Figure 3-6). Carbon atoms in the tether region are similarly labeled Cα, Cβ and so on. This system of nomenclature is very useful when comparing properties of our cyclophanes such as bond angles and NMR spectra.

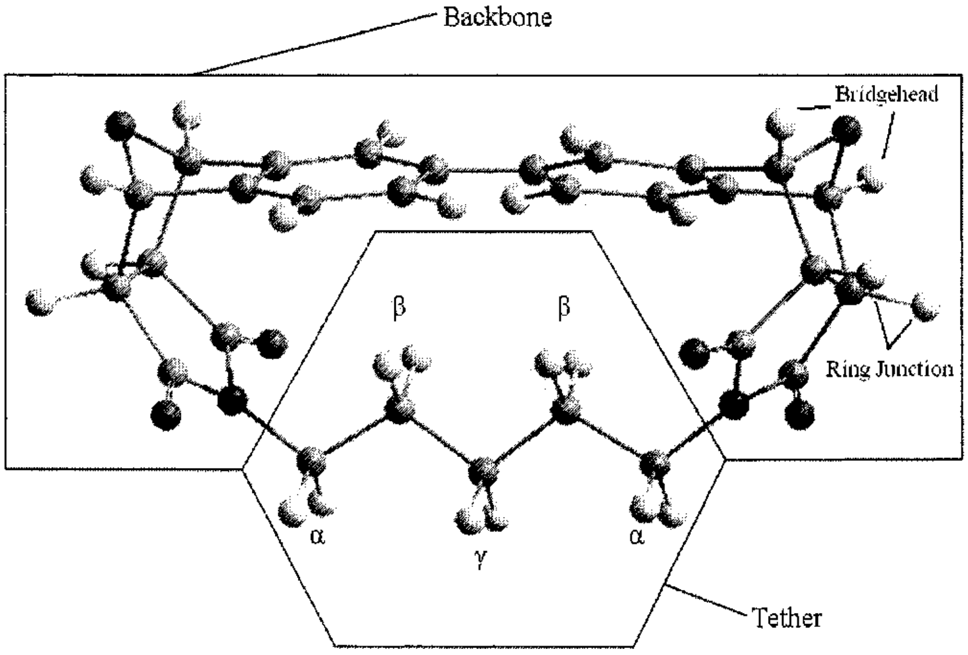
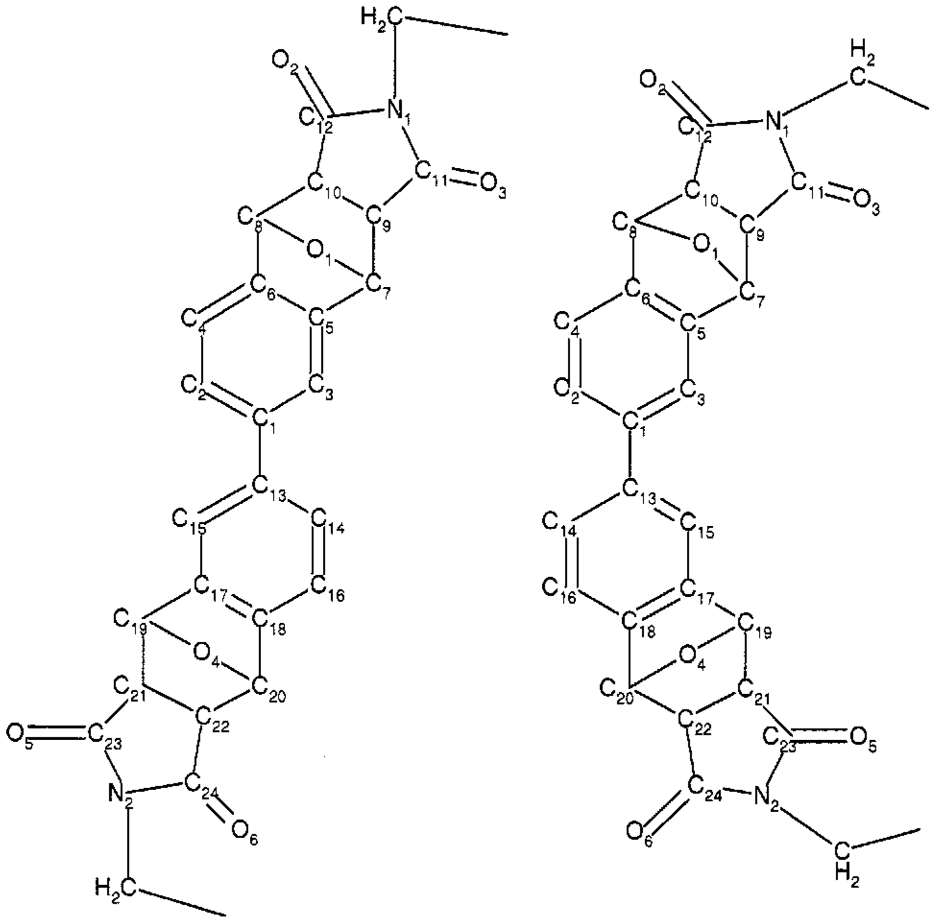


Figure 3-6: Cyclophane Nomenclature

In order to systematically compare structures of cyclophanes from bis(IBF), a more detailed examination of the backbone portion of the molecule is necessary. A common numbering scheme for the backbone of each isomer is therefore presented here. In both cases, C1 constitutes a reference point, namely one side (arbitrarily chosen) of the biphenyl single bond. From this point, two possible routes may be traced to N1, the nitrogen atom on the same side of the molecule as C1. The longer of the two routes contains seven bonds, and is termed the "long side" of the molecule. Atoms on this side of the molecule are given even numbers. The "short side" traces only six bonds to nitrogen, and atoms on the short side are given odd numbers. This scheme is symmetrical; adding 12 to each carbon atom will generate the number for the corresponding carbon atom on the opposite half of the molecule. Oxygen atoms do not necessarily follow this scheme, but are instead numbered sequentially starting with the long side (Figure 3-7).



anti- adduct backbone

syn-adduct backbone

Figure 3-7: Numbering Scheme of Cyclophane Backbone

3.4: Modeling Cyclophane Targets

Maleimide adduct 41 (Figure 3-4) was of particular interest to us, as it contains two nitrogen atoms suitable for substitution. Two possible products were modeled on a computer for the maleimide adduct, one for each symmetry point group. (Figure 3-8). Calculated AM1 distances between nitrogen atoms were 8.55Å for the C2 adduct (left), and 7.70Å in the case of the Cs adduct (right), with central bond torsions of 39.1° and 39.3°, respectively.

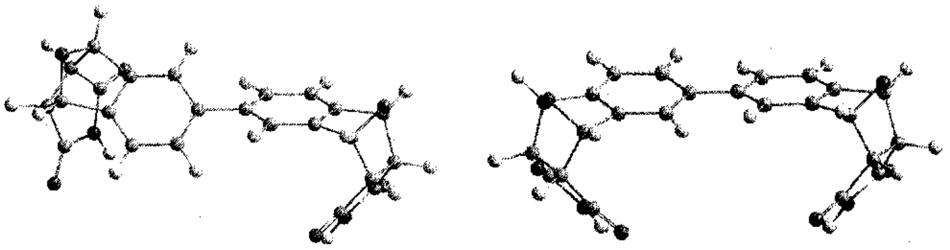


Figure 3-8: Maleimide Adduct Configuration. *C2* (left) and *Cs* (right) .

Inter-atomic distances between nitrogen atoms of the modeled compounds suggested that a carbon chain of 6 methylene units for the *anti-* adduct or 5 methylenes for the *syn-* adduct (8.76Å and 7.45Å respectively, allowing for staggered, terminal C-N bonds) would be most stable. Attaching the ends of the alkyl chain to both nitrogen atoms would result in a structurally interesting cyclophane bearing similarity to alicyclophanes (*see previous chapter*) synthesized by Butler and co-workers[65]. As with the simple maleimide adduct, two cyclophane products are possible, in which the nitrogen atoms are *anti-* and *syn-* to each other and exhibiting C2 and Cs symmetry, respectively (Figure 3-9).

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[65] Butler, D.N, Shang, M, Warrener, R.N. *Tet. Lett.* **2000**, *41*, 5985.

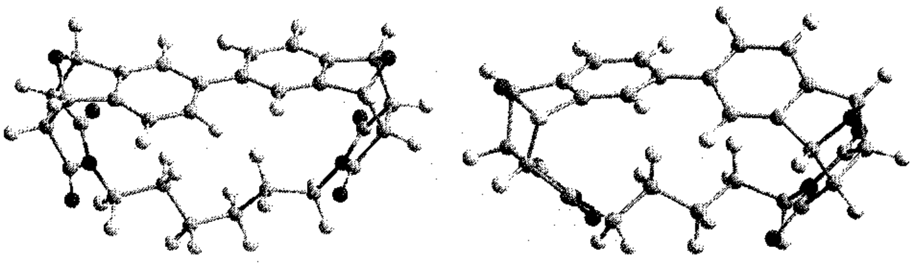

Figure 3-9: Calculated "Ideal" Cyclophane AM1 Models.
6C *anti*- cyclophane on the left, 5C *syn*- cyclophane on the right.

AM1 modelling[66] using HyperChem™[67] suggested that neither isomer would be thermodynamically favored over the other, given that the calculated energies at room temperature for the five-carbon cyclophane were -6871 and -6869 kcal/mol for the *syn*- and *anti*- adducts, respectively. As such, we expected both isomers to be present in our reaction mixtures. In the actual event however, shorter tether lengths invariably formed *anti*- cyclophane adducts, while longer tether lengths tended to favour *syn*- adducts. This will be more fully explained in section 3.6: *Syn/Anti Selectivity in Cyclophane Synthesis.*

3.5: Synthesis of Cyclophanes

We sought to apply our methodology to the synthesis of cyclophanes. Simply adding epoxide, bis(dienophile) and dipytet to chloroform proved fruitless, as polymer was by far the major product. Performing the reaction under high dilution conditions to keep intermolecular reactions to a minimum improved the yield, allowing for 2-10% isolated yields from 4,4'-dibromobiphenyl. Only under reflux did the reaction yields break 10%, which can be rationalized by again considering reaction geometry. It is unlikely that the two Diels-Alder reactions take place simultaneously, instead reacting in

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[66] AM1 parameters: Polak-Ribiere Algorithm, and RMS gradient of 0.1 kcal/Å mol.
[67] HyperChem 7.5 for Windows, 2002, Hypercube inc.

a stepwise manner (Figure 3-10). After the first reaction, the tether must adopt the correct geometry for reaction with the second isobenzofuran unit. Failure to adopt this geometry would result in polymer formation, as a nearby molecule could just as easily react. At high temperatures, the chance of achieving the correct geometry would be increased, resulting in increased yield in cyclophanic product over polymer[68].

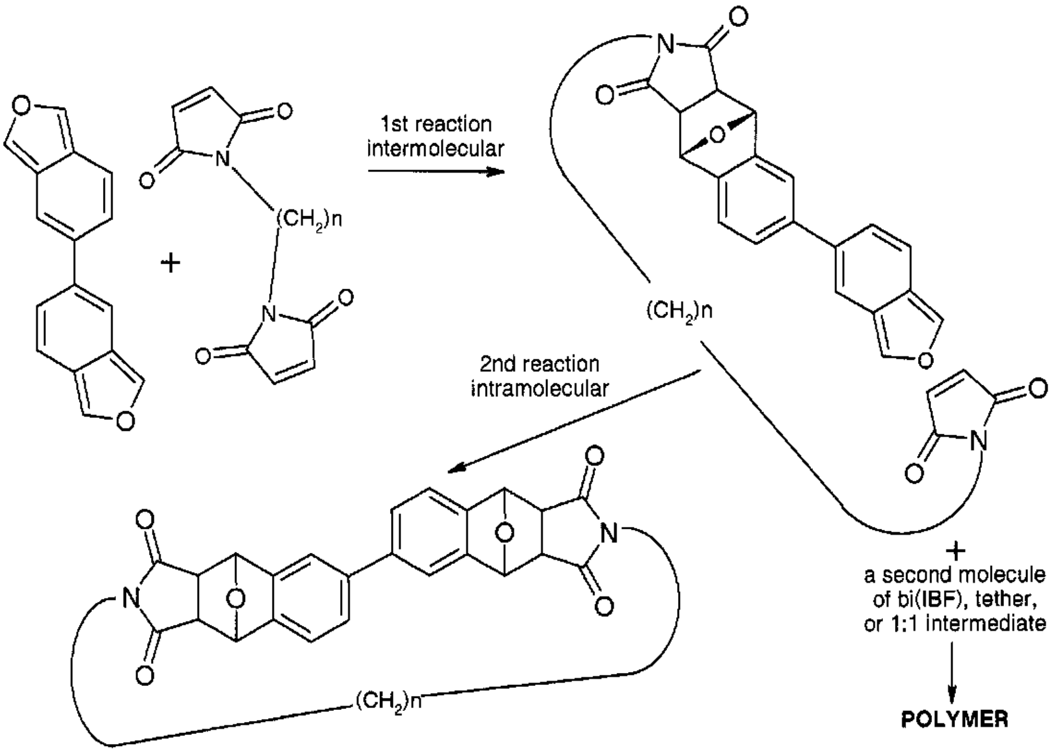

Figure 3-10: Reaction Scheme of Cyclophane Synthesis.

Our optimized synthesis involved adding the contents of two 50mL syringes, one containing bis(maleimide) and the other containing bis(isobenzofuran), simultaneously to a reaction vessel containing 500mL of refluxing solvent. This was done *via* syringe pump at a rate of 1mL every two minutes, keeping the reactants at a constant, dilute concentration to minimize intermolecular reactions. The mixture was refluxed to

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[68] Discussions with G.J. Bodwell led to our use of high-temperature, high-dilution conditions.

maximize the rate of conformational motion in the second, intramolecular Diels-Alder reaction. After reaction was complete, chromatography with a 5cm silica gel column using 1% acetic acid in chloroform as a mobile phase served to remove excess dipytet and tether. Further purification was accomplished through recrystallization. Utilization of this technique resulted in greatly increased yields, nearing 30% when the five-carbon tether was used.

3.5.1: SN2 Synthesis of Cyclophanes

In an alternative reaction, maleimide adduct **41** (Figure 3-4) can also be used to synthesize cyclophanes through standard substitution chemistry, using the maleimide nitrogen atoms as nucleophiles. Tethers employed in this alternative method require two leaving groups in acceptable positions to allow cyclophane formation over polymerization. Dilution conditions were not used with this method, with lower yields as a consequence. Where the double Diels-Alder route gave specific ratios of *syn-* and *anti-* isomers depending on tether length, however, the SN2 route yielded no selectivity; both isomers were observed in roughly equal amounts for all tether lengths.

3.5.2: Tether Possibilities

Limitations in cyclophane variation have more to do with tether geometry than N-N bond distance. Because of rotation around the biphenyl single bond "link", the actual distance between nitrogen atoms is capable of varying significantly with bond torsion. Alkyl chains of lengths from 5 to 9 carbon atoms form cyclophane with little difficulty, as do *para*-xylyl and other tethers possessed of significant rotational motion. However, *para*-phenyl cyclophanes do not form, as only one axis of rotation is present in 1,4-phenylenebis(maleimide). Attempted synthesis of cyclophanes with tethers containing more than 9 or less than 5 carbon atoms did give indications of very small (less than 1%) amounts of cyclophane, but only polymer was isolated from these reactions.

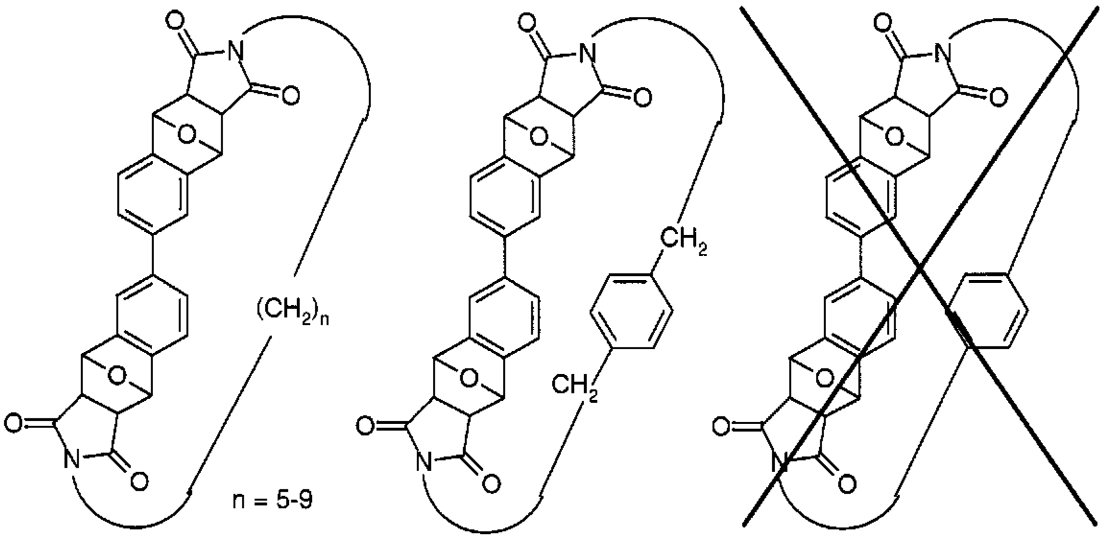

Figure 3-11: Tether Possibilities

3.5.3: Comparison to biphenyl

Because 5,5'-bis(isobenzofuran) is in reality simply a furan-annulated analogue of biphenyl, some comparison can be made between the structure of cyclophanes from bis(IBF) and that of biphenyl itself. The torsion angle of the biphenyl single bond is of particular importance. The original X-ray crystal structure examination by Trotter[69] showed that the two aromatic rings of biphenyl are co-planar in the crystalline state. While this is true for unsubstituted biphenyl however, recent work by Dinesh & Singh[70] has shown that simple substitutions such as methoxy- groups in any position on biphenyl interact in such a way as to change the dihedral angle to 37.5°. In addition, NMR and IR studies by Akiyama & Watanabe[71] determined a solution-state dihedral angle of approximately 37°. Because the cyclophanes presented here are essentially substituted

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[69] Trotter, J. *Acta Crystallogr.* **1961**, *14*, 1135
[70] Dinesh, R, Singh, D. *Bull. Mater. Sci.* **2004**, *27*, 31
[71] Akiyama, M, Watanabe, T. *J. Phys. Chem.* **1986**, *90*, 1752

biphenyls, a dihedral angle of 37° in both the solution and solid state shall be considered as typical of an unstrained derivative.

3.6: Syn/Anti Selectivity in Cyclophane Synthesis

Upon examining the NMR integration data of the crude product mixtures from both the double Diels-Alder and SN_2 methodologies, a significant trend emerges regarding *syn/anti* selectivity of the reaction (Table 3-1). As might be expected, no selectivity whatsoever accompanies the SN_2 method, since both isomers were pre-formed in the starting material. Because of this, equal proportions of each isomer may be found in the product of the SN_2 reaction. The double Diels-Alder synthesis shows a very distinct trend towards *anti* selectivity associated with short tether lengths. The xylyl, five, and six-carbon cyclophanes formed exclusively as the *anti* isomer, in complete contradiction of what was expected from the computer models (section 3.4) Some selectivity is lost with the seven-carbon cyclophane, with only about 80% *anti* selectivity. The eight-carbon cyclophane exhibited approximately 50% selectivity. Finally, the reaction for the nine-carbon cyclophane yielded 60% *syn-* selectivity. This trend was observed with both crude and purified material, although all of the cyclophanes for which X-ray quality crystals were obtained crystallized as their major isomer.

Table 3-1: Syn/Anti Selectivity of Double Diels-Alder Cyclophane Synthesis. Yield for 9C cyclophane is for the crystallized syn adduct.

Cyclophane	Yield	syn/anti ratio
Xylyl-		0 / 100
5C	19.6%	0 / 100
6C	17.1%	0 / 100
7C	16.5%	20 / 80
8C	15.9%	50 / 50
9C	8.5%	60 / 40

Reaction geometry may be used to explain the trend mentioned above (Figure 3-12). Shorter tether lengths have less rotational freedom, and therefore have more difficulty assuming the necessary reaction geometry for the *syn* isomer. Longer tether lengths are capable of assuming the required conformation. Also, because the *anti* isomer has its tether region suspended directly under the backbone region, steric hindrance increases with tether length. The *syn* isomer allows long tether lengths to assume a conformation in which the tether is no longer directly under the backbone, instead rotating out towards the side of the molecule. It is unfortunate that attempts at cyclophane synthesis with tether lengths longer than nine methylene units yielded nothing but polymer; it would be interesting to see how far the trend continues towards 100% *syn* selectivity.

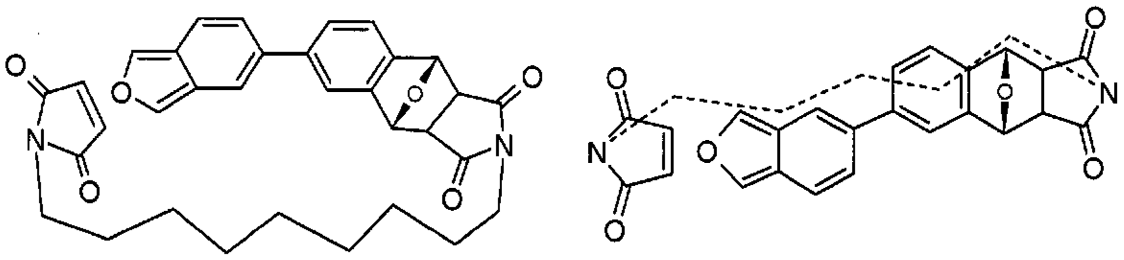

Figure 3-12: Depiction of Suspected Transition States for *syn*- (left, 9-carbon chain) and *anti*- (right, 5-carbon chain) Adducts. Longer chains "swing out" to the side, favoring *syn*- adducts.

3.7: Five-carbon cyclophane

The first compound to be synthesized, isolated and characterized by NMR was the 5 carbon cyclophane. This tether length was attempted first because it was calculated as one of the optimal lengths for cyclophane formation (see section 3.4: *Modeling Cyclophane Targets*), and so synthesis of the five-carbon cyclophane utilizing the methodology detailed above (section 3.5:) served as a first test case.

Analysis of proton, carbon-13 and COSY NMR experiments showed that only one isomer was present in both crude and purified samples. Proton NMR spectra for this cyclophane showed a number of different signals consistent with a molecule of C2 symmetry (Figure 3-13). Five separate resonances arising from the tether proved consistent with four pairs of diastereotopic protons and one pair of homotopic protons. Were this molecule to be the *syn-* isomer possessing Cs symmetry, one would expect an extra resonance, as the central methylene protons would then be diastereotopic, and six proton signals would be observed rather than five (Figure 3-14). Synthesis of the 5-carbon cyclophane using the SN2 route with 1,5-dibromopentane confirmed our hypothesis that only a single isomer was present from the double Diels-Alder reaction, as a distinct spectrum from the *syn-* cyclophane was observed overlapping that of the *anti-* cyclophane (Figure 3-15). To confirm the assignment of the proton signals, a COSY spectrum was used (Figure 3-16).

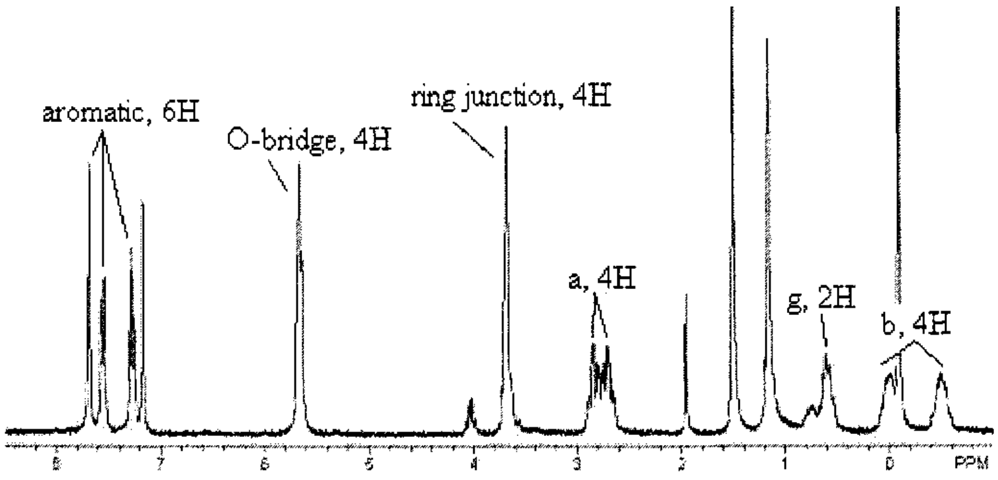

Figure 3-13: Proton NMR Spectrum of 5-C Cyclophane *via* Double Diels-Alder Route.

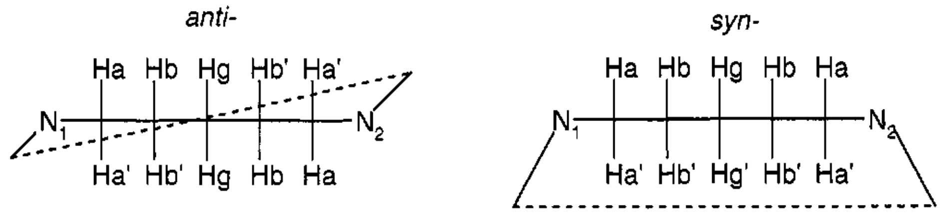

Figure 3-14: Diagram of Tether Proton Topicity. a = α, b = β, g = δ.

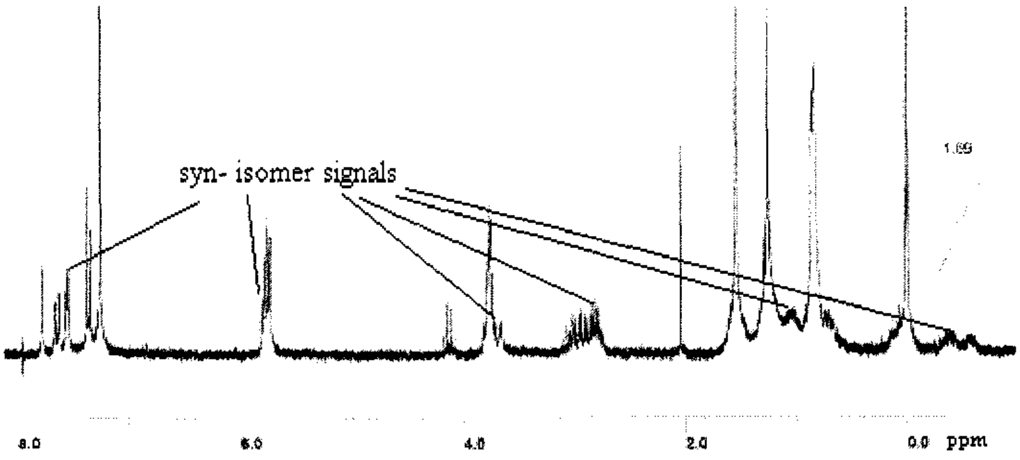

Figure 3-15: Proton NMR Spectrum of 5-C Cyclophane *via* SN2 Route.

