SYNTHESIS OF PERFLUORO[2.2]PARACYCLOPHANE AND ITS NUCLEOPHILIC SUBSTITUTIONS

By

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A DISSERTATION PRESENTED TO THE GRADUATE SCHOOL
OF THE UNIVERSITY OF FLORIDA IN PARTIAL FULFILLMENT
OF THE REQUIREMENTS FOR THE DEGREE OF
DOCTOR OF PHILOSOPHY

UNIVERSITY OF FLORIDA

2009

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To my wife, Jinfeng Peng, my son, Pengcheng, and my daughter, Nina,
with love

ACKNOWLEDGMENTS

I am deeply indebted to my supervisor, Professor William R. Dolbier, Jr., for his invaluable guidance, encouragement, and trust over years. It has been a rewarding experience and great honor to work with him.

I would also like to take this opportunity to express my sincere gratitude to Drs. Weihong Tan, Sukwon Hong, Lisa McElwee-White and Kenneth Sloan for their help, suggestions and time they have spent as my supervisory committee members.

I am extremely grateful to Dr. Ion Ghiviriga for his critical help to elucidate the ^{19}F NMR data to determine the regiochemistry of the multiple-substituted compounds.

I would like to give my special thanks to Henry Martinez for his helpful discussion and support for computer technologies. My thanks also go to all Dolbier group members and my friends outside who are too many to mention individually, for their support and friendship.

I deeply appreciate my parents for their unconditional love, support and encouragement, without which I cannot become a doctor.

Finally, I am extremely grateful to my wife, Jinfeng Peng for everything she has done for me.

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December 2009

Chairman: William R. Dolbier, Jr.
Major Department: Chemistry

Perfluoro[2.2]paracyclophane and perfluoro[2.2.2]paracyclophane have been successfully synthesized in 42% and 1.2% yield respectively from their precursor, 1,4-bis (chlorodifluoromethyl)-2,3,5,6-tetrafluorobenzene by its reaction with activated zinc dust when heated in anhydrous acetonitrile at 100 ^{o}C. Two preparations of the precursor, first from 1,4-dicyano-2,3,5,6-tetrachlorobenzene and an improved method beginning from 1,2,4,5-tetrachlorobenzene, are also described and discussed as are key comparisons to our related synthesis of AF4. Perfluoro[2.2]paracyclophane was then used as starting materials in reactions with a large variety of nucleophiles.

The aromatic fluorines of perfluoro[2.2]paracyclophane are extremely reactive with respect to nucleophilic substitution reactions. Chapter 3 emphasizes products of monosubstitution with hydroxide, alkoxide, *tert*-butyl lithium, thiolates, amines and dimethyl malonate in the presence of sodium hydride. Reactions of bidentate nucleophiles with perfluoro[2.2]paracyclophane provide cyclic products. All reactions appear to proceed via S_NAr mechanisms. Reactivity issues are discussed including the effects of substituents on the further reactivity and regiochemistry of multisubstitution.

The UV-vis absorption spectra of products show a progression toward longer wavelength absorption as the substitutents become increasingly electron donating.

Bis-nucleophilic substitutions of F8 with sodium thiolates show replacement of the fluorine atom *para* to the first substitutent on the same benzene ring. In comparison, treatment of F8 with sodium 4-fluorophenolate or secondary amines gives a mixture of bis-substituted F8 derivatives. Reaction of F8 with 4 equivalents of sodium thiolates furnishes tetrakis-substituted F8 derivatives which contain two regioisomers. Each benzene ring has two substituents *para* to each other. The ratio of the two isomers is dependent on the group that is attached to sulfur. Treatment of F8 with 4 equivalents of sodium 4-fluorophenolate gives only one isomer. The reaction of F8 with 8 equivalents of pyrrolidines provides two tri-substituted F8 isomers. Treatment of F8 with two equivalents of 1,2-benzene-dithiol in the presence of sodium hydride furnishes bis-cycloadducts on the same benzene ring as a major product. Transannular effects of these products are measured by UV-vis spectra.

CHAPTER 1
AN OVERVIEW: SYNTHETIC METHODS OF [2.2]PARACYCLOPHANE, FLUORINATED[2.2]PARACYCLOPHANES AND THEIR APPLICATIONS

1.1 Introduction

[2.2]Paracyclophane ([2.2]PCP) chemistry has grown considerably since the parent [2.2]PCP was first prepared in 1949.[1] Besides commercial application as monomers for parylene-type polymers,[2] these molecules have spawned an unusual and unique chemistry.[3] The two eclipsing aryl rings, or decks are held rigidly in place at the *para* positions by ethylene bridges. The proximity of the decks prohibits rotation of the rings without cleavage of one of the bridge C-C bonds, which normally does not occur below 180^{o}C. The separation of the two aromatic rings is less than the sum of the van der Waals radii for carbon (3.40 Å) ranging from 2.78 Å for the bridging carbons (C6-C11) to a maximum of 3.09 Å between C4-C13.[3] The rigid structure results in the bridge σ bonds (C1-C2 and C9-C10) being held almost perpendicular to the aryl rings allowing a strong σ-π interaction as observed by the lengthening of the C-C bond (1.63 vs 1.54 Å in ethane) (Figure 1-1). There is a strong repulsion between the two decks resulting in distortion of the aryl rings to give them a shallow boat-like geometry. It also engenders a strong π interaction between the rings that can lead to unique extended π systems. Both its distinct electronic structure and the distortion of the rings increases the basicity /nucleophilicity of the benzene group of [2.2]PCP; it undergoes electrophilic substitution more rapidly than simple aryl systems and has an enhanced ability to form π-complexes; for instance, the first order rate constant for the reaction of [2.2]PCP with $Cr(CO)_6$ is ca. 25% greater than for *p*-xylene.[4]

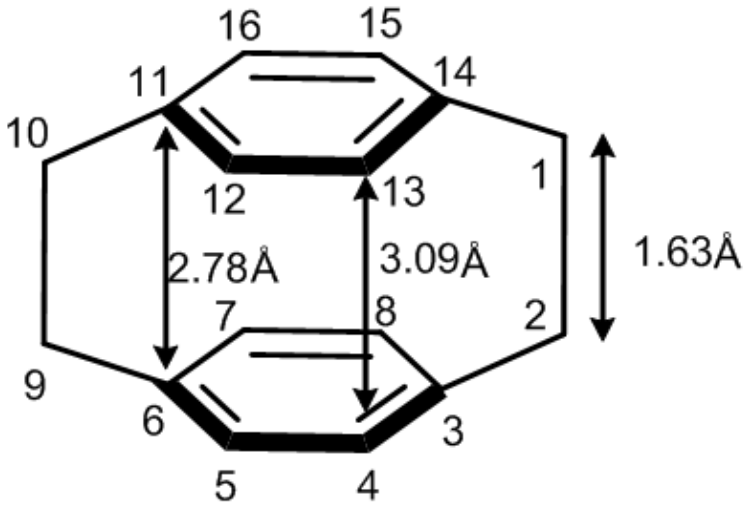


Figure 1-1 Structure of [2.2]paracyclophane

The chemistry of [2.2]PCP can generally be understood if one considers its unique structure. To a degree, its reactivity is that of a classic aromatic compound, keeping in mind that substituents on one deck can have a profound influence on the reactivity of the other deck. However, this simple srutucture (Figure 1-1) does not always hold up to close scrutiny; due to its distorted structure, steric effects, and the unique π-interactions, [2.2]paracyclophane derivatives are often resistant to conventional transformations.[5] The combination of all these facets often makes understanding the chemistry of [2.2]PCPs such an interesting challenge.

This overview will describe four aspects of [2.2]paracyclophane chemistry: 1. Synthetic methods of [2.2]paracyclophane and fluorinated[2.2]paracyclophanes. 2. Applications of [2.2]paracyclophane, octafluoro[2.2]paracyclophane and their derivatives. 3. Reactivity and reactions of [2.2]paracyclophane. 4. Reactions of octafluoro[2.2]paracyclophane and its derivatives.

1.2 Synthesis of [2.2]Paracyclophane and Fluoronated [2.2]paracyclophane

1.2.1 Synthetic Methods for [2.2]Paracyclophane

[2.2]PCP was first synthesized by C. J. Brown and A. C. Farthing.[1] *p*-Xylene was pyrolyzed at low pressure using the technique described by Szwarc,[6] and extraction of the polymer with chloroform yielded low molecular-weight compounds. This extract contained traces of an acetone-insoluble fraction, having m.p 285 ^{o}C, which after recrystallization from pyridine and glacial acetic acid yielded [2.2]PCP (Figure 1-2).

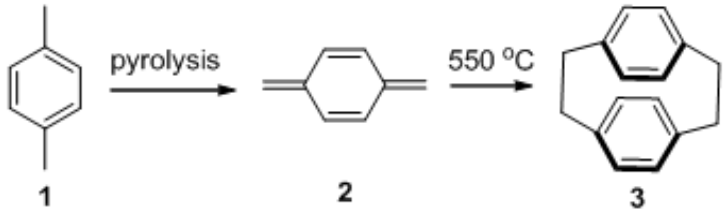


Figure 1-2 Synthesis of [2.2]PCP by pyrolysis of *p*-xylene

A second synthetic method for [2.2]PCP was developed by D. J. Cram and H. Steinberg[7] via an intramolecular Wurtz reaction with dibromide (**4**) to give only 2.1% yield. This reaction had two major disadvantages: 1. The yield was too low. 2. The reaction required tedious work with dibromide being added over 60 h period to sodium with stirring at 7000 r.p.m. (Figure 1-3). However, the observation of this reaction changed the mind of chemists, who had considered that the ring strain evidently present in the molecule could only be overcome by the extreme conditions of the pyrolysis reaction. These initial inferences were proved incorrect, when the [2.2]PCP was subsequently prepared by the intramolecular Wurtz reaction with dibromide. This reaction initiated further development of [2.2]PCP chemistry.

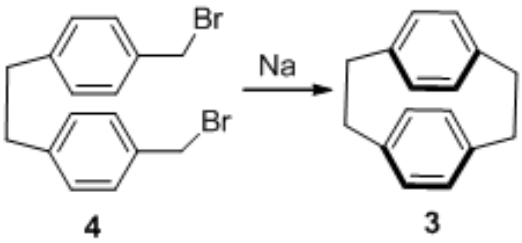


Figure 1-3 Synthesis of [2.2]PCP by intramolecular Wurtz reaction

The commercial production method for [2.2]PCP was eventually developed by T. Otsubo, H. Horita and S. Misumi.[8] *N,N,N*- Trimethyl-1-*p*-tolylmethanammonium chloride was pyrolyzed in xylene at 140 ^{o}C to form [2.2]PCP in 33% yield, when phenothiazine was used as an inhibitor to avoid radical polymerization of the quinodimethane (**2**) intermediate (Figure 1-4).

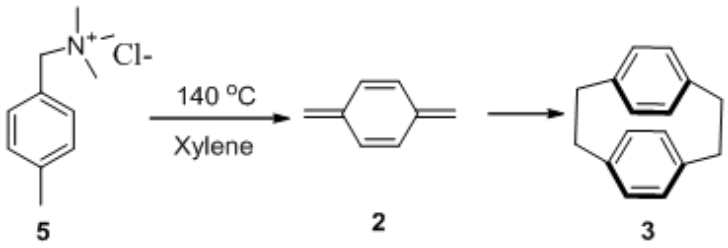


Figure 1-4 Preparation of [2.2]PCP by pyrolysis of ammonium salt (**5**)

1.2.2 Synthetic Methods for Octafluoro[2.2]paracyclophane

The first synthetic method for preparation of octafluoro[2.2]paracyclophane (AF4) was the tedious Chow procedure[9] (Figure 1-5). α, α'-Bis(alkylsulfonyl)-α, α, α', α'-tetrafluoro-*p*-xylene (**6**) was pyrolyzed at 600-800 ^{o}C with steam as diluent, After the pyrolysate was condensed in toluene, isolation and purification of octafluoro[2.2]para-cyclophane (**9**) was accomplished by evaporation, recrystallization, and sublimation. Variation of the alkyl groups in **6** from ethyl to butyl exhibited no significant difference in yields or in pyrolysis conditions. Steam-diluted pyrolysis of α, α'-dihalo-α, α, α', α'-tetrafluoro-*p*-xylene (**7**) under similar conditions also yielded **9**. Optimum yields (28.8%) were obtained when the pyrolysis chamber was packed with copper mesh. This method

provided enough material to obtain preliminary physical and chemical data on the dimer and its Parylene polymer to recognize the potential of the latter material.

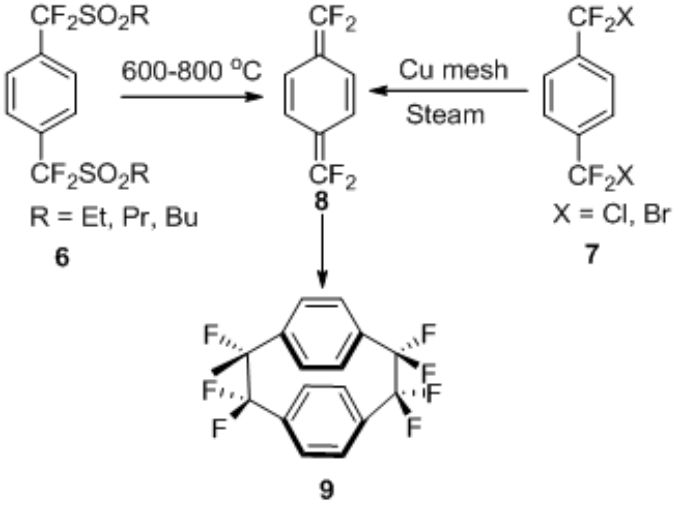


Figure 1-5 Synthesis of AF4 by pyrolysis of bisalkylsulfonyl (**6**) or dihalo-*p*-xylene (**7**)

Since then, Dolbier et al reported a reduction process utilizing Ti^0, using high dilution technology to generate and dimerize the *p*-xylylene monomer. This process allowed preparation of gram quantities of AF4 for the first time.[10,11] However, the process also proved virtually impossible to scale up significantly, with oligomerization of the *p*-xylylene monomer dominating dimerization as quantities were increased (Figure 1-6).

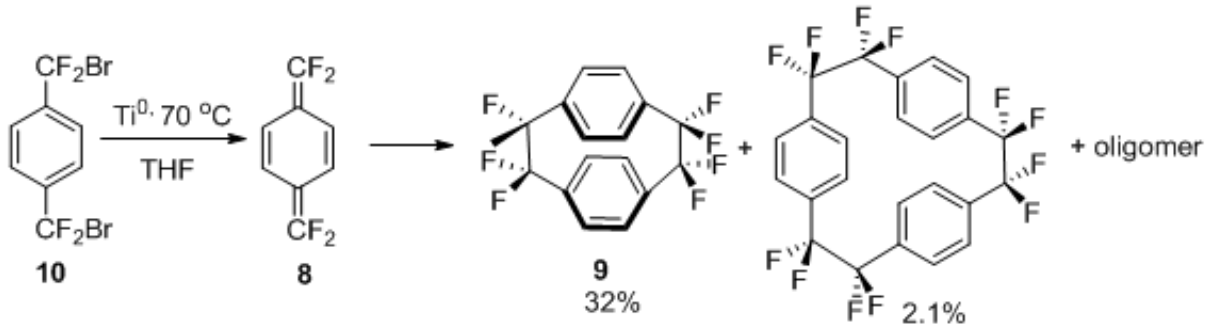


Figure 1-6 Preparation of AF4 using Ti^0 as reducing reagent

Subsequently, a process involving the use of (trimethylsilyl)tributyltin with CsF instead of Ti^0 resulted in a higher yield (40%), and scale-up was feasible in the

preparation of AF4[12,13]. Indeed, kilogram quantities of AF4 were prepared for the first time using this procedure in 72-L glass equipment. However, commercial use of this method was inhibited by the high costs of the required dibromide (**10**) and use of the tinsilane as a reducing agent including the potentially hazardous nature of the latter reagent (Figure 1-7).

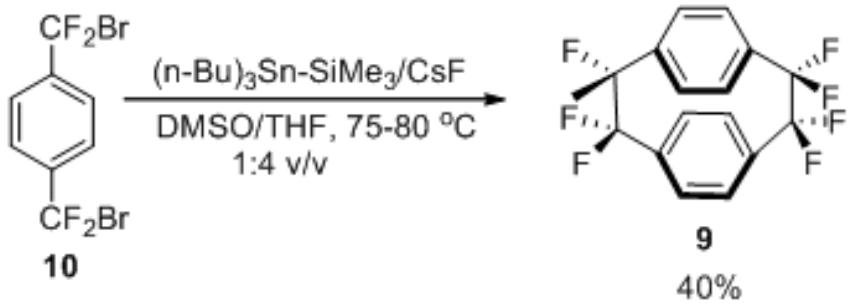


Figure 1-7 Preparation of AF4 using tinsilane as reducing reagent

The current commercial production procedure[14,15] for preparation of AF4 was discovered by Dolbier et al in 1998. A mixture of 1,4-bis-(chlorodifluoromethyl)benzene (**11**) and 4 equivalents of zinc dust in dimethylacetamide was heated to 100 ^{o}C for 4 h to produce AF4 in 60% yield. The precursor, 1,4-bis-(chlorodifluoromethyl)benzene (**11**) was prepared by the reaction of commercially available hexachloro-*p*-xylene with anhydrous HF at a low pressure in 80% yield. This procedure proved superior in every regard to the earlier methods. It used an inexpensive and readily accessible precursor , 1,4-bis-(chlorodifluoromethyl)benzene (**11**), an inexpensive, commercially available reducing reagent, zinc powder, and the AF4-forming reaction could be carried out by a non-high dilution procedure that proved to be highly scaleable (Figure 1-8). This invention was a milestone in the history of preparation of AF4.

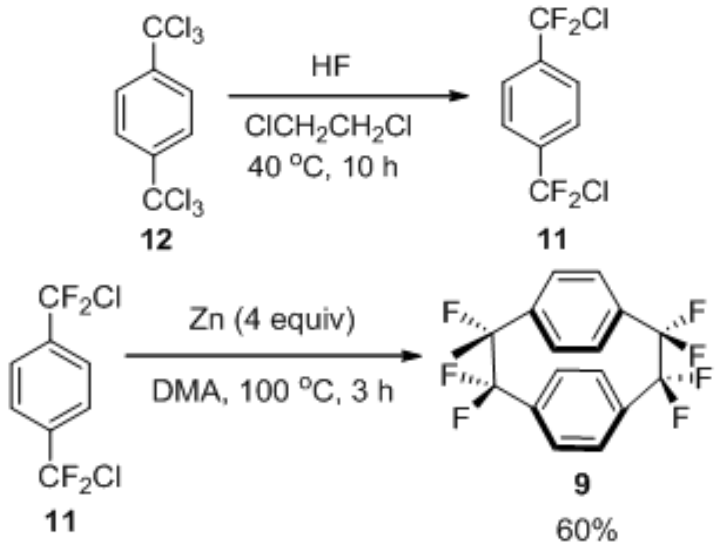


Figure 1-8 Synthesis of AF4 precursor (**11**) and AF4 using zinc as reducing reagent

1.2.3 Synthesis of 1,1,9,9-Tetrafluoro[2.2]paracyclophane and 1,1,10,10-Tetrafluoro-[2.2]paracyclophane

Bromination of [2.2]PCP with NBS in dry carbon tetrachloride[16] gave a mixture of 1,1,9,9-tetrabromo[2.2]PCP (**12**) and 1,1,10,10-tetrabromo[2.2]PCP (**13**) in a 2:3 ratio with a yield of 34%. The mixture of **12** and **13** was treated with $AgBF_4$ in anhydrous dichloromethane to provide a mixture of 1,1,9,9-tetrafluoro[2.2]PCP (**14**) and 1,1,10,10-tetafluoro[2.2]PCP (**15**),[17] followed by sublimation, column chromatography and fractional recrystallization to provide **14** and **15** in combined 50% yield (Figure 1-9).