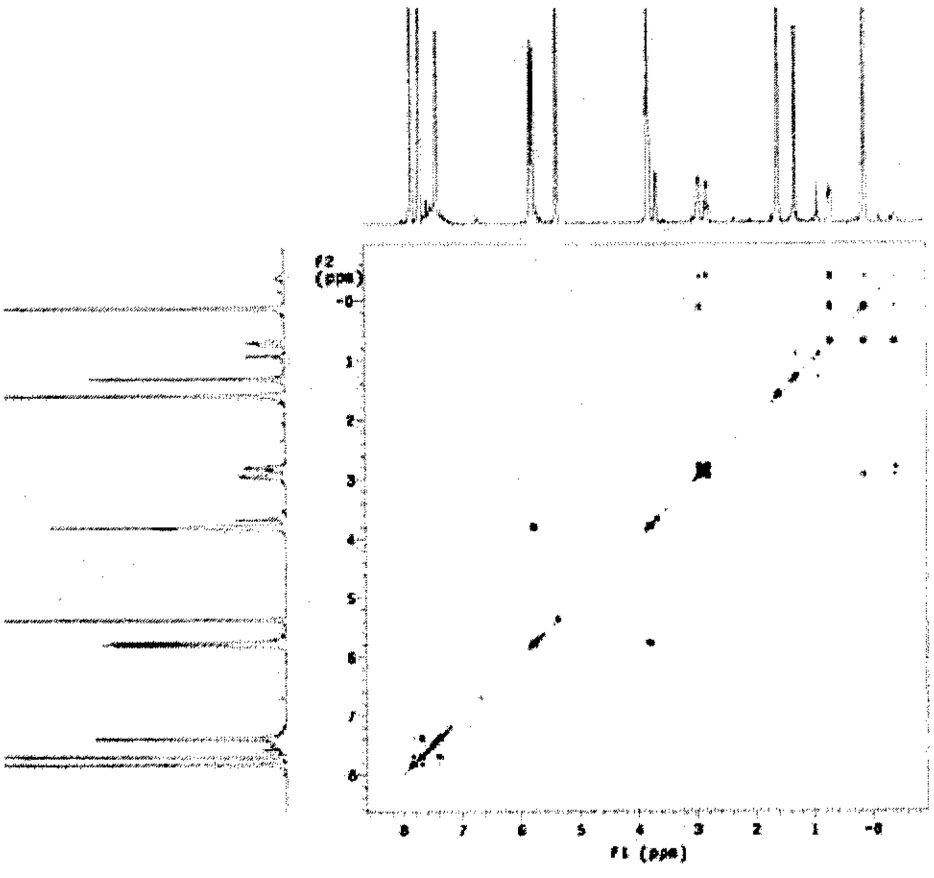

Figure 3-16: COSY Spectrum of 5-C Cyclophane at 500MHz in CD_2Cl_2

Crystallization of the five-carbon cyclophane for X-ray diffraction experiments proved difficult. Once crystals were finally grown, however, a number of interesting structural features were discovered. First of all, the aromatic rings are slightly warped, although to a lesser degree than similar pyrene-based cyclophanes discovered by Bodwell.[72] This warping leads to two biphenyl bond torsions C2-C1-C13-C15 at 4.33° and C3-C1-C13-C14 at 2.65°, a large variation from the "expected" angle of 37°. I postulate that the small torsion angle serves to minimize bond strain in the tether region by sacrificing a relatively small amount of energy from a larger dihedral angle. The other

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[72] Bodwell, G.J, Bridson, J.N, Chen, S-L, Poirier, R.A. *J. Am. Chem. Soc.* **2001**, *123*, 4704.

interesting feature of the backbone of this cyclophane is a small amount of deformation in the oxabicyclic ring system – most likely a result of crystal packing forces. The tether region, being one methylene unit shorter than optimal for the *anti-* isomer, is deformed; the Cα-Cβ-Cγ bond angles on each end of the tether are 115° - quite wide for sp_3-hybridized carbon atoms – while the other bond angles are all much more typical[73], averaging 109°. The tether deformation of this cyclophane is likely a result of repulsive tether/backbone electronic interactions[74].

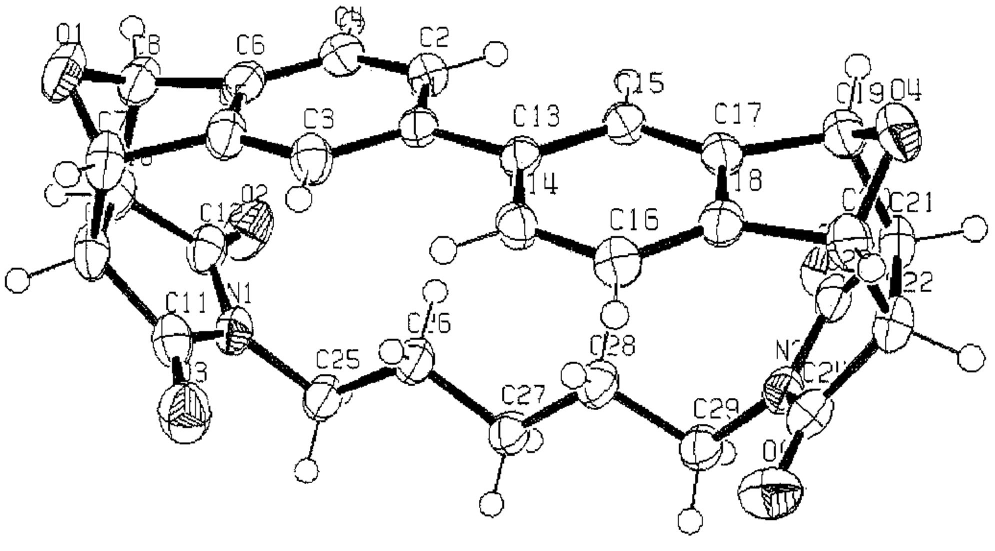

Figure 3-17: ORTEP diagram of 5C cyclophane Crystal Structure at the 50% Probability Level

3.8: Six-carbon cyclophane

The second cyclophane in the series contained six methylene units in its tether. In a similar fashion to the five-carbon cyclophane, the molecule exhibits six resonances, one

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[73] CRC handbook, 55th ed. The Chemical Rubber Publishing co, 1974, pg. F-203.

[74] Pascal, R.A. Jr, Winans, C.G, Engen, D.V. *J. Am. Chem. Soc.* **1989**, *111*, 3007.

for each diastereotopic pair of protons. Unlike the five-carbon cyclophane however, no homotopic proton pair exists, as there is no methylene group centred on the C2 axis of rotation. Again, only one isomer appeared to be present from the double Diels-Alder reaction, which was confirmed by synthesizing the cyclophane by SN2 chemistry from the maleimide adduct. The SN2 synthesis showed two distinct sets of proton and carbon NMR signals.

Six-carbon cyclophane molecules co-crystallized from a solution of 1% acetic acid in chloroform along with a molecule of acetic acid (Figure 3-18). The presence of acetic acid in the unit cell is an interesting and rare feature of the structure. In addition, the six methylene units are skewed slightly, preventing the molecule from having perfect C2 symmetry in the crystalline state – not unusual given that the cyclophane crystallizes in the P-1 space group. The additional methylene unit alleviates enough ring strain to remove any non-planarity in the aromatic rings, and the biphenyl bond torsion is 26.4° - much closer to the expected angle of 37°. A single *gauche-* interaction appeared in the tether next to one of the nitrogen atoms, marking the start of an interesting trend – each additional methylene unit adds an additional *gauche-* interaction to the tether. Finally, the C-C bond angles of the tether all exceed 110°, up to a maximum of 115.4° for the N2-Cα'-Cβ' bond angle (the skewed side of the tether).

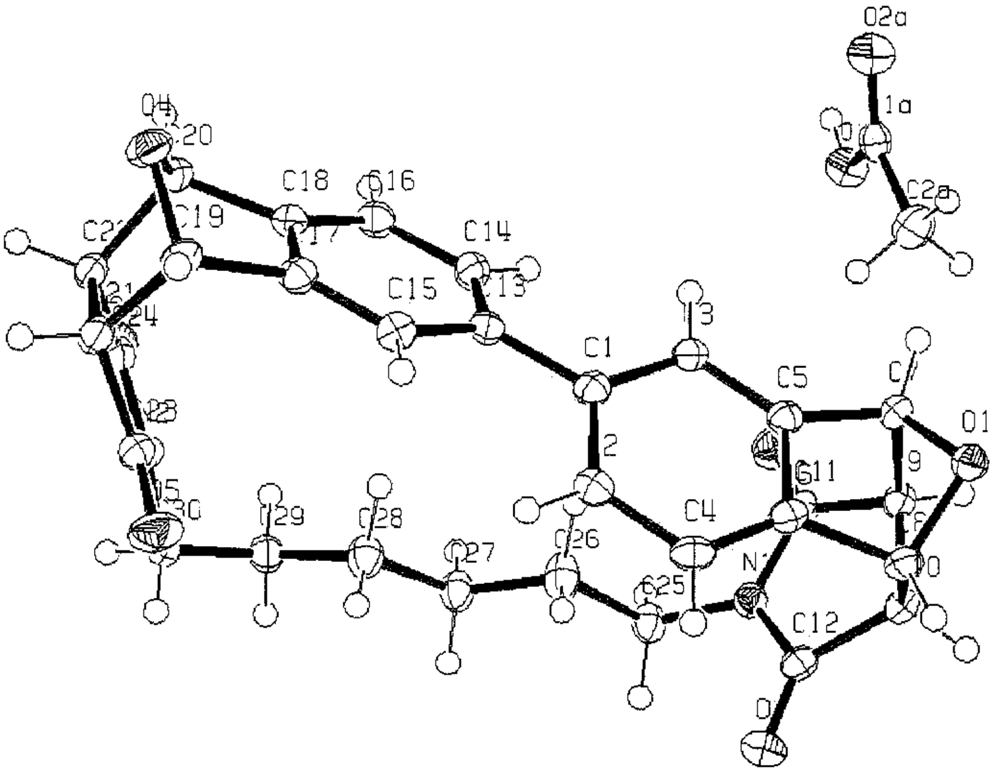

Figure 3-18: ORTEP diagram of 6C cyclophane Crystal Structure at the 50% Probability Level

3.9: Seven-carbon cyclophane

As with both the five- and six- carbon cyclophanes, the solution state behavior of the seven-carbon cyclophane was perfectly consistent with a single isomer of C2 symmetry. Because of the increasing number of overlapping proton signals, the proton NMR spectrum of the tether region proved much more difficult to interpret.

This molecule crystallized in a remarkable fashion, at first glance appearing to co-crystallize as two separate enantiomers (Figure 3-19). In the case of these molecules however, the conformation of the aliphatic tether is superimposable in each compound, destroying the symmetry of the enantiomers in the solid state. As a result of this destroyed symmetry, the molecules have crystallized in the P1 space group, an unusual phenomenon in molecules which are racemic or show no optical activity.

Structurally, this cyclophane contains the closest geometry to what was expected for a substituted biphenyl. The biphenyl dihedral angle is 35° for one isomer, 34.5° for the other. As with the five-carbon cyclophane, the tether bond angles varied; both Cβ-Cγ-Cδ bond angles were at approximately tetrahedral angles, but every other angle exceeded 113.8°, to a maximum of 117.2° for the Cγ-Cδ-Cγ' bond angle – nearing the optimal 120° angle for sp^2- hybridized carbon atoms. The reason for this is a matter of interaction between the aromatic *pi-* electron clouds and the tether protons. Unlike the shorter tethers, sufficient rotational motion in the tether region allowed the tether protons to achieve a greater distance from the *pi-* electrons, resulting in both a diminished proton NMR shielding effect and a tether rotated "sideways" from the orientation of the five-carbon tether.

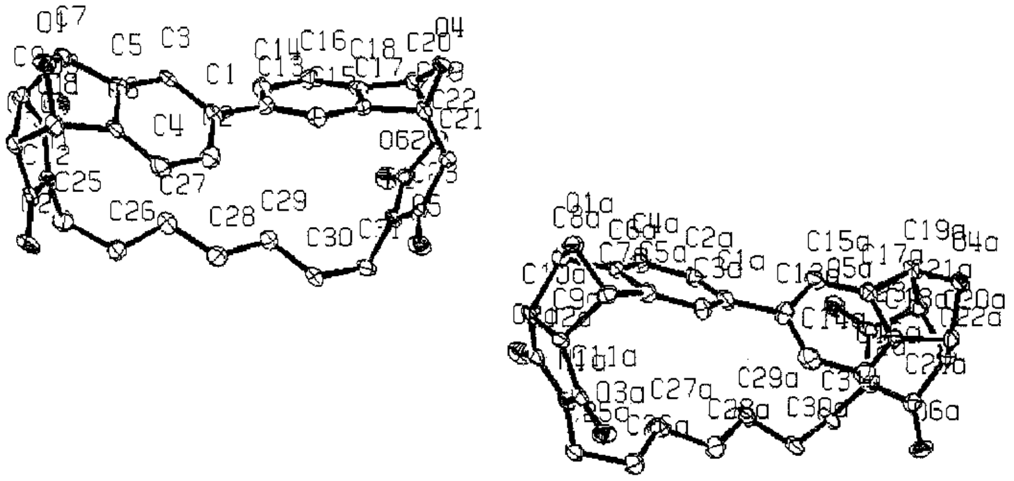

Figure 3-19: ORTEP diagram of "enantiomeric" 7C cyclophane at the 50% Probability Level. Hydrogen atoms omitted for clarity.

3.10: eight-carbon cyclophane

The cyclophane containing eight carbon atoms in its tether (Figure 3-20) did not crystallize, and a mass spectrum proved impossible to obtain by electron impact or electrospray ionization due to the extreme non-volatility characteristic of all of the cyclophanes synthesized. We therefore base most of our knowledge of this molecule on NMR data, particularly proton, COSY and carbon-13 spectra. It was determined that a mix of *syn-* and *anti-* isomers was present, evidenced by the doubling of peaks in the carbon-13 NMR spectrum. Peak matching and integration of the aromatic region of the proton spectrum (Figure 3-21) and comparison with the same region of the five-carbon cyclophane (Figure 3-22) revealed that the two isomers were present in roughly equal quantities. Neither isomer could be separated from the other by chromatography or recrystallization.

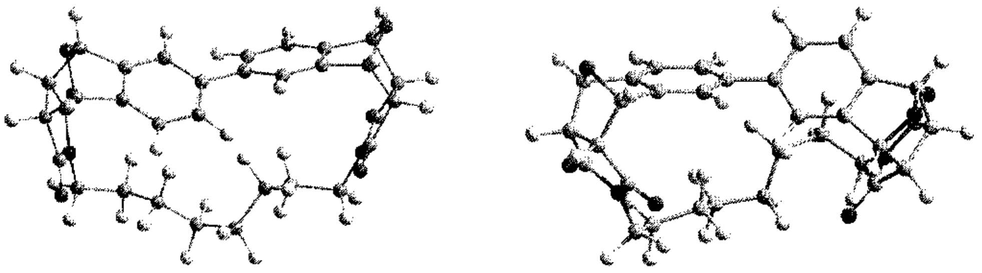

Figure 3-20: Hyperchem 7.5™ AM1 Models of 8C cyclophane. *Anti-* on left, *Syn-* on Right. X-ray Crystal Structures were not Obtained.

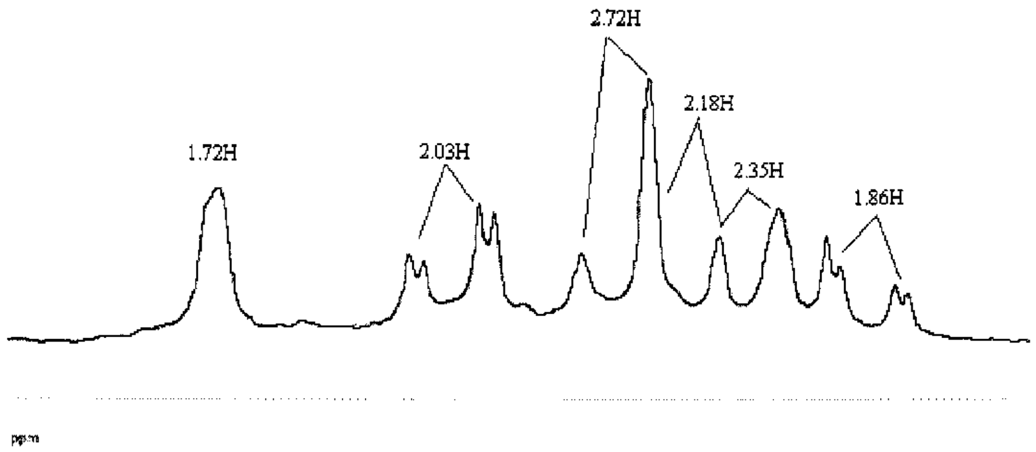

Figure 3-21: Aromatic Proton NMR Integration of 8C cyclophane, mix of *syn/anti* Isomers

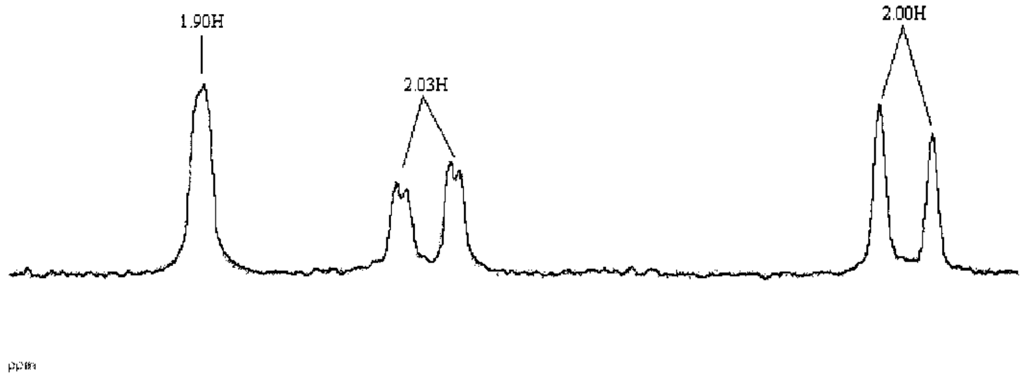

Figure 3-22: Aromotic Proton NMR Integration of 5C cyclophane, *anti* Isomer

3.11: nine-carbon cyclophane

Crystallizing as a single syn- isomer (Figure 3-23), the 9-carbon cyclophane exhibited a large amount of disorder in its tether. While attempting to model this molecule in hyperchem, different tether conformations of near-identical calculated energy were observed, depending on how the molecule was initially drawn. In the crystalline state it appears that two of these conformations have co-crystallized.

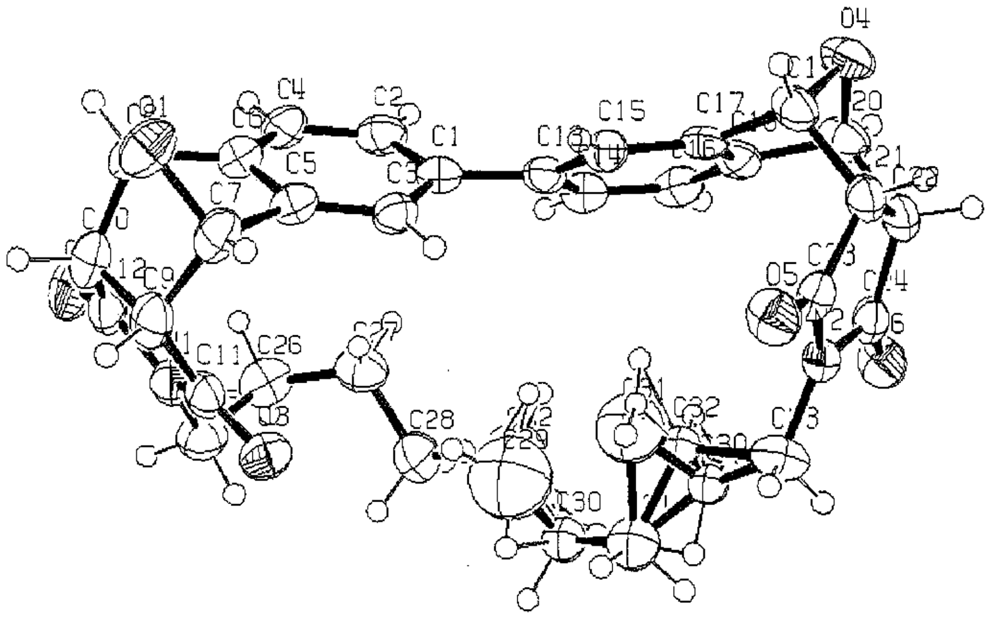

Figure 3-23: ORTEP diagram of 9C cyclophane at the 50% level, Disorder Model Shown.

Disorder in the tether was largely confined to four carbon atoms in a *gauche-*configuration, namely Cβ', Cγ', Cδ' and Cε. A disorder model was developed[75] in which one conformation was refined to 65% occupancy, the other with 35% occupancy. Inability of the least-squares refinement program to adequately describe the diffuse electron density of the 35% occupancy site may account for the relatively large thermal ellipsoid plot. Other remarkable structural features include a biphenyl torsion angle of

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[75] Thanks to Professor René Boeré, who came up with the original model.

41.1°, all non-disordered tether angles between 111-112°, and a very slight twist to the oxabicyclic ring containing atoms C7 to C12.

3.12: para-*xylyl cyclophane*

By far the easiest to crystallize, the para-xylyl cyclophane also proved to be one of the most interesting. Solution state NMR experiments follow the trends seen with all of the above molecules, consistent with C2 symmetry. The NMR spectra of this cyclophane (Figure 3-24) show typical resonances from the backbone, but the tether region is, as one might expect, somewhat different from the aliphatic series. The methylene protons are consistently diastereotopic, showing up as two doublets slightly downfield of 4 ppm. The four aromatic protons however exhibit a singlet upfield of 6 ppm, rather than the expected coupling pattern consistent with C2 symmetry. The single proton resonance for the aromatic ring of the tether suggests that some form of rapid exchange takes place, even when subjected to temperatures as low as -60°C. Each proton therefore spends enough time in proximity to the biphenyl rings to experience a shielding effect, but the overall shielding is not as great as with the five-carbon cyclophane, in which the methylene units are rotationally constrained relative to longer tether lengths.

As with the seven-carbon cyclophane, two isomers co-crystallized in an asymmetric unit with nearly identical tether regions (Figure 3-26). One molecule exhibits crystallographic C2 symmetry, with the aromatic ring of the tether situated precisely above the biphenyl single bond. The other has no imposed symmetry, with its tether aromatic ring slightly askew. Solution state data suggests that these molecules are enantiomers, which in the crystalline state have been reduced to diastereomers due to crystal packing forces.

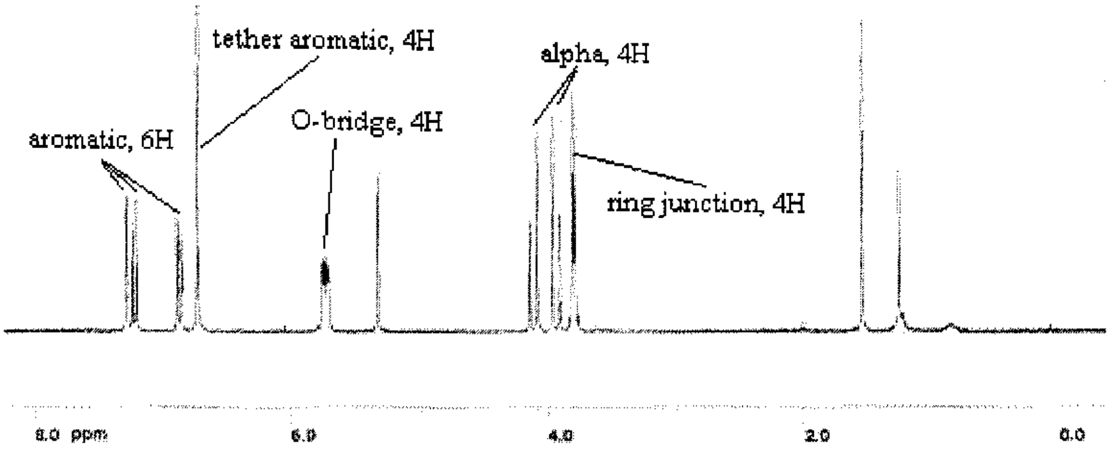

Figure 3-24: Proton NMR Spectrum of *para*-xylyl cyclophane

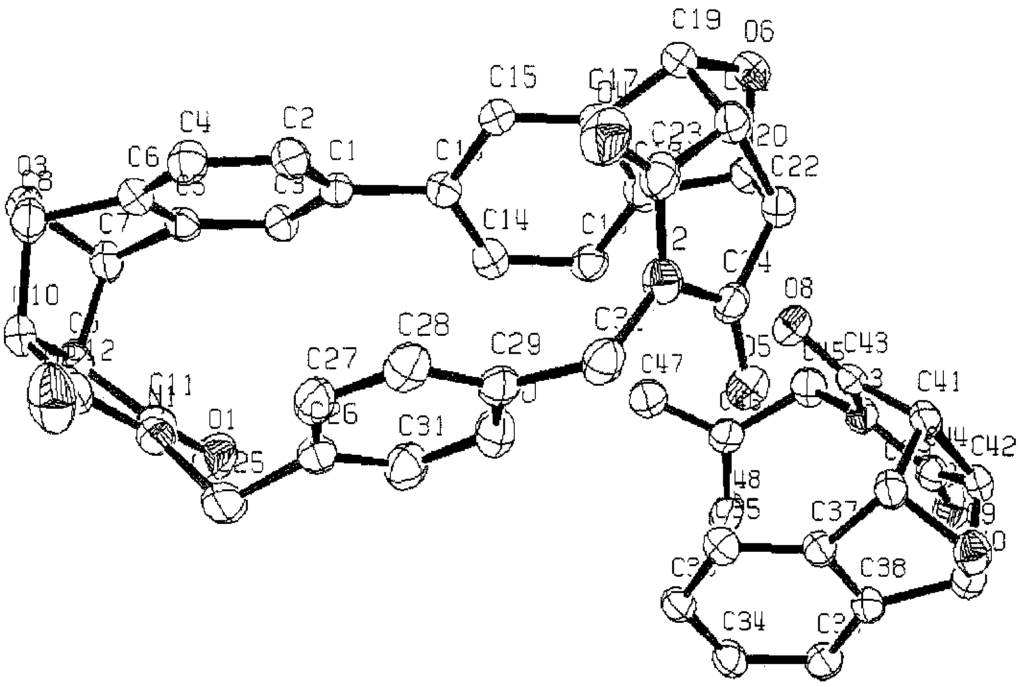

Figure 3-25: Labelled ORTEP of para-xylyl cyclophane. Assymetric unit shown. Hydrogen atoms omitted for clarity.

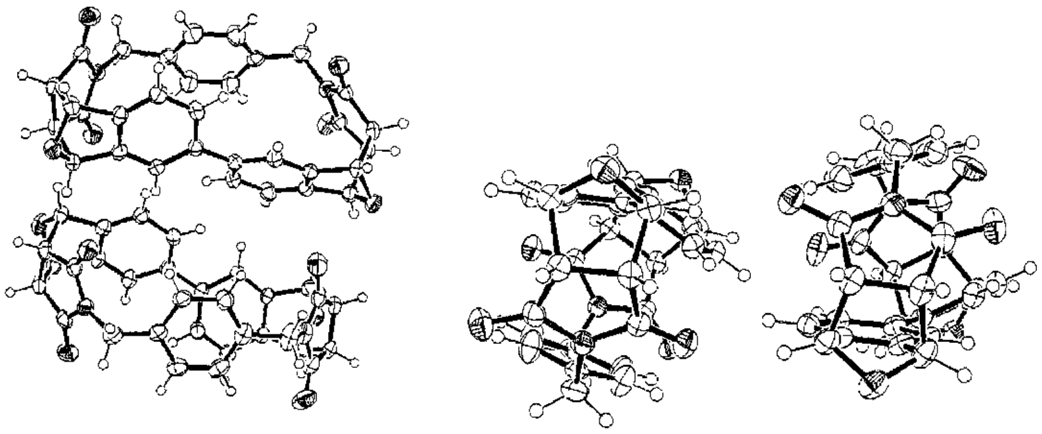
(front) (side)

Figure 3-26: ORTEP diagrams of *para*-xylyl cyclophane at the 50% Probability Level

The biphenyl-type torsion angle average of 32.5° between both enantiomers is very close to that of the seven-carbon cyclophane, the difference being 2°. The rest of the molecule follows standard bond lengths and angles[76], with only the N-Cα-Cβ bond angle being unusual – averaging 115.3° between both enantiomers.

3.13: Other Cyclophanes

While cyclophanes containing aliphatic tether regions were our initial interest, it is possible to incorporate tethers with a variety of functional groups by using the alternative method mentioned in section 3.5.1: SN2 Synthesis of Cyclophanes. In particular, alkenes, alkynes and oxygen atoms were introduced to the tether, suggesting future possibilities for the cyclophanes presented here.

3.14: 2-butene & 2-butyne cyclophanes

1,4-dichloro-cis-2-butene and 1,4-dichloro-trans-2-butene, as well as 1,4-dichloro-2-butyne all served as bis-alkylating agents when combined with the maleimide adduct **41** in DMF in the presence of potassium carbonate (Figure 3-27). Difficulty

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[76] CRC handbook, 55th ed. The Chemical Rubber Publishing co, 1974. pg. F-203.

purifying these compounds thwarted our efforts to crystallize them, and that combined with very small quantities of isolated cyclophane caused us to abandon their investigation for the time being. As a result, only NMR data is available on these compounds, with spectra consistent with the results from maleimide adduct **41**; a mix of *syn* and *anti* products, and shielding of β-protons (see experimental section for details).