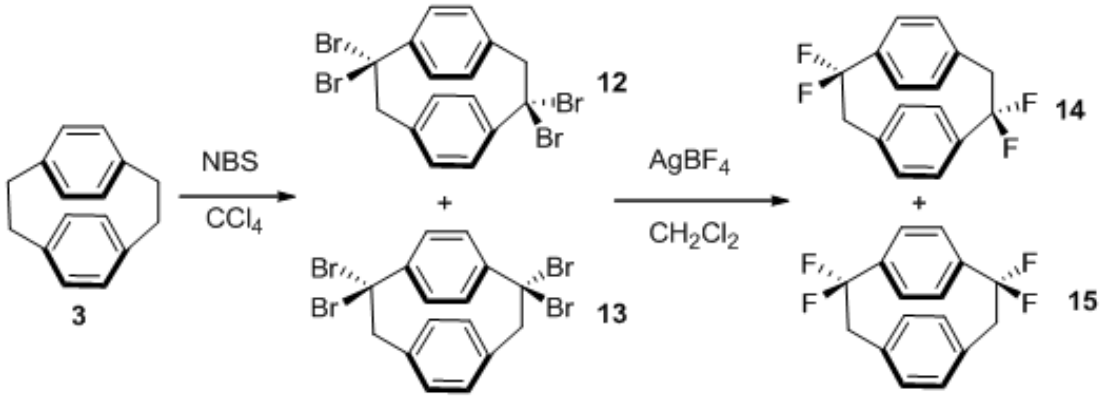


Figure 1-9 Synthesis of 1,1,9,9-tetrafluoro[2.2]PCP and 1,1,10,10-tetrafluoro[2.2]PCP

1.2.4 Synthesis of 4,5,7,8-Tetrafluoro and 4,5,7,8,12,13,15,16-Octafluoro[2.2]-paracyclophane

4,5,7,8,12,13,15,16-Octafluoro[2.2]PCP (**16**) was most efficiently prepared by 1,6 Hofmann elimination from the quaternary ammonium hydroxide compound derived from 4-methyl- tetrafluorobenzyl bromide via the unstable tetrafluoro-*p*-xylylene (Figure 1-10). With vigorous mixing in dilute solutions, **16** was obtained in 42% yield.[18]

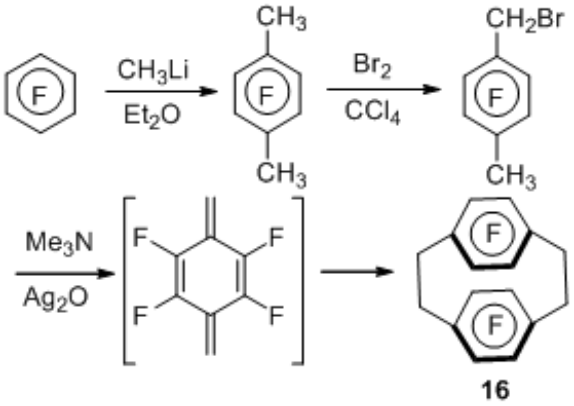


Figure 1-10 Synthesis of 4,5,7,8,12,13,15,16-octafluoro[2.2]PCP

5,6,8,9-Tetrafluoro-2,11-dithio[3.3]PCP (**17**) was obtained in high yields by condensation of either of two pairs of molecules. Extrusion of the two sulfur atoms in **17** afforded **18** in 24% yield[18] (Figure 1-11).

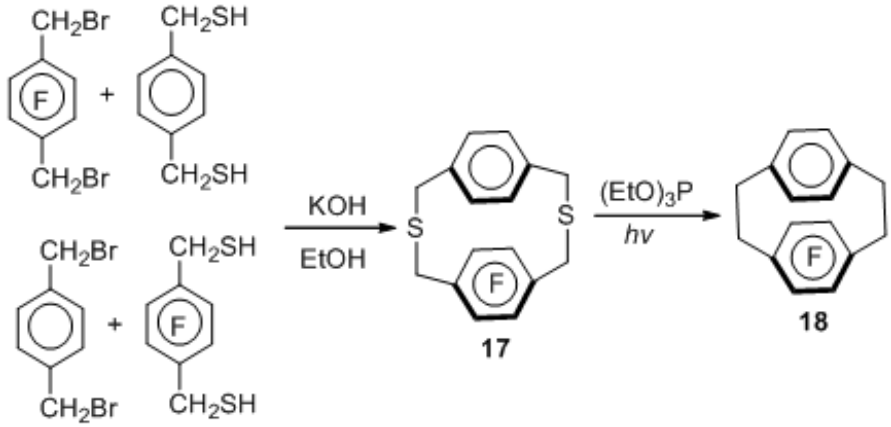


Figure 1-11 Synthesis of 4,5,7,8-tetrafluoro[2.2]PCP

1.3 Applications of [2.2]Paracyclophane, Octafluoro[2.2]Paracycyclophane and Their derivatives.

1.3.1 Application of [2.2]Paracyclophane

[2.2]PCPs are useful chemical vapor deposition (CVD) precursor of thin film polymers, known in the industry as Parylenes (Figure 1-12).[2] Such Parylenes are ideally suited for use as conformal coatings in a wide range of applications, such as in the automotive, medical, electronics, and semiconductor industries. Parylene coatings are chemically inert, transparent and have excellent barrier properties.[19] Parylene N, which is generated from the parent hydrocarbon (**3**) has been found to be useful for several hours at temperatures up to 130 ^{o}C. Compared to other polymers, Parylene-N coatings are well known for 1. gas phase deposition and polymerization, 2. pinhole-free deposition at room temperature, 3. adherence to metals, composites, plastics and elastomers, 4. infinitely controllable thickness, 5. effective gap fill.

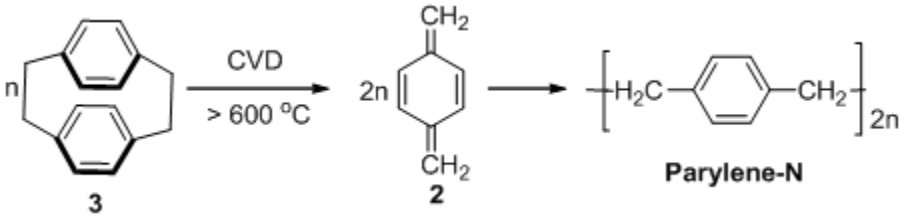
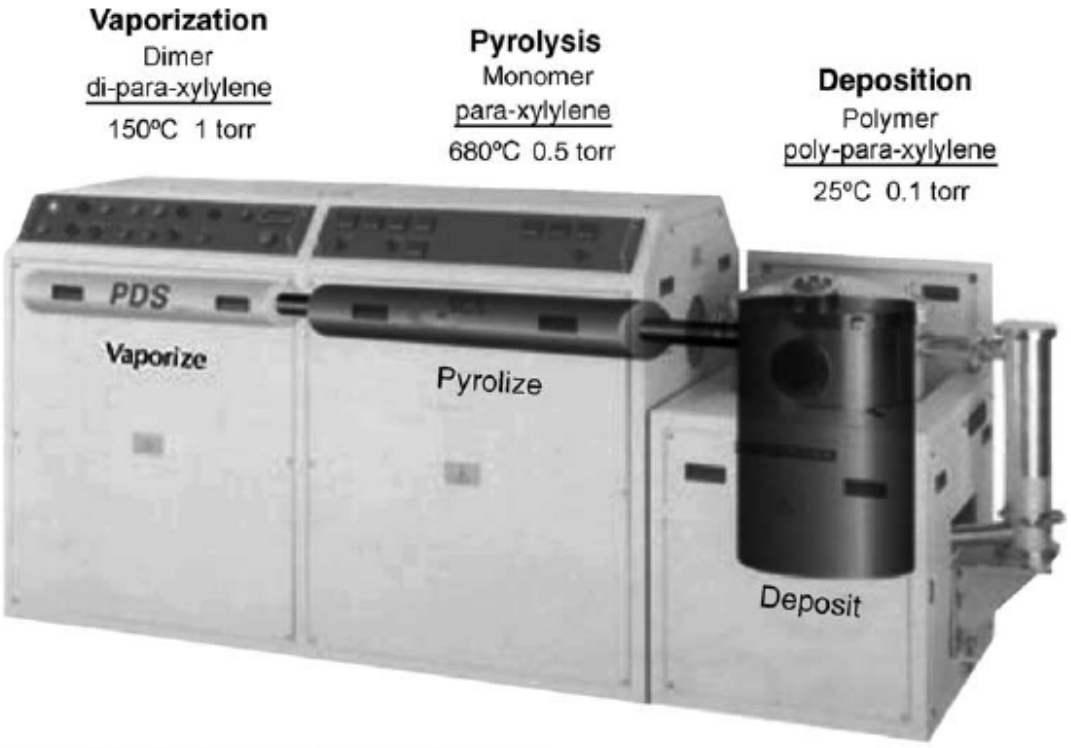


Figure 1-12 [2.2]PCP and the conversion to Parylene-N polymer

Why do chemists need to make the dimer first? It is a difficult job and very expensive. Can *p*-xylylene (**2**) be prepared from other precursors? The answer is yes. But by starting the coating process with dimer, one can generate the necessary *p*-xylylene (**2**) in the most unambiguous manner, without any gaseous by-products at all. The gaseous by-products produced by most other routes to *p*-xylylene (**2**) range from the corrosive gas (HCl, SO_2) to carbon dioxide and hydrocarbons, and they are produced in integral molar ratios relative to the *p*-xylylene (**2**).

What equipment can be used for the process shown in Figure 1-12? Gorham[2] designed the operation equipment for this process displayed in Figure 1-13. [2.2]PCP is vaporarized at 150 ^{o}C under vacuum (1 torr.) in the 1st chamber. The dimer is pyrolyzed to *p*-xylylene (monomer) at 680 ^{o}C (0.5 torr.) in the 2nd chamber. The monomer is polymerized into Parylene-N coatings at 25 ^{o}C (0.1 torr.) in the 3rd chamber. The process flow of *p*-xylylene monomer into the deposition chamber is on the order of 100 sccm (standard cubic centimeters per minute), depending to a major extent on payload surface area. This particular flow is equivalent to a little over 0.6 g/min. of Parylene-N.



source: http://www.scscookson.com/parylene/

Figure 1-13 Gorham process for conversion of [2.2]PCP to Parylene polymers

1.3.2 Application of Octafluoro[2.2]paracyclophane

Octafluoro[2.2]PCP (**9**) which was known in the industry as Parylene-HT was heated to more than 600 ^{o}C to pyrolyze it to the monomer **8**, which polymerized at low

temperature to form Parylene-HT polymer, poly(α,α,α',α'-tetrafluoro-*p*-xylylene) (Figure 1-14). In addition to keeping the properties of Parylene-N coatings, The Parylene-HT polymer combines a low dielectric constant (Parylene-HT polymer $(C_8H_4F_4)n$ of 2.25 prediction with a density of 1.584g/ mL versus Parylene-N $(C_8H_8)n$ of 2.76 with a density of 1.110 g/mL), with high thermal stability (<1% loss/ 2 h at 450^oC), low moisture absorption (<0.1%) and other advantageous properties. With such properties, and because its in *vacuo* deposition process ensures conformality to microcircuit features and superior submicron gap-filling capability, Parylene-HT could have considerable application as an interlayer dielectric for on-chip high speed semiconductor device interconnections.

It is predicted that the more fluorine-hydrogen replacements we make, the lower the dielectric constant will be. The perfluorinated version of Parylene, which we call Parylene F8 (the polymer of perfluorinated *p*-xylylene C_8F_8) is the logical end of this path, and is predicted to have an isotropic dielectric constant of 2.11 and a density of 1.93 g/mL). To our knowledge, no synthetic method of preparation of perfluoro[2.2]para-cyclophane (F8) existed, therefore, synthesis of F8 was a desirable research goal.

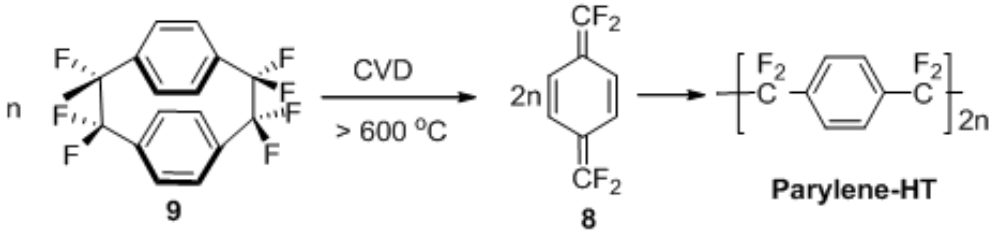


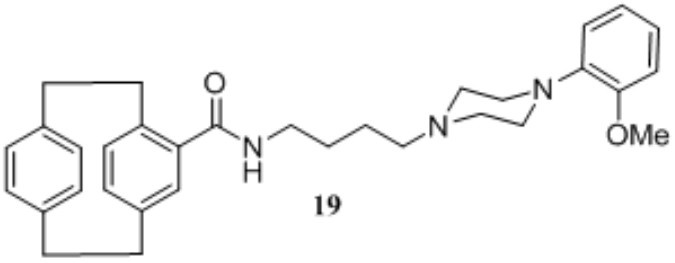
Figure 1-14 AF4 and their conversion to Parylene-HT polymers

1.3.3 Application of [2.2]Paracyclophane Derivatives

Traditionally, [2.2]PCP derivatives have been studied because of their unusual geometry, their steric, transannular and ring strain effects. They have been studied as

probes for investigation of theories on bonding, ring strain and π electron interactions.[3-5, 19-23]

Modern applications have seen [2.2]PCP used in biomedical research with various derivatives being employed as bioisoteres for a variety of heterocyclic systems.[24] For instance, Compound **19** displayed interesting binding profiles as a D3 antagonists, which might be a starting point for the development of highly beneficial CNS active drugs, especially for the treatment of schizophrenia. Because of



19

the planar chirality of the cyclophane skelton, stereochemical differentiation was observed when the (*R*)-enantiomer **(*R*)-19** showed significantly higher D3 affinity. Moreover, the high steric demand of the paracyclophanes of type **19** is well tolerated by the binding site of the dopamine D3 receptor, indicating substantial plasticity of the receptor-excluded volumes. Thus, the paracyclophane derived D3 antagonists should serve as valuable molecular probes for the investigation of GPCR-ligand interactions. It is quite remarkable that the relatively bulky [2.2]PCP moiety can be employed as a pharmaceutical element.

Recent research has seen its properties exploited in two main areas: Its electronic properties have been utilized in the design of electron donor-acceptor compounds[25] and a variety of molecular electronic materials such as linear and non-linear optoelectronics and conductive polymers.[26] [2.2]PCPs are serving as excellent

donating systems for electron donor-acceptor compounds comparable to classical aromatic compounds, and it has been proven that this behavior is mainly due to the presence of transannular electronic interactions between the two benzene rings in the cyclophane molecule. El-Shaieb et al used 4,13-diamino-[2.2]PCP (**20**) as electron donor to investigate its donating properties towards electron acceptors such as 7,7,8,8-tetracyanoquino- dimethane (TCNQ, **21**), 2-dicyanomethyleneindan-1,3-dione (CNIND, **22**), 2,3-dichloro-1,4-naphthoquinone (DCHNQ, **23**), 2,3-dicyano-1,4-naphthoquinone (DCNQ, **24**), and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ, **25**) to give corresponding electron donor-acceptor compounds **26-33** respectively. The results of the reactions between **20** and these acceptors are shown in Figure 1-15. The attack of the two molecules of the acceptor at the same nitrogen to give compounds **29**, **31** and **33** rather than forming compound **34** may be rationalized in terms of the stability of the resonance structures **36-38** (Figure 1-16). It is evident that in structure **35**, the two positively charged nitrogen atoms are located in a *pseudo-geminal* position so they are so close to each other to make this alternative adduct unstable because of electronic repulsion. On the other hand, in structures **37** and **38**, the lone pair of electrons on the disubstituted nitrogen atom enters into conjugation with the two-quinone moieties.

Valentini et al reported the synthesis and photoelectrical properties of two [2.2]PCP derivatives **39** and **40** (Figure 1-17), bearing conjugated alkyne units in the linear side-chain. These compounds were incorporated as an electroactive component with a conductive polymer, for example, poly (3-butylthiophene). The blend showed a photoelectrical response higher than that of the neat polymer. The application of an electric bias during the preparation of the blend led to an increase in the photocurrent

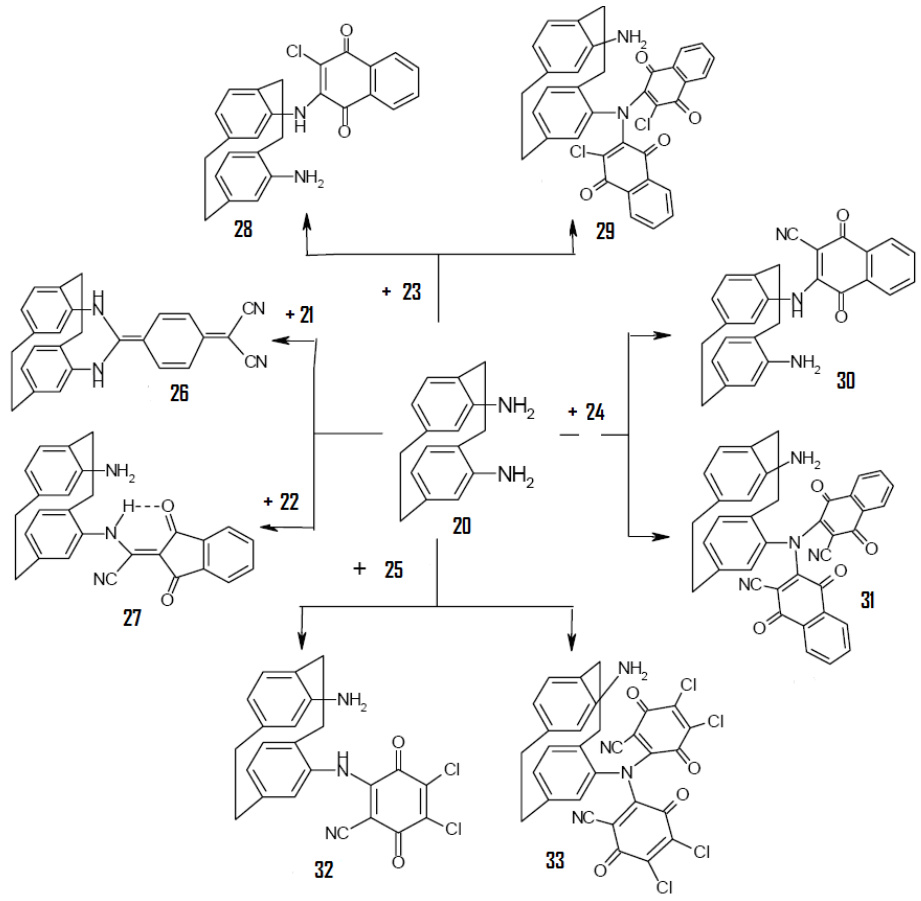


Figure 1-15 Formation of electron donor-acceptor compounds using 4,13-diamino-[2.2]PCP as electron donor

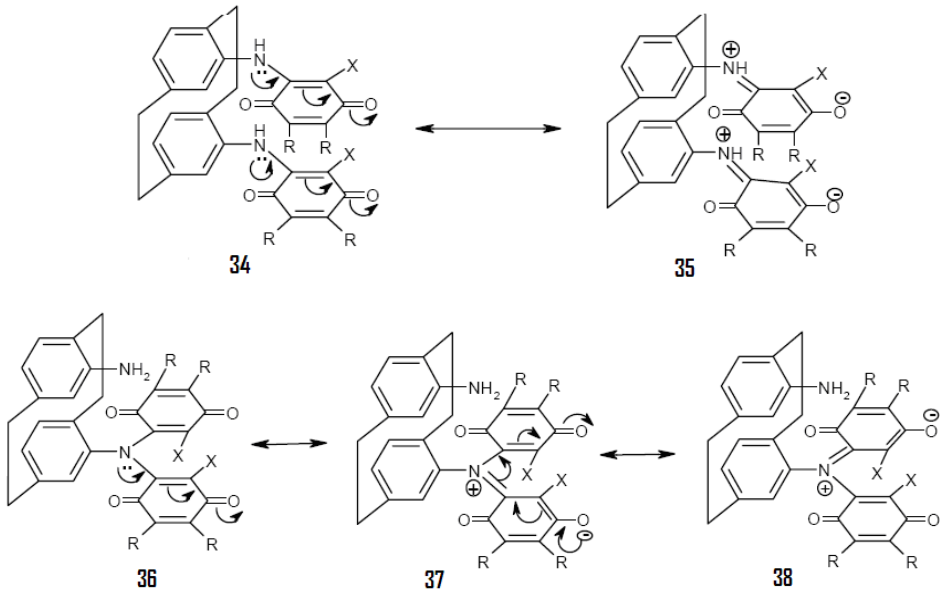


Figure 1-16 Rationalization of two molecules of the acceptor attack at the same nitrogen to give compounds **29**, **31** and **33** instead of forming compound **34**

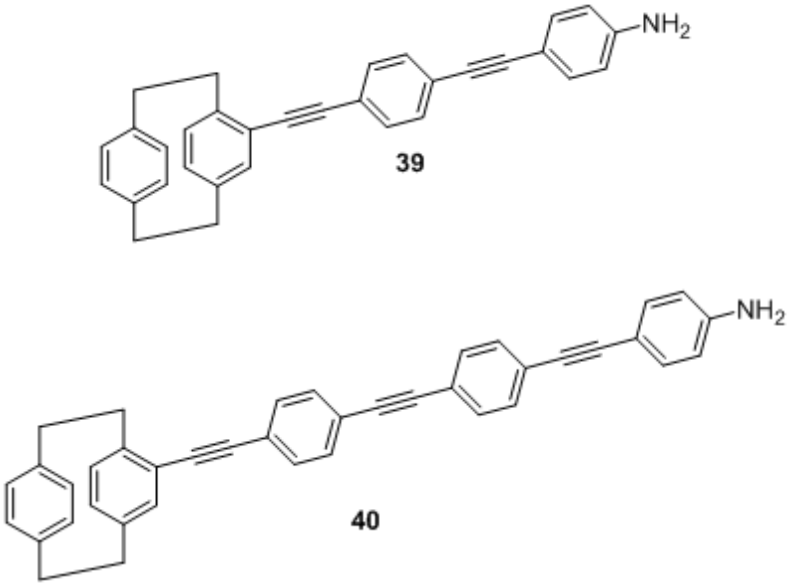


Figure 1-17 [2.2]PCP derivatives as electroactive component

Chiral [2.2]PCP derivatives have found considerable use in stereoselective synthesis. The use of [2.2]PCP derivatives as chiral auxiliaries, reagents and ligands has been summarized in two excellent reviews by Gibson[27] and Rozenberg.[28] The majority of [2.2]PCP ligands or reagents are based on one of four different substitution patterns (**41-44**, Figure 1-18), there are examples of derivatives that have been functionalized on the ethylene bridge (**45**) but these are rare.

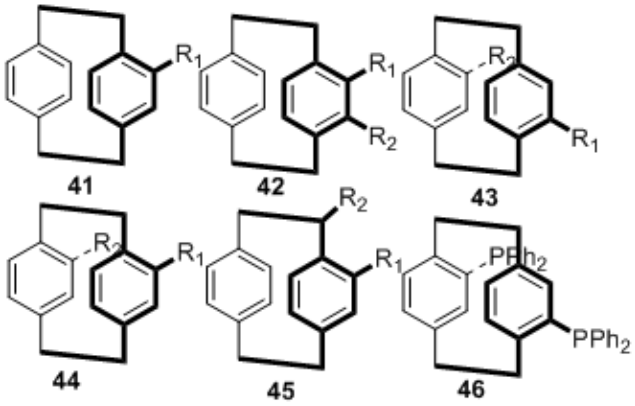


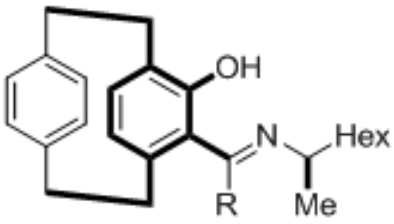
Figure 1-18 [2.2]PCP substitution patterns and ligands

Prior to the advent of PhanePhos, 4,12-bis-(diphenylphosphino)-[2.2]PCP **46**, a *pseudo-ortho* disubstituted derivative, as chiral ligand in 1997,[29-31] reports on the use of

[2.2]PCP in stereoselective synthesis were scarce. It is the great success of PhanePhos in enantioselective hydrogenations that has fuelled research into the utility of [2.2]PCP as a scaffold for the preparation of chiral ligands.

Unlike other common planar chiral scaffolds, such as metallocenes or metal-arene complexes that require two (or more) substituents on one ring to become chiral, [2.2]PCP only requires one substituent to break the symmetry of the molecule. A number of monosubstituted[2.2]PCP derivatives have been screened in enantioselective catalysis, but the majority show moderate to low enantioslectivities, presumably due to excessive conformational freedom.

The most studied substitution pattern is the *ortho* disubstituted [2.2]PCP (**42**) due to the ease of their preparation from monosubstituted derivatives. Amongst the most successful *ortho*-disubstituted[2.2]PCP ligands are the 4-hydoxy [2.2]paracyclophane aldimine **47a** and ketimines **47b**,**c** ligands of Brase[32](Figure 1-19). These ligands are amongst the most successful known for the 1,2-addition of alkyl, alkenyl and alkynylzinc reagents to aromatic and aliphatic aldehydes and imines. They can be considered bench marks not only for the success of [2.2]PCP-based ligands but in the addition of functionalized zinc reagents in general.



47a R = H
47b R = Me
47c R= Ph

Figure 1-19 [2.2]PCP-based ligands

The synthesis of *pseudo-geminal* or 4,13-disubstituted[2.2]PCP derivatives (**44**) from monosubstituted starting materials is also relatively simple, the transannular effect facilitates regioselective bromination. As a result, a large number of such ligands have been reported with varying degrees of success in enantioselective catalysis.[33-34]

Functionalization of the bridging ethylene groups is extremely rare (**45**). To our knowledge only Hou et al have investigated the activity of such compounds as ligands.[35] Significantly, sulfide **48** (Figure 1-20) was found to form a more reactive and more selective catalyst than the *ortho*-disubstituted analogue in palladium-catalyzed allylic alkylation reactions (94% vs 50-63% ee). It is believed that the bridge-substituted ligand **48** possesses a greater degree of flexibility than the *ortho*-disubstituted derivative and is therefore able to adopt a more favorable conformation on complexation. It should be noted that compound **45** was an unexpected by-product in the synthesis of the *ortho* substituted derivative.

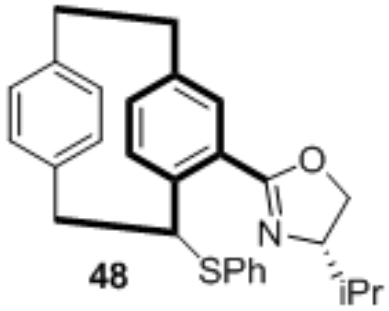


Figure 1-20 Bridge-substituted [2.2]PCP ligands

1.4 Reactivities and Reactions of [2.2]Paracyclophane

The inter-ring distance in the [2.2]PCP is significantly smaller than the distance between the layers of graphite, and repulsions between the π-electron density on the two rings results in a distortion of the benzene rings from planarity towards either chair or boat conformations. They therefore provide excellent models for the study of

molecular strain and its relationship to reactivity. The conformational simplicity and unique geometry of these molecules provide a means of investigating the transannular interactions between the aromatic rings, and yield information concerning the transmission of electronic effects from substituents on one ring to the second.

When compared to classical arenes, the most distinctive chemical property of the [2.2]PCPs is the ease with which they undergo addition reactions such as Diels-Alder cycloadditions, hydrogenations and ionic additions.[36] However, the typical regenerative behavior of aromatic molecules is not entirely suppressed, and substitution reactions such as bromination, Friedel-Crafts acylation and nitration are well established. Besides these reactions at the aromatic groups, reactions at the ethylene bridges such as cleavage, isomerization, and functionalization also occur.

1.4.1 Properties of [2.2]Paracyclophane

1.4.1.1 Structure and strain

The early X-ray structure of [2.2]PCP[1] indicated a rigid, face to face molecule with three mirror planes and bent benzene rings. A later and highly refined structure reveals that, even at 93 ^{o}K, the substance equilibrates between two structures in which the ethylene bridges are slightly deecilpsed.[37] In this molecular motion, the benzene rings rotate about axis perpendicular to and passing through the center of each face. The angle swept by this rotation is about 6 ^{o}. A cross section and face view of the molecule are found in Figure 1-21.

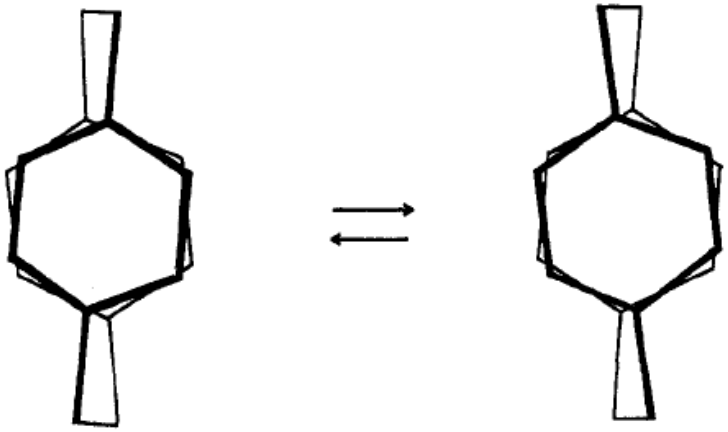


Figure 1-21 Structure of [2.2]PCP at 93 ^{o}K

The crystal structure demonstrates the presence of considerable strain and compression energy in the [2.2]PCP. The strain energy of [2.2]PCP is 31 kcal/mole.[38]

1.4.1.2 Steric inhibition of ring rotation

An engaging aspect of [2.2]PCP chemistry is the symmetry properties of the parent hydrocarbons and its derivatives. The smaller cycle is distributed more equally in the three dimensions than most other molecules. Most ball-like molecules are rigid by virtue of their bonding interactions. The [2.2]PCP is rigid because of its nonbonding interactions. The rigidity and small nonbonded atomic distances in the [2.2]PCP lead to the possibility of stable conformational isomers, and the energy barriers to ring rotation of both benzene nuclei and carbon bridges have been studied.

Structures **49a** and **49b** are enantiomeric and possibly interconvertible through state A (Figure 1-22). Carboxylic acid **50**[39], **51**[40], **52**[41] were resolved. Compound **53**[41]

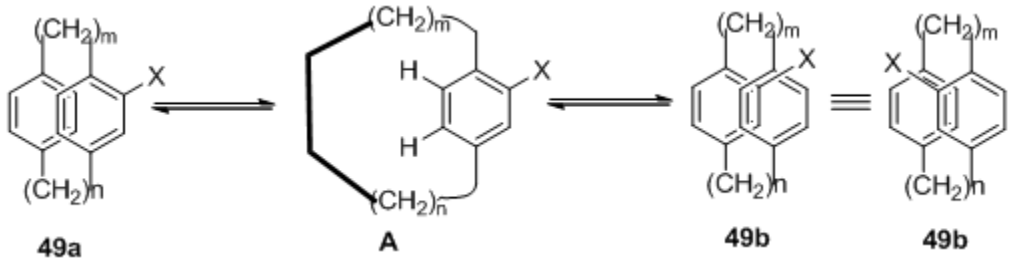
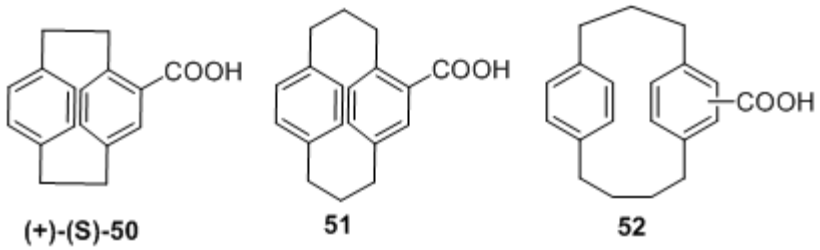


Figure 1-22 Structures **49a** and **49b** are enantiomeric and possibly interconvertible through state A

was not resolvable, indicating facile benzene ring rotation at room temperature. When heated to 160 ^{o}C, **52** racemized slowly with an estimated activation energy[42] of 33 kcal/mole, but acid **51** failed to racemize at temperature up to 240 ^{o}C [40]. The methyl ester of **50** did racemize at 200 ^{o}C, but only by an ethylene-bridge-cleaving mechanism[42]. From the temperature-dependent nmr spectra of diacetyl[4.4]PCP (**54)**, the barrier to ring rotation was estimated as ~15 kcal/mole at 15 ^{o}C. Rotation of the benzene ring around the aryl-alkyl bond (structure A, Figure 1-22) detectable by racemization in the paracyclophane systems, requires the two hydrogens to pass the other aromatic ring, and, in the case of bent benzene rings conversion from one boat form to the other. This interconversion occurs easily in the unstrained [4.4]PCP with 16 atoms in the large ring and does not occur at reasonable temperatures in [3.3]PCP with 14 atoms in the large ring. Stuart-Briegleb molecular models of compounds **50-53** uniquely allow both the assembly and the correct prediction of room temperatures behavior with respect to ring rotation.



1.4.1.3 Reactions that reflect the strain in the [2.2]paracyclophanes

The 31-kcal strain energy of [2.2]PCP, coupled with its almost rigid structure, gives rise to reactions of the bridge carbons that exhibit features peculiar to the system. Ring cleavage by a thermal process can relieve the strain in the molecule. The nature of the cleavage and fates of the intermediates have been investigated. Pyrolysis at 600 ^{o}C of [2.2]PCP and some of its derivatives produces two fragments[2] which are sufficiently stable under low pressure (<1 Torr) that recombination is delayed until the vapor comes in contact with a surface at 30 ^{o}C where it forms a polymer. Whether the intermediates are diradical **55** or *p*-xylylene **2**, they combine in quantitative yield to form a living polymer which retains a concentration of free radical of 5-10 × 10^{-4} mole/mole of tetraene (Figure 1-23).

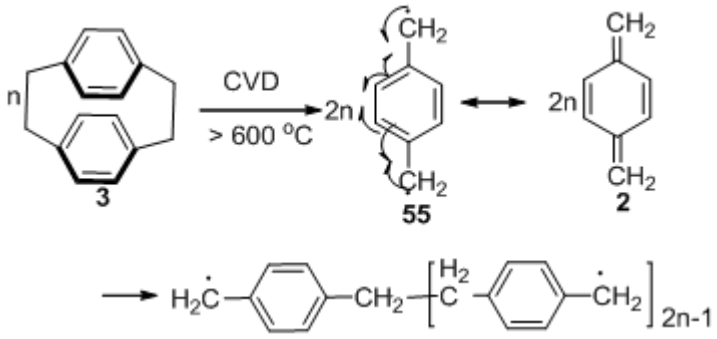


Figure 1-23 [2.2]PCP conversion to living polymers

Another example is the racemization without decomposition of optically active ester **56** when heated to 200 ^{o}C.[42] An examination of molecular models of **56** provides the convincing conclusion that ring rotation cannot occur in this system without ring rupture.

The data[42] show that cleavage of only one benzyl-benzyl bond occurred at this temperature, followed by aryl rotation and benzyl-benzyl bond formation (Figure 1-24).

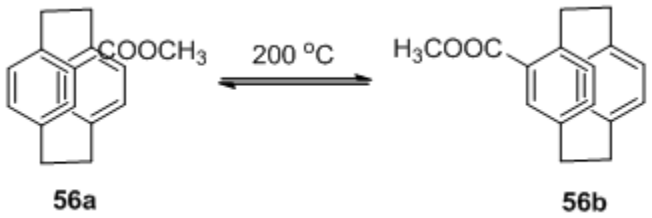


Figure 1-24 Racemization of optically active ester **56**

1.4.2 Reactions of [2.2]Paracyclophane

1.4.2.1 Reactions at the ethylene bridges of [2.2]paracyclophane

1.4.2.1.1 Radical cleavage

[2.2]PCP (**3**), pyrolysis at temperature above 200 °C in the presence of hydrogen donors like *p*-diisopropylbenzene or thiophenol leads to 4,4'-dimethylbibenzyl **57** (74% yield) (Figure 1-25).

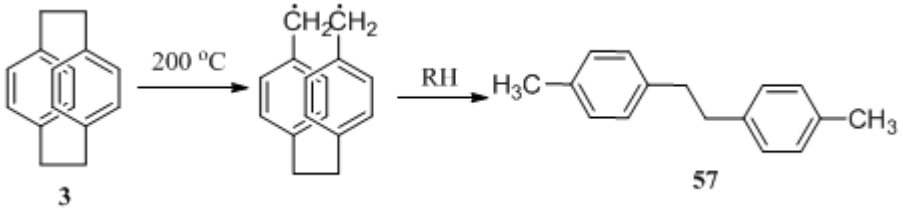


Figure 1-25 Radical cleavage of [2.2]PCP

1.4.2.1.2 Ionic reaction

Treatment of [2.2]PCP (**3**) with $AlCl_3$/HCl in methylene chloride at 0 °C provides [2.2]metaparacyclophane **60** in 44% yield. The driving force for this reaction, which presumably takes place via the σ-complexes **58** and **59** is most likely provided by the reduction of the strain energy **(***E*s of **3**: 134 kJ/mol; *E*s of **60**: 100 kJ/mol) (Figure 1-26).

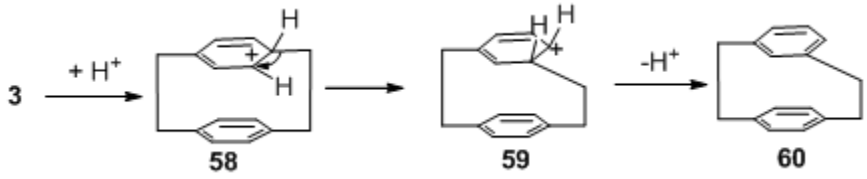


Figure 1-26 Ionic reaction of [2.2]PCP

1.4.2.2 Reactions at the benzene rings

1.4.2.2.1 Diels-Alder reaction

In contrast to the readiness of conjugated di- and trienes to participate in [2 + 4] cycloadditions as diene components, simple aromatic 6π-electron systems are normally extremely sluggish in Diels-Alder additions-one reason for the use of benzene, toluene, the various xylenes, and halobenzenes as solvents in these reactions. Despite the low reactivity of benzene, 6π-arenes can react as dienes if the reaction is performed at high temperatures or in presence of Lewis acid catysts; reactive dienophiles also add.[43] Nevertheless, the "superdienophile" 4-*N*-phenyl1,2,4-triazoline-3,5-dione (**61**) does not add to benzene or any of the polymethylbenzenes at room temperature after several weeks.[44] However, [2.2]PCP (as a formal dimer of *p*-xylene) reacts with **61** to afford the 1:2-cycloadduct (**62**) after ca. six days at room temperature in 99% yield (Figure 1-27).

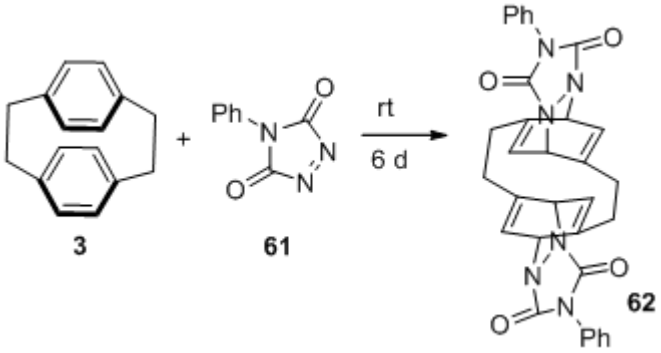


Figure 1-27 Reaction of [2.2]PCP with "superdienophile" **61**

1.4.2.2.2 Hydrogenation

Catalytic hydrogenation of [2.2]PCP under mild conditions produces a diene that either has structure **63** or **64**, whereas slightly more rigorous reaction conditions yield perhydro[2.2]PCP **65**[45] (Figure 1-28).

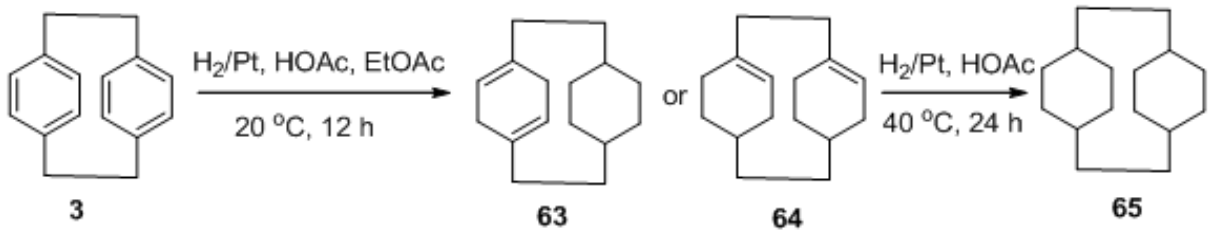


Figure 1-28 Hydrogenation of [2.2]PCP

Birch reduction of [2.2]PCP should take place readily because a substantial reduction in strain is expected for the transformation of non-planar aromatic nuclei into boat-configurated 1,4-cyclohexadiene units. Under the conditions given in Scheme 21, [2.2]PCP **3**, besides providing small amounts of the dihydro- compound **66**, mainly affords the tetrahydro derivative **67** as well as **68** (Figure 1-29).