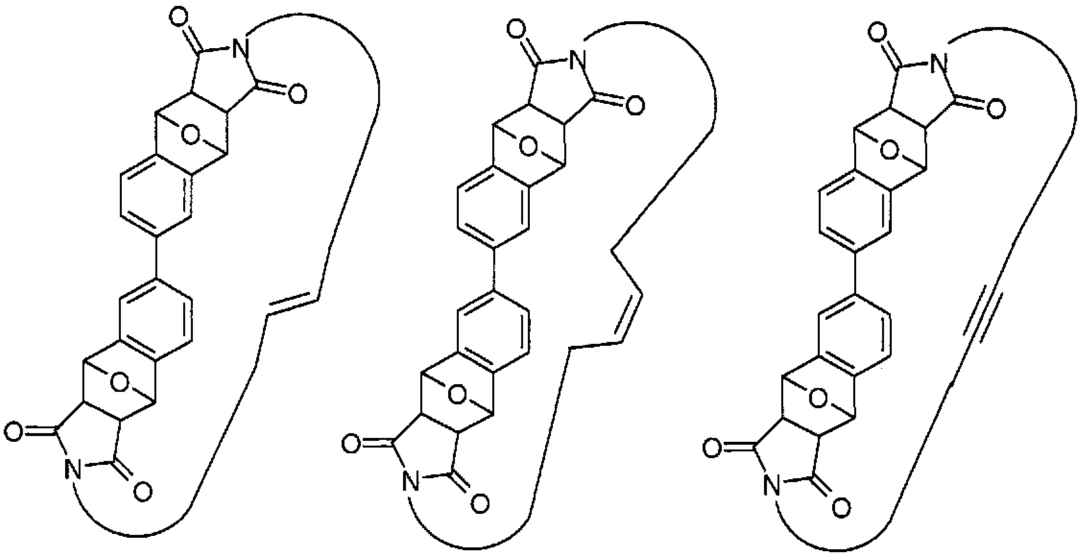

Figure 3-27: Trans-2-butene, cis-2-butene, and 2-butyne Cyclophanes

3.15: 3-oxapentane cyclophane

Taking inspiration from Butler's alicyclophane work[77], the final cyclophane presented in this thesis is structurally very similar to the five-carbon cyclophane, save for a single oxygen atom replacing the central methylene unit. Bis(2-chloroethyl) ether was the bis-alkylating agent in this case, and the resulting cyclophane was obtained in sufficient purity for NMR data to be acquired. The proton NMR spectrum (Figure 3-28) showed the typical resonances of the five-carbon cyclophane, save that the protons α- to the tether oxygen atom varied greatly in their chemical shift, by approximately 1.5 ppm. This suggests that one homotopic pair of protons is in relatively close proximity to the

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[77] Butler, D.N, Shang, M, Warrener, R.N. *Tet. Lett.* **2000**, *41*, 5985

aromatic pi- electron density, thereby being shielded. The other homotopic proton pair is pointing almost directly away from the pi- electrons, and experiences the full deshielding effect of its proximity to oxygen. The AM1 model (Figure 3-29) illustrates this point. Two β-protons are in very close proximity to the aromatic rings, while the other two β-protons are situated in a much more distant orientation.

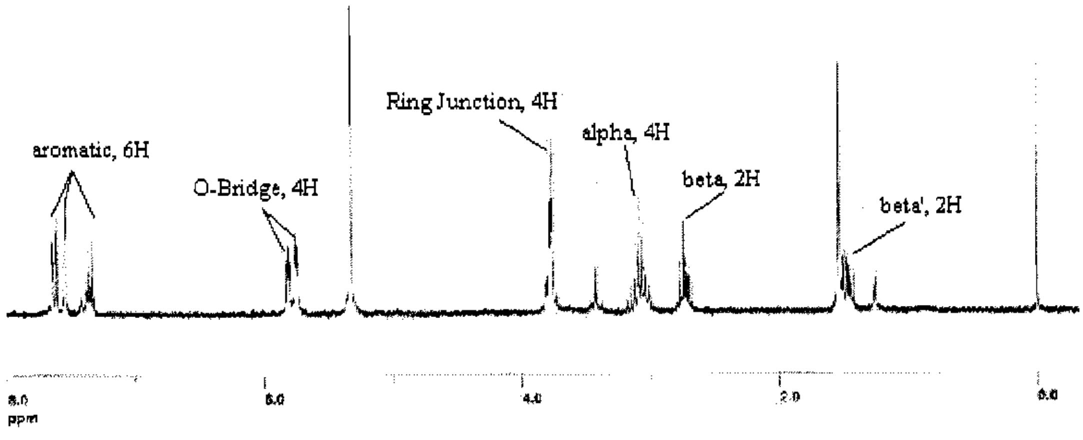

Figure 3-28: Proton NMR Spectrum of 3-oxapentane Cyclophane in CD_2Cl_2

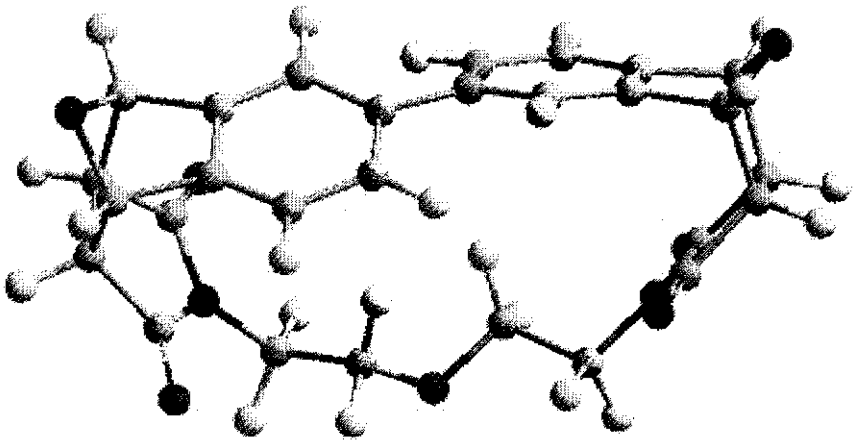

Figure 3-29: AM1 model of 3-oxapentane cyclophane. An X-ray crystal structure was not obtained.

3.16: Comparison of cyclophanes

By comparing proton NMR spectra of the various cyclophanes in both crude and recrystallized samples, it was possible to identify specific isomers, as the aromatic region of each product showed distinct coupling patterns. *Anti* adducts were seen exclusively with the five- and six-carbon chains. *Syn* cyclophanes began to form in small amounts at a tether length of seven carbon atoms, although the *anti* adduct crystallized preferentially from the mixture. The eight-carbon cyclophane contained approximately equal proportions of *syn* and *anti*, and the nine-carbon cyclophane was predominantly *syn* cyclophane. Both the eight- and nine-carbon cyclophanes appear to preferentially crystallize as the *syn* isomer judging from NMR data, although lack of X-ray data makes confirmation of isomerism difficult in the case of the eight-carbon cyclophane. Carbon-13 NMR experiments support the above hypothesis. In cases where only one isomer was present, a number of carbon signals corresponding to only one molecule was observed. The number of carbon signals exactly doubled when both isomers were present.

3.16.1: X-Ray Diffraction Analysis

Detailed examination of X-ray diffraction data revealed several interesting structural features of cyclophanes from 5,5'-bis(isobenzofuran). First, tether region bond angles were generally wider than 109.5° expected for saturated carbon atoms[78]. The only exception to this rule occurs with the five-carbon cyclophane, in which the relatively large amount of steric interaction between aromatic π-electrons and β-protons serves to "squeeze" the tether angles to as low as 108.5°. Second, the oxabicyclic ring structure of each cyclophane is deformed to a greater or lesser extent, depending on tether length (the seven-carbon cyclophane is least twisted).

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[78] CRC handbook, 55th ed. The Chemical Rubber Publishing co, 1974, pg. F-203.

Table 3-2: Tether Angles from X-ray Diffraction. Averages were taken for molecules with more than one molecule in the unit cell.

5-carbon cyclophane	
N1-Cα-Cβ	109.14(13)
Cα-Cβ-Cγ	115.65(14)
Cβ-Cγ-Cβ'	108.45(13)
Cγ-Cβ'-Cα'	115.11(14)
Cβ'-Cα'-N2	108.97(13)

6-carbon cyclophane	
N1-Cα-Cb	110.35(11)
Cα-Cβ-Cγ	113.51(12)
Cβ-Cγ-Cγ'	112.63(12)
Cγ-Cγ'-Cβ'	111.34(12)
Cγ'-Cβ'-Cα'	115.33(12)
Cβ'-Cα'-N2	115.43(11)

7-carbon cyclophane	
N1-Cα-Cβ	113.4(5)
Cα-Cβ-Cγ	114.7(6)
Cβ-Cγ-Cδ	109.4(6)
Cγ-Cδ-Cγ'	117.2(6)
Cδ-Cγ'-Cβ'	110.1(6)
Cγ'-Cβ'-Cα'	116.7(6)
Cβ'-Cα'-N2	114.4(5)

9-carbon cyclophane	
N1-Cα-Cβ	111.6(4)
Cα-Cβ-Cγ	112.8(4)
Cβ-Cγ-Cδ	112.6(4)
Cγ-Cδ-Cε	107.2(7)
Cδ-Cε-Cδ'	111.5(10)
Cε-Cδ'-Cγ'	110.6(8)
Cδ'-Cγ'-Cβ'	113.8(7)
Cγ'-Cβ'-Cα'	111.2(10)
Cβ'-Cα'-N2	105.7(6)

As the tether data illustrates (Table 3-2), angles vary by as much as 7° within the same molecule, with an overall maximum angle of 117.2° for the central methylene group of the seven-carbon cyclophane. An overall minimum angle of 105.7° in the nine-carbon cyclophane was observed, but disorder in the tether of that molecule makes this measurement highly suspect. Predictably, the degree and pattern of variation in tether angles is directly related to the amount of steric interaction between π-electrons and tether protons, with longer tethers oriented such that steric interactions are lessened.

The next parameters observed were the oxabicyclic ring angles (Table 3-3). Unlike the tether angles, these do not vary to any great degree with tether length or type – all are within a few degrees of angles calculated using AM1 models. Unlike the modeled systems however, one trend does stand out – each set of oxabicyclic ring angles varies within the molecule by 1-3°, imparting a "twist" to the rigid, non-aromatic region of the molecule (table 3-2).

Table 3-3: Oxabicyclic Ring Angles from X-ray Diffraction

Angle	5C	6C	7C ent.1	7C ent.2	9C	Xylyl ent.1	Xylyl ent.2
C5-C7-C9	108.26(14)	108.58(11)	107.3(5)	110.4(5)	108.3(4)	107.1(3)	106.8(3)
C6-C8-C10	107.76(14)	107.56(11)	109.6(5)	108.0(5)	110.0(4)	107.1(3)	106.7(3)
C17-C19-C21	110.53(13)	108.88(11)	110.0(5)	107.3(5)	110.3(4)	107.7(3)	106.8(3)
C18-C20-C22	107.07(13)	109.78(10)	108.5(5)	108.6(5)	111.5(4)	106.7(3)	106.7(3)
C7-O1-C8	96.93(12)	96.98(9)	97.6(5)	97.3(4)	97.2(3)	97.2(3)	97.1(3)

Adjoined to the oxabicyclic ring are the maleimide ring-junction angles (Table 3-4). Again, no large deviations from calculated values are observed, although a small increase in angle occurs with tether length. Deviations in the order of 1-4° within the same compound continue the theme of a slightly deformed molecule, the most apparent case of this theme being exhibited by the six-carbon cyclophane. As the six-carbon cyclophane also exhibits the least amount of symmetry in its tether region, the large difference in junction angle is understandable; the "twist" in said molecule is associated directly with a *gauche-* interaction on only one side of the tether.

Table 3-4: Maleimide Ring Junction Angles from X-Ray Diffraction

Angle	5C	6C	7C ent.1	7C ent.2	9C	Xylyl ent.1	Xylyl ent.2
C7-C9-C11	115.22(14)	115.38(10)	114.6(5)	116.9(5)	117.4(4)	114.3(3)	115.8(3)
C8-C10-C12	115.20(15)	114.14(11)	115.8(5)	117.9(5)	115.8(4)	115.9(3)	115.5(3)
C19-C21-C23	116.56(13)	116.46(11)	118.1(5)	115.4(5)	115.4(3)	114.9(3)	115.8(3)
C20-C22-C24	114.05(14)	118.76(11)	117.2(5)	116.3(5)	115.1(4)	116.1(3)	115.5(3)
C9-C10-C12	104.78(14)	104.94(11)	104.7(5)	104.9(5)	105.4(4)	104.4(3)	105.0(3)
C10-C9-C11	105.17(14)	105.02(11)	105.3(5)	105.9(5)	104.3(4)	105.5(3)	104.6(3)

Because all of the cyclophanes presented here are essentially substituted biphenyls, measurement and comparison of the torsion angle of the biphenyl single bond can provide some interesting data. In particular, comparison with AM1 models (Table 3-4) of different cyclophanes shows a drawback to using this particular modeling method – AM1 models are not particularly accurate in their prediction of biphenyl-like bond torsions in molecules of this type, particularly with very short or very long tether lengths.

Table 3-5: Interatomic N-N Distance and Biphenyl Bond Torsion of Cyclophanes

Tether	N-N distance (ang.)		Biphenyl Bond Torsion (deg.)	
	AM1	X-ray	AM1	Xray
5	7.38	7.31	23.3	3.49
6	7.94	7.96	32.8	26.5
7	8.34	8.74	31.2	35.6
8	9.1	N/A	35	N/A
9	8.8	9.09	31.3	40.8
xylyl	7.36	7.44	13.9	32.8

note: 8- and 9-carbon cyclophanes were both calculated as syn-isomers.

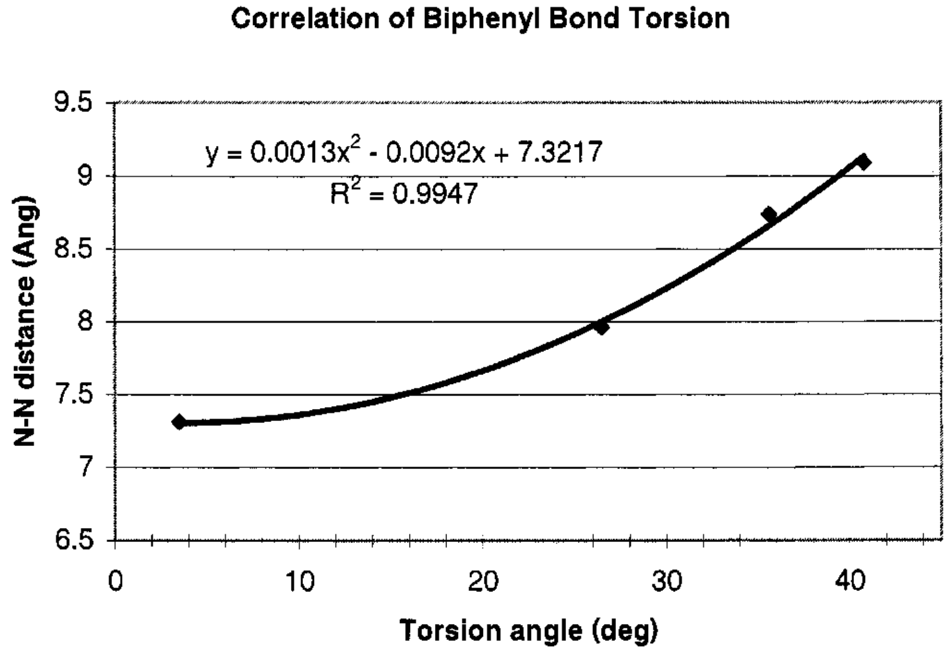

Figure 3-30: Tether Length and Interatomic N-N Distance from X-ray Diffraction Data

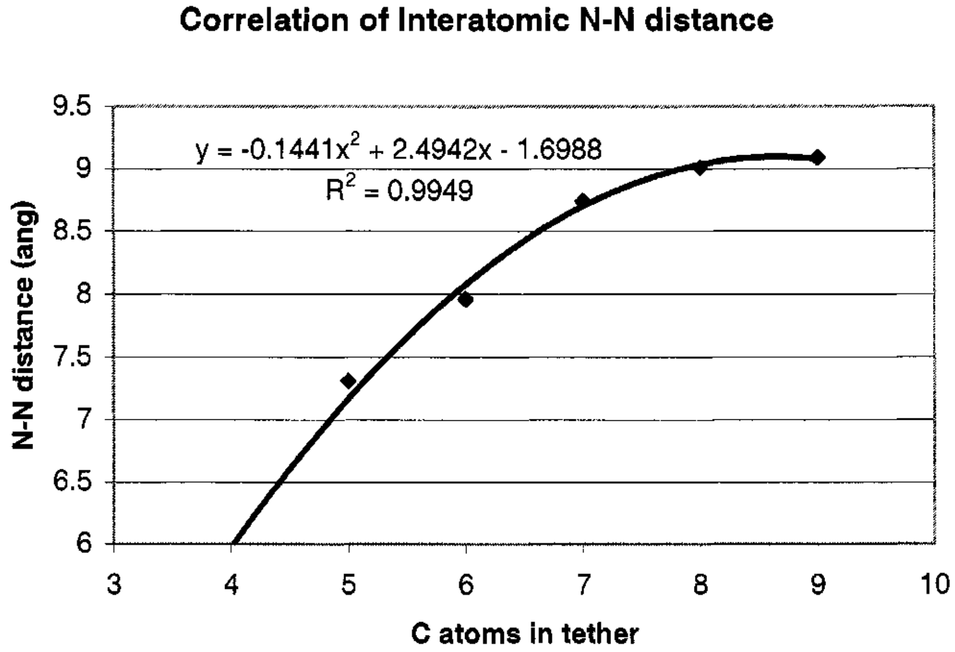

Figure 3-31: Tether Length and Interatomic N-N Distance from X-ray Diffraction Data

Correlation of interatomic N-N distance and bond torsion using AM1 models is of little value due to the inaccuracy involved, but examination of the same variables in the X-ray structures (Figure 3-30) reveals a polynomial relationship between these two variables. As the interatomic distance between nitrogen atoms increases (also a function of tether length, Figure 3-31), bond torsion increases to approximately 41°. At this point, rather than widen the N-N distance still further (by twisting or deforming bonds in the molecule), the tether adopts a less-than-optimal conformation, accepting a certain amount of steric interference between tether atoms rather than an increase in ring-strain. It is an unfortunate fact that longer tether lengths are so difficult to synthesize and purify; extension of the data to confirm this trend would be quite interesting, to see whether or not the trend towards *syn*-selectivity continues, or stabilizes at approximately 50%.

3.16.2: Ultraviolet Spectroscopy of Cyclophanes

It has long been established that the wavelength of absorption of the biphenyl chromophore in the near-ultraviolet region is directly related to the co-planarity of biphenyl's two aromatic rings[79,80]. As mentioned earlier, we shall consider the solution-state bond torsion of biphenyl to be 37.5°, which is significantly non-coplanar. Because of differences in chromophore absorption, maleimide adduct **41** was used as a reference rather than biphenyl. Adduct **41** absorbs at λmax 260nm, while the five-, seven-, and nine-carbon cyclophanes absorb at λmaxes of 272, 265, and 257nm, respectively. The fact that each additional tether carbon atom decreases the wavelength of absorption by almost exactly 3.5nm suggests very strongly that the amount of co-planarity between the aromatic rings decreases with increasing tether size.

The tendency towards aromatic ring co-planarity with decreasing tether length is reflected in the amount of resonance interaction between the two aromatic rings. With the five-carbon atom tether, both rings are very nearly co-planar, and so conjugation between aromatic π-bonds is at a maximum. As the tether length increases, conjugation decreases accordingly. Increasing conjugation may also be a factor in explaining the facility of cyclophane synthesis with shorter tether lengths.

3.16.3: NMR Analysis of Cyclophanes

Proton NMR spectrum analysis proved relatively consistent with X-ray diffraction data, although such a comparison is impossible in all but the most qualitative of examinations. Peaks arising from the backbones of the various cyclophanes exhibited

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[79] O'Shaughnessy, M.T, Rodebush, W.H. *J. Am. Chem. Soc.* **1940**, *62*, 2906

[80] Williams, B, Rodebush, W.H. *J. Am. Chem. Soc.* **1941**, *63*, 3018

little deviation from one cyclophane to another. The tether protons, however, exhibited highly shielded NMR signals as far upfield as -0.39ppm.

Table 3-6: NMR peak data for Cyclophanes

tether	*aromatic protons*			*oxabicyclic protons*				*tether protons*				
length	s	dd	d	O-bridge	ring	N-CH2		β	β'	γ	γ'	δ
5C	7.82	7.69	7.38	5.77	3.79	2.94	2.80	0.12	-0.39	0.70	N/A	N/A
6C	7.56	7.49	7.39	5.78	3.76	2.98	2.79	0.38	-0.08	1.01	0.88	N/A
7C	7.63	7.51	7.40	5.77	3.81	2.99		0.44	0.25	0.71	N/A	1.02
8C	7.53	7.40	7.29	5.73	3.81	3.02		0.39	N/A	0.89	N/A	0.67
9C	7.41	7.36	7.31	5.71	3.81	3.02		0.60	overlapping peaks ca. 1.0ppm			
p-xylyl	7.28	6.87	7.18	5.73	3.80	4.11	3.93	aromatic tether 6.72ppm				
5C-oxy	7.55	7.63	7.35	5.77	3.78	3.08		2.72	1.48	N/A	N/A	N/A

Shielding effects on protons in close proximity to aromatic π-electrons have been studied[81,82], and Schneider and co-workers have developed an empirical model for quantification of this effect[83]. As expected, tether protons in solution experience a shielding effect depending on the average distance of the proton to the center of the aromatic ring. In particular, β-protons in the shorter tether lengths (five- and six-methylene units) exhibit the largest shielding effects, and individual pairs of diastereotopic protons are resolvable. Longer tether lengths undergo conformational changes with sufficient rapidity at room temperature that the shielding effect is averaged on the NMR time scale. This averaging causes a "blurring" together of individual proton NMR signals, resulting in an irresolvable series of overlapping peaks.

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[81] Keehn, P.M, Rosenfeld, S.M, *Cyclophanes I*. Academic Press, 1983

[82] Vögtle, F. *Cyclophane Chemistry*. Translation from german by P.R. Jones, John Wiley & Sons, 1993

[83] Schneider, H.J, Rüdiger, V, Cuber, U. *J. Org. Chem.* **1995**, *60*, 996

3.17: 5,5'-Bis(isobenzofuranyl)acetylene

A second novel bis(isobenzofuran) has also been successfully synthesized and reacted with N-methylmaleimide. Bromoacetal **43** was previously synthesized in quantity by a former student. Sonogashira[84]-type coupling failed, due to the lack of reactivity of the aryl bromide towards this type of reaction. The molecule was instead subjected to Stille coupling[85] conditions, with bis(benzonitrile)palladium(II)chloride as the catalytic species, yielding approximately 15mg of purified bis(acetal) **44** (Figure 3-31). The proton NMR spectra of both of these compounds were identical; carbon-13 NMR confirmed the presence of a triple bond. Because of the small yield obtained, optimization of this reaction, or development of a new technique, would be a requirement if further study of this molecule is desired.

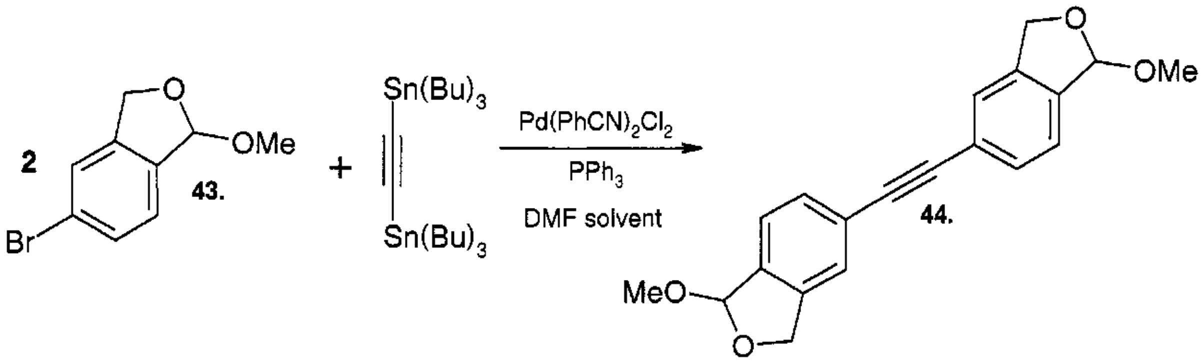

Figure 3-32: Stille coupling of 5-bromoisobenzofuran acetal

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[84] Sonogashira, K, Tohda, Y, Hagihara, N. *Tetrahedron Lett.* **1975**, *50*, 4467.
[85] Cummins, C.H. *Tetrahedron Lett.* **1994**, *6*, 857.

Because only a very small quantity of **44** was obtained, it was only possible to obtain a spectrum of the bis(isobenzofuran) and one adduct. The difuran was generated from the acetal using the base-induced procedure, and the proton NMR spectrum obtained. Finally, the difuran was trapped with N-methylmaleimide under the acid-catalyzed route to yield adduct **45** (Figure 3-33). Again, the presence of the triple bond was confirmed with carbon-13 NMR. The isolation of the N-methylmaleimide adduct confirmed that this series of reactions does in fact work in the synthesis of 5,5'-bis(isobenzofuranyl)acetylene.

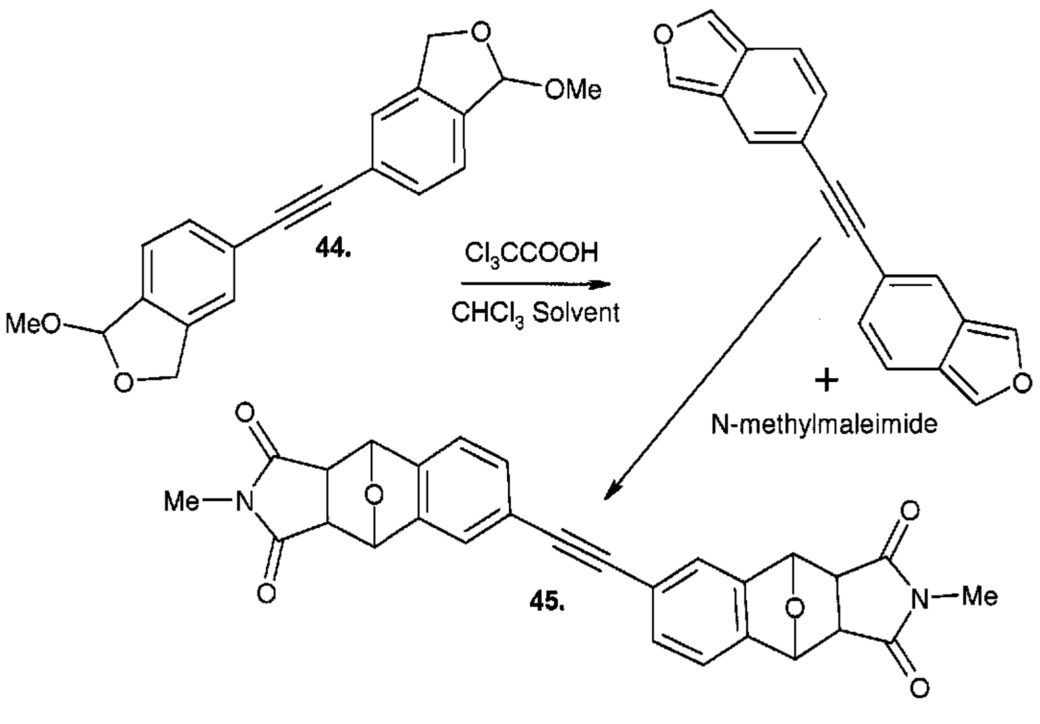

Figure 3-33: Trapping of 5,5'bis(isobenzofuranyl)acetylene with N-methylmaleimide

Chapter 4: Future Directions

Potential for future study of the 5,5'-bis(isobenzofuran) system remains high. In addition to the generation of cyclophanes from bis(IBF), a number of possible products may be obtained from the maleimide-difuran system. These products include alcohols (as in the case of N-hydroxymethylmaleimide), acid anhydrides (maleic anhydride), and other functional groups compatible with the maleimide moiety. In addition to intrinsically reactive functional groups, cyclophanes based on the butene- and butyne- tethers would allow for introduction of multiple functional groups *via* addition to the double or triple bond.

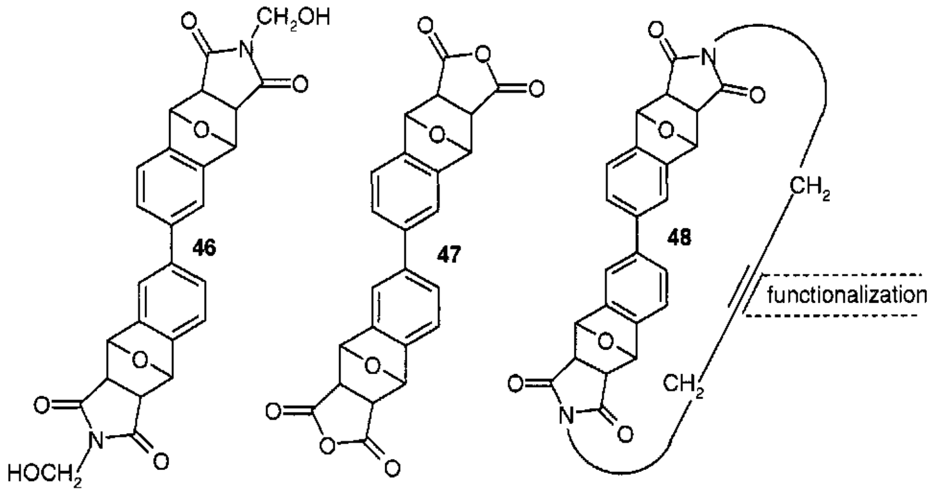

Figure 4-1: Adducts for Potential Complexation Chemistry

Successful synthesis of any or all of these compounds (Figure 4-1) would prove interesting in that they are all potential ligands for host-guest chemistry. Dialcohol **46** in particular could potentially be reacted or complexed with several metals, including the obvious group I alkali metals to form salts. Hydrolysis of dianhydride **47** to form a tetra-carboxylic acid would provide a similar substrate. Finally, the potential of 2-butyne cyclophane **48** as a potential host compound is limited only by the chemistry of the carbon-carbon triple bond.

Another area of potential interest lies in finding alternate syntheses of cyclophanes from 5,5'-bi(isobenzofuran) (Figure 4-2). The poor-to-modest yields obtained so far represent a major stumbling block in the future investigation of molecules of this type. One potential route to bi(IBF) is through the 5-bromoisobenzofuran acetal. A variant of the Suzuki-Miyaura[84] or Ullmann[85] coupling techniques may provide a route to the coupled acetal. The high yields generally seen with isobenzofurans generated through this route would undoubtedly be of great benefit in the synthesis of cyclophanes.

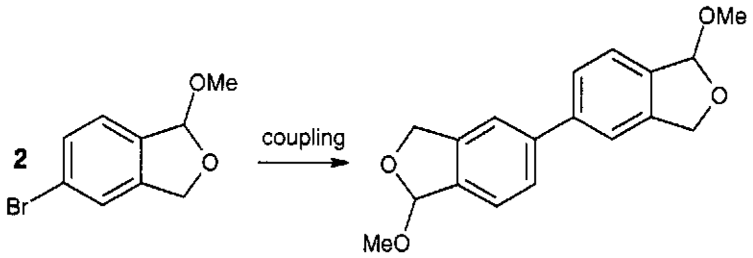

Figure 4-2: Alternate route to 5,5'-bis(isobenzofuran)

Of course, simply optimizing the present technique of dehydrohalogenation / Diels-Alder addition of furan may also prove fruitful. Changes in solvent, reaction time, or initial starting material, may all allow for "fine-tuning" of the reaction. More pertinently, changing the base from Caubere's complex base to some other strong base such as lithium diisopropylamide may avoid the large amounts of impurities generated using the current method.

Finally, control of the aromatic ring dihedral angle shows promise as future molecular switches (Figure 4-3). Because the co-planarity of the two aromatic rings in

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[84] Miyaura, N, Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457

[85] Fanta, P.E. *Synthesis*. **1974**, 9.

cyclophanes presented here has been shown to be dependent upon tether length, a tether which can be converted from one length to another and then back again would provide a method of controlling the amount of conjugation present in the biphenyl system. The first method of accomplishing this control that comes to mind is photocyclization. Under a given wavelength, the tether cyclizes, becoming shorter and bringing the aromatic rings into full conjugation. Another wavelength would allow the tether to de-cyclize, reducing the amount of conjugation and changing the UV/Visible absorption characteristics of the molecule.

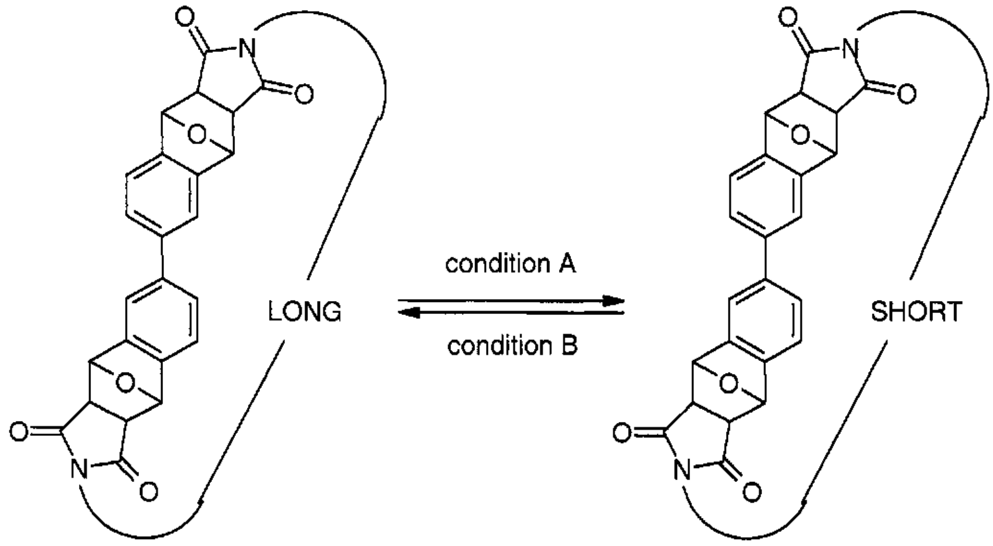

Figure 4-3: Molecular Switch based on Cyclophane from bis(IBF)

In addition to the bis(IBF) system, a similar difuran based on pyrene (Figure 4-4) would allow for future comparison of planarity and aromaticity. Because pyreno(1,2-c,6,7-c) difuran incorporates the bis(IBF) unit in its structure while removing the single-bond rotation possible with bis(IBF), a rigid cyclophane very similar in size to those synthesized from bis(IBF) would (at least on first glance) seem plausible. Research into this system is planned in the near future.

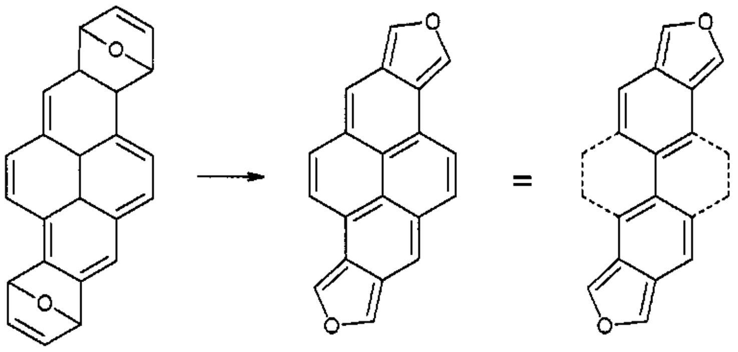

Figure 4-4: Pyreno(1,2-*c* 6,7-*c*)difuran as Bis(IBF Analogue)

Because of the fascinating structure of 5,5'-bis(isobenzofuranyl)acetylene, future investigation into improving yields and possible alternate syntheses remains a high priority. A possible solution to the extremely low yields currently achieved for the acetal precursor may be to form adducts with maleimide (or other suitable dienophile) prior to coupling with acetylene.

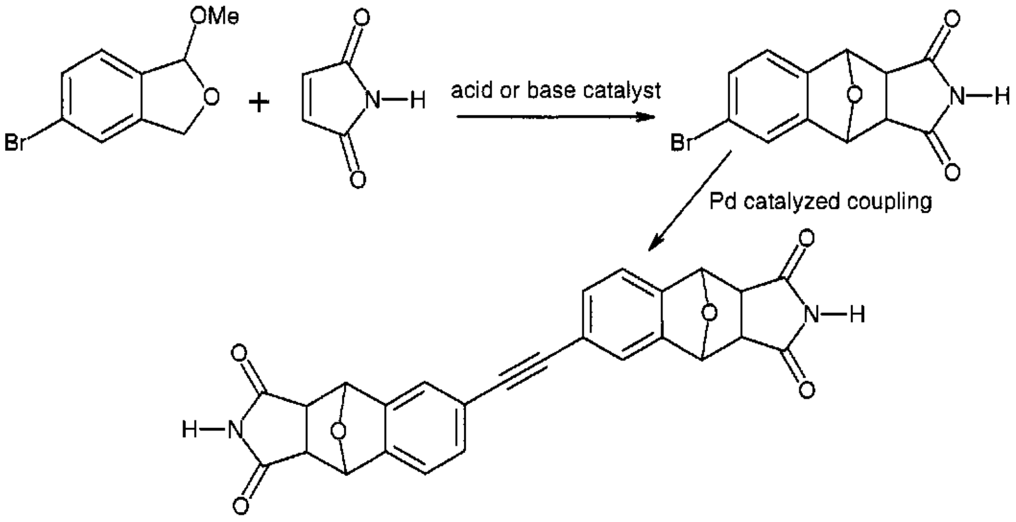

Figure 4-5: Alternative Coupling Process for 5-Bromoisobenzofuran Acetal

A second, perhaps more elegant alternative to palladium-catalyzed coupling reactions of Sonogashira and/or Stille type involves 4,4'-dibromostilbene as a precursor, a compound used by Thibault[86] in the synthesis of 5,5'-bis(isobenzofuranyl) ethene. Bromination of the stilbene, followed by treatment with a large excess of Caubere's base in the presence of furan should yield the diepoxide analogue of acetal **49** in two steps, allowing for generation of the difuran utilizing dipytet.

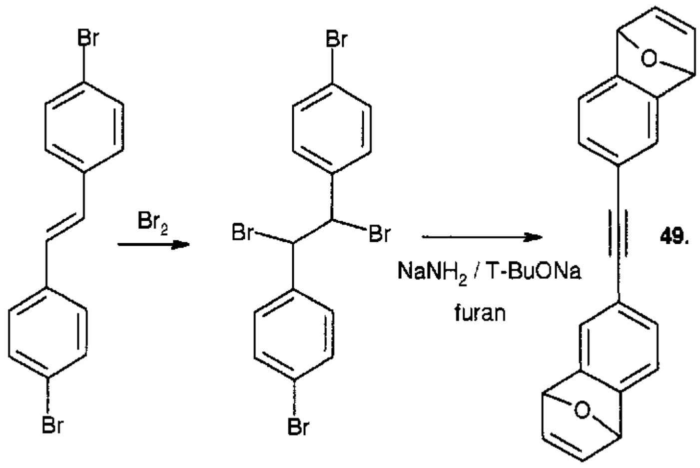

Figure 4-6: Diepoxide Precursor to 5,5'-bis(isobenzofuranyl) acetylene

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[86] Thibault, M.E. *Cyclophanes from bis(isobenzofuran)s.* Master's Thesis, 2004.

Chapter 5: Experimental Details

Unless otherwise noted, all compounds and reagents were used as received directly from the manufacturers. Solvents were distilled under nitrogen from an appropriate drying agent where indicated. Computer models were performed with Hyperchem™ 7.5 software[1] with the AM1 semi-empirical method. NMR spectra were obtained on Bruker AC250- and Varian INOVA 500MHz spectrometers, and IR spectra on a Nicolet Avatar FTIR spectrometer. Coupling constants (J values) are all in hertz. Ultraviolet spectra were collected on a Cary 1E spectrometer. Samples were sent to the University of Calgary for mass spectral and some X-ray analysis. Other X-ray diffraction experiments were performed at the University of Alberta. No elemental analyses were performed because of the limited quantities of products formed. *Note: Mass spectral data do not match calculated values in some cases. Machine calibration is the likely cause, as there were problems with the machine at the time of data acquisition.*

5.1: Synthesis of Precursors and Necessary Reagents

5.1.1: Synthesis of 3,6-di(2-pyridyl)-1,2,4,5-tetrazine "dipytet"

3,6-di(2-pyridyl)-1,2,4,5-tetrazine (dipytet) was synthesized according to a procedure developed by Geldard and Lions[2]. 20g of 2-cyanopyridine and 20mL of hydrazine monohydrate were warmed together on a steam bath for 3 hours, yielding 17.44g of a dark orange crystalline solid, 3,6-di(2-pyridyl)-1,2-dihydro-1,2,4,5-tetrazine. 7g of this solid was suspended in 1L of 60% acetic acid in water and cooled to 0°C. 18.4g of sodium nitrite dissolved in 50mL of water was slowly added to this solution, which turned a deep maroon colour and evolved brown NO_2 gas. The solution was neutralized

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[1] HyperChem 7.5 for Windows, 2002, Hypercube inc.

with concentrated ammonium hydroxide, and maroon crystals filtered off. These were used in subsequent reactions with no further purification.

3,6-di(2-pyridyl)-1,2,4,5-tetrazine: Yield 72%, m.p. 229-230°C.

^{1}H NMR (250MHz, CDCl$_3$): δ 9.00 (m, 2H); 8.78 (dt, 2H, J=8.0, 1.0); 8.03 (td, 2H, J=7.8, 1.7); 7.45 (ddd, 2H, J=7.5, 4.7, 1.0).

5.1.2: Synthesis of 5,5'-bi (isobenzofuran) precursor; 6,6'-bis(1,4-epoxy-1,4-dihydronaphthalene) (38):

3.27g (0.044mmol) of t-butanol (d=0.786) in 6mL of anhydrous THF was added slowly to a suspension of 4.66g (120mmol) of sodium amide in 6mL of anhydrous THF. The resulting suspension was allowed to stir at room temperature for 1.5 hours. 1.25g (4.01mmol) of 4,4'-dibromobiphenyl in 11.86mL furan (large excess) and enough THF to dissolve the dibromide was then added slowly to the NaNH$_2$ suspension and allowed to stir at room temperature. After a further 1.5 hours, the reaction mixture had turned a dark brown colour, at which point the entire reaction mixture was poured into a beaker of ice water and extracted with petroleum ether. The resulting yellow solution was dried with MgSO$_4$, filtered, and evaporated under reduced pressure to yield yellow foam. The crude product was used in subsequent reactions without further purification. A sample was recrystallized from toluene / hexanes for characterization purposes, yielding a pale yellow solid.

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[2] Geldard, J.F, Lions, F. *J. Org. Chem.* **1965**, *30*, 318

<u>*5,5'-bis(isobenzofuran) precursor (38):*</u> Yield 81%, m.p. 156-159° C.

^{1}H NMR (250MHz, CD_2Cl_2): δ 7.45, (d, 2H, J=0.9); 7.29, (d, 2H, J=7.4); 7.15 (dd, 2H, J=7.4, 1.5); 7.05 (s, 4H); 5.72 (s, 4H).

^{13}C NMR (250MHz, CD_2Cl_2): δ 151.1, 149.2, 143.71, 143.70, 139.3, 124.6, 121.0, 120.3, 83.2, 83.0.

FT-IR (KBr disc): 3007, 1447, 1278, 986, 867, 846, 823, 697 cm^{-1}.

5.1.3: General procedure for synthesis of bis-maleimide "tether" molecules[3,4]

4.00g (40.8 mmol, excess) of maleic anhydride dissolved in 16mL of glacial acetic acid in a 100mL round bottom flask. A solution of 18mmol of diamine in 6mL of glacial acetic acid was added to the dissolved anhydride and stirred under reflux for approximately 6 hours. The solvent was removed under vacuum, and the resulting tarry substance recrystallized from methanol to yield a white solid.

Yields varied from 30%-80%.

<u>*1,5-bis(maleimidyl)pentane:*</u> ^{1}H NMR (250MHz, $CDCl_3$) δ 6.69 (s, 4H); 3.50 (t, 4H, J=7.2); 1.61 (p, 4H, J=7.5); 1.27 (m, 2H). mp 103-104.5°C

<u>*1,6-bis(maleimidyl)hexane:*</u> ^{1}H NMR (250MHz, $CDCl_3$) δ 6.69 (s, 4H); 3.49, (t, 4H, J=7.2); 1.57 (m, 4H); 1.30 (m, 4H). mp 122-124°C

<u>*1,7-bis(malemidyl)heptane:*</u> ^{1}H NMR (250MHz, $CDCl_3$) δ 6.69 (s, 4H); 3.50 (t, 4H, J=7.3); 1.57 (m, 4H); 1.30 (m, 6H). mp 80-81°C

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[3] Metha, N.B, Phillips, A.P, Lui, L.F, Brooks, R.E. *J. Org. Chem.* **1960**, *25*, 1012
[4] Walker, M.A. *J. Org. Chem.* **1995**, *60*, 5352

1,8-bis(malemidyl)octane: ^{1}H NMR (250MHz, $CDCl_3$) δ 6.68 (s, 4H); 3.50 (t, 4H, J=7.2); 1.57 (m, 4H); 1.28 (m, 8H). mp 119-121°C

1,9-bis(maleimidyl)nonane: ^{1}H NMR (250MHz, $CDCl_3$) δ 6.69 (s, 4H); 3.50 (t, 4H, J=7.2); 1.56 (m, 4H); 1.27 (m, 10H). mp 80.5-88°C

para-*xylylenebismaleimide:* ^{1}H NMR (250MHz, $CDCl_3$) δ 7.28 (s, 4H); 6.70 (s, 4H); 4.64 (s, 4H). mp greater than 350°C

5.2: General procedures for bi-isobenzofuran reactions

5.2.1: Isolation of 5,5'-bi(isobenzofuran) (2):

1.00mmol (286mg) of diepoxide precursor and 2.00mmol (477mg) of 3,6-di(2-pyridyl)-1,2,4,5-tetrazine (dipytet) were dissolved in 50mL of chloroform and stirred under nitrogen for two hours. The solution was then filtered through a short pad of silica gel to purify the difuran. Solvent was removed *in vacuo* at ambient temperature, and a proton NMR spectrum was obtained directly from the residue. All proton signals arising from the difuran disappeared after standing at ambient temperature for two hours, giving poly-5,5'-bi(isobenzofuran).

5,5'-bi(isobenzofuran) (2):

^{1}H NMR (250MHz, $CDCl_3$) δ 8.07 (t, 2H, J=1.5); 8.03 (t, 2H, J=1.5); 7.60 (dd, 2H, J=2.3, 1.0); 7.49 (dt, 2H, J=9.0, 1.0); 7.20 (dd, 2H, J=9.3, 1.5)

5.2.2: Synthesis of Simple Adducts:

1.00mmol (286mg) of diepoxide precursor, 2.00mmol (476mg) of 3,6-di(2-pyridyl)-1,2,4,5-tetrazine (dipytet) and 2.00mmol of an appropriate dienophile were dissolved in 50mL of chloroform and stirred under nitrogen for two hours. The crude mixture was extracted with 1M hydrochloric acid, removing the basic dipytet and its reaction byproduct. Solvent was dried with anhydrous magnesium sulfate and evaporated *in vacuo*. If further purification proved necessary, the product was recrystallized from chloroform / hexanes or chloroform / toluene.

5.2.3: Synthesis of Cyclophanes:

1.00mmol (286mg) of diepoxide precursor and 2.00mmol (476mg) of dipytet were dissolved in 50ml of chloroform and stirred under nitrogen until evolution of gas was complete. A separate solution containing 1.00mmol of a suitable bis(dienophile) in 50mL of chloroform was also prepared. Both solutions were added simultaneously at a rate of 25mL/hour *via* double syringe pump to a 1L 3-neck flask containing 500ml of chloroform under reflux. Once addition was complete, the reaction was allowed to stir under reflux overnight. Solvent was removed under reduced pressure to yield a red solid. The crude mixture was filtered through a short column of silica gel with 1% acetic acid in chloroform. Solvent was removed from product-containing fractions *in vacuo*. The remaining residue was treated with three (more if necessary) 100ml portions of boiling hexanes to dissolve unwanted byproducts of the reaction, leaving behind the cyclophane as an off-white solid.

5.2.4: SN2 Synthesis of Cyclophanes

100mg (0.233mmol) of maleimide adduct was dissolved in approximately 5mL of dry DMF over excess potassium carbonate. To this mixture, an equimolar amount of terminal dibromide was added. The reaction was allowed to proceed to completion overnight. Solvent was removed by vacuum pump and the residue taken up into chloroform. This solution was then to remove any remaining potassium carbonate. The cyclophane was precipitated by adding a small quantity of hexanes, and filtered to yield an off-white solid.

5.2.5: Aromatization of Simple Adducts

Several simple adducts exhibited very complicated NMR spectra due to the presence of multiple isomers of each adduct. In order to simplify these complex mixtures, adducts were aromatized *via* dehydration with methanesulfonic acid. Once aromatization was complete the mixture was extracted with 10% sodium hydroxide solution, dried, evaporated and finally recrystallized from toluene to yield small quantities of substituted binaphthyls. Aromatization of several cyclophanes was also attempted, with the goal of creating a cyclophane with a highly strained aromatic region. All of these attempts failed, instead yielding black, unidentifiable tar.

5.3: Simple Adducts from 5,5'-bis(isobenzofuran)

Maleimide adduct (41): Yield 35 %, mp softened at 225°C, decomposed at 261°C

^{1}H NMR (250MHz, DMSO-d_6) δ 7.54 (s, 2H); 7.51 (m, 2H); 7.35 (d, 2H, J=1.0); 5.77 (m, 4H); 5.67 (s, 2H); 3.80 (m, 4H)

^{13}C NMR (250MHz, DMSO-d_6) δ 175.52, 142.81, 140.99, 139.04, 126.06, 121.07, 118.92, 80.68, 79.22, 49.35

FT-IR (KBr disc): 3213, 3073, 1713, 1349, 1284, 1185, 987, 822 cm^{-1}.

N-Methyl maleimide adduct (6): Yield 41%, m.p. 255-258°C

^{1}H NMR (250MHz, CD_2Cl_2) δ 7.39 (s, 2H); 7.36-7.28 (multiple peaks, 4H); 5.74 (m, 4H); 3.77 (dd, 4H, J=3.8, 2.0); 2.22 (s, 6H)

^{13}C NMR (250MHz, $CDCl_3$) δ174.42, 141.97, 141.12, 140.39, 127.47, 127.32, 121.52, 120.12, 80.69, 80.56, 48.79, 48.93, 24.03

Mass Spectrum M/z: MI 456.1313 (5.30%), 345.1002 (64.47%), 234.0680 (100%), 202.0783 (9.33%), 117.0342 (23.48%) Calculated mass: 448.4838

FT-IR (KBr disc): 3011, 1700, 1433, 1288, 986, 862 cm^{-1}.

(2,2'-Binaphthyl-6,6'-dicarboxylic acid dimethyl ester) (4):

Yield 9.3%, m.p. 268-270°C

^{1}H NMR (250MHz, $CDCl_3$) δ 8.67 (s, 2H); 8.22 (s, 2H); 8.13 (dd, 2H, J=8.5,1.7); 8.10 (d, 2H, J=8.0); 7.99 (d, 2H, J=10.5), 7.95 (dd, 2H, J=8.5, 1.8); 4.01 (m, 6H)

^{13}C NMR (250MHz, $CDCl_3$) δ 167.43, 140.69, 136.22, 132.34, 131.14, 130.43, 128.82, 128.24, 126.71, 126.54, 126.30, 52.48

Mass Spectrum M/z: MI 370.1202 (100%), 339.1019 (41.67%), 311.1068 (21.52%), 252.0935 (31.53%), 126.0467 (9.54%) Calculated Mass: 370.4045

FT-IR (KBr disc): 2956, 1719, 1434, 1303, 1241, 1095, 808 cm^{-1}.

(2,2'-Binaphthyl-6,6',7,7'-tetracarboxylic acid, tetramethyl ester) (5):

m.p. 214-219°C, yield 32.4%

^{1}H NMR (250MHz, $CDCl_3$) δ 8.35 (s, 2H); 8.33 (s, 2H); 8.23 (s, 2H); 8.08 (d, 2H, J=8.7); 7.99 (dd, 2H, J=8.9, 1.7); 3.99 (s, 12H)

^{13}C NMR (250MHz, $CDCl_3$) δ 168.26, 168.14, 140.51, 134.07, 133.10, 130.61, 130.22, 129.78, 129.73, 129.19, 128.34, 127.24, 52.88, 52.87

Mass Spectrum M/z: MI 486.1314 (100%), 455.1129 (86.56%), 409.0709 (16.51%), 338.0937 (15.61%), 252.0932 (8.87%), 212.0472 (23.31%). Calculated Mass: 486.4779

FT-IR (KBr disc): 2951, 1722, 1463, 1434, 1269, 1124, 1051 cm^{-1}.

5.4: Cyclophanes from 5,5'-bis(isobenzofuran)

In all cases, cyclophanes derived from 5,5'-bis(isobenzofuran) were synthesized according to the general procedure listed above (section 5.2.3), except where mentioned. Two possible isomers of each product are theoretically possible, but only in the 8- and 9-carbon tether lengths was a significant amount of *syn-* adduct observed.

Five-carbon cyclophane (7, n=5): Yield 19.6%, m.p. >350° C

^1H NMR (500MHz, CD_2Cl_2) δ 7.82 (s, 2H); 7.69 (dd, 2H, J=7.5, 1.5); 7.38 (d, 2H, J=8.0); 5.79 (d, 2H, J=5.5); 5.75 (d, 2H, J=5.5); 3.79 (m, 4H); 2.94 (td, 2H, J=13.0, 4.5); 2.80 (td, 2H, J=13.0, 4.5); 0.70 (m, 2H); 0.11 (m, 2H); -0.39 (m, 2H)

^{13}C NMR (500MHz, CD_2Cl_2) δ 174.28, 173.92, 142.76, 141.79, 138.45, 126.50, 121.96, 117.55, 80.92, 80.40, 48.88, 48.44, 37.78, 29.91, 29.08

Mass Spectrum M/z: MI 496.1631 (52.28%), 234.0680 (100%), 202.0780 (6.58%), 117.0339 (12.4%). Calculated Mass: 488.5486

FT-IR (KBr disc): 2940, 2857, 1772, 1700, 1397, 1343, 1175, 860, 821 cm^{-1}.

UV-Vis (CH_2Cl_2): 272, 285 nm

Oxapentane cyclophane (fig. 3-29): Yield not measured, m.p. >350° C

^1H NMR (250MHz, CD_2Cl_2) δ 7.62 (dd, 2H, J=7.8, 1.7); 7.54 (s, 2H); 7.35 (d, 2H, J=7.8); 5.81 (m, 2H); 5.74 (m, 2H); 3.77 (m, 4H); 3.08 (m, 4H); 2.72 (m, 2H); 1.46 (m, 2H)

This Molecule was synthesized by the SN2 route (section 5.2.4).

<u>*Six-carbon cyclophane (7, n=6):*</u> Yield 17.1%, m.p. >350° C

^{1}H NMR (250MHz, CD_2Cl_2) δ 7.52 (s, 2H); 7.34 (d, 4H, J=1.0); 5.74 (m, 4H); 3.74 (m, 4H); 2.94 (m, 2H); 2.76 (m, 2H); 0.97 (m, 2H); 0.83 (m, 2H); 0.33 (m, 2H); -0.05 (m, 2H)

^{13}C NMR (500MHz, CD_2Cl_2) δ 174.14, 174.02, 142.41, 140.83, 140.71, 127.88, 121.69, 119.34, 80.52, 80.24, 49.00, 48.52, 38.89, 26.61, 26.15

Mass Spectrum M/z: MI 510.1787 (24.84%), 234.0682 (100%), 202.0783 (5.12%), 117.0339 (8.38%). Calculated Mass: 502.5754

FT-IR (KBr disc): 2940, 2851, 1773, 1693, 1398, 1350, 1243, 1148, 980, 861, 819 cm^{-1}.