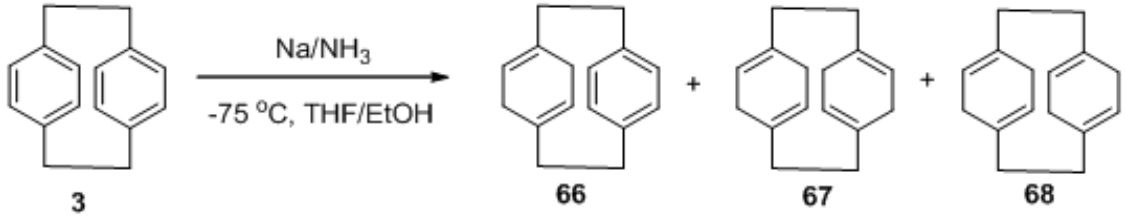


Figure 1-29 Birch reduction of [2.2]PCP

The known strong dependence of the product composition in Birch reduction on small variations in the reaction conditions is also observed for **3**. Whereas addition of a solution of **3** in tetrahydrofuran to a refluxing solution/ suspension of sodium in liquid ammonia, followed by addition of ethanol yields 4,4'-dimethylbibenzyl **57** in 94% yield. Slow addition of **3** in THF/ethanol to a solution of sodium in refluxing ammonia leads quantitatively to **68**.

1.4.2.2.3 Electrophilic substitution

1.4.2.2.3.1 Acetylation with acetyl chloride/aluminum chloride

Acetylation of [2.2]PCP with acetyl chloride in the presence of aluminum chloride provides 4-acetyl[2.2]PCP as major product together with two isomeric methyl ketones

($C_{36}H_{36}O_2$). Careful chromatography on silica gel and fractional crystallization of the acetylated reaction mixture give **69** (75%), **70** (9%, mp 257^{o}C) and **71** (9%, mp 98-101 ^{o}C). Both **70** and **71** possess the same molecular formula $C_{36}H_{36}O_2$ (Figure 1-30). Compounds **70** and **71** are formed under Friedel-Craft acylation. One acetyl group substituted in the [2.2]PCP nucleus deactivates both rings toward electrophilic attack. Thus it seems reasonable to expect that the nucleus was first alkylated and then acylated in a second stage. The strain in the [2.2]PCP is probably responsible for the ease with which it undergoes ring opening with $AlCl_3$. An attractive general mechanistic scheme is formulated (Figure 1-31).

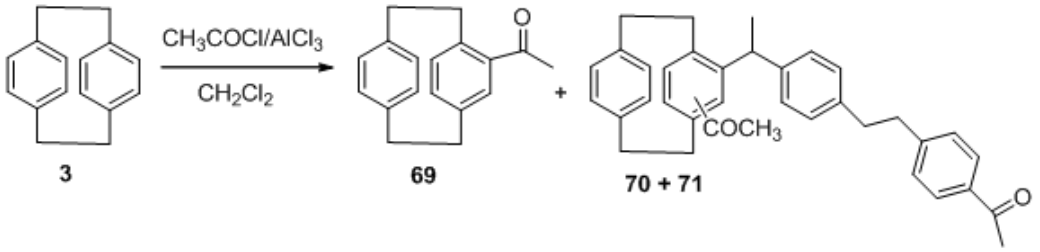


Figure 1-30 Acetylation of [2.2]PCP with acetyl chloride

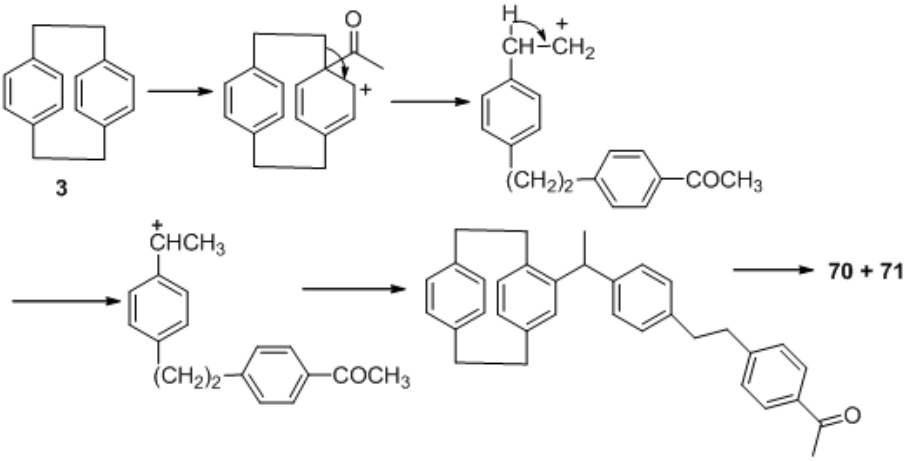


Figure 1-31 Proposed mechanism for the formation of by-products **70** and **71**

1.4.2.2.3.2 Nitration of [2.2]paracyclophane

Nitration of **3** with fuming nitric acid in glacial acetic acid for 15 min provides mainly 4-nitro[2.2]paracyclophane.[45] When the reaction time was extended, a large

number of products were generated, which were *pseudo-gem*(**72**, yield: 0.7%)*, pseudo-meta*(**73**, yield: 2%), *pseudo-ortho*(**74**, yield: 2%) and *pseudo-para* (**75**, yield: 1.4%) dinitro[2.2]PCPs (Figure 1-32).

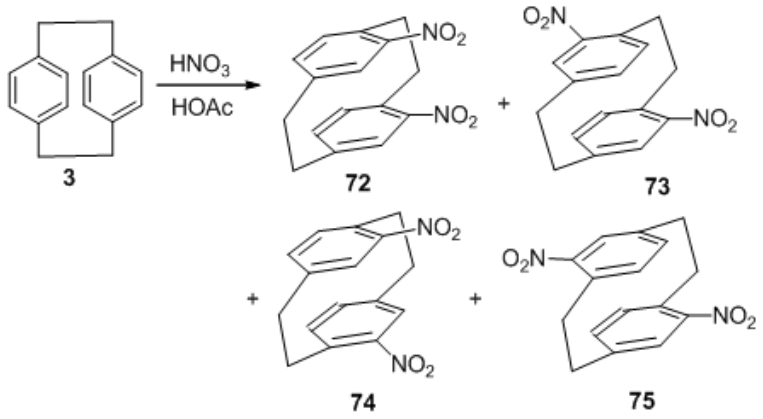


Figure 1-32 Dinitration of [2.2]PCP with HNO_3/CH_3COOH

1.4.2.2.3.3 Bromination of [2.2]paracyclophane

Iron-catalyzed bromination of **3** with 2 equivalents of bromine in carbon tetrachloride gave four isomeric dibromides in the yields indicated in Figure 1-33. The compounds were separated by a combination of chromatographic and crystallization techniques.

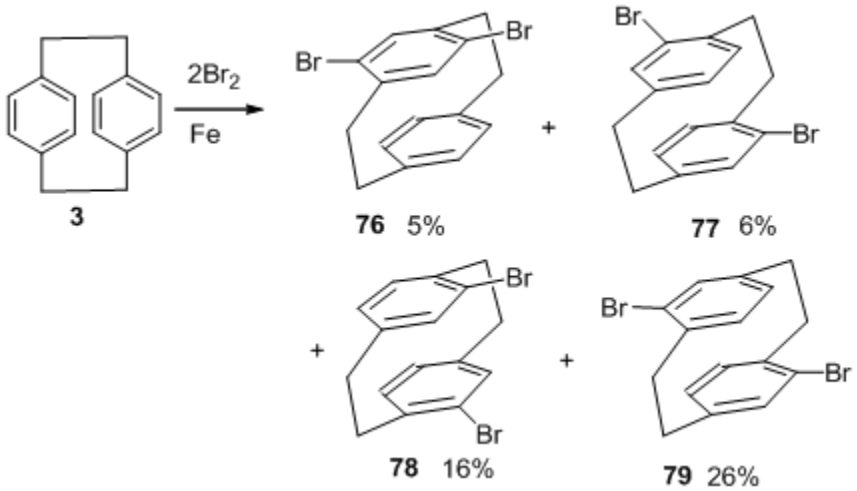


Figure 1-33 Dibromination of [2.2]PCP with Br_2/Fe

Use of excess bromine in the presence of an iron catalyst gave two products (total isolated yield: 57%) after chromatography. The faster moving component (yield: 29%) was 4,7,12,15-tetrabromo[2.2]PCP (**80**). The second slower moving tetrabromo isomer was 4,5,15,16-tetrabromo[2.2]PCP (**81**) and isolated in 28% yield (Figure 1-34).

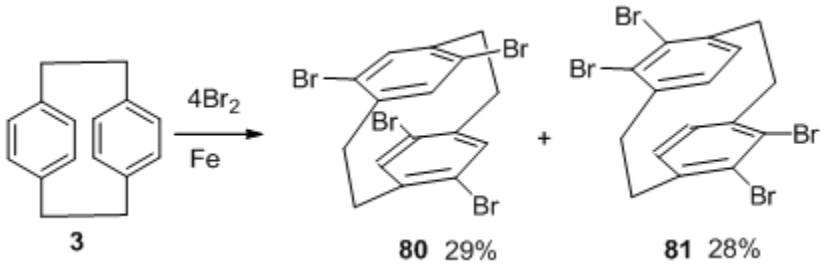


Figure 1-34 Tetrabromination of [2.2]PCP with Br_2/Fe

1.4.2.2.3.4 Dichlorination of [2.2]paracyclophane

The iodine-catalyzed dichlorination of [2.2]PCP did not proceed as discretely as the bromination. Substantial amounts of monochloro and trichloro products were generated when 2 mol of chlorine had been consumed. Only the insoluble *pseudo-para*-dichloro[2.2]paracyclophane (**82**) was isolated (10% yield, Figure 1-35).

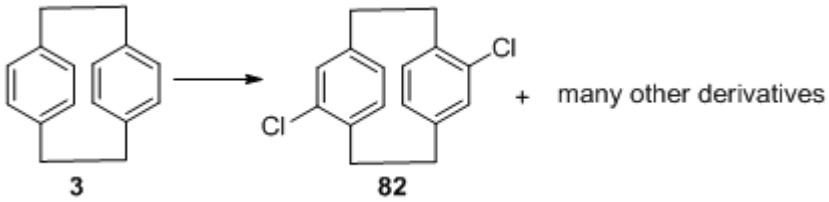


Figure 1-35 Dichlorination of [2.2]PCP with Cl_2 in the presence of iodine

1.4.2.2.3.5 Transannular directive influences in electrophilic substitution of monosubstituted [2.2]paracyclophane

Chemical and spectral evidence indicate the presence of strong transannular electronic interactions in [2.2]PCP and its derivatives.[46] When second substituent is introduced into monosubstituted [2.2]PCP, the first substituent should have a directive influence on the same benzene ring and a transannular directive impact on another

benzene ring. Table 1-1[47] records the results of an investigation of such directive influences.

Table 1-1 Pattern of electrophilic substitution of monosubstituted [2.2]paracyclophanes

			%	% *pseudo*			
Entry	X	Reagent	*para*	*ortho*	*para*	*meta*	*gem*
1	$COOCH_3$	Br_2, Fe					89
2	$COCH_3$	Br_2, Fe					56
3	COOH	Br_2, Fe					63
4	NO_2	Br_2, Fe		2	6	8	70
5	CN	Br_2, Fe		16	25	26	
6	Br	Br_2, Fe	5	16	26	6	
7	OH	$C_6H_5N_2Cl$	98				

The data of Table 1-1 indicate that electophilic substitution of paracyclophane with strong electron-donating groups orients *para* in the ring bearing the substituent, as in diazonium coupling of 4-hydoxy[2.2]PCP (entry 7), for weaker electron-donating group, besides *para*-bis-substituted[2.2]PCP, *pseudo-para*, *pseudo-ortho* and *pseudo-meta*-bis[2.2]PCP were produced, bromination of 4-bromo-[2.2]PCP gives 5% *para*, 16% *pseudo-ortho*, 26% *pseudo-para* and 6% *pseudo-meta*-bisbromo[2.2]PCP (entry 6).

The presence of one electron-withdrawing substituent in one ring deactivated both rings toward further electophilic attack. For the acetyl, carbomethoxy, carboxy, and nitro derivatives of [2.2]PCP, bromination occurs exclusively or predominantly in the position *pseudo-gem* to these groups to give the thermodynamically least stable isomer. The oxygens of these groups are ideally positioned to accept a proton from the *pseudo-gem* position. The lower specificity of the nitro compound probably reflects its lower basicity (entry 1-4). The cyano group apparently cannot function as an internal base because of its linear structure, and no *pseudo-gem* product pattern was observed in

entry 5. The random product pattern in entry 5 rules out specific conjugative or inductive effects on positions of substitution. The mechanism favored by the data is illustrated with 4-bromo-[2.2]PCP as substrate (entries 6). In the over-all scheme, the electrophile attacks the face of the unsubstituted ring, a proton is transferred from ring to ring, and the proton departs from the face of the originally substituted ring. Thus, electrophiles enter and leave from the system by the least hindered paths (Figure 1-36)

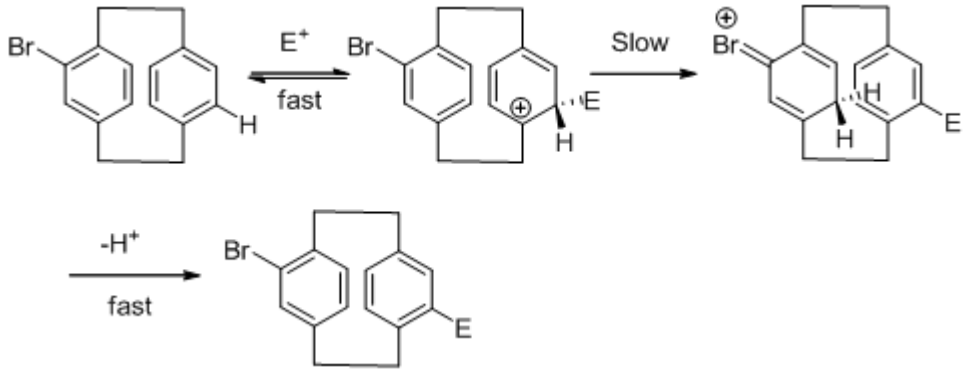


Figure 1-36 Transannular directive influences second electrophilic substitution of 4-bromo-[2.2]PCP

1.5 Reactions of Octafluoro[2.2]paracyclophane and Its Derivatives

1.5.1 Reactions of Octafluoro[2.2]paracyclophane

Octafluoro[2.2]PCP (AF4) is a deactivated aromatic system because of fluoroalkyl group. Thus, the Friedel-Craft type aromatic bromination, acylation and alkylation chemistry do not work.[49] However, nitration of AF4 is successful, and nitration of AF4 with nitronium tetrafluoroborate in sulfolane at room temperature afforded mononitro-AF4 (**84**) in 86% isolated yield[49] with no dinitro derivatives observed. Reduction of 4-nitro-AF4 provides 4-amino-AF4 in 82% yield (**85**). Examining the diazotization and Sandmeyer-type chemistry of **85,** a number of other derivatives including halo-, hydroxyl- and phenyl- AF4 derivatives can be produced in yields ranging from poor to good (Figure 1-38).

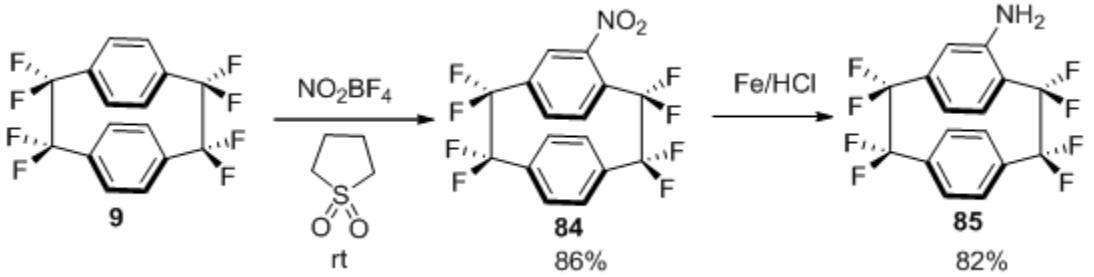


Figure 1-37 Synthesis of monosubstituted AF4 derivatives

When nitration was carried out under the more forcing conditions of 5 equivalents of nitronium tetrafluoroborate and a temperature of 80 ^{o}C, the products generated were a mixture of *pseudo-meta*(**86a**), *pseudo-para* (**86b**), and *pseudo-ortho*(**86c**) dinitro-AF4 derivatives in 81% combined isolated yield[50], with the ratio of 1:1:1. *pseudo-ortho* Isomer could be separated from *pseudo-meta* and *pseudo-para* isomers by column chromatography, but *pseudo-meta* and *pseudo-para* isomers could not be separated by column chromatography, however, the *pseudo-meta* and *pseudo-para* isomer mixture could be enriched in one isomer or the other by fractional crystallization, or sublimation. Reduction of the three isomeric dinitro-AF4 compounds provides corresponding the diamino-AF4 compounds in 82-84% yield (**87a-c**). The double diazotization of these diamino-systems, followed by Sandmeyer-type chemistry furnishes the three isomeric dibromo-(**88a-c**), diiodides-(**89a-c**) and diphenyl-AF4 (**90a-c**) in good isolated yield (60-78%) (Figure 1-39). Trifluoromethylation of the of the *pseudo-meta* and *pseudo-para* diodes **89a,b** with methyl 2-(fluorosulfonyl)-difluoroacetate in the presence of catalytic amount of $PdCl_2$ provides high yields of corresponding bis-(trifluoromethyl)-AF4 products (**91a-b**).

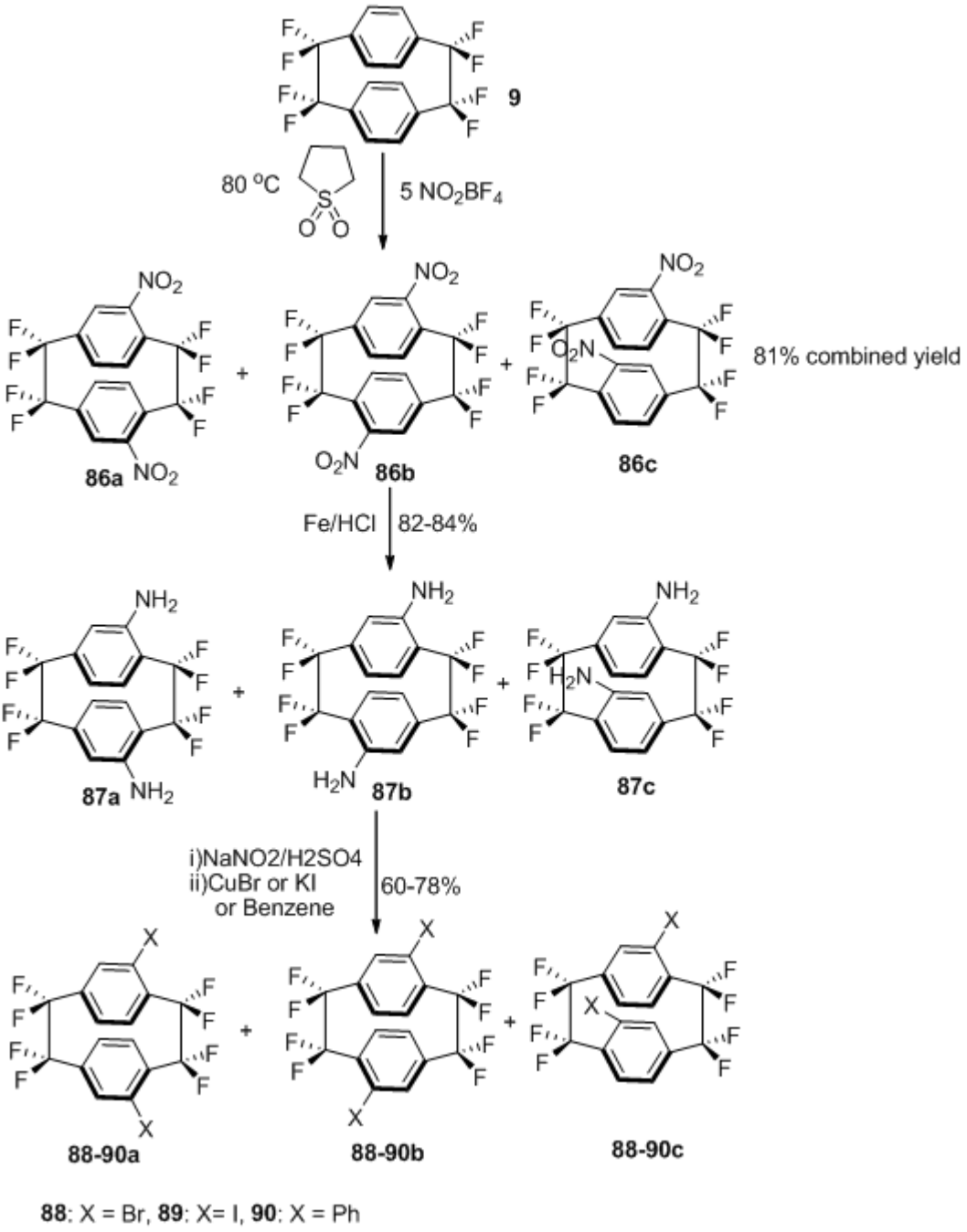


Figure 1-38 Synthesis of bis-substituted AF4 derivatives

1.5.2 Thermal Isomerizations of AF4 Derivatives

It is known that [2.2]PCP derivatives can be racemized at 200 °C. Since replacement of hydrogen by fluorine in saturated systems usually increases thermal and chemical stability,[51] together with the lower stability of difluorobenzyl radicals relative to

benzyl radicals,[52] AF4 derivatives would be predicted to require a much higher temperature to undergo such isomerization. Indeed, *pseudo-ortho*- bis(trifluoro-acetamido)-AF4 (**92a**) proved to be perfectly stable and unchanged when heated neat at 300 ^{o}C for 8 h, but when it was heated to 390 ^{o}C for 2 h, NMR analysis indicated that it had been converted to a 5:1 ratio of **92a** and *pseudo-para* isomer (**92b**). The above mixture was further heated at 360 ^{o}C for 24 h, and the ratio of **92a:92b** was found to have changed to 1:7 (Figure 1-39).