<u>*Seven-carbon cyclophane (7, n=7):*</u> Yield 16.5%, m.p. >350° C

^{1}H NMR (250MHz, CD_2Cl_2) δ 7.52 (s, 2H); 7.46 (dd, 2H, J=7.8, 1.6); 7.35 (d, 2H, J=7.8); 5.73 (m, 4H); 3.78 (dd, 4H, J=3.8, 2.0); 2.97 (m, 4H); 1.12 (m, 1H); 0.74 (m, 1H); 0.69 (m, 4H); 0.56 (m, 2H); 0.22 (m, 2H)

^{13}C NMR (500MHz, CD_2Cl_2) δ 174.34, 174.26, 142.77, 141.38, 139.88, 126.60, 121.62, 119.50, 80.46, 80.24, 48.66, 48.57, 37.24, 27.00, 25.10, 23.08

Mass Spectrum M/z: MI 524.1938 (33.26%), 234.0680 (100%), 202.0779 (4.73%), 117.0337 (8.11%). Calculated Mass: 516.6023

FT-IR (KBr disc): 2939, 2856, 1767, 1700, 1399, 1340, 1179, 860, 820 cm^{-1}.

UV-Vis (CH_2Cl_2): 265nm, distinct shoulder at approx. 275nm

Eight-carbon cyclophane, major product (presumed to be syn-) (7, n=8):

Yield 15.9%, m.p. >350° C

^{1}H NMR (250MHz, $CDCl_3$): δ 7.38 (d, 2H, J=7.5); 7.31 (s, 2H); 7.28 (dd, 2H, J=7.3, 1.5); 5.74 (d, 2H, J=5.0); 5.70 (d, 2H, J=5.0); 3.79 (m, 4H); 3.02 (m, 4H); 0.91 (m, 4H); 0.71 (m, 4H); 0.41 (m, 4H).

^{13}C NMR (500MHz, $CDCl_3$) δ 174.06, 170.91, 141.96, 141.61, 140.69, 127.17, 121.44, 121.23, 80.17, 79.94, 48.34, 48.01, 37.84, 28.93, 28.47, 26.59

FT-IR (KBr disc): 2930, 2850, 1767, 1700, 1404, 1346, 1152, 864, 822 cm^{-1}.

Nine-carbon cyclophane, syn-product (7, n=9):

Yield: 8.5%, m.p. >350° C

^{1}H NMR (250MHz, CD_2Cl_2) δ 7.37 (d, 2H, J=7.0); 7.32-7.27 (overlapping m, 4H); 5.72 (m, 4H); 3.81 (m, 4H); 3.02 (m, 4H); 1.15-0.50 (multiple peaks, 14H)

^{13}C NMR (250MHz, CD_2Cl_3) δ 174.35, 174.25, 142.62, 141.72, 141.03, 127.12, 121.77, 121.58, 80.55, 80.35, 48.72, 48.65, 39.10, 28.94, 27.38 26.43, 25.78

Mass Spectrum M/z: MI 552.2256 (57.70%), 234.0680 (100%), 202.0781 (4.36%), 117.0338 (5.89%). Calculated Mass: 544.6561

FT-IR (KBr disc): 2938, 2858, 1767, 1700, 1462, 1437, 1395, 1345, 1170, 974, 854, 829 cm^{-1}.

UV-Vis (CH_2Cl_2): 257nm, small hump at approx. 275nm

Para-xylyl cyclophane (42):

^{1}H NMR (250MHz, CD_2Cl_2) δ 7.28 (m, 2H); 7.20 (d, 2H, J=7.8); 6.86 (dd, 2H, J=7.8, 1.5); 6.72 (s, 4H); 5.74 (m, 4H); 4.10 (d, 2H, J=14.0); 3.93 (d, 2H, J=14.0); 3.80 (m, 4H)

No other data available, due to lack of material. Mass Spectra were inconclusive. ^{13}C NMR sample was not strong enough for a spectrum.

trans-*2-butene cyclophane, (figure 3-27, left):*

^{1}H NMR (500MHz, $CDCl_3$) δ 7.48 (s, 2H); 7.44 (dd, 2H, J=7.6, 1.6); 7.36 (d, 2H, J=8.0); 5.76 (m, 4H); 5.42 (m, 1H); 4.69 (m, 1H); 3.81 (m, 4H); 3.53 (m, 4H)

^{13}C NMR (500MHz, $CDCl_3$) δ 173.92, 173.74, 156.22, 142.19, 140.48, 140.13, 139.14, 132.43, 130.26, 128.79, 127.02, 126.41, 122.51, 121.77, 119.56, 110.00, 80.53, 80.34, 48.76, 48.72

FT-IR (KBr disc): 3012, 1772, 1705, 1428, 1394, 1337, 1179, 862, 819 cm^{-1}.

This Molecule was synthesized by the SN2 route (section 5.2.4).

cis-*2-butene cyclophane, (figure 3-27, middle):*

^{1}H NMR (500MHz, $CDCl_3$) δ 7.45 (s, 2H); 7.42 (dd, 2H, J=8.0, 1.5); 7.34 (d, 2H, J=8.0); 5.78 (m, 4H); 5.31 (m, 1H); 4.22 (m, 1H); 3.98 (m, 2H); 3.82 (m, 4H); 3.62 (m, 2H)

No other data available, due to contamination by oligomer, which obscured the spectral peaks in ^{13}C NMR.

This Molecule was synthesized by the SN2 route (section 5.2.4).

2-butyne cyclophane, (figure 3-27, right):

^1H NMR (500MHz, $CDCl_3$) δ 7.48 (s, 2H); 7.44 (dd, 2H, J=7.6, 1.6); 7.36 (d, 2H, J=8.0); 5.80 (m, 4H); 3.86 (m, 4H); 3.68 (m, 4H)

^{13}C NMR (500MHz, $CDCl_3$) δ 173.07, 172.97, 141.85, 140.43, 140.20, 139.34, 132.38, 128.92, 127.12, 122.44, 121.64, 119.60, 80.51, 80.32, 78.63, 48.97, 48.92

FT-IR (KBr disc): 2922, 1711, 1419, 1394, 1348, 1178, 817 cm^{-1}.

This Molecule was synthesized by the SN2 route (section 5.2.4).

5-bromo-1,3-dihydro-1-methoxyisobenzofuran (acetal precursor of 5-bromoIBF) (43):

This product was synthesized by another student; NMR data is given here for completeness and comparison.

^1H NMR (250MHz, $CDCl_3$) δ 7.45 (d, 1H, J=7.9); 7.41 (s, 1H); 7.26 (d, 1H, J=8.0); 6.13 (d, 1H, J=2.1); 5.16 (d, 1H, J=12.7); 5.01 (d, 1H, J=13.1); 3.43 (s, 3H)

^{13}C NMR (250MHz, $CDCl_3$) δ 142.78, 136.96, 131.23, 124.80, 124.71, 123.63, 107.51, 72.02, 54.59

bis(1,3-dihydro-1-methoxyisobenzofuranyl)acetylene (44):

1 mmol (229mg) of acetal precursor **43**, along with 0.5mmol (302mg) of bis(tributylstannyl)acetylene, was dissolved in dry toluene. To this solution, 10 mol percent each of bis(benzonitrile)palladium(II)chloride and triphenylphosphine was added, and the mixture was held at reflux temperature overnight. The product was

isolated by silica gel chromatography on a 10cm column with ethyl acetate. The solvent was then evaporated, yielding 15mg of pure bis(acetal) **44**.

^{1}H NMR (250MHz, $CDCl_3$) δ 7.51 (d, 2H, J=7.9); 7.44 (s, 2H); 7.39 (d, 2H, J=8.0); 6.18 (d, 2H, J=2.0); 5.21 (d, 2H, J=12.0); 5.04 (d, 2H, J=13.0); 3.45 (s, 6H)

^{13}C NMR (250MHz, $CDCl_3$) δ 140.70, 137.94, 131.54, 124.44, 124.39, 123.31, 107.61, 89.78, 72.22, 54.47

5,5'-bis(isobenzofuranyl)acetylene (fig.3-33):

7mg (0.022mmol) of bis(5-bromo-1,3-dihydro-1-methoxyisobenzofuranyl) acetylene was dissolved in 5mL diethyl ether, and cooled to 0°C. To this solution, 10 molar equivalents of lithium diisopropylamide was added, and the mixture stirred for 30 minutes. The reaction was then quenched with water, extracted with ether, dried over magnesium sulfate, and evaporated to yield a yellow residue. This residue was taken up into deuterated chloroform, and an NMR spectrum obtained.

^{1}H NMR (250MHz, $CDCl_3$) δ 8.04 (t, 2H, J=1.3); 8.00 (t, 2H, J=1.3); 7.65 (d, 2H, J=1.1); 7.39 (dt, 2H, J=9.0, 1.1); 6.94 (dd, 2H, J=9.0, 1.0)

N-methyl maleimide adduct of 5,5'-bis(isobenzofuranyl)acetylene (45):

7mg of bis(acetal) (0.022mmol) was combined with 5mg (2 molar equivalents) of N-methylmaleimide and a single crystal of trichloroacetic acid in 5mL of toluene. The solvent was evaporated, quantitatively yielding N-methylmaleimide adduct **45**.

^{1}H NMR (250MHz, $CDCl_3$) δ 7.43 (s, 2H); 7.39 (d, 2H, J=1.2); 7.29 (d, 2H, J=7.6); 5.77 (dd, 4H, J=3.7, 1.8); 3.85 (dd, 4H, J=3.5, 1.7); 2.39 (s, 6H)

^{13}C NMR (250MHz, $CDCl_3$) δ 175.03, 141.22, 141.05, 132.10, 131.99, 124.18, 121.30, 81.74, 80.61, 80.52, 48.91

Appendix A. 5-carbon cyclophane X-ray data

Crystals were grown by slow evaporation from a mixture of chloroform and toluene. These crystals were sent to the University of Alberta for X-ray diffraction experiments. The molecule crystallized in Wyckoff site *i,* with two enantiomers centred on an inversion site.

The structure was solved using direct methods[1] and expanded using Fourier techniques.[2] Non-hydrogen atoms were refined anisotropically. Hydrogen atoms were first refined isotropically, then fixed at geometrically idealized positions using a riding model. The final cycle of full-matrix least-squares refinement using SHELXTL 5.1[3] converged (largest parameter shift was 0.00 times its esd) with unweighted and weighted agreement factors, R = 0.042 and wR = 0.137 (all data), respectively, and goodness of fit, S = 0.89. The weighting scheme was based on counting statistics and the final difference map was essentially featureless. Figures were plotted using ORTEP-3 for windows[4].

Proton NMR experiments on the dry crystals showed a non-stoichiometric amount of toluene present in the crystal lattice, to the order of approximately 0.5 : 1 toluene : cyclophane. During refinement, this toluene exhibited a very high amount of disorder, eventually proving impossible to accurately model with the software at hand. PLATON[5] software was therefore used to model the disordered electron density via the SQUEEZE command.

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[1] Altomare, A, Cascarano, M, Giacovazzo, C & Guagliardi, A. (1993). *SIR92.* J. Appl. Cryst., **26**, 343

[2] Beurskens, P.T., Admiraal, G., Beurskens, G., Bosman, W.P., de Gelder, R., Israel, R. & Smits, J.M.M. (1994). The *DIRDIF-94* program system, Technical Report of the Crystallography Laboratory, University of Nijmegen, The Netherlands

[3] **SHELXTL 5.1**, Bruker AXS. Copyright 1998.

[4] **ORTEP-3 v.1.076**, Farrugia, L.J, *J. Appl. Cryst.* (1997), 30, 565

[5] **PLATON v1.07**. Spek, A.L, *Acta. Cryst.* (1990), A46, C34.

A-1: Crystal data and structure refinement for 5-carbon cyclophane.

Identification code	kf5C	
Empirical formula	$C_{29} H_{24} N_2 O_6$	
Formula weight	496.55	
Temperature	193(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 8.5329(8) Å	α = 113.8580(10)°
	b = 11.9053(11) Å	β = 99.1310(10)°
	c = 14.2650(13) Å	γ = 100.8160(10)°
Volume	1256.6(2) $Å^3$	
Z	2	
Density (calculated)	1.434 Mg/m^3	
Absorption coefficient	0.100 mm^{-1}	
F(000)	570	
Crystal size	0.33 x 0.30 x 0.11 mm^3	
Theta range for data collection	1.62 to 26.41°.	
Index ranges	-10<=h<=10, -14<=k<=14, -17<=l<=17	
Reflections collected	9718	
Independent reflections	5114 [R(int) = 0.0256]	
Completeness to theta = 26.41°	98.9 %	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5114 / 0 / 359	
Goodness-of-fit on F^2	0.894	
Final R indices [I>2sigma(I)]	R1 = 0.0423, wR2 = 0.1240	
R indices (all data)	R1 = 0.0613, wR2 = 0.1366	
Largest diff. peak and hole	0.251 and -0.150 $e.Å^{-3}$	

A-2: Atomic coordinates (x 104) and equivalent isotropic displacement parameters (Å2x 103) for 5-carbon cyclophane.

U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
N(1)	9468(2)	6900(1)	-2053(1)	34(1)
O(1)	5547(2)	7266(1)	-3945(1)	49(1)
C(1)	5643(2)	8085(2)	-490(1)	28(1)
N(2)	8627(2)	8080(1)	3258(1)	32(1)
O(2)	10779(2)	8844(1)	-1915(1)	53(1)
C(2)	6577(2)	9268(2)	-341(1)	34(1)
O(3)	7716(2)	4941(1)	-2546(1)	51(1)
C(3)	5192(2)	7048(2)	-1519(1)	33(1)
O(4)	4261(1)	9027(1)	3713(1)	37(1)
C(4)	7084(2)	9456(2)	-1160(1)	37(1)
O(5)	9728(1)	10239(1)	3883(1)	41(1)
C(5)	5674(2)	7257(2)	-2325(1)	36(1)
O(6)	7015(2)	6085(1)	2861(1)	48(1)
C(6)	6615(2)	8442(2)	-2151(1)	36(1)
C(7)	5543(2)	6387(2)	-3476(1)	41(1)
C(8)	7011(2)	8244(2)	-3193(1)	41(1)
C(9)	7261(2)	6145(2)	-3557(1)	39(1)
C(10)	8299(2)	7456(2)	-3351(1)	39(1)
C(11)	8112(2)	5874(2)	-2696(1)	37(1)
C(12)	9681(2)	7863(2)	-2367(1)	36(1)
C(13)	5243(2)	7914(2)	436(1)	28(1)
C(14)	4461(2)	6704(2)	331(1)	31(1)
C(15)	5706(2)	8962(2)	1453(1)	29(1)
C(16)	4142(2)	6510(2)	1187(1)	32(1)
C(17)	5348(2)	8763(2)	2295(1)	29(1)
C(18)	4572(2)	7558(2)	2168(1)	30(1)
C(19)	5663(2)	9641(2)	3468(1)	33(1)
C(20)	4478(2)	7753(2)	3266(1)	35(1)
C(21)	7079(2)	9395(2)	4141(1)	33(1)
C(22)	6279(2)	8014(2)	3920(1)	35(1)
C(23)	8638(2)	9355(2)	3774(1)	32(1)
C(24)	7289(2)	7240(2)	3287(1)	34(1)
C(25)	10456(2)	6974(2)	-1080(1)	35(1)
C(26)	9538(2)	7358(2)	-220(1)	36(1)
C(27)	10270(2)	7275(2)	789(1)	33(1)
C(28)	9203(2)	7690(2)	1554(1)	38(1)
C(29)	9780(2)	7677(2)	2614(1)	35(1)

A-3: Bond lengths [Å] and angles [°] for 5-carbon cyclophane.

Bond Lengths	
N(1)-C(11)	1.377(2)
N(1)-C(12)	1.381(2)
N(1)-C(25)	1.466(2)
O(1)-C(7)	1.451(2)
O(1)-C(8)	1.444(2)
C(1)-C(2)	1.395(2)
C(1)-C(3)	1.416(2)
C(1)-C(13)	1.495(2)
N(2)-C(23)	1.391(2)
N(2)-C(24)	1.388(2)
N(2)-C(29)	1.466(2)
O(2)-C(12)	1.203(2)
C(2)-C(4)	1.392(2)
O(3)-C(11)	1.211(2)
C(3)-C(5)	1.377(2)
O(4)-C(20)	1.450(2)
O(4)-C(19)	1.4484(19)
C(4)-C(6)	1.369(2)
O(5)-C(23)	1.2044(19)
C(5)-C(6)	1.387(2)
C(5)-C(7)	1.517(2)
O(6)-C(24)	1.213(2)
C(6)-C(8)	1.513(2)
C(7)-C(9)	1.560(3)
C(8)-C(10)	1.560(3)
C(9)-C(11)	1.505(3)
C(9)-C(10)	1.527(3)
C(10)-C(12)	1.519(2)
C(13)-C(14)	1.405(2)
C(13)-C(15)	1.409(2)
C(14)-C(16)	1.389(2)
C(15)-C(17)	1.383(2)
C(16)-C(18)	1.379(2)
C(17)-C(18)	1.388(2)
C(17)-C(19)	1.517(2)
C(18)-C(20)	1.507(2)
C(19)-C(21)	1.568(2)
C(20)-C(22)	1.569(2)
C(21)-C(23)	1.506(2)
C(21)-C(22)	1.537(2)
C(22)-C(24)	1.510(3)
C(25)-C(26)	1.520(2)
C(26)-C(27)	1.526(2)
C(27)-C(28)	1.520(2)
C(28)-C(29)	1.522(2)

Bond Angles	
C(11)-N(1)-C(12)	113.60(14)
C(11)-N(1)-C(25)	121.23(14)
C(12)-N(1)-C(25)	124.91(14)
C(7)-O(1)-C(8)	96.93(12)
C(2)-C(1)-C(3)	118.10(14)
C(2)-C(1)-C(13)	120.15(14)
C(3)-C(1)-C(13)	121.62(14)
C(23)-N(2)-C(24)	113.38(14)
C(23)-N(2)-C(29)	122.05(14)
C(24)-N(2)-C(29)	123.93(15)
C(4)-C(2)-C(1)	122.49(15)
C(5)-C(3)-C(1)	118.68(15)
C(20)-O(4)-C(19)	96.72(12)
C(6)-C(4)-C(2)	118.26(16)
C(3)-C(5)-C(6)	121.88(16)
C(3)-C(5)-C(7)	133.57(17)
C(6)-C(5)-C(7)	104.28(14)
C(4)-C(6)-C(5)	120.56(15)
C(4)-C(6)-C(8)	133.67(17)
C(5)-C(6)-C(8)	105.56(15)
O(1)-C(7)-C(5)	101.58(15)
O(1)-C(7)-C(9)	99.65(13)
C(5)-C(7)-C(9)	108.26(14)
O(1)-C(8)-C(6)	101.25(14)
O(1)-C(8)-C(10)	99.94(14)
C(6)-C(8)-C(10)	107.76(14)
C(11)-C(9)-C(10)	105.17(14)
C(11)-C(9)-C(7)	115.22(14)
C(10)-C(9)-C(7)	101.83(15)
C(12)-C(10)-C(9)	104.78(14)
C(12)-C(10)-C(8)	115.20(15)
C(9)-C(10)-C(8)	101.85(14)
O(3)-C(11)-N(1)	123.36(17)
O(3)-C(11)-C(9)	128.17(16)
N(1)-C(11)-C(9)	108.46(15)

O(2)-C(12)-N(1)	124.52(16)
O(2)-C(12)-C(10)	127.49(16)
N(1)-C(12)-C(10)	107.98(14)
C(14)-C(13)-C(15)	118.03(14)
C(14)-C(13)-C(1)	121.37(14)
C(15)-C(13)-C(1)	120.55(14)
C(16)-C(14)-C(13)	122.50(14)
C(17)-C(15)-C(13)	119.01(14)
C(18)-C(16)-C(14)	118.21(15)
C(15)-C(17)-C(18)	121.70(14)
C(15)-C(17)-C(19)	133.19(15)
C(18)-C(17)-C(19)	105.10(13)
C(16)-C(18)-C(17)	120.52(15)
C(16)-C(18)-C(20)	134.68(15)
C(17)-C(18)-C(20)	104.73(14)
O(4)-C(19)-C(17)	101.01(12)
O(4)-C(19)-C(21)	99.03(12)
C(17)-C(19)-C(21)	110.53(13)
O(4)-C(20)-C(18)	101.31(13)
O(4)-C(20)-C(22)	100.80(13)
C(18)-C(20)-C(22)	107.07(13)
C(23)-C(21)-C(22)	105.15(14)
C(23)-C(21)-C(19)	116.56(13)
C(22)-C(21)-C(19)	100.87(13)
C(24)-C(22)-C(21)	104.64(13)
C(24)-C(22)-C(20)	114.05(14)
C(21)-C(22)-C(20)	102.01(13)
O(5)-C(23)-N(2)	123.94(15)
O(5)-C(23)-C(21)	128.18(16)
N(2)-C(23)-C(21)	107.87(14)
O(6)-C(24)-N(2)	124.21(17)
O(6)-C(24)-C(22)	127.58(16)
N(2)-C(24)-C(22)	108.21(14)
N(1)-C(25)-C(26)	109.14(13)
C(27)-C(26)-C(25)	115.65(14)
C(28)-C(27)-C(26)	108.45(13)
C(27)-C(28)-C(29)	115.11(14)
N(2)-C(29)-C(28)	108.97(13)

A-4: Anisotropic displacement parameters ($Å^2 x 10^3$) for 5-carbon cyclophane.

The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
N(1)	35(1)	43(1)	25(1)	15(1)	9(1)	11(1)
O(1)	39(1)	80(1)	29(1)	27(1)	6(1)	18(1)
C(1)	25(1)	36(1)	25(1)	13(1)	6(1)	14(1)
N(2)	32(1)	41(1)	26(1)	17(1)	7(1)	12(1)
O(2)	46(1)	57(1)	47(1)	29(1)	-1(1)	-5(1)
C(2)	42(1)	34(1)	28(1)	13(1)	10(1)	16(1)
O(3)	59(1)	43(1)	43(1)	17(1)	11(1)	4(1)
C(3)	27(1)	39(1)	27(1)	10(1)	6(1)	7(1)
O(4)	34(1)	42(1)	30(1)	9(1)	14(1)	10(1)
C(4)	45(1)	37(1)	36(1)	19(1)	13(1)	16(1)
O(5)	36(1)	43(1)	39(1)	19(1)	8(1)	3(1)
C(5)	29(1)	50(1)	25(1)	14(1)	6(1)	13(1)
O(6)	47(1)	41(1)	57(1)	25(1)	8(1)	12(1)
C(6)	35(1)	49(1)	30(1)	22(1)	9(1)	18(1)
C(7)	34(1)	56(1)	25(1)	13(1)	6(1)	7(1)
C(8)	41(1)	56(1)	30(1)	23(1)	9(1)	16(1)
C(9)	38(1)	52(1)	22(1)	10(1)	10(1)	11(1)
C(10)	35(1)	58(1)	27(1)	21(1)	11(1)	13(1)
C(11)	36(1)	42(1)	29(1)	11(1)	12(1)	9(1)
C(12)	33(1)	47(1)	30(1)	19(1)	11(1)	9(1)
C(13)	24(1)	36(1)	24(1)	13(1)	5(1)	13(1)
C(14)	30(1)	32(1)	25(1)	8(1)	5(1)	10(1)
C(15)	27(1)	31(1)	27(1)	12(1)	6(1)	10(1)
C(16)	29(1)	32(1)	31(1)	13(1)	7(1)	7(1)
C(17)	23(1)	35(1)	26(1)	10(1)	5(1)	11(1)
C(18)	24(1)	39(1)	28(1)	15(1)	7(1)	11(1)
C(19)	31(1)	37(1)	29(1)	12(1)	9(1)	10(1)
C(20)	32(1)	39(1)	31(1)	13(1)	11(1)	6(1)
C(21)	34(1)	41(1)	20(1)	10(1)	8(1)	8(1)
C(22)	37(1)	45(1)	26(1)	18(1)	9(1)	7(1)
C(23)	32(1)	41(1)	21(1)	14(1)	3(1)	9(1)
C(24)	34(1)	41(1)	30(1)	20(1)	3(1)	9(1)
C(25)	34(1)	47(1)	28(1)	19(1)	7(1)	14(1)
C(26)	33(1)	50(1)	28(1)	19(1)	9(1)	18(1)
C(27)	31(1)	42(1)	30(1)	18(1)	9(1)	15(1)
C(28)	34(1)	53(1)	32(1)	21(1)	10(1)	20(1)
C(29)	32(1)	46(1)	32(1)	19(1)	9(1)	17(1)

A-5: Hydrogen coordinates (x 104) and isotropic displacement parameters (Å2x 10 3) for 5-carbon cyclophane.

	x	y	z	U(eq)
H(2)	6878	9972	346	40(5)
H(3)	4568	6225	-1651	29(4)
H(4)	7739	10267	-1034	48(5)
H(7)	4582	5602	-3824	48(5)
H(8)	7297	9033	-3296	40(5)
H(9)	7198	5475	-4278	49(5)
H(10)	8743	7410	-3969	32(4)
H(14)	4139	5992	-352	26(4)
H(15)	6255	9792	1558	23(4)
H(16)	3642	5679	1099	29(4)
H(19)	5780	10561	3647	31(4)
H(20)	3617	7078	3294	43(5)
H(21)	7330	9995	4913	27(4)
H(22)	6287	7932	4592	36(5)
H(25A)	11543	7612	-843	36(5)
H(25B)	10648	6133	-1217	42(5)
H(26A)	9499	8248	-25	48(5)
H(26B)	8385	6805	-522	40(5)
H(27A)	10295	6386	619	41(5)
H(27B)	11416	7838	1118	30(4)
H(28B)	8062	7120	1204	50(6)
H(28A)	9163	8567	1691	42(5)
H(29A)	9819	6805	2495	34(5)
H(29B)	10905	8265	2989	32(4)

Appendix B. 6-carbon cyclophane X-ray data

A crystal of this cyclophane was grown *via* slow evaporation from 1% acetic acid in chloroform, and sent to the University of Calgary for X-ray diffraction experiments. The structure was solved independently by both the technician at U of C and the author of this thesis, the latter of which is presented here. As with the five-carbon cyclophane, two units, each containing one molecule of cyclophane and acetic acid, are centred on an inversion site in Wyckoff position *i*, meaning that there are two enantiomers present in the unit cell.

The structure was solved by direct methods and expanded using Fourier techniques. Non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined isotropically, then fixed at geometrically idealized positions using a riding model. The final cycle of full-matrix least-squares refinement using SHELXTL 5.1 converged (largest parameter shift was 0.00 times its esd) with unweighted and weighted agreement factors, $R = 0.039$ and $wR = 0.106$ (all data) respectively, and goodness of fit, $S = 1.02$. The weighting scheme was based on counting statistics and the final difference map was essentially featureless. Figures were plotted using ORTEP-3 for windows.

A stoichiometric amount of acetic acid was found to co-crystallize with this cyclophane in the ratio 1:1. Proton NMR experiments on the dry crystals confirm this ratio, with integration from aromatic protons and acetic acid methyl protons yielding the predicted ratio of 2:1.

B-1: Crystal data and structure refinement for 6-carbon cyclophane.

Identification code	kf6c	
Empirical formula	$C_{32} H_{30} N_2 O_8$	
Formula weight	570.58	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 8.4100(17) Å	α= 65.30(3)°.
	b = 12.355(3) Å	β= 74.57(3)°.
	c = 14.322(3) Å	γ = 81.18(3)°.
Volume	1301.7(5) $Å^3$	
Z	2	
Density (calculated)	1.456 Mg/m^3	
Absorption coefficient	0.105 mm^{-1}	
F(000)	600	
Crystal size	0.20 x 0.18 x 0.16 mm^3	
Theta range for data collection	3.28 to 27.41°.	
Index ranges	-10<=h<=10, -15<=k<=15, -18<=l<=18	
Reflections collected	11087	
Independent reflections	5866 [R(int) = 0.0193]	
Completeness to theta = 27.41°	99.2 %	
Absorption correction	None	
Max. and min. transmission	0.9833 and 0.9792	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5866 / 0 / 381	
Goodness-of-fit on F^2	1.022	
Final R indices [I>2sigma(I)]	R1 = 0.0390, wR2 = 0.0986	
R indices (all data)	R1 = 0.0513, wR2 = 0.1063	
Largest diff. peak and hole	0.277 and -0.223 e.$Å^{-3}$	

B-2: Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for 6-carbon cyclophane.