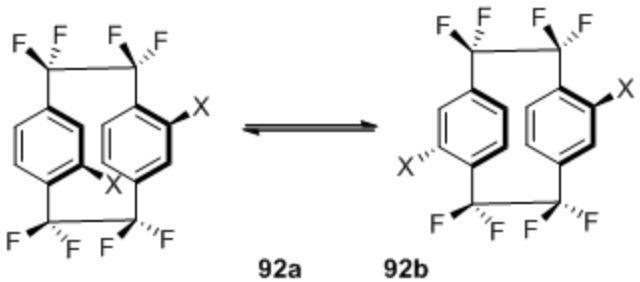


Figure 1-39 Thermal isomerrization of *pseudo-ortho*-bis(trifluoro-acetamido)-AF4

Therefore, the AF4 derivative has considerably more kinetic thermal stability than the hydrocarbon [2.2]PCP system. This not only demonstrates the stabilizing effect of exchanging fluorine for hydrogen, but could have serious implications regarding the use of these AF4 derivatives as chiral ligands, catalysts and auxiliaries, since they display far superior resistance to thermal isomerization than hydrocarbon analogues.

1.5.3 Reactions of AF4 Derivatives

1.5.3.1 Aryne chemistry of octafluoro[2.2]paracyclophane

Dehydroiodination of 4-iodo-octafluoro[2.2]PCP by treatment with *t*-BuOK in the presence of benzene, naphthalene and anthracene affords each of the corresponding Diels-Alder cycloadducts derived from the presumed aryne intermediates in high yield

(Figure 1-42).[53] When 4,15-diiodo-octafluoro[2.2]PCP is used as starting material instead of 4-iodo-octafluoro[2.2]PCP, Diels-Alder bis-cycloadducts are obtained in excellent yield.[53] A double Diels-Alder reaction of the formal *syn*-bis(dehydro)-octafluoro[2.2]PCP with anthracene leads to formation of a novel cage compound that contains a highly pyramidal double bond (Figure 1-40).[54] When 4-acetamido-octafluoro[2.2]PCP is treated with *p*-chlorobenzoyl nitrite in the presence of various dienes, similar results[55] are obtained as shown in Figure 1-41.

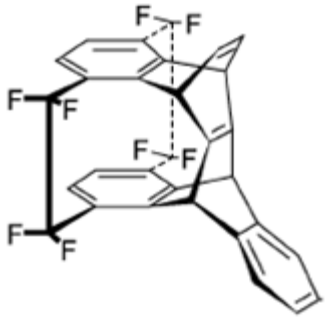


Figure 1-40 Highly pyramidalized cage alkene formed via the double Diels-Alder cycloaddition of *syn*-4,5,13,14-bis(dehydro)octafluoro[2.2]PCP to anthracene

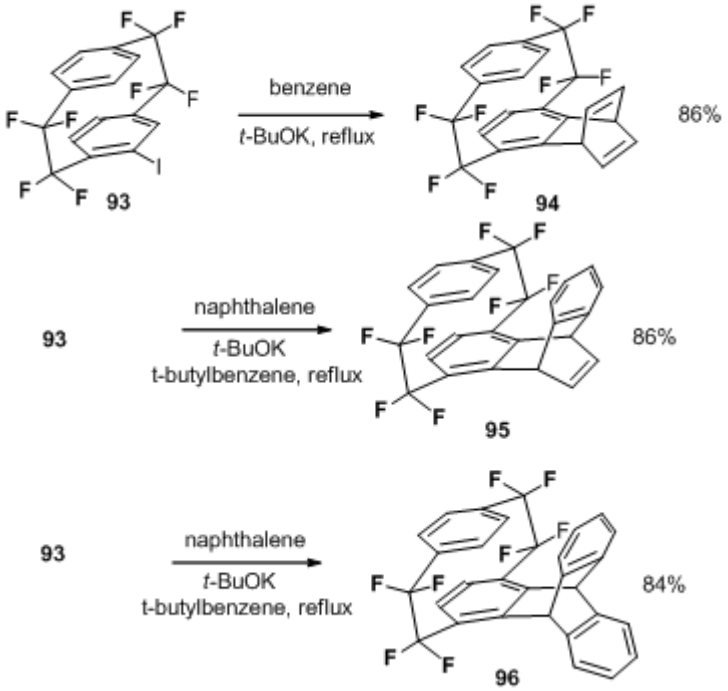


Figure 1-41 Reaction of 4-iodo-AF4 with various dienes in the presence of *t*-BuOK

1.5.3.2 Novel ring-cleaving reaction of 4-nitro-octafluoro [2.2]paracyclophane with nucleophiles

When 4-nitro-octafluoro[2.2]PCP is treated with nucleophiles such as alkoxides and cyanide, a novel ring opening reaction is observed via a S_NAr mechanism. The nucleophile apparently attacks the bridgehead aryl carbon vicinal to the nitro group, followed by subsequent aryl-CF_2 bond cleavage to form **97a**, **b** type products in moderate to good yields (52-78%) (Figure 1-42).[56]

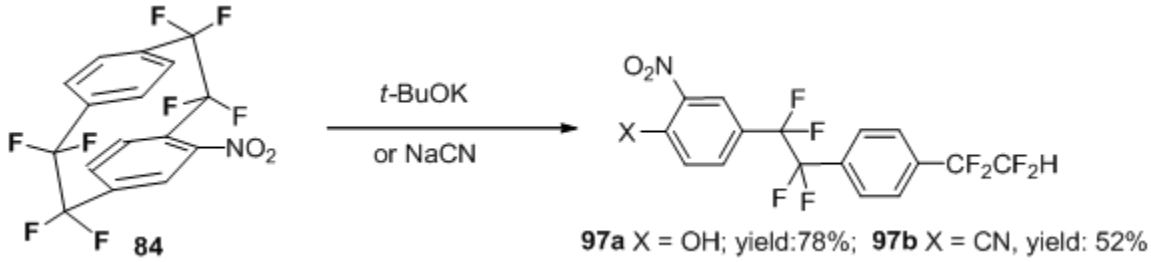


Figure 1-42 Ring opening reaction of 4-nitro-octafluoro[2.2]PCP

1.5.3.2 Nucleophilic substitution of 4-iodo-octafluoro [2.2]PCP

Reactions of 4-iodo-AF4 with thiophenol and dimethyl malonate in the presence of sodium hydride under irradiation of sunlamp provide corresponding products **98**, **99** in high yields. In the absence of irradiation with sunlamp, the reaction cannot proceed even at 120 ^oC (Figure 1-43).[57] Thus these reactions appear to proceed via $S_{RN}1$ mechanisms

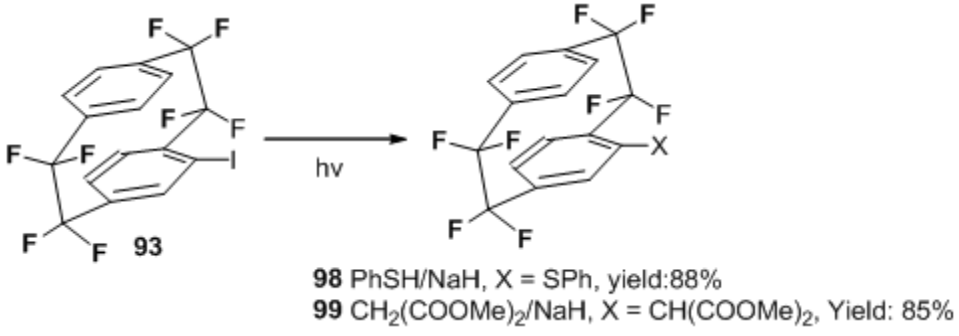


Figure 1-43 Nucleophilic substitution of 4-iodo-octafluoro [2.2]PCP

In conclusion, studies of [2.2]PCP has probed theories on bonding, ring strain and π electron interactions in addition to their use in commercial application as monomers for Parylene-type polymers. The electronic properties of [2.2]PCP were employed in the design of charge transfer complexes and variety of molecular electronic materials such as linear and non-linear optoelectronics and conductive polymers. The planar properties of [2.2]PCP were used in the preparation of chiral ligands and biomedical research. A successful synthetic method for preparation of AF4 was discovered in 1996. Besides the industrial application of this compound as a monomer for the Parylene-HT polymer, studies of the chemistry of AF4 began in 1999 because of the commercial availability of AF4. It is hoped that commercial applications for AF4 derivatives will be found much like their hydrocarbon analogues.

CHAPTER 2
SYNTHESIS OF PERFLUORO[2.2]PARACYCLOPHANE AND PERFLUORO[2.2.2]PARACYCLOPHANE

2.1 Abstract

A method for preparing perfluoro[2.2]paracyclophane has been sought ever since the partially fluorinated octafluoro[2.2]paracyclophane (AF4) was first synthesized. This compound has now been prepared in 42% yield from the precursor, 1,4-bis(chloro-difluoromethyl)-2,3,5,6-tetrafluorobenzene by its reaction with zinc dust when heated in anhydrous acetonitrile at 100 ^{o}C. Two preparations of the precursor, first from 1,4-dicyano-2,3,5,6-tetrachlorobenzene and an improved method beginning from 1,2,4,5-tetrachlorobenzene, are also described as are key comparisons to our related synthesis of AF4.

2.2 Introduction

[2.2]Paracyclophanes are useful chemical vapor deposition (CVD) precursors of a family of thin film polymers known as Parylenes.[58] Parylene polymers are conformal coatings that are ideally suited for a wide variety of applications within the automotive, medical, electronics and semiconductor industries. Parylene coatings are transparent, chemically inert, and they have excellent barrier properties.

The process of conversion of [2.2]paracyclophane into a Parylene polymer is exemplified in Figure 2-1 for the parent hydrocarbon system. The hydrocarbon version

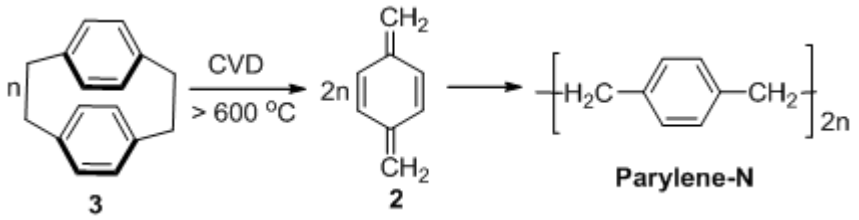


Figure 2-1 [2.2]Paracyclophane and its conversion to Parylene polymers

of polymer, Parylene N, has good thermal stability, remaining useful (for several hours) at temperatures up to 130 ^{o}C. However, for those applications that require a coating of greater thermal stability, the bridge-fluorinated Parylene-HT, which exhibits only 0.3% weight loss per hour at 450 ^{o}C, is preferred. The precursor for Parylene HT is 1,1,2,2,9,9,10,10-octafluoro[2.2]paracyclophane, commonly known as AF4, and which for the last 15 years has been the subject of considerable synthetic interest. Since Dr. Dolbier initially published its preparation method in 1993,[11] which allowed gram quantities of AF4 to be prepared, four subsequent papers have provided procedures that would allow larger, even commercial quantities to be prepared.[13,15,59,60] The best of our procedures, where 1,4-bis(chlorodifluoromethyl)benzene was allowed to react with zinc in dimethylacetamide under non-high-dilution conditions, is shown in Figure 2-2.[15] This process is currently used to manufacture AF4 for use in the Parylene industry.

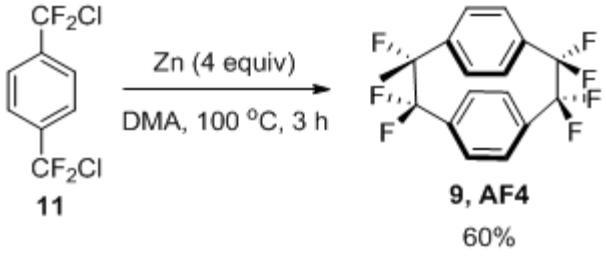


Figure 2-2 Preparation of AF4 by reduction of dichloride (**11**) with zinc

Perfluoro[2.2]paracyclophane, herein referred to as F8, has been the subject of much interest as a potential Parylene precursor ever since AF4 was found to be so useful. It was predicted that the polymer derived from F8 would retain the high thermal stability of the AF4 derived polymer while having a lower dielectric constant, better dielectric strength, a very low coefficient of friction, plus transparency in the regions of spectra (IR spectra, in particular) that involve C-H bonds. Nevertheless, until this report

no synthesis of F8 has been reported.[61,62] The method described below the first synthetic method for F8.

The approach to the synthesis of F8 that ultimately proved successful emulated the method shown above for AF4. However, significant changes in the key steps were required because of the presence of the ring fluorines. A completely different synthesis of the logical [2.2]paracyclophane precursor 1,4-bis(chlorodifluoromethyl)-2,3,5,6-tetrafluorobenzene (**100**) proved necessary because the ring fluorines effectively inhibited both the chlorination and bromination steps of our published procedure for synthesis of the AF4 precursor.[63]

Instead, we utilized alternative synthetic schemes to prepare precursor **100**. Our initial approach utilized commercially available 2,3,5,6-tetrachloro-1,4-dicyanobenzene (**101**) as the starting material (Figure 2-3). Tetrafluoro compound **102** was prepared in 89% yield by facile Cl-F exchange using KF in anhydrous DMF in the presence of 2% phase transfer agent tetrabutyl ammonium bromide.[64] The cyano groups were then reduced using DIBAL-H in toluene to form dialdehyde **103** in 69% yield.[64,65] Dialdehyde **103** could be efficiently converted (87%) to the bis(difluoromethyl) compound **104** via reaction with SF_4 in the presence of HF. Chlorination of compound **104** provided the desired precursor **100** in 56% yield.

Although this procedure allowed the synthesis of the required precursor **100**, the required use of DIBAL-H and SF_4 insured that this overall process would be too expensive to utilize for making larger quantities of F8. The chlorination step took 56 h

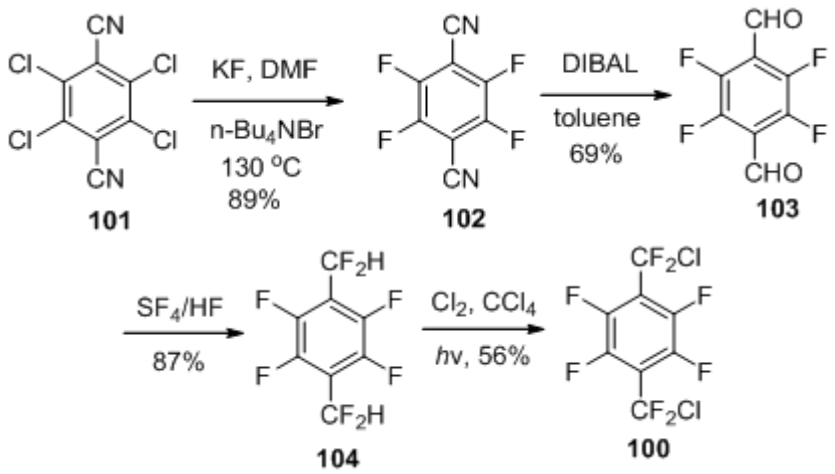


Figure 2-3 First synthesis of F8 precursor **100** (Method A)

and the yield was only 56%. My contribution was developing a three step approach to the synthesis of **100**, based on the preparation by Castaner and Riera of 1,4-bis(dichloromethyl)-2,3,5,6-tetrachlorobenzene (**106**) by $AlCl_3$-catalyzed condensation of chloroform with 1,2,4,5-tetrachlorobenzene (**105**).[66] Thus, as shown in Figure 2-4,1,4-bis(difluoromethyl) -2,3,5,6-tetrafluorobenzene (**104**) could be prepared with overall yield of 65% from the inexpensive 1,2,4,5-tetrachlorobenzene. The yield of chlorination of compound **104** was improved to 81% from 56% and the reaction time was reduced to 17 h simply by increasing reaction temperature from 60 ^{o}C to reflux (84 ^{o}C). In order to further reduce the price of 1,4-bis(chlorodifluoromethyl) -2,3,5,6-tetrafluorobenzene (**100**), 1,2,4,5-tetrafluorobenzene was used as starting material instead of 1,2,4,5-tetrachlorobenzene for $AlCl_3$–catalyzed condensation with chloroform, but the reaction did not work. Another attempt was applied the same procedure for the Cl-F exchange step by the use of KF or technical grade CsF replacing reagent grade CsF, but this reaction did not succeed either.

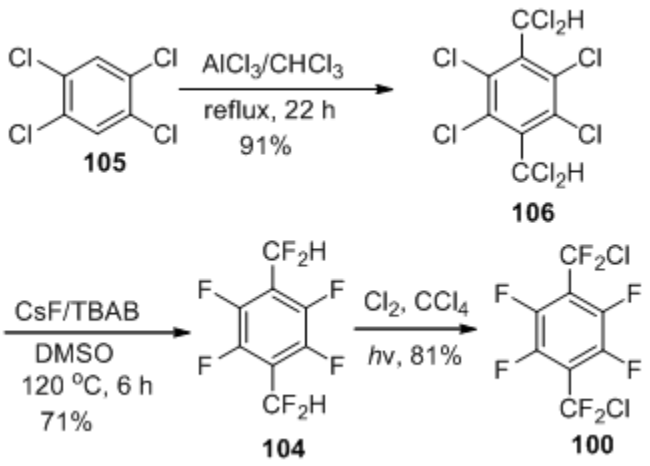


Figure 2-4 Improved synthesis of F8 precursor **100** (Method B)

Conversion of dichloride precursor **100** to the paracyclophane F8 provided its own challenges, since the exact procedure used to synthesize AF4 when applied to **100** gave no perfluoro[2.2]paracyclophane product. Indeed, when precursor **100** was allowed to react with zinc in various polar aprotic solvents, a reaction proceeded very smoothly to consume **100** (Figure 2-5).

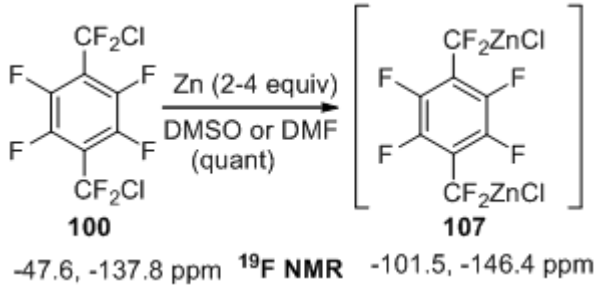


Figure 2-5 Application of AF4 procedure to preparation of F8

A fluorine NMR spectrum of the reaction mixture indicated that **100** had been converted cleanly to a single product that exhibited two singlet signals, at -101.5 and -146.4 ppm, signals that were not inconsistent with the product actually being the desired perfluoro[2.2]paracyclophane. However, any attempt to work up the reaction gave no isolable fluorine-containing product. It finally was concluded that these new

signals were due to formation of the over reduced bis-zinc reagent **107**. This conclusion was based on two reactions of the intermediate, both of which were consistent with it being bis-zinc reagent **107** (Figure 2-6). Addition of bromine to the reaction mixture containing **107** led to formation of *bis*-bromodifluoromethyl product **108**. Whereas addition of acetic acid produced bis-difluoromethyl compound **104**.[67] Also the observed fluorine chemical shift of **107** is consistent with its structure.[68,69]

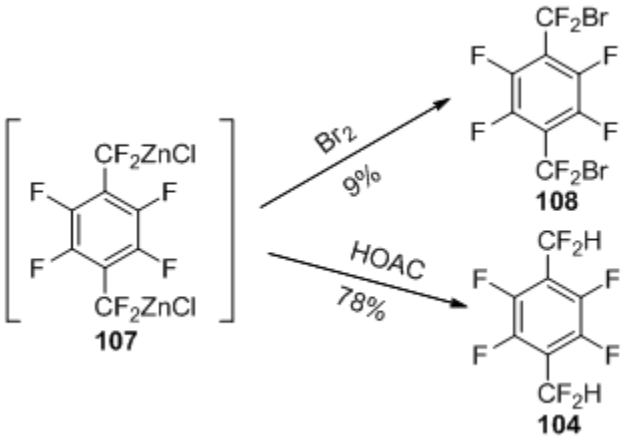


Figure 2-6 Chemical characterization of bis-zinc reagent **107**

In view of these results, it was thought that using zinc in a less polar solvent might inhibit the over-reduction that led to the bis-Zn reagent **107**. Indeed when acetonitrile was used as the reaction medium, a new product appeared in relatively low yield (20%) which also had two signals in the fluorine NMR, this time at -102.8 and -132.4 ppm (Figure 2-8). Upon isolation and characterization, this product proved to be the desired perfluoro[2.2]paracyclophane, F8, as characterized by ^{13}C, ^{19}F NMR, HRMS, elemental analysis and X-ray structure analysis (X-ray structure of F8 see Appendix in Figure 1).

The following optimization led to a pure product and higher yield. First, the reaction temperature was reduced from 120 ^{o}C to 100 ^{o}C (oil bath temperature) by

activating the zinc with 2% hydrochloric acid. The reaction is believed to be more favorable for dimerization rather than polymerization at low temperature. Secondly, precursor **100** must be very pure; if precursor **100** contains even trace amounts of compound **104**, smooth reaction is inhibited. As result of these optimization, this reaction yield was able to be increased to 42% of high purity product. In addition to giving F8, this reaction also produced the bridge-unsaturated product (**110**) and trimer perfluoro[2.2.2]paracyclophane (**111**) (X-ray structure of **111** see Appendix in Figure 2).

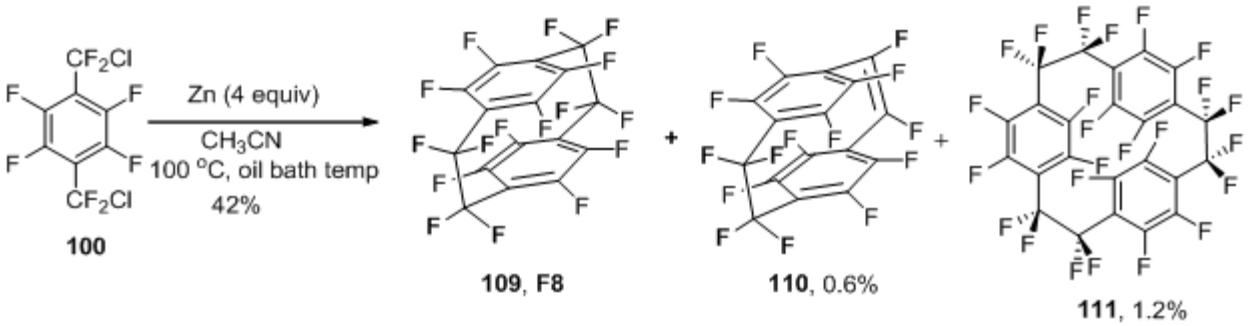


Figure 2-7 Synthesis of F8 and trimer perfluoro[2.2.2]paracyclophane

Thus, for the first time, the perfluoro[2.2]paracyclophane is available for deposition experiments to determine the impact of perfluorination on properties of the respective Parylene polymer. Scale up experiments have now allowed us to produce more than 200 g of pure F8 for Specialty Coating System, Inc. for preparation and testing films.

2.3 Experimental Section

1,4-Dicyano-2,3,5,6-tetrafluorobenzene (101)[64]: 1,4-Dicyano-2,3,5,6-tetra-chlorobenzene (purity 95%) (40 g, 0.15 mol), KF (43.7 g, 5 equiv), and tetrabutuyl-ammonium bromide (TBAB) (0.99 g, 2 mol%) were added to a flask containing dry DMF (250 mL), and the mixture was stirred overnight at 120 ^{o}C under N_2. The reaction mixture was poured into ice-water (2 L). The resulting precipitate was filtered and

washed with water. The crude product was recrystallized from acetone to give 1,4-dicyano-2,3,5,6-tetrafluorobenzene (25.5 g, 89%) as yellowish crystals. mp 197-199 ^{o}C; ^{19}F NMR δ -128.5 (s).[64]

2,3,5,6-Tetrafluorobenzene-1,4-dicarbaldehyde (103)[64,65,70]: To a solution of 1,4-dicyano-2,3,5,6-tetrachlorobenzene (**102**) (20.0 g, 0.1 mol) and toluene (300 mL) at 0 ^{o}C was added 1 M diisopropylaluminum hydride (DIBAL-H) toluene solution dropwise under nitrogen. The reaction mixture was stirred at 0 ^{o}C for 1 h and then slowly warmed to room temperature and stirred overnight. The reaction was quenched by addition of 2 N hydrochloric acid (300 mL) until pH<2, and the mixture was stirred for 30 min. The resulting precipitate was filtered and washed with dichloromethane. The organic layer was separated from the filtrate and the aqueous layer was extracted with dichloromethane (50 mL × 6). The combined organic layers were washed with saturated sodium bicarbonate and brine, dried over $MgSO_4$, filtered and concentrated to give crude product (16 g), which was recrystallized from dichloromethane to obtain 2,3,5,6-tetrafluorobenzene-1,4-dicarbaldehyde (**103**) (14.2 g, 69%). mp 197-199 ^{o}C; ^{1}H NMR δ 10.33 (s);[64] ^{19}F NMR δ -144.2 (s);[64] MS 207 (M+H, 100).

1,4-Bis(difluoromethyl)-2,3,5,6-tetrafluorobenzene (104) (Method A)[67]: 2,3,5,6-Tetrafluorobenzene-1,4-dicarbaldehyde (**103**) (27.3 g, 0.132 mol) and dichloromethane (50 mL) were added into a 250 mL autoclave, which was then cooled with a dry ice acetone bath. HF (8.0 g) and SF_4 (135 g) was added, and the reaction mixture was stirred at 180 ^{o}C for 48 h. The reaction mixture was washed out with dichloromethane (200 mL) and kept overnight to release HF and other gaseous products. The reaction mixture was filtered and the filtrate was washed with brine (60 mL × 3), dried over

$MgSO_4$, evaporated to dryness, and recrystallized from dichloromethane to afford product **104** (28.9 g, 87%): mp 68-70^oC (lit.[67] mp 45-50 ^oC); ^1H NMR δ 6.97 (t, J_{FH} = 53 Hz); ^{13}C δ 108.22 (t, J_{FC} = 242 Hz), 115.97 (br. S), 144.79 (d, J_{FC} = 262 Hz), ^{19}F NMR δ -115.2 (d, J_{FH} = 52 Hz), -142.2 (s). Anal. Calcd for $C_8H_2F_8$: C, 38.42; H, 0.81. Found: C, 38.07; H, 0.68.

1,4-Bis(dichloromethyl)-2,3,5,6-tetrachlorobenzene (106)[66]: A mixture of 1,2,4,5-tetrachlorobenzene (22.6 g, 0.1 mol) and aluminum chloride (30 g, 0.225 mol) in anhydrous chloroform (300 mL) was refluxed for 22 h. The reaction mixture was cooled to room temperature, diluted with chloroform (200 mL) and poured into a mixture of hydrochloric acid (30 mL) and ice-water (300 mL). The organic layer was separated, dried over magnesium sulfate, and concentrated to give crude product (45 g), which was recrystallized from hexanes (225 mL) to give **106** (31.6 g) as yellow solid. The mother liquor was concentrated to a volume of 45 mL, after which a second crop of product (4.1 g) was obtained. The total yield was 91.1%. mp 134-136 ^oC (lit.[66] mp 127-129 ^oC); ^1H NMR δ 7.59 (br. s), 7.63 (br. s) (equal intensity, due to atropismers deriving from restricted rotation of the dichloromethyl group);[71] ^{13}C NMR δ 66.52, 137.29 (C1/C4 carbons not observed).

1,4-Bis(difluoromethyl)-2,3,5,6-tetrafluorobenzene (104) (Method B): A mixture of octachloro-*p*-xylene (120g, 314.1 mmol), cesium fluoride (476 g, 3.14 mol) and tetrabutylammonium bromide (4.2 g, 12.7 mmol) in anhydrous DMSO (520 mL) was heated to 120 ^oC for 6 h. The reaction mixture was then cooled down to room temperature and poured into ice water (1100 mL), then extracted with diethyl ether (2 × 500 mL). The combined organic layers were washed with water (1000 mL), dried over

magnesium sulfate, concentrated to remove solvent. The residue was distilled at 72 ^{o}C with reduced pressure (20 mm Hg) to give crude product (60 g), which was recrystallized from hexanes (60 mL) to furnish octafluoro-*p*-xylene (55.8 g, yield: 71.1%, mp: 70-72 ^{o}C) as white crystals. ^{1}H NMR δ 6.97 (t, J_{FH} = 53 Hz); ^{13}C δ 108.22 (t, J_{FC} = 242 Hz), 115.97 (br. S), 144.79 (d, J_{FC} = 262 Hz), ^{19}F NMR δ -115.2 (d, J_{FH} = 52 Hz), -142.2 (s). Anal. Calcd for $C_8H_2F_8$: C, 38.42; H, 0.81. Found: C, 38.07; H, 0.68.

1, 4-Bis-(chlorodifluoromethyl)-2,3,4,5-tetrafluorobenzene (100): To a solution of octafluoro-*p*-xylene (18.7 g, 74.8 mmol) in carbon tetrachloride (250 mL) was bulbed chlorine under sunlamp for 17 h. The reaction mixture was slowly evaporated to remove carbon tetrachloride. The residue was distilled under reduced pressure (85-87 ^{o}C/20 mmHg) to give 1, 4-bis-(chlorodifluoromethyl)-2,3,4,5-tetrafluorobenzene (19.4 g, yield: 81.3%) as a colorless oil. ^{13}C NMR δ 121.10 (t, J_{FC} = 295 Hz), 143.61 (d, J_{FC} = 268 Hz), ^{19}F NMR δ -47.6 (m, 4F), -137.9 (m, 4F). HRMS calcd for $C_8F_8Cl_2$ 317.9249, found 317.9239; GC-EI-MS ($C_8F_8Cl_2$, 319, C_8F_8Cl, 283, C_8F_8, 248).

1.4-Bis(bromodifluoromethyl)-2,3,5,6-tetrafluorobenzene (108): A mixture of 1, 4-bis-(chlorodifluoromethyl)-2,3,4,5-tetrafluorobenzene (**100**) (1 g, 3.13 mmol) and zinc (0.82 g, 12.5 mmol) in anhydrous DMF (5 mL) was heated to 100 ^{o}C for 0.5 h. The reaction mixture was cooled to room temperature, and a ^{19}F NMR spectrum of the mixture revealed two equal intensity singlets at -100.3 and -145.0 ppm. These two peaks were attributed to the presence of bis-zinc intermediate **107**: ^{19}F NMR δ -100.3 and -145.0 (equal intensity). Bromine (0.65 g, 8 mmol) was then added to the reaction mixture, and this mixture was stirred at room temperature for 4 h, quenched with ice-water (30 g), extracted with diethyl ether (2 × 10 mL). The combined ethereal layers

were dried over magnesium sulfate, and concentrated to give crude product, which was purified by column chromatography (silica gel, hexanes) to provide 1.4-bis(bromo-difluoromethyl)-2,3,5,6-tetrafluorobenzene (0.11 g, yield: 8.6%) as sticky colorless oil. . ^{13}C δ 110.4 (t, J_{FC} = 308 Hz), 143. 1 (d, J_{FC} = 284 Hz) (other carbon not seen); ^{19}F NMR δ -43.8 (m, 4F), -137.9 (m, 4F). HRMS (all three isotopic combinations) calcd for $C_8F_8[79]Br_2$ 405.8239, found 405.8214; calcd for $C_8F_8[79]Br[81Br$ 407.8219, found 407.8228; calcd for $C_8F_8[81]Br_2$ 409.8198, found 409.8234.

Perfluoro[2.2]paracyclophane (109): A mixture of 1,4-bis-(chlorodifluoromethyl)-2,3,5,6-tetrafluorobenzene (10 g, 31.3 mmol) and zinc (8.2 g, 125.2 mmol) in anhydrous acetonitrile (100 mL) was heated to 100 ^oC (oil bath temperature) under nitrogen atmosphere. The reaction mixture was refluxed gently for 38 h. The reaction mixture was then cooled to room temperature, filtered and washed with acetone (3 × 30 mL). The combined filtrates were concentrated to dryness. The residue was purified by column chromatography (silica gel, hexanes) to give crude product (3.8 g) as white powder. The crude product was recrystallized from chloroform (40 mL) to furnish 2.9 g of pure product as white needles. The mother liquor was concentrated to dryness. The residue was recrystallized from chloroform (10 mL) to give second crop of pure product (0.37 g) as white needles. The yield is 42.1% based on isolated pure product. mp 195-196 ^oC; ^{13}C δ 118.0 (tt, J_{FC} = 283.29 Hz), 147.4 (dd, J_{FC} = 267.22 Hz), bridgehead carbon not seen; ^{19}F NMR δ -102.8 (s, 8F), -132.4 (s, 8F). HRMS calcd for $C_{16}F_{16}$ 495.9739, found 495.9719; Anal. Calcd for $C_{16}F_{16}$: C, 38.73; H, 0.00; N, 0.00. Found: C, 39.07; H, 0.00; N, 0.04.

Perfluoro[2.2.2]paracyclophane (111): The accumulated mother liquor enriched with perfluoro [2.2.2]paracyclophane (**111**) and bridge-unsaturated compound (**110**), was concentrated to dryness (12 g), and was purified by column chromatography (silica gel, hexanes). The first fraction was compound **110** (1.2 g, yield: 0.6%) as a white powder. The third fraction (3.6 g) contains compound **111,** which was not pure. Recrystallization it from acetonitrile (40 mL) gave perfluoro[2.2.2]paracyclophane (2.4 g, yield: 1.2%) as white crystals. mp 245-246 ^{o}C; ^{19}F NMR δ -104.28 (s, 12F), -134.17 (s, 12F). HRMS calcd for $C_{24}F_{24}$ 743.9617, found 743.9609; Anal. Calcd for $C_{24}F_{24}$: C, 38.73; H, 0.00; N, 0.00. Found: C, 38.54; H, 0.00; N, 0.263. Compound **110**: mp 135-137 ^{o}C; ^{19}F NMR δ -103.72 (m, 4F), -122.67 (s, 2F), -129.47 (d, *J* = 10.4 Hz, 4F), -134.11 (d, *J* = 12.7 Hz, 4F). HRMS calcd for $C_{16}F_{14}$ 457.9776, found 457.9758; Anal. Calcd for $C_{16}F_{14}$: C, 41.95; H, 0.00; N, 0.00. Found: C, 42.00; H, 0.00; N, 0.02.

CHAPTER 3
REACTIONS OF NUCLEOPHILES WITH PERFLUORO[2.2]PARACYCLOPHANE

3.1 Introduction

Fluorine substituents on alkenes or aromatic rings are known to significantly enhance the electron deficiency of these unsaturated systems and as a result increase their reactivity towards nucleophiles.[72-74] Trifluoromethyl substituents, although not as effective as a nitrile group, are even more effective activating groups for such nucleophilic attack.[74-76] Such activation derives, of course, from the ability of these groups to stabilize the carbanion "Meisenheimer" intermediates that would be formed, for example, during a nucleophilic aromatic substitution reaction proceeding via an S_NAr mechanism. Such a process, proceeding by a carbanion intermediate is the most common by which nucleophilic aromatic substitution reactions occur, such mechanism being facilitated by substituents that will increase the electron deficiency of the system.

Because of the presence of multiple fluorine substituents, hexafluorobenzene and pentafluoropyridine exhibit high reactivity towards nucleophiles (Figure 3-1), [73,74,77,78] as do trifluoromethyl-substituted analogues, such as perfluorotoluene.[74,75,79] In a kinetic study of the reactivity of perfluoropolymethylbenzenes towards nucleophiles, it was observed that in its reaction with $^-OCH_3/HOCH_3$ at 25 ^oC, perfluorotoluene is 7000 times as reactive as hexafluorobenzene. Adding a second (*para*) trifluoromethyl group (as in perfluoro-*p*-xylene) leads to a somewhat lower reactivity, but it is still 2900 times more reactive than hexafluorobenzene.

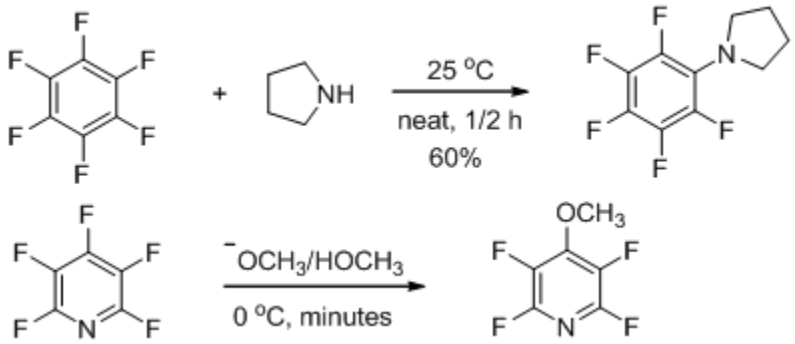


Figure 3-1 Reactivity of hexafluorobenzene and pentafluoropyridine with nucleophiles

Perfluoro[2.2]paracyclophane (F8) has recently been synthesized[80] and because its aromatic rings resemble those of perfluoro-*p*-xylene, it should be expected to exhibit high reactivity towards nucleophiles, although the reactivity may be somewhat diminished because of the non-planarity of F8's benzene rings.

3.2 Results

Indeed, F8 proved to be very reactive with a large variety of nucleophiles. In this chapter, reactions that led mainly to mono-substitution will be emphasized, with discussions centered on definition of factors that favor mono-substitution. Subsequent chapter will deal with multi-substitution reactions of F8, the regiochemistry of multi-substitution, and characterization of the multi-substituted products, including detailed multidimensional NMR analysis of these products.

When F8 was allowed to react at room temperature with up to eight equivalents of NaOH in aqueous THF a single, mono-hydroxy product **112a** was formed in 99% yield (Figure 3-2). A similar reaction of 2.2 equivalents of NaOMe in THF yielded the mono-substituted product **112b** in 49% yield along with 14% of a dimethoxy product, the *pseudo-para* isomer **113**. Providing further contrast, a reaction of F8 with one equivalent of sodium thiophenolate yielded no mono-substituted product at all. Instead,

the *para*-bis-(phenylthio) product **114a** was obtained in 30% yield along with small amounts of tetrakis- and hexakis-(phenylthio) products.