U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1A)	10609(1)	1499(1)	-267(1)	31(1)
O(1)	4207(1)	5251(1)	1328(1)	25(1)
N(1)	8655(1)	5383(1)	2033(1)	23(1)
C(1)	5508(2)	2518(1)	4420(1)	20(1)
C(1A)	8985(2)	1494(1)	11(1)	26(1)
O(2)	7188(1)	6822(1)	2582(1)	31(1)
C(2)	4795(2)	3449(1)	4735(1)	22(1)
N(2)	8944(1)	543(1)	7800(1)	24(1)
O(2A)	8231(1)	611(1)	235(1)	33(1)
C(2A)	8162(2)	2637(1)	34(1)	35(1)
O(3)	9571(1)	4007(1)	1290(1)	31(1)
C(3)	5804(2)	2715(1)	3346(1)	21(1)
O(4)	5630(1)	-1953(1)	8281(1)	29(1)
C(4)	4387(2)	4568(1)	4015(1)	23(1)
O(5)	6538(1)	1521(1)	8323(1)	37(1)
C(5)	5378(2)	3824(1)	2640(1)	20(1)
O(6)	10924(1)	-869(1)	7545(1)	32(1)
C(6)	4676(2)	4744(1)	2969(1)	21(1)
C(7)	5596(2)	4388(1)	1450(1)	22(1)
C(8)	4515(2)	5813(1)	1969(1)	23(1)
C(9)	7051(2)	5260(1)	966(1)	22(1)
C(10)	6291(2)	6254(1)	1360(1)	23(1)
C(11)	8571(2)	4783(1)	1415(1)	23(1)
C(12)	7375(2)	6234(1)	2059(1)	23(1)
C(13)	6023(2)	1364(1)	5209(1)	20(1)
C(14)	7346(2)	658(1)	4898(1)	24(1)
C(15)	5242(2)	995(1)	6286(1)	22(1)
C(16)	7921(2)	-401(1)	5624(1)	24(1)
C(17)	5798(2)	-63(1)	6989(1)	22(1)
C(18)	7123(2)	-755(1)	6673(1)	22(1)
C(19)	5265(2)	-721(1)	8168(1)	25(1)
C(20)	7329(2)	-1808(1)	7680(1)	25(1)
C(21)	6593(2)	-599(1)	8694(1)	23(1)
C(22)	8046(2)	-1391(1)	8369(1)	23(1)
C(23)	7278(2)	622(1)	8266(1)	25(1)
C(24)	9493(2)	-593(1)	7846(1)	24(1)
C(25)	9826(2)	5016(1)	2717(1)	26(1)
C(26)	9114(2)	4053(1)	3783(1)	32(1)
C(27)	10304(2)	3565(1)	4513(1)	27(1)
C(28)	9493(2)	2722(1)	5626(1)	29(1)
C(29)	10769(2)	2087(1)	6281(1)	27(1)

C(30)	10080(2)	1494(1)	7464(1)	29(1)

B-3: Bond lengths [Å] and angles [°] for 6-carbon cyclophane.

Bond Lengths	
O(1A)-C(1A)	1.3179(18)
O(1)-C(8)	1.4516(16)
O(1)-C(7)	1.4495(16)
N(1)-C(12)	1.3897(18)
N(1)-C(11)	1.3912(17)
N(1)-C(25)	1.4636(17)
C(1)-C(2)	1.4007(18)
C(1)-C(3)	1.4110(18)
C(1)-C(13)	1.4902(19)
C(1A)-O(2A)	1.2274(18)
C(1A)-C(2A)	1.483(2)
O(2)-C(12)	1.2130(16)
C(2)-C(4)	1.3949(19)
N(2)-C(24)	1.3886(17)
N(2)-C(23)	1.3905(19)
N(2)-C(30)	1.4672(18)
O(3)-C(11)	1.2140(17)
C(3)-C(5)	1.3834(18)
O(4)-C(19)	1.4539(16)
O(4)-C(20)	1.4521(18)
C(4)-C(6)	1.3784(19)
O(5)-C(23)	1.2098(17)
C(5)-C(6)	1.3980(18)
C(5)-C(7)	1.5188(18)
O(6)-C(24)	1.2131(17)
C(6)-C(8)	1.5107(19)
C(7)-C(9)	1.5705(19)
C(8)-C(10)	1.564(2)
C(9)-C(11)	1.5113(19)
C(9)-C(10)	1.5438(18)
C(10)-C(12)	1.5141(19)
C(13)-C(14)	1.4003(19)
C(13)-C(15)	1.4077(18)
C(14)-C(16)	1.4017(19)
C(15)-C(17)	1.3794(19)
C(16)-C(18)	1.3796(19)
C(17)-C(18)	1.3930(19)
C(17)-C(19)	1.5089(19)
C(18)-C(20)	1.5161(19)
C(19)-C(21)	1.559(2)
C(20)-C(22)	1.5616(19)
C(21)-C(23)	1.5125(19)
C(21)-C(22)	1.5426(19)
C(22)-C(24)	1.510(2)
C(25)-C(26)	1.523(2)
C(26)-C(27)	1.517(2)
C(27)-C(28)	1.530(2)
C(28)-C(29)	1.520(2)
C(29)-C(30)	1.5203(19)

Bond Angles	
C(8)-O(1)-C(7)	96.98(9)
C(12)-N(1)-C(11)	113.62(11)
C(12)-N(1)-C(25)	123.19(11)
C(11)-N(1)-C(25)	122.50(11)
C(2)-C(1)-C(3)	119.09(12)
C(2)-C(1)-C(13)	119.74(11)
C(3)-C(1)-C(13)	121.08(12)
O(2A)-C(1A)-O(1A)	122.29(13)
O(2A)-C(1A)-C(2A)	123.42(13)
O(1A)-C(1A)-C(2A)	114.28(13)
C(4)-C(2)-C(1)	121.86(12)
C(24)-N(2)-C(23)	113.30(12)
C(24)-N(2)-C(30)	122.37(12)
C(23)-N(2)-C(30)	123.50(11)
C(5)-C(3)-C(1)	118.56(12)
C(19)-O(4)-C(20)	96.88(10)
C(6)-C(4)-C(2)	118.33(12)
C(3)-C(5)-C(6)	121.48(12)
C(3)-C(5)-C(7)	133.83(12)
C(6)-C(5)-C(7)	104.55(11)
C(4)-C(6)-C(5)	120.66(12)
C(4)-C(6)-C(8)	134.10(12)
C(5)-C(6)-C(8)	105.07(11)
O(1)-C(7)-C(5)	101.58(10)
O(1)-C(7)-C(9)	99.67(10)
C(5)-C(7)-C(9)	108.58(11)
O(1)-C(8)-C(6)	101.48(10)

O(1)-C(8)-C(10)	100.30(10)
C(6)-C(8)-C(10)	107.56(11)
C(11)-C(9)-C(10)	105.02(11)
C(11)-C(9)-C(7)	115.38(10)
C(10)-C(9)-C(7)	101.27(10)
C(12)-C(10)-C(9)	104.94(11)
C(12)-C(10)-C(8)	114.14(11)
C(9)-C(10)-C(8)	101.85(10)
O(3)-C(11)-N(1)	123.79(12)
O(3)-C(11)-C(9)	128.02(12)
N(1)-C(11)-C(9)	108.19(11)
O(2)-C(12)-N(1)	123.97(13)
O(2)-C(12)-C(10)	127.88(13)
N(1)-C(12)-C(10)	108.14(11)
C(14)-C(13)-C(15)	118.89(12)
C(14)-C(13)-C(1)	120.43(12)
C(15)-C(13)-C(1)	120.60(12)
C(13)-C(14)-C(16)	122.11(12)
C(17)-C(15)-C(13)	118.38(12)
C(18)-C(16)-C(14)	118.01(12)
C(15)-C(17)-C(18)	122.33(12)
C(15)-C(17)-C(19)	132.69(12)
C(18)-C(17)-C(19)	104.97(11)
C(16)-C(18)-C(17)	120.25(12)
C(16)-C(18)-C(20)	134.78(12)
C(17)-C(18)-C(20)	104.96(11)
O(4)-C(19)-C(17)	101.26(11)
O(4)-C(19)-C(21)	99.62(10)
C(17)-C(19)-C(21)	108.88(11)
O(4)-C(20)-C(18)	101.07(11)
O(4)-C(20)-C(22)	99.14(10)
C(18)-C(20)-C(22)	109.78(10)
C(23)-C(21)-C(22)	105.02(11)
C(23)-C(21)-C(19)	116.46(11)
C(22)-C(21)-C(19)	101.92(10)
C(24)-C(22)-C(21)	104.77(11)
C(24)-C(22)-C(20)	118.76(11)
C(21)-C(22)-C(20)	101.43(11)
O(5)-C(23)-N(2)	124.77(13)
O(5)-C(23)-C(21)	127.01(13)
N(2)-C(23)-C(21)	108.21(11)
O(6)-C(24)-N(2)	123.69(13)
O(6)-C(24)-C(22)	127.69(12)
N(2)-C(24)-C(22)	108.55(11)
N(1)-C(25)-C(26)	110.35(11)
C(27)-C(26)-C(25)	113.51(12)
C(26)-C(27)-C(28)	112.63(12)
C(29)-C(28)-C(27)	111.34(12)
C(30)-C(29)-C(28)	115.33(12)
N(2)-C(30)-C(29)	115.43(11)

B-4: Anisotropic displacement parameters (Å^{2}x 10^3) for 6-carbon cyclophane.

The anisotropic displacement factor exponent takes the form: $-2\pi^2[\, h^2 a^{*2}U^{11} + ... + 2\, h\, k\, a^*\, b^*\, U^{12}\,]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1A)	27(1)	35(1)	33(1)	-18(1)	-3(1)	-1(1)
O(1)	27(1)	21(1)	33(1)	-11(1)	-14(1)	4(1)
N(1)	23(1)	22(1)	21(1)	-6(1)	-6(1)	-3(1)
C(1)	18(1)	20(1)	23(1)	-8(1)	-4(1)	-4(1)
C(1A)	28(1)	32(1)	18(1)	-10(1)	-4(1)	0(1)
O(2)	35(1)	29(1)	35(1)	-18(1)	-8(1)	-4(1)
C(2)	20(1)	24(1)	22(1)	-10(1)	-2(1)	-4(1)
N(2)	31(1)	19(1)	21(1)	-7(1)	-6(1)	-3(1)
O(2A)	27(1)	35(1)	39(1)	-19(1)	-2(1)	-1(1)
C(2A)	35(1)	31(1)	35(1)	-12(1)	-8(1)	3(1)
O(3)	29(1)	30(1)	34(1)	-15(1)	-8(1)	6(1)
C(3)	21(1)	19(1)	23(1)	-9(1)	-5(1)	-2(1)
O(4)	33(1)	20(1)	29(1)	-6(1)	-2(1)	-7(1)
C(4)	20(1)	21(1)	29(1)	-13(1)	-2(1)	-1(1)
O(5)	43(1)	24(1)	47(1)	-18(1)	-11(1)	7(1)
C(5)	19(1)	20(1)	22(1)	-9(1)	-5(1)	-3(1)
O(6)	29(1)	34(1)	29(1)	-13(1)	-4(1)	2(1)
C(6)	19(1)	17(1)	27(1)	-8(1)	-5(1)	-2(1)
C(7)	25(1)	18(1)	24(1)	-8(1)	-9(1)	3(1)
C(8)	25(1)	19(1)	28(1)	-11(1)	-9(1)	2(1)
C(9)	27(1)	19(1)	19(1)	-5(1)	-6(1)	-1(1)
C(10)	28(1)	17(1)	22(1)	-5(1)	-8(1)	-1(1)
C(11)	24(1)	21(1)	18(1)	-4(1)	-2(1)	-4(1)
C(12)	26(1)	19(1)	22(1)	-5(1)	-4(1)	-6(1)
C(13)	19(1)	20(1)	22(1)	-8(1)	-5(1)	-4(1)
C(14)	26(1)	24(1)	20(1)	-9(1)	-4(1)	-1(1)
C(15)	19(1)	23(1)	24(1)	-9(1)	-3(1)	-1(1)
C(16)	27(1)	24(1)	25(1)	-13(1)	-6(1)	2(1)
C(17)	22(1)	22(1)	22(1)	-8(1)	-3(1)	-4(1)
C(18)	26(1)	19(1)	24(1)	-9(1)	-8(1)	-2(1)
C(19)	26(1)	20(1)	24(1)	-6(1)	-2(1)	-3(1)
C(20)	31(1)	18(1)	25(1)	-8(1)	-5(1)	-1(1)
C(21)	29(1)	19(1)	18(1)	-6(1)	-3(1)	0(1)
C(22)	30(1)	17(1)	18(1)	-6(1)	-5(1)	1(1)
C(23)	34(1)	20(1)	21(1)	-8(1)	-8(1)	2(1)
C(24)	31(1)	23(1)	16(1)	-7(1)	-7(1)	1(1)

C(25)	24(1)	28(1)	24(1)	-5(1)	-8(1)	-6(1)
C(26)	27(1)	38(1)	25(1)	-1(1)	-8(1)	-11(1)
C(27)	26(1)	29(1)	24(1)	-5(1)	-9(1)	-6(1)
C(28)	27(1)	32(1)	25(1)	-5(1)	-7(1)	-7(1)
C(29)	29(1)	27(1)	24(1)	-7(1)	-8(1)	-7(1)
C(30)	40(1)	25(1)	23(1)	-7(1)	-11(1)	-9(1)

B-5: Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for 6-carbon cyclophane.

	x	y	z	U(eq)
H(1A)	10995	834	-276	47
H(2)	4583	3313	5460	26
H(2A)	6973	2620	106	52
H(2B)	8618	3297	-623	52
H(2C)	8351	2748	633	52
H(3)	6286	2098	3112	25
H(4)	3923	5194	4240	28
H(7)	5660	3815	1112	26
H(8)	3673	6445	2065	28
H(9)	7337	5575	178	27
H(10)	6261	7049	762	27
H(14)	7869	905	4171	28
H(15)	4354	1462	6522	27
H(16)	8834	-861	5400	29
H(19)	4101	-535	8486	30
H(20)	7900	-2536	7580	30
H(21)	6197	-911	9478	28
H(22)	8278	-2090	9005	27
H(25A)	10070	5713	2818	31
H(25B)	10873	4706	2379	31
H(26A)	8103	4387	4131	39
H(26B)	8790	3388	3669	39
H(27A)	10743	4238	4554	33
H(27B)	11245	3131	4212	33
H(28A)	8683	3184	5976	35
H(28B)	8891	2124	5580	35
H(29A)	11383	1471	6033	32
H(29B)	11570	2672	6150	32
H(30A)	11017	1157	7814	34
H(30B)	9495	2115	7715	34

B-6: Hydrogen bonds for 6Crack [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(1A)-H(1A)...O(2A)	0.84	1.79	2.6259(15)	177.5

Symmetry transformations used to generate equivalent atoms:
#1 (-x-1), (-y+1), (-z+1)

Appendix C. 7-carbon cyclophane X-ray data

A crystal of this cyclophane was grown *via* slow evaporation from 1% acetic acid in chloroform, and sent to the University of Calgary for X-ray diffraction experiments. The structure was solved independently by both the technician in Calgary and the author of this thesis. The latter is presented here. This cyclophane crystallized in Wyckoff position *a*, with one asymmetric unit containing two "enantiomeric" molecules in the unit cell.

The structure was solved by the direct methods and expanded using Fourier techniques, revealing two independent molecules in an asymmetric unit. The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were not refined, but included at geometrically idealized positions using a riding model. The final cycle of full-matrix least-squares refinement using SHELXTL 5.1 converged (largest parameter shift was 0.00 times its esd) with unweighted and weighted agreement factors, R = 0.075 and wR = 0.232 (all data), respectively, and goodness of fit, S = 0.913. The weighting scheme was based on counting statistics and the final difference map was essentially featureless. An absolute structure could not be established in this analysis. Figures were plotted using ORTEP-3 for windows.

C-1: Crystal data and structure refinement for 7-carbon cyclophane.

Identification code	kf7c	
Empirical formula	$C_{31} H_{28} N_2 O_6$	
Formula weight	524.55	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P1	
Unit cell dimensions	a = 8.2300(16) Å	α = 88.11(3)°.
	b = 11.872(2) Å	β = 72.40(3)°.
	c = 13.597(3) Å	γ = 82.70(3)°.
Volume	1256.0(4) Å^3	
Z	2	
Density (calculated)	1.387 Mg/m^3	
Absorption coefficient	0.097 mm^{-1}	
F(000)	552	
Crystal size	0.20 x 0.14 x 0.06 mm^3	
Theta range for data collection	5.52 to 27.49°	
Index ranges	-10<=h<=10, -15<=k<=15, -17<=l<=17	
Reflections collected	22127	
Independent reflections	5671 [R(int) = 0.1071]	
Completeness to theta = 27.49°	98.4 %	
Max. and min. transmission	0.9942 and 0.9809	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5671 / 3 / 704	
Goodness-of-fit on F^2	0.913	
Final R indices [I>2sigma(I)]	R1 = 0.0749, wR2 = 0.2012	
R indices (all data)	R1 = 0.1012, wR2 = 0.2317	
Absolute structure parameter	0(10)	
Largest diff. peak and hole	0.583 and -0.470 e.Å^{-3}	

C-2: Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for 7-carbon cyclophane.

U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	845(6)	2271(4)	11170(4)	26(1)
C(1)	4077(8)	2194(5)	7781(5)	23(1)
N(1)	6128(7)	1697(5)	10504(4)	22(1)
O(2)	5830(7)	3514(4)	11106(4)	31(1)
N(2)	9218(7)	2539(5)	3807(4)	23(1)
C(2)	4119(9)	3320(6)	8021(5)	28(1)
O(3)	5689(7)	-107(4)	10176(4)	32(1)
C(3)	3399(8)	1435(5)	8593(5)	21(1)
O(4)	4838(6)	1557(4)	3344(4)	26(1)
C(4)	3530(9)	3725(6)	9035(5)	26(1)
O(5)	7809(7)	4327(4)	3870(4)	29(1)
C(5)	2776(8)	1855(5)	9595(5)	21(1)
O(6)	10249(7)	665(4)	3437(4)	32(1)
C(6)	2824(8)	2984(5)	9805(5)	22(1)
C(7)	1979(8)	1334(6)	10625(5)	22(1)
C(8)	2083(9)	3084(6)	10974(5)	24(1)
C(9)	3349(8)	1209(5)	11217(5)	21(1)
C(10)	3369(8)	2454(5)	11482(5)	21(1)
C(11)	5135(9)	814(5)	10567(5)	24(1)
C(12)	5202(8)	2664(6)	11022(4)	23(1)
C(13)	4723(8)	1773(6)	6695(5)	23(1)
C(14)	5549(9)	682(6)	6475(5)	26(1)
C(15)	4546(8)	2499(5)	5891(5)	21(1)
C(16)	6121(9)	254(5)	5456(5)	22(1)
C(17)	5105(8)	2071(5)	4889(5)	19(1)
C(18)	5857(8)	963(5)	4681(5)	21(1)
C(19)	5046(8)	2560(5)	3851(5)	20(1)
C(20)	6247(8)	821(5)	3534(5)	22(1)
C(21)	6873(8)	2749(5)	3177(5)	21(1)
C(22)	7750(8)	1522(5)	2978(5)	22(1)
C(23)	7966(8)	3330(5)	3660(5)	20(1)
C(24)	9225(8)	1462(5)	3418(5)	21(1)
C(25)	7977(9)	1610(7)	10025(5)	29(1)
C(26)	8532(9)	2339(6)	9062(5)	26(1)
C(27)	8616(11)	1811(7)	8049(6)	34(2)
C(28)	9117(10)	2658(6)	7180(5)	32(2)
C(29)	9561(10)	2213(7)	6081(5)	29(2)
C(30)	9987(10)	3186(6)	5319(5)	28(1)
C(31)	10593(9)	2839(6)	4197(5)	27(1)
O(1A)	5593(6)	6562(4)	1838(4)	25(1)
N(1A)	10432(7)	7529(5)	1372(4)	23(1)

C(1A)	8849(9)	6782(6)	-1509(5)	24(1)
O(2A)	11097(7)	5664(4)	1740(4)	32(1)
N(2A)	14043(7)	6694(5)	-5327(4)	23(1)
C(2A)	9417(8)	5682(6)	-1286(5)	24(1)
O(3A)	9086(6)	9328(4)	1309(4)	28(1)
C(3A)	7822(8)	7498(5)	-707(5)	22(1)
O(4A)	9423(6)	7281(4)	-5989(3)	24(1)
C(4A)	8996(9)	5255(5)	-282(5)	24(1)
O(5A)	13271(7)	4895(4)	-4993(4)	31(1)
C(5A)	7382(9)	7065(6)	299(5)	24(1)
O(6A)	14338(7)	8516(4)	-5919(4)	32(1)
C(6A)	7949(8)	5965(5)	498(4)	20(1)
C(7A)	6307(8)	7563(5)	1323(5)	21(1)
C(8A)	7176(9)	5831(5)	1646(5)	23(1)
C(9A)	7467(8)	7746(5)	2016(5)	20(1)
C(10A)	8137(8)	6527(5)	2203(5)	21(1)
C(11A)	9035(8)	8333(5)	1527(5)	21(1)
C(12A)	10068(9)	6460(5)	1768(5)	22(1)
C(13A)	9277(8)	7193(6)	-2597(5)	24(1)
C(14A)	9548(9)	8316(6)	-2834(5)	28(1)
C(15A)	9394(9)	6439(5)	-3405(5)	23(1)
C(16A)	9980(9)	8726(6)	-3847(5)	26(1)
C(17A)	9766(8)	6857(5)	-4402(5)	20(1)
C(18A)	10051(7)	7987(5)	-4625(4)	19(1)
C(19A)	10019(8)	6329(5)	-5446(5)	21(1)
C(20A)	10459(9)	8085(5)	-5793(5)	23(1)
C(21A)	11970(8)	6208(5)	-6028(5)	23(1)
C(22A)	12266(9)	7447(6)	-6301(5)	23(1)
C(23A)	13133(8)	5809(5)	-5385(5)	19(1)
C(24A)	13645(8)	7663(5)	-5845(5)	22(1)
C(25A)	12194(8)	7840(6)	995(5)	25(1)
C(26A)	12705(10)	8191(6)	-137(5)	30(2)
C(27A)	13047(10)	7212(6)	-889(5)	31(2)
C(28A)	13702(11)	7660(7)	-1993(5)	34(2)
C(29A)	14080(9)	6816(6)	-2864(5)	29(2)
C(30A)	15003(9)	7337(6)	-3874(5)	26(1)
C(31A)	15413(8)	6611(6)	-4837(5)	27(1)

C-3: Bond lengths [Å] and angles [°] for 7-carbon cyclophane.

Bond Lengths

O(1)-C(7)	1.424(8)
O(1)-C(8)	1.453(8)
C(1)-C(2)	1.394(9)
C(1)-C(3)	1.425(9)
C(1)-C(13)	1.490(9)
N(1)-C(12)	1.379(9)
N(1)-C(11)	1.394(8)
N(1)-C(25)	1.455(9)
O(2)-C(12)	1.214(8)
N(2)-C(23)	1.361(8)
N(2)-C(24)	1.398(8)
N(2)-C(31)	1.472(8)
C(2)-C(4)	1.396(10)
O(3)-C(11)	1.205(8)
C(3)-C(5)	1.387(9)
O(4)-C(20)	1.444(8)
O(4)-C(19)	1.450(7)
C(4)-C(6)	1.381(10)
O(5)-C(23)	1.209(8)
C(5)-C(6)	1.388(8)
C(5)-C(7)	1.505(9)
O(6)-C(24)	1.190(8)
C(6)-C(8)	1.523(9)
C(7)-C(9)	1.562(9)
C(8)-C(10)	1.538(9)
C(9)-C(11)	1.493(9)
C(9)-C(10)	1.536(9)
C(10)-C(12)	1.498(9)
C(13)-C(14)	1.382(10)
C(13)-C(15)	1.401(9)
C(14)-C(16)	1.411(9)
C(15)-C(17)	1.391(8)
C(16)-C(18)	1.378(9)
C(17)-C(18)	1.380(9)
C(17)-C(19)	1.519(8)
C(18)-C(20)	1.505(9)
C(19)-C(21)	1.546(9)
C(20)-C(22)	1.565(9)
C(21)-C(23)	1.503(8)
C(21)-C(22)	1.535(9)
C(22)-C(24)	1.500(9)
C(25)-C(26)	1.528(9)
C(26)-C(27)	1.511(10)
C(27)-C(28)	1.520(10)
C(28)-C(29)	1.523(9)
C(29)-C(30)	1.528(10)
C(30)-C(31)	1.509(9)
O(1A)-C(8A)	1.428(8)
O(1A)-C(7A)	1.456(8)
N(1A)-C(11A)	1.365(8)
N(1A)-C(12A)	1.394(8)
N(1A)-C(25A)	1.475(8)
C(1A)-C(3A)	1.396(9)
C(1A)-C(2A)	1.386(10)
C(1A)-C(13A)	1.494(9)
O(2A)-C(12A)	1.180(8)
N(2A)-C(23A)	1.383(8)
N(2A)-C(24A)	1.385(9)
N(2A)-C(31A)	1.465(8)
C(2A)-C(4A)	1.398(9)
O(3A)-C(11A)	1.212(8)
C(3A)-C(5A)	1.402(9)
O(4A)-C(20A)	1.438(8)
O(4A)-C(19A)	1.445(8)
C(4A)-C(6A)	1.378(9)
O(5A)-C(23A)	1.201(8)
C(5A)-C(6A)	1.377(9)
C(5A)-C(7A)	1.500(9)
O(6A)-C(24A)	1.211(8)
C(6A)-C(8A)	1.508(8)
C(7A)-C(9A)	1.567(8)
C(8A)-C(10A)	1.566(8)
C(9A)-C(11A)	1.507(9)
C(9A)-C(10A)	1.524(9)
C(10A)-C(12A)	1.511(9)
C(13A)-C(14A)	1.391(9)
C(13A)-C(15A)	1.413(9)
C(14A)-C(16A)	1.401(10)
C(15A)-C(17A)	1.386(9)
C(16A)-C(18A)	1.380(9)
C(17A)-C(18A)	1.399(8)
C(17A)-C(19A)	1.516(8)
C(18A)-C(20A)	1.524(8)
C(19A)-C(21A)	1.551(9)

C(20A)-C(22A)	1.546(10)
C(21A)-C(23A)	1.506(9)
C(21A)-C(22A)	1.537(9)
C(22A)-C(24A)	1.498(9)
C(25A)-C(26A)	1.527(9)
C(26A)-C(27A)	1.515(9)
C(27A)-C(28A)	1.536(10)
C(28A)-C(29A)	1.510(9)
C(29A)-C(30A)	1.509(10)
C(30A)-C(31A)	1.519(9)

Bond Angles

C(7)-O(1)-C(8)	97.6(5)
C(2)-C(1)-C(3)	119.1(6)
C(2)-C(1)-C(13)	121.3(6)
C(3)-C(1)-C(13)	119.6(6)
C(12)-N(1)-C(11)	113.1(6)
C(12)-N(1)-C(25)	121.8(6)
C(11)-N(1)-C(25)	124.9(6)
C(23)-N(2)-C(24)	114.1(5)
C(23)-N(2)-C(31)	122.2(5)
C(24)-N(2)-C(31)	123.1(6)
C(4)-C(2)-C(1)	121.9(6)
C(5)-C(3)-C(1)	118.5(6)
C(20)-O(4)-C(19)	97.2(4)
C(6)-C(4)-C(2)	117.9(6)
C(6)-C(5)-C(3)	120.8(6)
C(6)-C(5)-C(7)	105.4(5)
C(3)-C(5)-C(7)	133.8(6)
C(5)-C(6)-C(4)	121.7(6)
C(5)-C(6)-C(8)	104.3(5)
C(4)-C(6)-C(8)	133.9(6)
O(1)-C(7)-C(5)	101.7(5)
O(1)-C(7)-C(9)	100.2(5)
C(5)-C(7)-C(9)	107.3(5)
O(1)-C(8)-C(6)	100.4(5)
O(1)-C(8)-C(10)	99.3(5)
C(6)-C(8)-C(10)	109.6(5)
C(11)-C(9)-C(10)	105.3(5)
C(11)-C(9)-C(7)	114.6(5)
C(10)-C(9)-C(7)	101.2(5)
C(12)-C(10)-C(9)	104.7(5)
C(12)-C(10)-C(8)	115.8(5)
C(9)-C(10)-C(8)	102.2(5)
O(3)-C(11)-N(1)	124.0(7)
O(3)-C(11)-C(9)	127.9(6)
N(1)-C(11)-C(9)	108.1(5)
O(2)-C(12)-N(1)	123.9(6)
O(2)-C(12)-C(10)	127.4(6)
N(1)-C(12)-C(10)	108.6(5)
C(14)-C(13)-C(15)	119.9(6)
C(14)-C(13)-C(1)	120.3(6)
C(15)-C(13)-C(1)	119.8(6)
C(13)-C(14)-C(16)	121.1(6)
C(17)-C(15)-C(13)	118.6(6)
C(18)-C(16)-C(14)	118.1(6)
C(18)-C(17)-C(15)	121.1(6)
C(18)-C(17)-C(19)	105.1(5)
C(15)-C(17)-C(19)	133.8(6)
C(17)-C(18)-C(16)	121.1(6)
C(17)-C(18)-C(20)	105.2(5)
C(16)-C(18)-C(20)	133.7(6)
O(4)-C(19)-C(17)	100.7(5)
O(4)-C(19)-C(21)	99.2(5)
C(17)-C(19)-C(21)	110.0(5)
O(4)-C(20)-C(18)	101.2(5)
O(4)-C(20)-C(22)	99.1(5)
C(18)-C(20)-C(22)	108.5(5)
C(23)-C(21)-C(22)	105.2(5)
C(23)-C(21)-C(19)	118.1(5)
C(22)-C(21)-C(19)	101.4(5)
C(24)-C(22)-C(21)	104.9(5)
C(24)-C(22)-C(20)	117.2(5)
C(21)-C(22)-C(20)	102.1(5)
O(5)-C(23)-N(2)	124.7(6)
O(5)-C(23)-C(21)	127.1(6)
N(2)-C(23)-C(21)	108.1(5)
O(6)-C(24)-N(2)	124.5(6)
O(6)-C(24)-C(22)	127.9(6)
N(2)-C(24)-C(22)	107.6(5)
N(1)-C(25)-C(26)	114.3(6)
C(27)-C(26)-C(25)	116.6(6)
C(28)-C(27)-C(26)	109.9(6)
C(29)-C(28)-C(27)	117.2(6)
C(28)-C(29)-C(30)	109.7(6)
C(31)-C(30)-C(29)	114.9(6)
N(2)-C(31)-C(30)	113.8(5)
C(8A)-O(1A)-C(7A)	97.3(4)
C(11A)-N(1A)-C(12A)	114.9(5)
C(11A)-N(1A)-C(25A)	121.2(5)
C(12A)-N(1A)-C(25A)	122.9(6)
C(3A)-C(1A)-C(2A)	119.2(6)