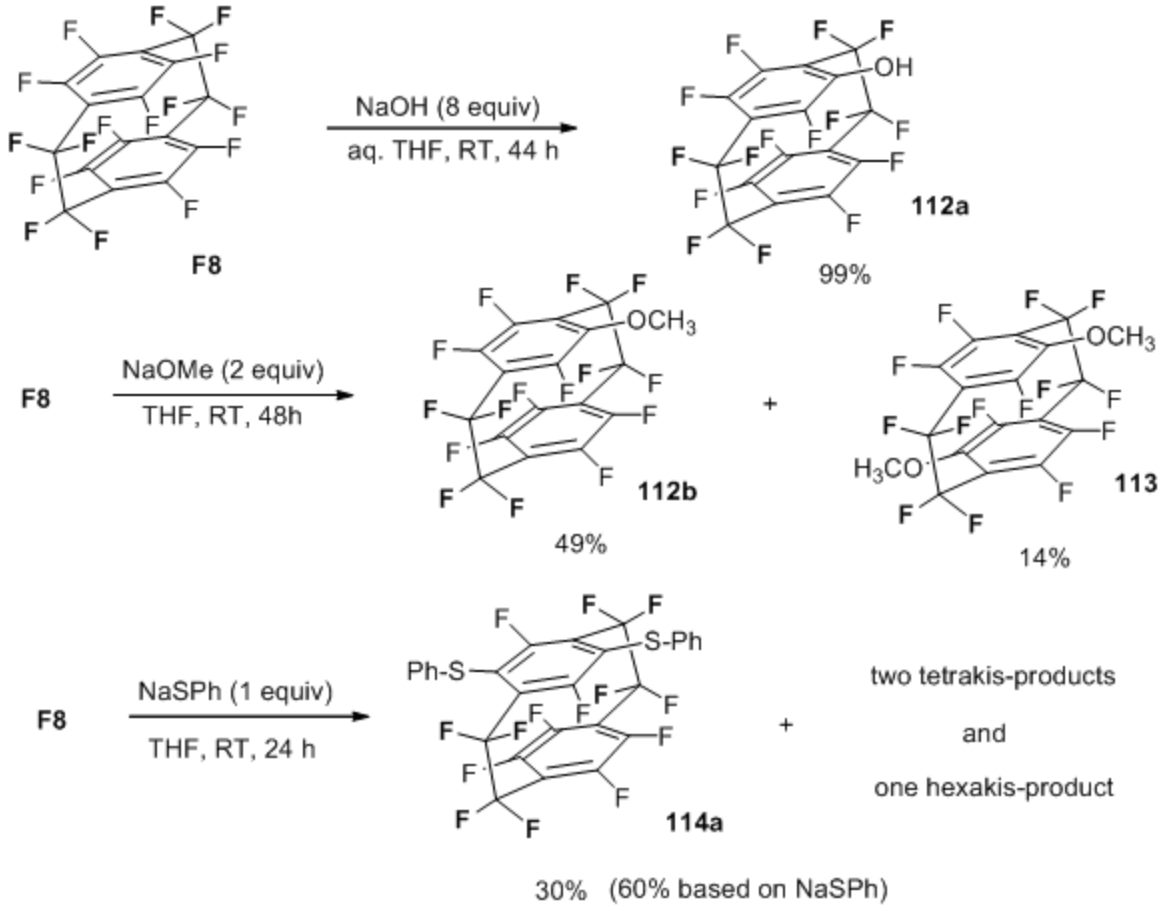


Figure 3-2 Reactions of F8 with nucleophiles

All three of the above nucleophiles were highly reactive in their respective substitution reactions with F8, with the reactions being complete after two days at room temperature for hydroxide and methoxide. The reaction with phenyl thiolate required only one day. The differences exhibited by these nucleophiles with respect to multiple substitution can be explained based on the variable effects of the different substituents (O^-, OMe and SPh) of the monoadducts on their reactions with a second equivalent of nucleophile. Substitution of fluorine by hydroxide to form phenol derivative **112a** will, of course, under the reaction conditions actually form the deprotonated phenolate anion,

and the O^- substituent will act as a powerful donor to the aromatic system that will strongly inhibit further reaction of a nucleophile with the ring bearing the O^-. Not only that, but the impact of the O^- must also be significantly transmitted to the other benzene ring of the paracyclophane, since a second strong hydroxide nucleophile is also not observed to add to that ring either. As a weaker donor, the methoxy substituent of **112b** appears to inhibit its reaction with a second equivalent of methoxide, but its influence is not sufficiently strong to prevent substitution of the other, unsubstituted benzene ring of **112b**. In contrast, the results obtained from the reaction of F8 with thiophenolate anion clearly indicate that the SPh substituent of the putative monoadduct must activate that ring towards addition of a second nucleophile. Such results are consistent with the previously observed formation of only *p*-bis-(phenylthio)-2,3,5,6-tetrafluorobenzene from the reaction of either one or two equivalents of phenylthiolate anion with hexafluorobenzene.[81]

Dimethyl malonate anion behaves much like hydroxide in its reaction with F8, forming only a monoadduct even when the nucleophile is present in great excess. The reason for this is much the same, since the monoadduct would become immediately deprotonated to form the highly unreactive carbanion. Other nucleophiles, generally oxygen and nitrogen nucleophiles that serve to deactivate the ring to which they become attached, have also been utilized in reaction with F8, with the results from all of these reactions being summarized in Table 3-1.

Some negative results were obtained during the trials between F8 and various nucleophiles. If methyl lithium, n-butyl lithium, phenyl lithium and *N*,*N*-diethyl-cyclohex-1-enamine were used as nucleophiles, no desired products were obtained. When F8

reacted with nitromethane or 2-nitropropane in the presence of 2 equivalents of NaH in anhydrous THF at room temperature or reflux, only the starting material F8 was recovered. No reaction was observed between F8 and aniline, phenyl hydrazine, or the Reformatsky reagent 1(-ethoxyvinyloxy)zinc (II) bromide probably due to these reagents being too weak base. There is also no reaction when ethynyltrimethylsilane was used as nucleophile in the presence of CsF.

Table 3-1 Reaction of nucleophiles with F8 in THF at RT

Nucleophile	Equivalents	Reaction Time hr	Product No. and Yield (%)	Color
HO^-	8	44	**112a** (99)	Yellow
MeO^-	2	48	**112b** (49)	White
4-F-C_6H_4-O^-	1	18	**112c** (77)	White
$^-CH(CO_2Me)_2$	4	48	**112d**(73)	White
tert-Butyllithium	1.1	18	**112e**(54)	White
Et_2NH	4.4	20	**112f**(91)	Yellow
$(CH_2)_4NH$	2.2	24	**112g**(84)	Yellow
$PhCH_2NHCH_3$	2.2	24	**112h**(68)	Yellow
$(CH_3)_2NH$ (aq)	2.2	1	**112i**(70)	Yellow

All of the above reactions were carried out preparatively for times of between 18 and 48 h, but it was later determined that the reactions of F8 with most of the nucleophiles were complete in less than an hour. Indeed, while conducting relative reactivity experiments it was determined that the reactions of methoxide with F8, hexafluorobenzene and pentafluoropyridine in THF were all complete within 15 minutes. Under conditions of direct competition, in the presence of equal amounts of F8 and pentafluoropyridine, methoxide reacted exclusively with pentafluoropyridine. Likewise, F8 reacted exclusively in competition with hexafluorobenzene. Thus in reactions with nucleophiles, pentafluoropyridine is much more reactive than F8, which is itself much more reactive than hexafluorobenzene.

Interestingly, even when 4.4 equivalents of diethylamine were used, the only formed product was **111f**, no bis-substituted product was detected due to steric hindrance. As with aqueous dimethylamine, the only product was **112i**, no **112a** was detected by ^{19}F NMR because nitrogen is more reactive than hydroxide group as nucleophiles.

All of the reaction mixtures were observed to develop a yellow color during reaction. Among the monosubstituted products, the ether, malonate and *t*-butyl products were colorless, whereas the hydroxy, sulfide and amine products were various shades of yellow. The UV spectra of these products show a progression towards longer wavelength absorption as the substituent becomes increasingly electron donating (Figures 3-3 and 3-4 and 3-5)

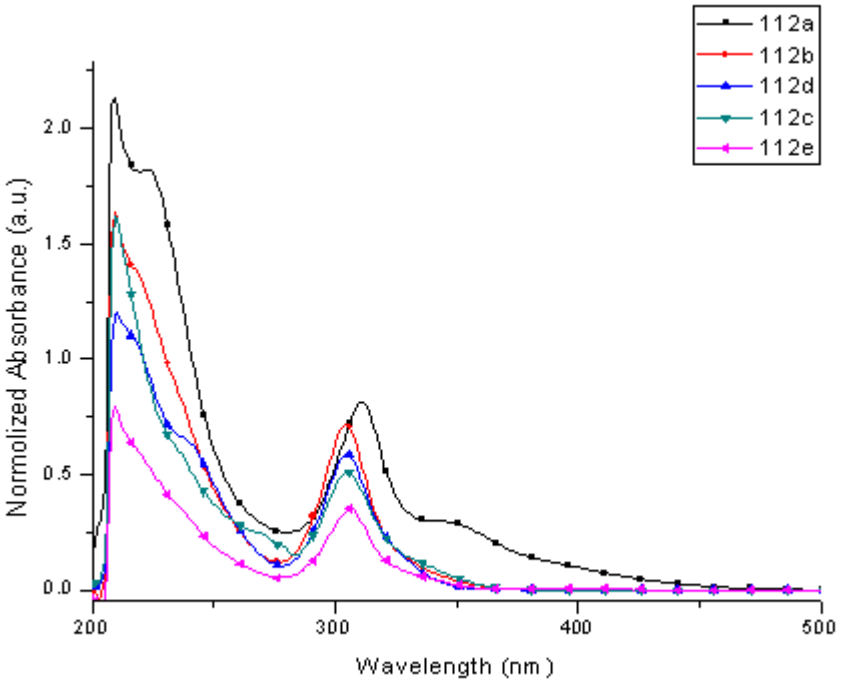


Figure 3-3 UV spectra of monosubstituted F8 compounds

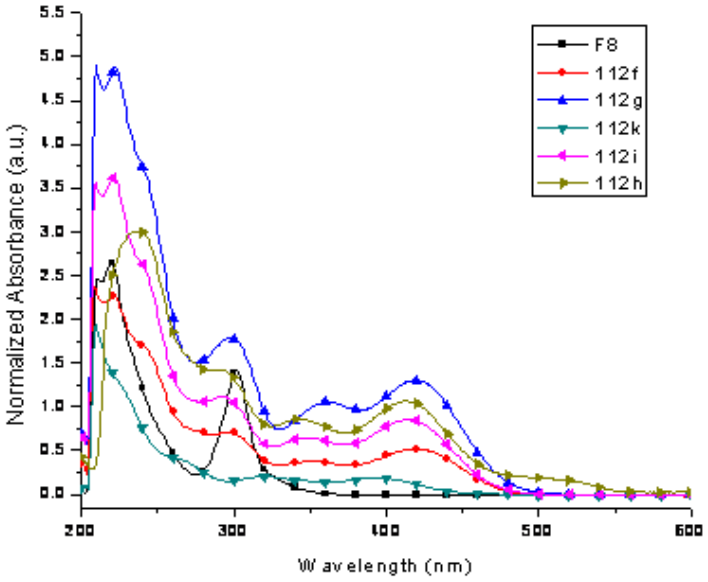


Figure 3-4 UV spectra of monosubstituted F8 compounds

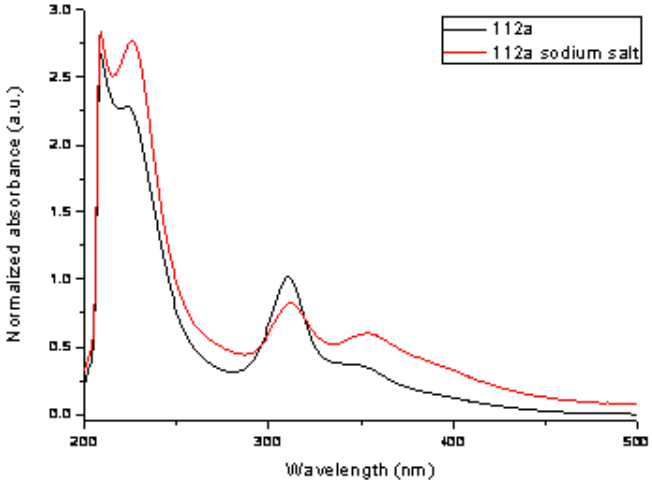


Figure 3-5 Comparison of UV spectra of F8 phenol and phenolate species

Bidentate nucleophiles were also examined to determine whether the intramolecular mode of reaction for the second nucleophile might provide sufficient kinetic advantage to observe cyclic products (Figure 3-6 and Table 3-2). Reaction of ethylene glycol in the presence of excess NaH led simply to formation of the

monoadduct **112j**. Attempts to stimulate cyclization by raising the temperature of the reaction led only to decomposition. In contrast, catechol (o-dihydroxybenzene) gave the cyclic diether, **115a**, resulting from consecutive nucleophilic substitution of F8 by the ortho-phenolate anions, even when 2 equivalents of catechol in the presence of 4.4 equivalents of NaH were used, only monoadduct was formed. Compound **115b** and **115c** were obtained respectively when 4-nitrocatechol and 1,2-benzenedithiol were used as nucleophiles. UV spectra of these compounds were displayed in Figure 3-7. Likewise, reactions of the primary and secondary bis-amines, 1,2-diaminoethane and 1,2-di(ethylamino)ethane, also resulted in formation of the respective cyclic disubstituted products **116a** and **116b**. These two compounds were both red in color, with their uv bands extending past 500 nm (Figure 3-8).

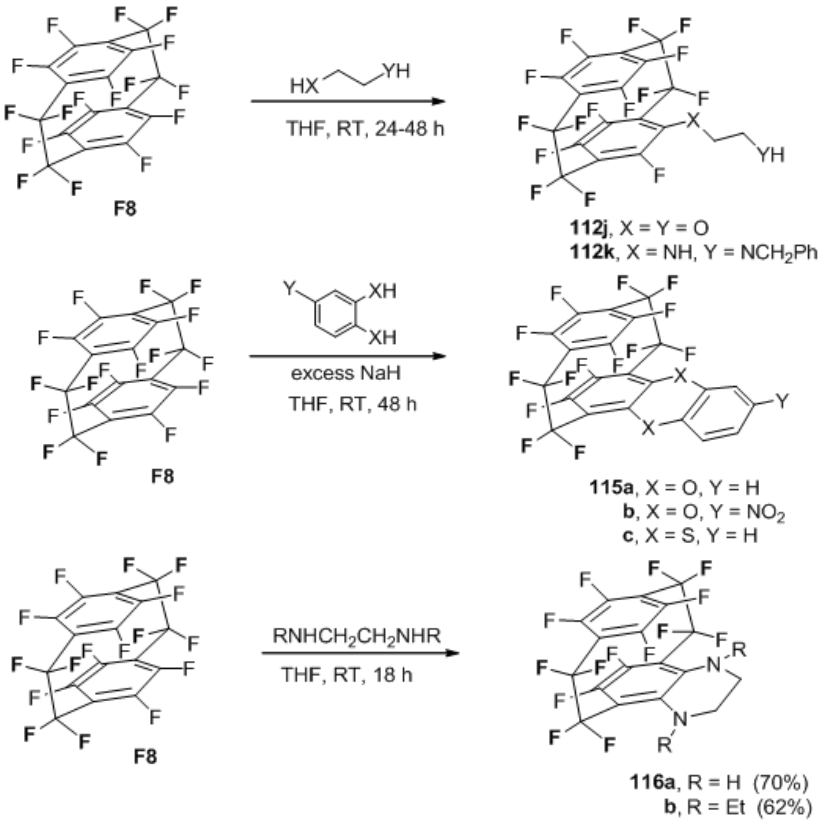


Figure 3-6 Reaction of F8 with bidentate nucleophiles

Table 3-2 Reaction of bidentate nucleophiles with F8 in THF at RT

Bidentate Nucleophile	Equivalents	Reaction Time hr	Product No. and Yield (%)	Color
$HOCH_2CH_2OH$	1.1 (excess NaH)	48	**112j**(50)	White
$NH_2CH_2CH_2NHCH_2Ph$	2.2	24	**112k**(58)	Yellow
1,2-dihydroxybenzene	1.1 (excess NaH)	48	**115a**(78)	Lt. yellow
1,2-dihydroxy-4-nitrobenzene	1.1 (excess NaH)	48	**115b**(56)	Lt. yellow
1,2-benzene-dithiol	1.1 (excess NaH)	18	**115c** (86)	Brown
$NH_2CH_2CH_2NH_2$	2.2	18	**116a** (70)	Red
$EtNHCH_2CH_2NHEt$	2.2	18	**116b** (62)	Red

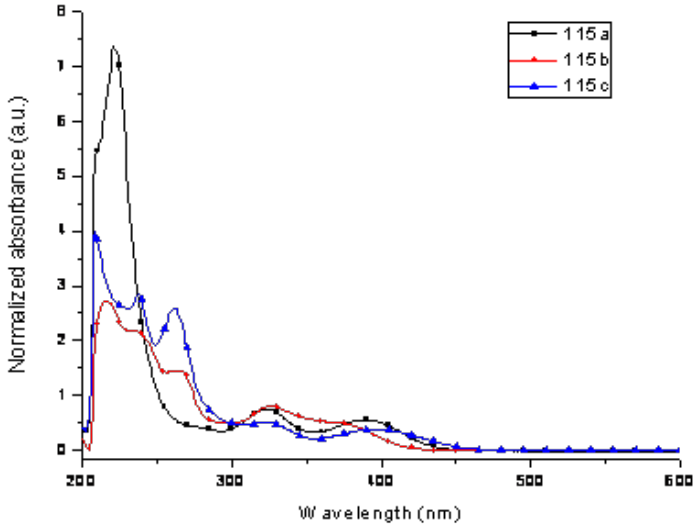


Figure 3-7 UV spectra of F8 adducts with benzene-1,2-diols and 1,2-bis-thiol

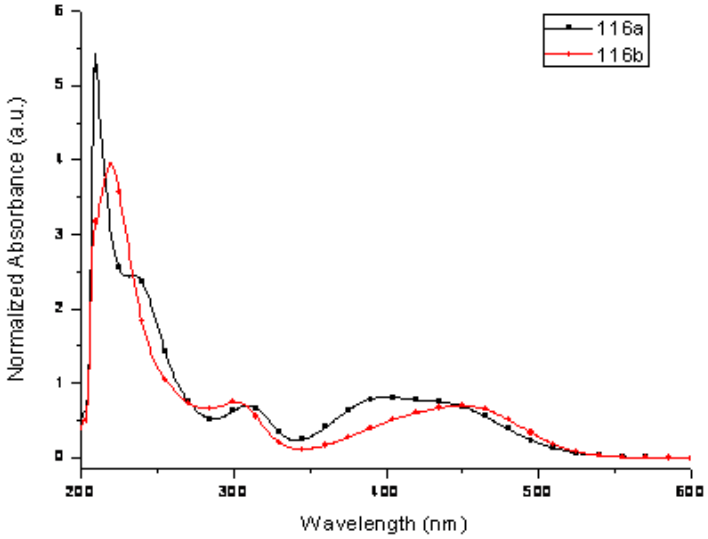


Figure 3-8 UV spectra of F8-bisamine adducts

3.3 Discussion

Although all of the reactions of F8 with nucleophiles can be understood within the context of the conventional S_NAr addition-elimination mechanism involving formation of a Meisenheimer (carbanion) intermediate, because of the extreme electron deficiency of the F8 substrate and the obvious electron-transfer ability of many of the nucleophiles in Table 3-1, it was considered prudent to also consider the possibility that the reactions might proceed via an electron-transfer, free radical chain $S_{RN}1$ mechanism. In pursuit of evidence regarding this issue, the reduction potential of F8 was determined via cyclic voltammetry, and ESR studies were carried out to determine whether the F8 radical anion might be detected, either electrochemically or during the course of any of the reactions of F8 with the various nucleophiles.

Electrochemistry. Electrochemical characterization of F8 was performed by cyclic voltammetry (CV) and differential pulse voltammetry (DPV) in acetonitrile with 0.1 M tetrabutylammonium hexafluorophosphate (Bu_4NPF_6) as a supporting electrolyte. The cyclic voltammogram of F8 shows an irreversible reduction wave with a peak at -1.24 V (vs. SCE) (Figure 3-9). The voltammogram of F8 shows anodic current in the reverse scan, peaked at -0.80 V (vs. SCE), corresponding to the oxidation of reduced species. In addition, no change in the voltammogram was observed when scanning cycles were repeated 10 times, which suggests the chemically reversible nature of the redox process. The results suggest probable delocalization of the charge through the stacked π-system of F8 stabilizing the intermediate radical anion species.