C(3A)-C(1A)-C(13A)	119.9(6)
C(2A)-C(1A)-C(13A)	120.8(6)
C(23A)-N(2A)-C(24A)	114.2(5)
C(23A)-N(2A)-C(31A)	124.1(6)
C(24A)-N(2A)-C(31A)	121.6(6)
C(1A)-C(2A)-C(4A)	122.5(6)
C(1A)-C(3A)-C(5A)	118.3(6)
C(20A)-O(4A)-C(19A)	97.8(4)
C(6A)-C(4A)-C(2A)	117.5(6)
C(6A)-C(5A)-C(3A)	121.3(6)
C(6A)-C(5A)-C(7A)	105.6(6)
C(3A)-C(5A)-C(7A)	133.1(6)
C(5A)-C(6A)-C(4A)	121.2(6)
C(5A)-C(6A)-C(8A)	104.8(5)
C(4A)-C(6A)-C(8A)	134.1(6)
O(1A)-C(7A)-C(5A)	100.7(5)
O(1A)-C(7A)-C(9A)	98.0(5)
C(5A)-C(7A)-C(9A)	110.4(5)
O(1A)-C(8A)-C(6A)	101.6(5)
O(1A)-C(8A)-C(10A)	99.6(5)
C(6A)-C(8A)-C(10A)	108.0(5)
C(11A)-C(9A)-C(10A)	105.9(5)
C(11A)-C(9A)-C(7A)	116.9(5)
C(10A)-C(9A)-C(7A)	101.5(5)
C(12A)-C(10A)-C(9A)	104.9(5)
C(12A)-C(10A)-C(8A)	117.9(5)
C(9A)-C(10A)-C(8A)	102.0(5)
O(3A)-C(11A)-N(1A)	125.2(6)
O(3A)-C(11A)-C(9A)	127.6(6)
N(1A)-C(11A)-C(9A)	107.2(5)
O(2A)-C(12A)-N(1A)	125.3(6)
O(2A)-C(12A)-C(10A)	127.8(6)
N(1A)-C(12A)-C(10A)	106.9(5)
C(14A)-C(13A)-C(15A)	118.9(6)
C(14A)-C(13A)-C(1A)	121.1(6)
C(15A)-C(13A)-C(1A)	120.0(6)
C(13A)-C(14A)-C(16A)	122.6(6)
C(17A)-C(15A)-C(13A)	118.3(6)
C(18A)-C(16A)-C(14A)	117.8(6)
C(18A)-C(17A)-C(15A)	122.0(6)
C(18A)-C(17A)-C(19A)	104.2(5)
C(15A)-C(17A)-C(19A)	133.8(6)
C(17A)-C(18A)-C(16A)	120.4(6)
C(17A)-C(18A)-C(20A)	105.3(5)
C(16A)-C(18A)-C(20A)	134.3(6)
O(4A)-C(19A)-C(17A)	101.4(5)
O(4A)-C(19A)-C(21A)	100.1(5)
C(17A)-C(19A)-C(21A)	107.3(5)
O(4A)-C(20A)-C(18A)	100.7(5)
O(4A)-C(20A)-C(22A)	99.7(5)
C(18A)-C(20A)-C(22A)	108.6(5)
C(23A)-C(21A)-C(22A)	105.5(5)
C(23A)-C(21A)-C(19A)	115.4(5)
C(22A)-C(21A)-C(19A)	102.0(5)
C(24A)-C(22A)-C(21A)	104.8(5)
C(24A)-C(22A)-C(20A)	116.3(5)
C(21A)-C(22A)-C(20A)	101.7(5)
O(5A)-C(23A)-N(2A)	125.4(6)
O(5A)-C(23A)-C(21A)	127.3(6)
N(2A)-C(23A)-C(21A)	107.3(5)
O(6A)-C(24A)-N(2A)	124.5(6)
O(6A)-C(24A)-C(22A)	127.4(6)
N(2A)-C(24A)-C(22A)	108.1(5)
N(1A)-C(25A)-C(26A)	113.1(5)
C(27A)-C(26A)-C(25A)	114.1(6)
C(26A)-C(27A)-C(28A)	108.9(6)
C(29A)-C(28A)-C(27A)	117.2(6)
C(28A)-C(29A)-C(30A)	110.3(6)
C(31A)-C(30A)-C(29A)	116.9(6)
N(2A)-C(31A)-C(30A)	114.6(5)

C-4: Anisotropic displacement parameters ($Å^2$x 10^3) for 7-carbon cyclophane.

The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	15(2)	35(3)	26(2)	-9(2)	-4(2)	-4(2)
C(1)	26(3)	25(3)	21(3)	-6(2)	-13(3)	0(2)
N(1)	19(3)	30(3)	19(2)	-1(2)	-8(2)	-1(2)
O(2)	39(3)	31(3)	32(3)	-7(2)	-19(2)	-13(2)
N(2)	23(3)	30(3)	18(2)	-1(2)	-9(2)	-8(2)
C(2)	33(4)	23(3)	29(3)	5(3)	-13(3)	-4(3)
O(3)	32(3)	23(2)	41(3)	-8(2)	-11(2)	2(2)
C(3)	24(3)	24(3)	20(3)	-4(2)	-12(2)	-8(2)
O(4)	30(2)	28(2)	26(2)	-3(2)	-16(2)	-5(2)
C(4)	37(4)	18(3)	26(3)	-3(2)	-15(3)	-2(3)
O(5)	38(3)	20(2)	34(3)	-5(2)	-15(2)	-7(2)
C(5)	19(3)	20(3)	26(3)	-6(2)	-9(2)	-4(2)
O(6)	30(3)	26(3)	39(3)	-1(2)	-11(2)	0(2)
C(6)	21(3)	29(3)	19(3)	-4(2)	-12(2)	-6(2)
C(7)	21(3)	29(3)	19(3)	-2(2)	-9(2)	-4(2)
C(8)	29(3)	24(3)	20(3)	-6(2)	-7(3)	-3(3)
C(9)	26(3)	20(3)	16(3)	1(2)	-3(2)	-3(2)
C(10)	24(3)	27(3)	16(3)	-3(2)	-8(2)	-4(2)
C(11)	28(3)	22(3)	24(3)	2(2)	-12(3)	-8(3)
C(12)	26(3)	32(3)	13(3)	-2(2)	-10(2)	-6(3)
C(13)	23(3)	26(3)	19(3)	1(2)	-5(2)	-8(2)
C(14)	31(3)	27(3)	23(3)	0(3)	-12(3)	-3(3)
C(15)	21(3)	19(3)	21(3)	-4(2)	-4(2)	0(2)
C(16)	27(3)	17(3)	22(3)	2(2)	-5(2)	-3(2)
C(17)	16(3)	24(3)	17(3)	2(2)	-5(2)	-6(2)
C(18)	16(3)	22(3)	26(3)	-4(2)	-8(2)	-4(2)
C(19)	22(3)	24(3)	17(3)	-2(2)	-10(2)	-3(2)
C(20)	24(3)	18(3)	25(3)	1(2)	-10(3)	-3(2)
C(21)	23(3)	21(3)	21(3)	1(2)	-10(2)	-5(2)
C(22)	23(3)	22(3)	21(3)	-4(2)	-6(2)	-8(2)
C(23)	18(3)	23(3)	16(3)	2(2)	-1(2)	-6(2)
C(24)	25(3)	20(3)	17(3)	-1(2)	-3(2)	-3(2)
C(25)	22(3)	39(4)	28(3)	3(3)	-9(3)	-4(3)
C(26)	22(3)	36(4)	21(3)	1(3)	-5(3)	-8(3)
C(27)	42(4)	36(4)	27(4)	-1(3)	-15(3)	-11(3)
C(28)	41(4)	33(4)	25(3)	-2(3)	-9(3)	-14(3)
C(29)	33(4)	38(4)	20(3)	-2(3)	-8(3)	-14(3)
C(30)	34(4)	34(4)	22(3)	1(3)	-16(3)	-11(3)

C(31)	24(3)	36(4)	24(3)	-4(3)	-7(3)	-13(3)
O(1A)	24(2)	24(2)	26(2)	1(2)	-6(2)	-11(2)
N(1A)	27(3)	27(3)	20(3)	-4(2)	-12(2)	-8(2)
C(1A)	24(3)	29(3)	21(3)	-2(2)	-9(2)	-5(3)
O(2A)	32(3)	29(3)	39(3)	-6(2)	-17(2)	1(2)
N(2A)	18(3)	30(3)	20(2)	-5(2)	-5(2)	-3(2)
C(2A)	25(3)	27(3)	18(3)	-9(2)	-4(2)	-5(3)
O(3A)	33(3)	18(2)	36(3)	-2(2)	-12(2)	-6(2)
C(3A)	24(3)	23(3)	18(3)	-2(2)	-7(2)	1(2)
O(4A)	23(2)	30(2)	24(2)	0(2)	-13(2)	-5(2)
C(4A)	29(3)	19(3)	24(3)	-2(2)	-11(3)	-1(2)
O(5A)	35(3)	23(2)	41(3)	1(2)	-22(2)	-2(2)
C(5A)	25(3)	25(3)	21(3)	-4(2)	-5(3)	-6(3)
O(6A)	31(3)	33(3)	31(3)	3(2)	-4(2)	-17(2)
C(6A)	20(3)	24(3)	16(3)	0(2)	-6(2)	-7(2)
C(7A)	19(3)	20(3)	22(3)	-1(2)	-3(2)	-3(2)
C(8A)	32(3)	18(3)	20(3)	0(2)	-9(3)	-7(3)
C(9A)	23(3)	21(3)	17(3)	-4(2)	-7(2)	-8(2)
C(10A)	25(3)	26(3)	16(3)	-6(2)	-9(2)	-9(2)
C(11A)	23(3)	27(3)	15(3)	-7(2)	-8(2)	-2(2)
C(12A)	30(3)	22(3)	17(3)	-2(2)	-11(2)	-6(3)
C(13A)	23(3)	25(3)	20(3)	0(2)	-3(2)	0(2)
C(14A)	33(4)	23(3)	26(3)	-9(3)	-9(3)	0(3)
C(15A)	26(3)	19(3)	26(3)	-4(2)	-12(3)	-1(2)
C(16A)	34(4)	19(3)	26(3)	-2(2)	-7(3)	-4(3)
C(17A)	20(3)	20(3)	22(3)	-4(2)	-9(2)	0(2)
C(18A)	15(3)	23(3)	17(3)	0(2)	-1(2)	-1(2)
C(19A)	24(3)	24(3)	19(3)	-1(2)	-11(2)	-5(2)
C(20A)	30(3)	20(3)	22(3)	5(2)	-12(3)	-2(3)
C(21A)	24(3)	25(3)	21(3)	-3(2)	-7(2)	-4(3)
C(22A)	26(3)	27(3)	18(3)	2(2)	-7(2)	-7(3)
C(23A)	16(3)	22(3)	19(3)	-9(2)	-3(2)	-3(2)
C(24A)	20(3)	25(3)	16(3)	-2(2)	1(2)	-4(2)
C(25A)	21(3)	34(3)	21(3)	-1(3)	-9(2)	-7(3)
C(26A)	38(4)	31(4)	21(3)	-6(3)	-6(3)	-10(3)
C(27A)	36(4)	33(4)	24(3)	-6(3)	-6(3)	-12(3)
C(28A)	43(4)	36(4)	20(3)	-4(3)	-4(3)	-11(3)
C(29A)	28(3)	37(4)	25(3)	-7(3)	-8(3)	-9(3)
C(30A)	24(3)	37(4)	22(3)	-7(3)	-12(3)	-6(3)
C(31A)	18(3)	40(4)	26(3)	-9(3)	-10(3)	-1(3)

C-5: Hydrogen coordinates (x 10^4) and isotropic displacement parameters (Å^{2}x 10^3) for 7-carbon cyclophane.

	x	y	z	U(eq)
H(2)	4562	3827	7478	29(3)
H(3)	3375	661	8451	29(3)
H(4)	3612	4486	9192	29(3)
H(7)	1433	634	10599	29(3)
H(8)	1601	3869	11243	29(3)
H(9)	2994	738	11852	29(3)
H(10)	2975	2581	12246	29(3)
H(14)	5735	211	7019	29(3)
H(15)	4054	3268	6027	29(3)
H(16)	6671	-501	5308	29(3)
H(19)	4143	3220	3888	29(3)
H(20)	6388	20	3287	29(3)
H(21)	6834	3125	2514	29(3)
H(22)	8172	1349	2222	29(3)
H(25A)	8419	806	9837	29(3)
H(25B)	8513	1836	10538	29(3)
H(26A)	7726	3049	9164	29(3)
H(26B)	9681	2551	9006	29(3)
H(27A)	9471	1124	7908	29(3)
H(27B)	7483	1580	8090	29(3)
H(28A)	8157	3280	7283	29(3)
H(28B)	10120	2994	7247	29(3)
H(29A)	8575	1874	5992	29(3)
H(29B)	10558	1616	5945	29(3)
H(30A)	8950	3750	5436	29(3)
H(30B)	10889	3566	5469	29(3)
H(31A)	11121	3471	3780	29(3)
H(31B)	11492	2179	4102	29(3)
H(2A)	10118	5200	-1835	29(3)
H(3A)	7432	8260	-838	29(3)
H(4A)	9416	4503	-142	29(3)
H(7A)	5442	8224	1291	29(3)
H(8A)	7067	5032	1887	29(3)
H(9A)	6764	8126	2681	29(3)
H(10A)	7798	6359	2958	29(3)
H(14A)	9435	8826	-2286	29(3)
H(15A)	9223	5666	-3269	29(3)
H(16A)	10217	9486	-3992	29(3)
H(19A)	9452	5629	-5430	29(3)
H(20A)	10247	8869	-6056	29(3)
H(21A)	12249	5732	-6664	29(3)
H(22A)	12636	7560	-7065	29(3)

H(25C)	13009	7185	1085	29(3)
H(25D)	12290	8475	1420	29(3)
H(26C)	11776	8747	-250	29(3)
H(26D)	13752	8576	-288	29(3)
H(27C)	11977	6868	-800	29(3)
H(27D)	13916	6621	-755	29(3)
H(28C)	12836	8278	-2091	29(3)
H(28D)	14765	8002	-2056	29(3)
H(29C)	12992	6579	-2907	29(3)
H(29D)	14802	6132	-2727	29(3)
H(30C)	14293	8046	-3970	29(3)
H(30D)	16095	7552	-3817	29(3)
H(31C)	16463	6834	-5345	29(3)
H(31D)	15668	5808	-4654	29(3)

Appendix D. 9-carbon cyclophane X-ray data

A crystal of this cyclophane was grown *via* slow evaporation from chloroform, and sent to the University of Alberta for X-ray diffraction experiments. This molecule crystallized in Wyckoff position *e*, with four molecules arranged in a "staircase" fashion.

The structure was solved by the direct methods and expanded using Fourier techniques. A large amount of disorder was discovered in four carbon atoms of the tether region of the molecule. Non-disordered, non-hydrogen atoms were refined anisotropically. Disordered non-hydrogen atoms were refined isotropically in several positions with differing site occupancy factors. Hydrogen atoms were not refined, but included at geometrically idealized positions using a riding model. The final cycle of full-matrix least-squares refinement using SHELXTL 5.1 converged (largest parameter shift was 0.00 times its esd) with unweighted and weighted agreement factors, R = 0.075 and wR = 0.218 (all data) respectively, and goodness of fit, S = 0.935. The weighting scheme was based on counting statistics and the final difference map was essentially featureless. Figures were plotted using ORTEP-3 for windows.

D-1: Crystal data and structure refinement for 9-carbon cyclophane.

Identification code	kf9C	
Empirical formula	$C_{33} H_{36} N_2 O_6$	
Formula weight	556.64	
Temperature	193(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P21/C	
Unit cell dimensions	a = 13.7266(12) Å	α = 90°
	b = 15.7146(15) Å	β =105.307(2)°
	c = 12.9781(12) Å	γ = 90°
Volume	2700.2(4) $Å^3$	
Z	4	
Density (calculated)	1.369 Mg/m^3	
Absorption coefficient	0.094 mm^{-1}	
F(000)	1184	
Crystal size	0.17 x 0.17 x 0.06 mm^3	
Theta range for data collection	1.54 to 26.41°	
Index ranges	-17<=h<=17, -19<=k<=19, -16<=l<=15	
Reflections collected	20364	
Independent reflections	5536 [R(int) = 0.1813]	
Completeness to theta = 26.41°	99.9 %	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	5536 / 0 / 418	
Goodness-of-fit on F^2	0.935	
Final R indices [I>2sigma(I)]	R1 = 0.0753, wR2 = 0.1594	
R indices (all data)	R1 = 0.2054, wR2 = 0.2177	
Largest diff. peak and hole	0.299 and -0.210 e.$Å^{-3}$	

D-2: Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for 9-carbon cyclophane.

U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	7356(2)	-1419(2)	11170(3)	61(1)
N(1)	6992(3)	-374(2)	8129(3)	43(1)
C(1)	4615(3)	-2387(3)	8704(3)	37(1)
N(2)	348(2)	-1312(2)	7613(3)	35(1)
O(2)	8364(2)	-1196(2)	8150(3)	67(1)
C(2)	5361(3)	-2866(3)	8421(4)	44(1)
O(3)	5736(2)	394(2)	8596(3)	52(1)
C(3)	4912(3)	-1696(3)	9397(3)	37(1)
O(4)	654(2)	-3808(2)	8677(2)	51(1)
C(4)	6379(3)	-2704(3)	8836(4)	44(1)
O(5)	958(2)	-1009(2)	9399(3)	52(1)
C(5)	5929(3)	-1546(3)	9823(3)	40(1)
O(6)	-379(2)	-1931(2)	5995(3)	51(1)
C(6)	6655(3)	-2061(3)	9571(4)	44(1)
C(7)	6514(3)	-893(3)	10589(4)	47(1)
C(8)	7657(4)	-1728(3)	10254(4)	54(1)
C(9)	7066(3)	-298(3)	9964(4)	46(1)
C(10)	7915(3)	-874(3)	9801(4)	50(1)
C(11)	6496(3)	-39(3)	8847(4)	42(1)
C(12)	7820(3)	-859(3)	8629(4)	50(1)
C(13)	3532(3)	-2624(3)	8306(3)	36(1)
C(14)	3121(3)	-2903(3)	7267(3)	39(1)
C(15)	2925(3)	-2601(3)	9015(3)	37(1)
C(16)	2129(3)	-3174(3)	6917(4)	42(1)
C(17)	1945(3)	-2891(2)	8679(3)	34(1)
C(18)	1548(3)	-3181(3)	7641(4)	39(1)
C(19)	1112(3)	-3046(3)	9217(4)	41(1)
C(20)	497(4)	-3473(3)	7605(4)	49(1)
C(21)	239(3)	-2400(3)	8809(3)	40(1)
C(22)	-205(3)	-2713(3)	7659(3)	44(1)
C(23)	562(3)	-1499(3)	8689(4)	40(1)
C(24)	-119(3)	-1970(3)	6960(4)	38(1)
C(25)	6692(4)	-251(3)	6971(4)	52(1)
C(26)	6222(4)	-1055(3)	6386(4)	56(1)
C(27)	5176(4)	-1230(3)	6506(4)	52(1)
C(28)	4394(4)	-624(4)	5860(5)	68(2)
C(29)	3543(11)	-559(10)	6426(15)	18(8)
C(29)	3290(17)	-237(15)	6706(15)	145(11)
C(30)	2619(6)	12(6)	5752(7)	42(4)
C(30)	1228(16)	-417(12)	6518(17)	33(7)
C(31)	1874(6)	167(5)	6376(6)	58(4)

C(31)	2140(20)	-620(20)	7290(30)	95(13)
C(32)	1583(12)	-630(7)	6889(12)	33(5)
C(32)	3327(11)	-716(10)	5920(20)	89(7)
C(33)	573(4)	-499(3)	7204(4)	50(1)

D-3: Bond lengths [Å] and angles [°] for 9-carbon cyclophane.

Bond Lengths	
O(1)-C(8)	1.442(5)
O(1)-C(7)	1.459(5)
N(1)-C(12)	1.380(6)
N(1)-C(11)	1.394(5)
N(1)-C(25)	1.463(5)
C(1)-C(2)	1.396(6)
C(1)-C(3)	1.399(6)
C(1)-C(13)	1.486(6)
N(2)-C(23)	1.380(5)
N(2)-C(24)	1.383(5)
N(2)-C(33)	1.447(5)
O(2)-C(12)	1.213(5)
C(2)-C(4)	1.381(6)
O(3)-C(11)	1.216(5)
C(3)-C(5)	1.380(6)
O(4)-C(19)	1.444(5)
O(4)-C(20)	1.450(5)
C(4)-C(6)	1.373(6)
O(5)-C(23)	1.215(5)
C(5)-C(6)	1.388(6)
C(5)-C(7)	1.503(6)
O(6)-C(24)	1.210(5)
C(6)-C(8)	1.519(6)
C(7)-C(9)	1.559(6)
C(8)-C(10)	1.543(7)
C(9)-C(11)	1.511(6)
C(9)-C(10)	1.533(6)
C(10)-C(12)	1.492(7)
C(13)-C(14)	1.387(5)
C(13)-C(15)	1.395(6)
C(14)-C(16)	1.385(6)
C(15)-C(17)	1.378(5)
C(16)-C(18)	1.383(6)
C(17)-C(18)	1.389(6)
C(17)-C(19)	1.509(6)
C(18)-C(20)	1.503(6)
C(19)-C(21)	1.554(6)
C(20)-C(22)	1.548(6)
C(21)-C(23)	1.503(6)
C(21)-C(22)	1.537(6)
C(22)-C(24)	1.502(6)
C(25)-C(26)	1.526(6)
C(26)-C(27)	1.511(6)
C(27)-C(28)	1.512(7)
C(28)-C(32)	1.494(12)
C(28)-C(29)	1.538(16)
C(29)-C(30)	1.611(17)
C(29)-C(32)	1.28(3)
C(29)-C(31)	2.02(4)
C(30)-C(31)	1.482(10)
C(30)-C(31)	1.42(4)
C(30)-C(33)	1.429(15)
C(31)-C(32)	1.521(14)
C(32)-C(33)	1.559(13)

Bond Angles	
C(8)-O(1)-C(7)	97.2(3)
C(12)-N(1)-C(11)	112.4(4)
C(12)-N(1)-C(25)	122.0(4)
C(11)-N(1)-C(25)	125.6(4)
C(2)-C(1)-C(3)	118.5(4)
C(2)-C(1)-C(13)	120.6(4)
C(3)-C(1)-C(13)	120.9(4)
C(23)-N(2)-C(24)	113.6(4)
C(23)-N(2)-C(33)	123.4(4)
C(24)-N(2)-C(33)	123.0(4)
C(4)-C(2)-C(1)	122.4(4)
C(5)-C(3)-C(1)	118.9(4)
C(19)-O(4)-C(20)	95.7(3)
C(6)-C(4)-C(2)	118.1(4)

C(3)-C(5)-C(6)	121.2(4)
C(3)-C(5)-C(7)	133.6(4)
C(6)-C(5)-C(7)	105.2(4)
C(4)-C(6)-C(5)	120.6(4)
C(4)-C(6)-C(8)	134.5(4)
C(5)-C(6)-C(8)	104.9(4)
O(1)-C(7)-C(5)	99.6(4)
O(1)-C(7)-C(9)	100.4(3)
C(5)-C(7)-C(9)	108.3(4)
O(1)-C(8)-C(6)	100.6(4)
O(1)-C(8)-C(10)	99.5(4)
C(6)-C(8)-C(10)	110.0(4)
C(11)-C(9)-C(10)	104.3(4)
C(11)-C(9)-C(7)	117.4(4)
C(10)-C(9)-C(7)	102.1(4)
C(12)-C(10)-C(9)	105.4(4)
C(12)-C(10)-C(8)	115.8(4)
C(9)-C(10)-C(8)	101.6(4)
O(3)-C(11)-N(1)	124.6(4)
O(3)-C(11)-C(9)	126.8(4)
N(1)-C(11)-C(9)	108.6(4)
O(2)-C(12)-N(1)	122.8(5)
O(2)-C(12)-C(10)	128.0(5)
N(1)-C(12)-C(10)	109.1(4)
C(14)-C(13)-C(15)	119.2(4)
C(14)-C(13)-C(1)	122.0(4)
C(15)-C(13)-C(1)	118.7(4)
C(16)-C(14)-C(13)	121.9(4)
C(17)-C(15)-C(13)	119.1(4)
C(18)-C(16)-C(14)	118.2(4)
C(15)-C(17)-C(18)	121.0(4)
C(15)-C(17)-C(19)	134.7(4)
C(18)-C(17)-C(19)	104.2(4)
C(16)-C(18)-C(17)	120.5(4)
C(16)-C(18)-C(20)	134.5(4)
C(17)-C(18)-C(20)	105.0(4)
O(4)-C(19)-C(17)	101.3(3)
O(4)-C(19)-C(21)	100.4(3)
C(17)-C(19)-C(21)	110.3(4)
O(4)-C(20)-C(18)	100.5(3)
O(4)-C(20)-C(22)	100.0(4)
C(18)-C(20)-C(22)	111.5(4)
C(23)-C(21)-C(22)	104.6(4)
C(23)-C(21)-C(19)	115.4(3)
C(22)-C(21)-C(19)	101.2(4)
C(24)-C(22)-C(21)	105.3(4)
C(24)-C(22)-C(20)	115.1(4)
C(21)-C(22)-C(20)	101.5(4)
O(5)-C(23)-N(2)	124.4(4)
O(5)-C(23)-C(21)	127.1(4)
N(2)-C(23)-C(21)	108.4(4)
O(6)-C(24)-N(2)	124.0(4)
O(6)-C(24)-C(22)	128.0(4)
N(2)-C(24)-C(22)	108.0(4)
N(1)-C(25)-C(26)	111.6(4)
C(27)-C(26)-C(25)	112.8(4)
C(26)-C(27)-C(28)	112.6(4)
C(32)-C(28)-C(27)	118.2(8)
C(32)-C(28)-C(29)	26.2(7)
C(27)-C(28)-C(29)	107.2(7)
C(28)-C(29)-C(30)	111.5(10)
C(32)-C(29)-C(31)	108.8(14)
C(31)-C(30)-C(29)	110.6(8)
C(31)-C(30)-C(33)	97(2)
C(30)-C(31)-C(32)	113.8(7)
C(30)-C(31)-C(29)	107(3)
C(31)-C(32)-C(33)	111.2(10)
C(29)-C(32)-C(28)	103.4(17)
C(30)-C(33)-N(2)	122.6(9)
C(30)-C(33)-C(32)	25.7(8)
N(2)-C(33)-C(32)	105.7(6)

D-4: Anisotropic displacement parameters ($Å^2 x\ 10^3$) for 9-carbon cyclophane.

The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2}U^{11} + ... + 2 h k a^* b^* U^{12}]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	57(2)	74(3)	43(2)	3(2)	-3(2)	8(2)
N(1)	39(2)	43(2)	47(3)	-2(2)	11(2)	-1(2)
C(1)	44(3)	32(3)	33(3)	6(2)	10(2)	3(2)
N(2)	29(2)	37(2)	37(2)	1(2)	7(2)	-1(2)
O(2)	38(2)	90(3)	76(3)	-3(2)	20(2)	9(2)
C(2)	56(3)	29(3)	45(3)	-2(2)	9(2)	4(2)
O(3)	49(2)	43(2)	64(2)	1(2)	14(2)	9(2)
C(3)	39(3)	33(3)	41(3)	3(2)	12(2)	7(2)
O(4)	62(2)	41(2)	47(2)	9(2)	8(2)	-15(2)
C(4)	38(3)	39(3)	57(3)	2(2)	16(2)	14(2)
O(5)	54(2)	52(2)	44(2)	-7(2)	6(2)	-9(2)
C(5)	42(3)	40(3)	34(3)	5(2)	6(2)	5(2)
O(6)	51(2)	59(2)	38(2)	-1(2)	2(2)	-10(2)
C(6)	39(3)	42(3)	47(3)	8(2)	7(2)	4(2)
C(7)	40(3)	53(3)	42(3)	-5(2)	-1(2)	5(2)
C(8)	47(3)	59(4)	48(3)	5(3)	2(2)	14(3)
C(9)	38(3)	49(3)	45(3)	-14(2)	1(2)	-6(2)
C(10)	33(3)	63(4)	47(3)	-5(3)	-2(2)	-1(2)
C(11)	36(3)	34(3)	52(3)	-8(2)	8(2)	-7(2)
C(12)	27(3)	54(3)	68(4)	-3(3)	13(3)	-2(2)
C(13)	41(3)	27(2)	41(3)	4(2)	12(2)	2(2)
C(14)	48(3)	35(3)	33(3)	-1(2)	12(2)	3(2)
C(15)	39(3)	33(3)	31(3)	-3(2)	-5(2)	-5(2)
C(16)	53(3)	32(3)	32(3)	-5(2)	-3(2)	3(2)
C(17)	46(3)	21(2)	32(3)	1(2)	7(2)	-1(2)
C(18)	44(3)	23(2)	46(3)	-3(2)	6(2)	-3(2)
C(19)	45(3)	39(3)	36(3)	0(2)	5(2)	-12(2)
C(20)	59(3)	40(3)	43(3)	-1(2)	6(2)	-13(2)
C(21)	32(2)	46(3)	40(3)	5(2)	5(2)	-8(2)
C(22)	32(3)	47(3)	48(3)	4(2)	4(2)	-11(2)
C(23)	27(2)	46(3)	45(3)	0(2)	7(2)	4(2)
C(24)	26(2)	44(3)	42(3)	-2(2)	4(2)	-3(2)
C(25)	55(3)	54(3)	46(3)	9(3)	15(3)	3(3)
C(26)	60(3)	58(4)	49(3)	1(3)	16(3)	9(3)
C(27)	66(4)	47(3)	42(3)	2(2)	13(2)	-2(3)
C(28)	49(3)	74(4)	82(5)	27(3)	17(3)	-5(3)
C(33)	70(4)	37(3)	48(3)	1(3)	24(3)	0(2)

D-5: Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for 9-carbon cyclophane.

	x	y	z	U(eq)
H(2)	5162	-3319	7926	32(11)
H(3)	4422	-1337	9571	24(10)
H(4)	6873	-3029	8618	31(11)
H(7)	6129	-598	11039	69(16)
H(8)	8218	-2154	10418	68(15)
H(9)	7350	211	10402	81(17)
H(10)	8592	-662	10215	74(16)
H(14)	3533	-2907	6782	8(8)
H(15)	3184	-2388	9719	28(10)
H(16)	1854	-3352	6199	19(9)
H(19)	1346	-3098	10012	45(12)
H(20)	206	-3892	7024	51(13)
H(21)	-269	-2429	9237	51(13)
H(22)	-923	-2900	7540	32(11)
H(25A)	7291	-90	6727	71(16)
H(25B)	6198	221	6792	60(14)
H(26A)	6188	-996	5618	56(14)
H(26B)	6664	-1546	6667	51(13)
H(27B)	5185	-1183	7269	52(13)
H(27A)	4981	-1821	6274	78(17)
H(28B)	4125	-842	5124	67(17)
H(28A)	4698	-58	5823	92(19)
H(29A)	3813	-304	7142	21
H(29B)	3293	-1137	6522	21
H(29C)	3185	361	6465	174
H(29D)	3934	-273	7271	174
H(30A)	2880	563	5569	50
H(30B)	2284	-283	5077	50
H(30C)	1065	-829	5920	40
H(30D)	1234	168	6237	40
H(31A)	1257	418	5899	70
H(31B)	2159	587	6944	70
H(31C)	2179	-1243	7422	114
H(31D)	2167	-328	7972	114
H(32A)	2126	-775	7534	40
H(32B)	1508	-1112	6382	40
H(32C)	2846	-522	5253	106
H(32D)	3174	-1314	6060	106
H(33A)	650	-52	7758	81(17)
H(33B)	26	-329	6574	75(17)

Appendix E. *para*-xylyl cyclophane X-ray data.

A crystal of this cyclophane was grown *via* slow evaporation from deuterated chloroform in an NMR tube, and sent to the University of Calgary for X-ray diffraction experiments. The structure was solved independently by both the technician in Calgary and the author of this thesis. the latter is presented here. Twelve molecules are present in the unit cell, with eight on Wyckoff position *f*, and four on Wyckoff position *e*.

The structure was solved by the direct methods and expanded using Fourier techniques. The structure is composed of two independent molecules one of which is centered. Non-hydrogen atoms were refined anisotropically. Hydrogen atoms were not refined, but included at geometrically idealized positions using a riding model. The final cycle of full-matrix least-squares refinement using SHELXTL 5.1 converged (largest parameter shift was 0.00 times its esd) with unweighted and weighted agreement factors, R = 0.054 and wR = 0.134 (all data) respectively, and goodness of fit, S = 0.990. The weighting scheme was based on counting statistics and the final difference map was essentially featureless. The figures were plotted using ORTEP-3 for windows.

E-1: Crystal data and structure refinement for para-***xylyl cyclophane.***

Identification code	kfxyl	
Empirical formula	$C_{32} H_{22} N_2 O_6$	
Formula weight	530.52	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	C2/c	
Unit cell dimensions	a = 24.046(4) Å	α = 90°.
	b = 7.9500(10) Å	β = 90.355(6)°.
	c = 38.356(7) Å	γ = 90°.
Volume	7332(2) $Å^3$	
Z	12	
Density (calculated)	1.442 Mg/m^3	
Absorption coefficient	0.101 mm^{-1}	
F(000)	3312	
Crystal size	0.24 x 0.24 x 0.18 mm^3	
Theta range for data collection	6.47 to 25.04°.	
Index ranges	-27<=h<=-6, -9<=k<=-1, -43<=l<=44	
Reflections collected	3947	
Independent reflections	3947 [R(int) = 0.0000]	
Completeness to theta = 25.04°	60.9 %	
Absorption correction	None	
Max. and min. transmission	0.9821 and 0.9762	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3947 / 0 / 541	
Goodness-of-fit on F^2	0.990	
Final R indices [I>2sigma(I)]	R1 = 0.0535, wR2 = 0.1055	
R indices (all data)	R1 = 0.1151, wR2 = 0.1341	
Largest diff. peak and hole	0.368 and -0.224 e.$Å^{-3}$	

E-2: Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3)for para-xylyl cyclophane.

U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	-1559(1)	6855(4)	1148(1)	54(1)
N(1)	-1403(1)	9179(4)	808(1)	36(1)
C(11)	-1614(1)	7587(6)	873(1)	37(1)
O(2)	-1434(1)	11176(4)	379(1)	60(1)
N(2)	1639(1)	9215(4)	1176(1)	32(1)
C(9)	-1904(1)	6971(5)	552(1)	32(1)
O(3)	-1762(1)	5856(3)	5(1)	33(1)
N(3)	1546(1)	2453(4)	2574(1)	29(1)
C(7)	-1599(1)	5502(5)	362(1)	30(1)
O(4)	1862(1)	9686(4)	603(1)	47(1)
C(5)	-986(1)	5939(5)	358(1)	27(1)
O(5)	1623(1)	8298(4)	1743(1)	39(1)
C(3)	-539(1)	5445(5)	565(1)	28(1)
O(6)	2289(1)	4475(3)	981(1)	38(1)
C(1)	-24(1)	6234(5)	512(1)	27(1)
O(7)	1670(1)	1981(4)	3160(1)	42(1)
C(2)	19(1)	7474(5)	261(1)	33(1)
O(8)	1573(1)	3463(4)	2014(1)	38(1)
C(4)	-434(1)	8011(6)	63(1)	34(1)
O(9)	2108(1)	7259(3)	2825(1)	34(1)
C(6)	-937(1)	7199(5)	117(1)	29(1)
C(8)	-1523(1)	7519(5)	-16(1)	34(1)
C(10)	-1850(1)	8397(5)	285(1)	32(1)
C(12)	-1541(1)	9771(6)	478(1)	38(1)
C(23)	1913(1)	8876(5)	867(1)	35(1)
C(21)	2277(1)	7344(5)	925(1)	34(1)
C(19)	2073(1)	5713(6)	739(1)	35(1)
C(17)	1457(1)	5569(6)	797(1)	30(1)
C(15)	1004(1)	5917(6)	583(1)	31(1)
C(13)	469(1)	5788(5)	732(1)	29(1)
C(14)	416(1)	5331(5)	1076(1)	30(1)
C(16)	877(1)	4991(6)	1298(1)	29(1)
C(18)	1401(1)	5129(5)	1144(1)	31(1)
C(20)	1988(1)	5037(5)	1284(1)	32(1)
C(22)	2204(1)	6887(5)	1311(1)	32(1)
C(24)	1797(1)	8164(5)	1446(1)	29(1)
C(25)	-1132(1)	10207(7)	1076(2)	51(2)
C(26)	-500(1)	10136(6)	1081(1)	37(1)
C(27)	-188(1)	11040(6)	840(2)	40(1)
C(28)	383(1)	11143(6)	879(2)	38(1)

C(29)	656(1)	10337(5)	1152(1)	31(1)
C(30)	349(1)	9347(6)	1375(1)	39(1)
C(31)	-226(1)	9243(6)	1342(1)	40(1)
C(32)	1271(1)	10684(6)	1218(1)	36(1)
C(44)	1759(1)	2817(5)	2899(1)	29(1)
C(42)	2115(1)	4370(5)	2871(1)	31(1)
C(40)	1879(1)	5979(5)	3054(1)	31(1)
C(38)	1268(1)	6073(5)	2960(1)	29(1)
C(36)	789(1)	5644(6)	3140(1)	31(1)
C(34)	290(1)	5715(5)	2948(1)	32(1)
C(33)	267(1)	6163(6)	2600(1)	28(1)
C(35)	760(1)	6577(5)	2420(1)	28(1)
C(37)	1254(1)	6509(5)	2614(1)	27(1)
C(39)	1849(1)	6677(5)	2506(1)	29(1)
C(41)	2090(1)	4864(5)	2485(1)	28(1)
C(43)	1716(1)	3562(5)	2318(1)	26(1)
C(45)	1207(1)	944(6)	2497(1)	35(1)
C(46)	585(1)	1220(5)	2500(1)	30(1)
C(47)	286(1)	1273(7)	2192(2)	46(2)
C(48)	290(1)	1257(7)	2810(2)	46(2)

E-3: Bond lengths [Å] and angles [°] for para-xylyl cyclophane.

Bond Lengths	
O(1)-C(11)	1.211(5)
N(1)-C(12)	1.387(6)
N(1)-C(11)	1.386(5)
N(1)-C(25)	1.463(6)
C(11)-C(9)	1.494(6)
O(2)-C(12)	1.209(5)
N(2)-C(24)	1.381(5)
N(2)-C(23)	1.386(6)
N(2)-C(32)	1.476(5)
C(9)-C(10)	1.535(6)
C(9)-C(7)	1.561(6)
O(3)-C(8)	1.444(5)
O(3)-C(7)	1.452(5)
N(3)-C(44)	1.375(5)
N(3)-C(43)	1.385(5)
N(3)-C(45)	1.480(5)
C(7)-C(5)	1.513(5)
O(4)-C(23)	1.205(5)
C(5)-C(3)	1.389(6)
C(5)-C(6)	1.367(6)
O(5)-C(24)	1.221(5)
C(3)-C(1)	1.405(5)
O(6)-C(19)	1.446(5)
O(6)-C(20)	1.444(5)
C(1)-C(2)	1.382(6)
C(1)-C(13)	1.493(6)
O(7)-C(44)	1.223(5)
C(2)-C(4)	1.391(6)
O(8)-C(43)	1.214(5)
C(4)-C(6)	1.388(6)
O(9)-C(39)	1.446(5)
O(9)-C(40)	1.455(5)
C(6)-C(8)	1.518(5)
C(8)-C(10)	1.565(6)
C(10)-C(12)	1.513(6)
C(23)-C(21)	1.516(6)
C(21)-C(22)	1.533(6)
C(21)-C(19)	1.557(6)
C(19)-C(17)	1.504(5)
C(17)-C(15)	1.388(6)
C(17)-C(18)	1.384(7)
C(15)-C(13)	1.413(5)
C(13)-C(14)	1.375(7)
C(14)-C(16)	1.421(6)

C(16)-C(18)	1.398(5)
C(18)-C(20)	1.508(5)
C(20)-C(22)	1.563(6)
C(22)-C(24)	1.504(6)
C(25)-C(26)	1.521(5)
C(26)-C(31)	1.392(7)
C(26)-C(27)	1.394(7)
C(27)-C(28)	1.382(5)
C(28)-C(29)	1.391(7)
C(29)-C(30)	1.381(7)
C(29)-C(32)	1.523(5)
C(30)-C(31)	1.389(5)
C(44)-C(42)	1.505(6)
C(42)-C(41)	1.536(6)
C(42)-C(40)	1.566(6)
C(40)-C(38)	1.512(5)
C(38)-C(36)	1.391(6)
C(38)-C(37)	1.371(7)
C(36)-C(34)	1.406(6)
C(34)-C(33)	1.380(7)
C(33)-C(35)	1.416(5)
C(33)-C(33)#1	1.491(8)
C(35)-C(37)	1.399(6)
C(37)-C(39)	1.499(5)
C(39)-C(41)	1.555(5)
C(41)-C(43)	1.512(5)
C(45)-C(46)	1.511(5)
C(46)-C(47)	1.379(7)
C(46)-C(48)	1.389(7)
C(47)-C(48)#1	1.385(5)
C(48)-C(47)#1	1.385(5)

Bond Angles

C(12)-N(1)-C(11)	112.9(3)
C(12)-N(1)-C(25)	123.6(4)
C(11)-N(1)-C(25)	123.0(4)
O(1)-C(11)-N(1)	123.9(4)
O(1)-C(11)-C(9)	127.4(4)
N(1)-C(11)-C(9)	108.7(4)
C(24)-N(2)-C(23)	113.1(3)
C(24)-N(2)-C(32)	123.9(4)
C(23)-N(2)-C(32)	122.5(4)
C(11)-C(9)-C(10)	105.5(3)
C(11)-C(9)-C(7)	114.3(3)
C(10)-C(9)-C(7)	101.5(3)
C(8)-O(3)-C(7)	97.2(3)
C(44)-N(3)-C(43)	113.5(3)
C(44)-N(3)-C(45)	123.7(3)
C(43)-N(3)-C(45)	122.6(4)
O(3)-C(7)-C(5)	101.7(3)
O(3)-C(7)-C(9)	99.8(3)
C(5)-C(7)-C(9)	107.1(3)
C(3)-C(5)-C(6)	121.5(3)
C(3)-C(5)-C(7)	132.7(4)
C(6)-C(5)-C(7)	105.3(3)
C(5)-C(3)-C(1)	118.1(4)
C(19)-O(6)-C(20)	97.2(3)
C(2)-C(1)-C(3)	119.3(3)
C(2)-C(1)-C(13)	120.0(3)
C(3)-C(1)-C(13)	120.7(4)
C(4)-C(2)-C(1)	122.5(3)
C(6)-C(4)-C(2)	117.1(5)
C(39)-O(9)-C(40)	97.1(3)
C(4)-C(6)-C(5)	121.4(3)
C(4)-C(6)-C(8)	132.8(4)
C(5)-C(6)-C(8)	105.5(3)
O(3)-C(8)-C(6)	101.4(3)
O(3)-C(8)-C(10)	99.5(3)
C(6)-C(8)-C(10)	107.1(3)
C(12)-C(10)-C(9)	104.4(3)
C(12)-C(10)-C(8)	115.9(3)
C(9)-C(10)-C(8)	102.0(3)
O(2)-C(12)-N(1)	123.5(4)
O(2)-C(12)-C(10)	128.0(4)
N(1)-C(12)-C(10)	108.4(4)
O(4)-C(23)-N(2)	124.6(4)
O(4)-C(23)-C(21)	127.6(4)
N(2)-C(23)-C(21)	107.8(4)
C(23)-C(21)-C(22)	105.3(3)
C(23)-C(21)-C(19)	114.9(3)
C(22)-C(21)-C(19)	101.9(3)
O(6)-C(19)-C(17)	101.7(3)
O(6)-C(19)-C(21)	99.4(3)
C(17)-C(19)-C(21)	107.7(3)
C(15)-C(17)-C(18)	122.6(3)
C(15)-C(17)-C(19)	131.9(5)
C(18)-C(17)-C(19)	105.2(3)
C(17)-C(15)-C(13)	117.4(5)
C(14)-C(13)-C(15)	119.8(3)
C(14)-C(13)-C(1)	121.7(3)
C(15)-C(13)-C(1)	118.4(4)
C(13)-C(14)-C(16)	123.2(3)

C(18)-C(16)-C(14)	115.8(5)
C(16)-C(18)-C(17)	121.2(3)
C(16)-C(18)-C(20)	133.7(5)
C(17)-C(18)-C(20)	105.0(3)
O(6)-C(20)-C(18)	101.6(4)
O(6)-C(20)-C(22)	100.1(3)
C(18)-C(20)-C(22)	106.7(3)
C(24)-C(22)-C(21)	104.5(3)
C(24)-C(22)-C(20)	116.1(3)
C(21)-C(22)-C(20)	101.5(3)
O(5)-C(24)-N(2)	123.5(3)
O(5)-C(24)-C(22)	127.4(4)
N(2)-C(24)-C(22)	109.1(3)
N(1)-C(25)-C(26)	115.3(3)
C(31)-C(26)-C(27)	119.1(3)
C(31)-C(26)-C(25)	119.7(4)
C(27)-C(26)-C(25)	121.0(4)
C(28)-C(27)-C(26)	119.8(4)
C(29)-C(28)-C(27)	121.2(4)
C(28)-C(29)-C(30)	118.5(3)
C(28)-C(29)-C(32)	119.7(4)
C(30)-C(29)-C(32)	121.5(4)
C(29)-C(30)-C(31)	120.9(4)
C(26)-C(31)-C(30)	120.1(4)
N(2)-C(32)-C(29)	114.9(3)
O(7)-C(44)-N(3)	124.1(3)
O(7)-C(44)-C(42)	127.3(4)
N(3)-C(44)-C(42)	108.6(3)
C(44)-C(42)-C(41)	105.0(3)
C(44)-C(42)-C(40)	115.5(3)
C(41)-C(42)-C(40)	102.2(3)
O(9)-C(40)-C(38)	101.1(3)
O(9)-C(40)-C(42)	99.3(3)
C(38)-C(40)-C(42)	106.7(3)
C(36)-C(38)-C(37)	121.8(3)
C(36)-C(38)-C(40)	132.5(5)
C(37)-C(38)-C(40)	105.2(3)
C(38)-C(36)-C(34)	115.9(5)
C(36)-C(34)-C(33)	123.1(3)
C(35)-C(33)-C(34)	120.2(3)
C(35)-C(33)-C(33)#1	118.0(6)
C(34)-C(33)-C(33)#1	121.8(4)
C(37)-C(35)-C(33)	116.2(5)
C(35)-C(37)-C(38)	122.8(4)
C(35)-C(37)-C(39)	131.1(5)
C(38)-C(37)-C(39)	105.8(3)
O(9)-C(39)-C(37)	101.6(3)
O(9)-C(39)-C(41)	100.5(3)
C(37)-C(39)-C(41)	106.8(3)
C(43)-C(41)-C(42)	104.6(3)
C(43)-C(41)-C(39)	115.8(3)
C(42)-C(41)-C(39)	101.4(3)
O(8)-C(43)-N(3)	123.9(3)
O(8)-C(43)-C(41)	127.9(3)
N(3)-C(43)-C(41)	108.2(3)
N(3)-C(45)-C(46)	115.1(3)
C(47)-C(46)-C(48)	117.8(4)
C(47)-C(46)-C(45)	120.6(4)
C(48)-C(46)-C(45)	121.3(4)
C(48)#1-C(47)-C(46)	121.5(4)
C(47)#1-C(48)-C(46)	120.6(4)

Symmetry transformations used to generate equivalent atoms:
#1 (-x), (y), (-z+1/2)

E-4: Anisotropic displacement parameters (Å2x 103) for para-xylyl cyclophane. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	47(2)	84(3)	32(2)	7(2)	1(1)	2(1)
N(1)	27(2)	44(2)	37(3)	-14(2)	-4(1)	6(1)
C(11)	28(2)	53(3)	29(3)	-2(2)	4(1)	8(2)
O(2)	61(2)	32(2)	85(3)	5(2)	-27(2)	4(1)
N(2)	29(2)	30(2)	35(3)	1(2)	-2(1)	-1(1)
C(9)	20(2)	41(2)	35(3)	-1(2)	3(1)	3(1)
O(3)	30(1)	39(2)	30(2)	-7(1)	-5(1)	0(1)
N(3)	28(2)	29(2)	30(2)	-1(2)	-4(1)	2(1)
C(7)	25(2)	34(3)	32(3)	2(2)	-4(1)	1(1)
O(4)	49(2)	58(2)	35(2)	16(2)	-1(1)	-6(1)
C(5)	25(2)	24(3)	30(3)	-6(2)	-1(1)	4(1)
O(5)	40(1)	45(2)	31(2)	-2(1)	-3(1)	2(1)
C(3)	28(2)	28(3)	28(3)	0(2)	-2(1)	5(1)
O(6)	29(1)	48(2)	37(2)	-8(2)	-2(1)	13(1)
C(1)	27(2)	28(3)	27(3)	-7(2)	-4(1)	6(1)
O(7)	43(2)	45(2)	37(2)	9(2)	-9(1)	-4(1)
C(2)	25(2)	41(3)	33(3)	-3(2)	0(1)	-1(1)
O(8)	39(1)	47(2)	27(2)	-1(2)	-4(1)	1(1)
C(4)	32(2)	41(3)	30(3)	7(2)	0(1)	-3(1)
O(9)	28(1)	35(2)	40(2)	-1(1)	-3(1)	-7(1)
C(6)	26(2)	34(3)	27(3)	-1(2)	0(1)	5(1)
C(8)	29(2)	41(3)	32(3)	4(2)	-5(1)	2(1)
C(10)	26(2)	38(2)	32(3)	1(2)	-7(1)	6(1)
C(12)	28(2)	37(3)	51(4)	-5(2)	-7(2)	11(2)
C(23)	28(2)	48(3)	30(3)	5(2)	-2(2)	-9(1)
C(21)	22(2)	52(3)	29(3)	-1(2)	-1(1)	-2(1)
C(19)	25(2)	51(3)	28(3)	-5(2)	1(2)	7(2)
C(17)	29(2)	35(3)	27(4)	-10(2)	-1(2)	5(1)
C(15)	27(2)	42(3)	24(4)	-5(2)	-1(1)	5(1)
C(13)	27(2)	31(3)	29(4)	-4(2)	-1(1)	3(1)
C(14)	27(2)	27(2)	36(3)	0(2)	-1(2)	0(1)
C(16)	34(2)	28(3)	24(3)	2(2)	0(1)	3(1)
C(18)	27(2)	28(3)	37(4)	-6(2)	-2(2)	3(1)
C(20)	27(2)	43(3)	27(3)	0(2)	1(1)	7(1)
C(22)	24(2)	45(3)	28(3)	-2(2)	-4(1)	-1(1)
C(24)	27(2)	35(2)	24(3)	-2(2)	-4(1)	-4(1)
C(25)	38(2)	59(4)	57(4)	-33(3)	-11(2)	12(2)
C(26)	34(2)	40(3)	38(3)	-16(2)	-7(2)	8(2)
C(27)	47(2)	33(3)	39(4)	-6(3)	-13(2)	10(2)
C(28)	48(2)	28(3)	37(4)	-1(2)	-6(2)	-1(2)
C(29)	36(2)	25(3)	32(3)	-7(2)	-4(2)	2(1)

C(30)	41(2)	37(3)	40(4)	3(3)	-10(2)	2(2)
C(31)	38(2)	43(3)	39(4)	-4(3)	-4(2)	-7(2)
C(32)	41(2)	30(3)	36(3)	-4(2)	-9(2)	-1(1)
C(44)	27(2)	33(2)	28(3)	5(2)	-2(1)	6(1)
C(42)	18(2)	43(3)	32(3)	-2(2)	-3(1)	3(1)
C(40)	28(2)	39(3)	27(3)	0(2)	-1(1)	-1(1)
C(38)	24(2)	31(3)	33(4)	-6(2)	-2(1)	0(1)
C(36)	34(2)	38(3)	22(3)	5(2)	2(1)	2(1)
C(34)	22(2)	36(3)	36(4)	0(2)	5(1)	-1(1)
C(33)	23(2)	28(3)	33(3)	-3(2)	1(1)	0(1)
C(35)	29(2)	25(2)	30(4)	5(2)	2(2)	1(1)
C(37)	24(2)	27(3)	31(4)	-3(2)	-1(2)	2(1)
C(39)	23(2)	33(3)	31(3)	1(2)	-2(1)	-1(1)
C(41)	21(2)	34(2)	30(3)	3(2)	0(1)	1(1)
C(43)	23(2)	29(2)	26(3)	-2(2)	0(1)	7(1)
C(45)	36(2)	24(3)	44(4)	-3(2)	-6(2)	3(1)
C(46)	35(2)	19(2)	34(3)	-3(2)	-4(2)	1(1)
C(47)	38(2)	68(4)	31(4)	0(3)	2(2)	5(2)
C(48)	40(2)	64(4)	33(4)	1(3)	-10(2)	-4(2)

E-5: Hydrogen coordinates (x 104) and isotropic displacement parameters (Å2x 10 3) for para-xylyl cyclophane.

	x	y	z	U(eq)
H(9)	-2302	6689	598	38
H(7)	-1690	4346	448	37
H(3)	-581	4598	738	33
H(2)	372	7979	222	39
H(4)	-401	8895	-102	41
H(8)	-1550	8076	-250	41
H(10)	-2223	8793	203	38
H(21)	2675	7590	870	41
H(19)	2196	5580	492	41
H(15)	1051	6231	346	37
H(14)	52	5238	1169	36
H(16)	833	4689	1535	35
H(20)	2039	4338	1499	39
H(22)	2566	6946	1440	39
H(25A)	-1269	9843	1307	61
H(25B)	-1248	11392	1042	61
H(27)	-367	11583	649	47
H(28)	592	11777	716	45
H(30)	532	8730	1554	47
H(31)	-432	8560	1498	48
H(32A)	1393	11579	1056	43

H(32B)	1315	11120	1458	43
H(42)	2506	4138	2948	37
H(40)	1971	6102	3307	37
H(36)	798	5323	3379	38
H(34)	-47	5442	3062	38
H(35)	756	6884	2180	34
H(39)	1915	7397	2296	34
H(41)	2469	4859	2378	34
H(45A)	1299	63	2670	42
H(45B)	1313	511	2265	42
H(47)	479	1321	1977	55
H(48)	486	1271	3026	55