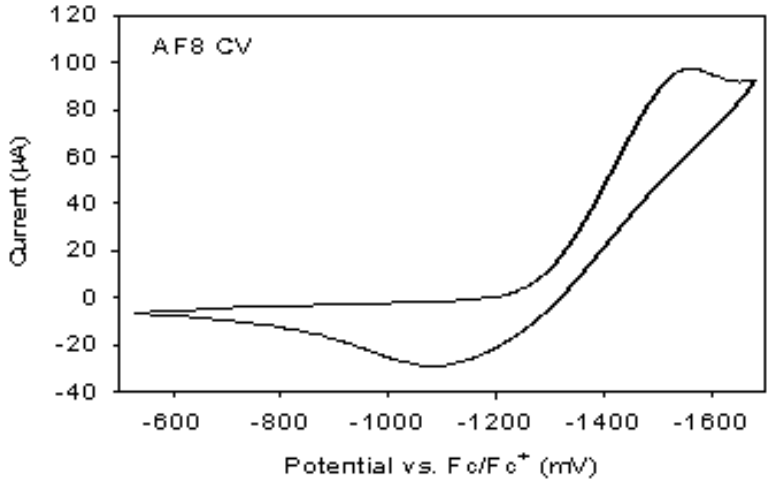


Figure 3-9 Cyclic voltammogram (CV) of F8

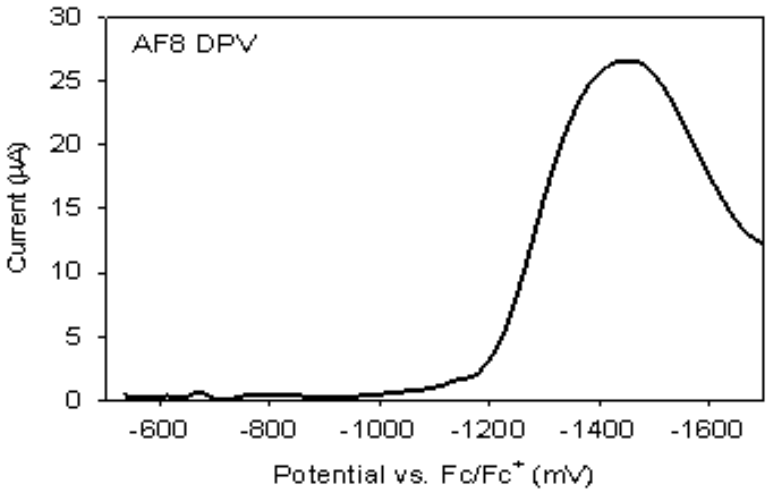


Figure 3-10 Differential Pulse Voltammogram (DPV) of F8

Because of the electrochemically irreversible nature of the redox process, the DPV technique was utilized to determine the reduction potential of F8. The DPV voltammogram shows a reduction peak at -1.12 V (vs SCE) (Figure 3-10). Although the presence of a possible second reduction wave was observed, the results were inconclusive due to overlapping solvent reduction waves. The reduction potential of F8 in acetonitrile (-1.12V vs SCE) is virtually the same as those of nitrobenzene (-1.14V) and *p*-fluoronitrobenzene (-1.13V),[82] and more negative than that of 4-nitro-AF4 (the

nitro derivative of the bridge-fluorinated [2.2]paracyclophane, AF4) (-0.86V), but more positive than that of hexafluorobenzene (-2.2V).[83]

Halonitroaromatics generally do not undergo substitution by the free radical chain $S_{RN}1$ mechanism, mainly because the intermediate nitro-stabilized aromatic radical anions appear to be too stable to allow dissociation of halide to form the propagating aryl radical in a kinetically-competitive manner.[84,85] Moreover, fluoride has proved to be by far the worst halide leaving group for an $S_{RN}1$ reaction.[86,87] Thus, it seems unlikely that F8, which has a similarly-stabilized radical anion and with only fluoride leaving groups, would participate in a productive $S_{RN}1$ reaction.

An attempt to directly observe the F8 radical anion by EPR under conditions of electrochemical generation failed, although the F8 was destroyed by the potential; nor could this radical anion be detected in situ, during the reaction of F8 with PhS^-Na^+ in THF. Electron transfer obviously was occurring during the electrochemical experiment; thus the lack of an observable EPR spectrum indicates that the intermediate radical anion (and any other radical species that are formed subsequently) must have been destroyed too rapidly to be observed. All that one can conclude by the lack of an EPR signal during the chemical reactions is that if the reaction proceeds via an SET (single electron transfer) process, any radical anion/radical intermediates must be too short-lived to be observed in the experiment.

The fate of the F8 radical anion was determined by subjecting F8 to exhaustive electrochemical reduction in acetonitrile, wherein the products that were observed exhibited only alkyl hydrogen incorporation. No aromatic hydrogen was observed in the NMR spectrum of the isolated product mixture. This means that if and when F8's

radical anion is formed, it prefers kinetically to lose fluoride from its bridges, rather than from its aromatic rings. Again, this result appears to preclude involvement of an $S_{RN}1$ mechanism in the reaction of F8 with nucleophiles.

Additional mechanistic experiments. The intervention of any free radical chain mechanism was additionally tested by an experiment in which the reaction of pyrrolidine with F8 was carried out in the presence of one equivalent of free radical trap, TEMPO. The reaction was not inhibited and proceeded to in a normal manner. This result again speaks clearly against involvement of a free radical chain process.

Lastly, the involvement of a FRC process in the reaction of F8 with methoxide can be specifically ruled out by earlier work by Bunnett[88] and Saveant,[89] which indicated that methoxide's preferred reaction with aryl radicals is hydrogen atom abstraction to form the $\bullet CH_2O^-$ radical anion. No such reductive reaction was observed in any of our reactions.

All of these results lead one to conclude that the reactions of F8 with nucleophiles cannot be proceeding via the free radical chain $S_{RN}1$ mechanism, and that the most probable mechanism for these reactions is the S_NAr mechanism proceeding via its usual delocalized (Meisenheimer) carbanion intermediate. One cannot completely rule out electron transfer or at least formation of a charge transfer complex as the initial step of the nucleophilic substitution mechanism, since non-radical chain SET processes, where an intermediate charge transfer complex of radical anion and radical collapse within the solvent cage to form the Meisenheimer complex have been proposed previously.[90]

3.4 Synthetic Conclusion

The aromatic rings of perfluoro[2.2]paracyclophane are exceptionally receptive to nucleophilic substitution, and all of the observations related to F8's reactivity and regiochemistry of reactions with the various nucleophiles that have been presented and discussed in this chapter can be readily rationalized within the framework of the S_NAr mechanism.

3.5 Characterization

Parent perfluoro[2.2]paracyclophane (F8) shows only two singlets (δ -102.8, -132.4 ppm)[80] for its eight equivalent bridge fluorines and eight equivalent aromatic fluorines in the ^{19}F NMR spectrum due to its symmetric nature. When a single substituent is introduced into one of the rings, the symmetry is destroyed, and all fifteen fluorines become nonequivalent.

F8 derivatives display a multitude of ^{19}F-^{19}F couplings, ranging from ca. 250 Hz for the geminal coupling to couplings smaller than 3 Hz, which are visible only when the line is not broaden by other small couplings. Couplings over 3 Hz, were identified in the DQF-COSY spectrum, were confirmed and measured in selective decoupling experiments, that were refined through simulation in gNMR. The experimental and simulated spectrum for compound **112d** are given in Figure 3-11. Chemical shifts and coupling constants are given in Table 3-3.

The largest couplings only were used for the assignment of the fluorine signals. It has previously been demonstrated that in fluoro-AF4s a bridge fluorine couples with a large coupling constant (20-30 Hz) with the aromatic fluorine *ortho* and *syn*, and with a somehow smaller constant (20-10 Hz) with the aromatic fluorine which is *pseudo-gem* to the fluorine *ortho* and *syn*.[91] The other large couplings used for the assignment were

the *ortho* coupling of the aromatic fluorines, *ca*. 20 Hz, significantly larger than the *meta* or *para* couplings, *ca*. 6-10 Hz. The steps of the assignment procedure are presented in Figure 3-12: **a**) the pairs of geminal fluorines were identified by a large coupling, *ca*. 250 Hz. **b**) couplings larger than 50 Hz identified the aromatic fluorines (*a9, a14, a15*) *ortho* and *syn* to some of the bridge fluorines (*a8, a7* and *a6*, correspondingly). **c**) couplings of 10-40 Hz of these later bridge fluorines identified the aromatic fluorines (*a13*, *a10* and *a11*) *pseudo-gem* to the their *ortho* and *syn* partners. **d**) other couplings larger than 20 Hz of these later aromatic fluorines (*a13*, *a10* and *a11*) identified the bridge protons *ortho* and *syn* to them (*a3*, *a2* and *a4*, correspondingly), which established the identity and relative orientation of the fluorines in a tetrafluoroethylene unit. In most cases, this assignment can be confirmed by couplings of 8-10 Hz between the bridge fluorines which are vicinal and *syn*. The couplings with aromatic fluorines of the bridge fluorines in the tetrafluoroethylene unit *a2, a3, a7, a8* displays a 'diagonal pattern', *i.e.* the bridge fluorines displaying couplings over 50 Hz with the *ortho* and *syn* and couplings over 10 Hz with the fluorines *pseudo-gem* to the ones *ortho* and *syn*, are vicinal and *anti*. This diagonal pattern can be applied to assign *a12* as *ortho* and *syn* to *a1*, since *a12* displays couplings with comparable constants with both *a1* and *a5*. The position of *a12* can also be established later on, based on the *ortho* coupling of the aromatic fluorines. ***e)*** just one *ortho* coupling of the aromatic fluorines is necessary at this point to join the two 'half-molecules' determined in step *d*. The other two *ortho* couplings confirm the whole assignments and determine/confirm the position of the aromatic fluorines which display comparable couplings with two bridge ones, like *a12*.

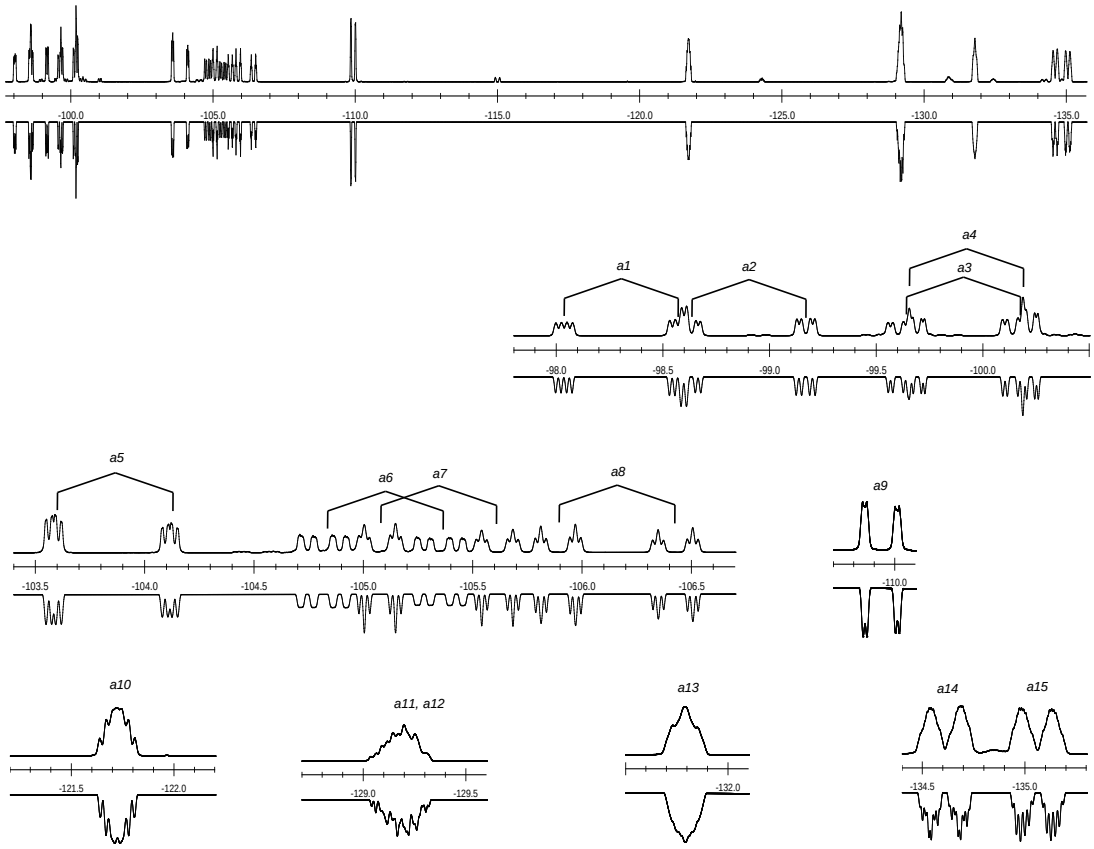


Figure 3-11 ^{19}F spectrum of compound **1**, experimental (top) and simulated (bottom)

Table 3-3 Chemical shifts (ppm) and coupling constants (Hz) in the ^{19}F spectrum of compound **112d**

	δ	$J_{an\text{-}a1}$	$J_{an\text{-}a2}$	$J_{an\text{-}a3}$	$J_{an\text{-}a4}$	$J_{an\text{-}a5}$	$J_{an\text{-}a6}$	$J_{an\text{-}a7}$	$J_{an\text{-}a8}$	$J_{an\text{-}a9}$	$J_{an\text{-}a10}$	$J_{an\text{-}a11}$	$J_{an\text{-}a12}$	$J_{an\text{-}a13}$	$J_{an\text{-}a14}$
a1	-98.31														
a2	-98.91	0.0													
a3	-99.88	0.0	0.0												
a4	-99.98	0.0	0.0	0.0											
a5	-103.83	12.0	0.0	0.0	249.8										
a6	-105.07	250.7	0.0	0.0	8.0	0.0									
a7	-105.33	0.0	12.0	252.2	0.0	0.0	0.0								
a8	-106.15	0.0	0	252.10.0	0.0	0.0	0.0	0.0							
a9	-109.93	0.0	2.0	2.0	0.0	0.0	0.0	0.0	74.2						
a10	-121.72	0.0	29.8	0.0	0.0	3.5	0.0	11.5	0.0	0.0					
a11	-129.14	0.0	0.0	0.0	25.6	0.0	28.1	0.0	0.0	9.0	22.0				
a12	-129.24	24.3	0.0	0.0	0.0	21.0	0.0	0.0	0.0	0.0	0.0	0.0			
a13	-131.79	0.0	0.0	33.2	0.0	0.0	4.0	0.0	13.0	3.0	0.0	0.0	20.0		
a14	-134.61	0.0	0.0	0.0	0.0	0.0	0.0	67.4	0.0	0.0	14.7	0.0	6.0	6.0	
a15	-135.06	2.0	0.0	0.0	0.0	0.0	69.7	0.0	0.0	0.0	0.0	10.0	8.0	8.0	20.0

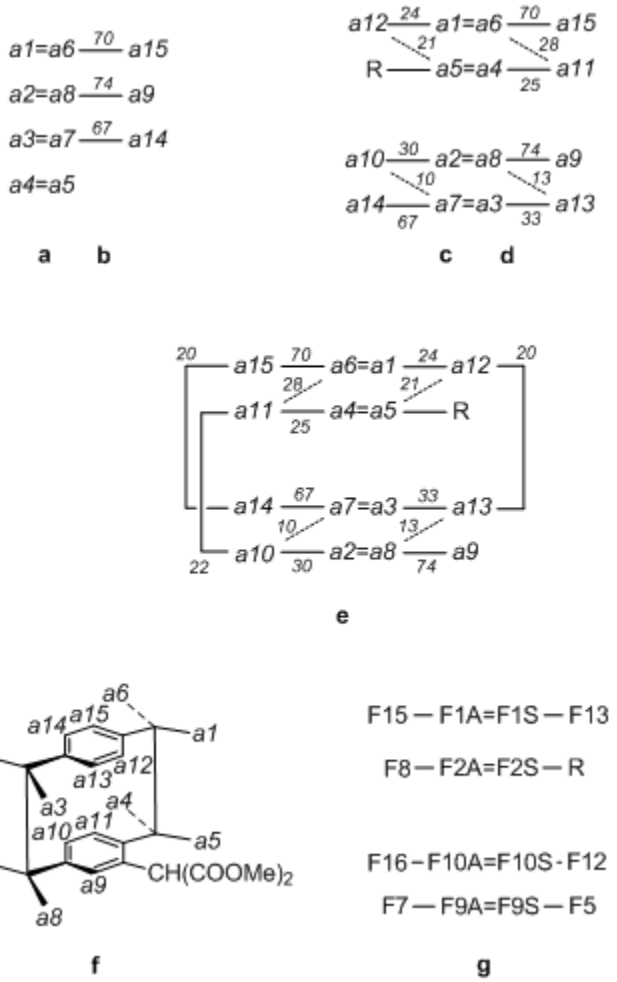


Figure 3-12 Step-by-step assignment of the ^{19}F signals in compound **112d**

The complete assignments are given on the structure in Figure 3-12f. Alternately, the positions of the fluorines in the representation of Fig. 3-12e are given in Figure 3-12g.

The ^{19}F spectrum of **112d** (Figure 3-11) displays a pattern for the bridge fluorines which was seen in all of the compounds **112a-112k**, namely there are four more shielded and four more deshielded fluorines, and each of the fluorines in the deshielded region has a geminal partner in the shielded region. The most shielded bridge fluorines (*a5-a8*) are the ones which display the largest coupling constants with the aromatic fluorine over four bonds and *syn,* $^4J_{\text{bridge-arom.}}$ These fluorines are on one side of the

‘upper deck’ of the PCP (e.g. F1A and F10A in **112d**) and on the opposite side of the ‘lower deck’ (F9S in **112d**), suggesting a skewed geometry in which the upper deck moves towards or away from the substituent. In a move towards the substituent, F1S, F2A, F9A and F10S are drawn closer to both the aromatic fluorine four bonds away and *syn* and to the aromatic fluorine on the remote deck five bonds away and *syn*. The through-space couplings between the bridge fluorine and these aromatic fluorines are expected to become larger. This is the case of compounds **112a** and **112b**. In compounds **112d** and **112g**, F9S, F10A and F1A display larger couplings both over four bounds with the aromatic fluorines *syn* and over five bonds with the aromatic fluorines on the opposite deck and *syn*, in agreement with a move of the upper deck away from the substituent. This is to be expected, considering the larger size of the substituents in **112d** and **112d**, compared to **112a** and **112b**.

Smaller couplings, between 2 and 5 Hz, have been noticed in the DQF-COSY spectra, and have then been optimized through simulation. The long-range coupling constants between aromatic and bridge fluorines support also the skewed geometry, if one assumes that the angular dependence of the ^{19}F-^{19}F couplings parallels the one of the ^{1}H-^{1}H couplings. The bridge fluorine which is further away from the plane of the aromatic ring displays a small (ca. 5 Hz) coupling with the aromatic fluorine four bonds away and anti. This is similar to the cisoid allylic coupling, which reaches a maximum when the C-H bond of the allyl proton is perpendicular to the plane of the double bond.[92]. The bridge fluorine which is closer to the plane of the aromatic ring and displays a coupling over 50 Hz with the aromatic fluorine *ortho* and *syn*, also displays a coupling over five bonds with the aromatic fluorine *meta* and *anti*. Similar couplings

between the benzylic proton in the plane of the aromatic ring and the proton *meta* and *anti* have been reported.[93] We have reported for the 4-fluoro-AF4 a coupling of F4 and F9A, which agrees with a skewed geometry in which the upper deck is displaced towards the fluorine substituent, geometry indicated by the larger couplings F4-F1S and F4-F2S.[92] More literature on the parallel displacement of the aromatic rings in Journal of Organic Chemistry 2007, 2469.[94]

Other couplings, in the range of 4-12 Hz, have been detected between *vicinal* and *syn* bridge fluorines. They are similar to the couplings seen in mono- and di-fluoro-AF4s, and are expected to be larger than the couplings between bridge fluorines vicinal and anti, based on the Karplus relationship, which was demonstrated to hold for fluorines too.

Table 3-4 NMR data for the aliphatic fluorines in compound **112d** in benzene-*d6*

Position	δ (ppm)	T1 (s)	^{2}J (Hz)	^{3}J (Hz)	$^{4}J_{syn}$ (Hz)	$^{5}J_{syn}$ (Hz)	other ^{n}J (Hz)
1S	-98.31	0.58	251	12 (F1S-F2S) 8 (F1A-F2A)	24	-	<3 (F15)
1A	-105.07	0.69			67	28	<3 (F12)
2S	-103.83	0.80	250		-	21	<3 (F7)
2A	-99.98	0.64			26	0	
9S	-106.15	0.75	252	12 (F9A-F10A) 10 (F9S-F10S)	74	13	<3 (F8)
9A	-98.91	0.70			30	0	<3 (F5)
10S	-99.88	0.73	252		33	<3	<3 (F16)
10A	-105.33	0.83			67	12	<3 (F13)

Table 3-5 NMR data for the aromatic fluorines in compound **112d** in benzene-*d6*

Position	δ (ppm)	T1 (s)	$^{3}J_{ortho}$ (Hz)	$^{4}J_{meta}$ (Hz)	$^{5}J_{para}$ (Hz)	$^{7}J_{pseudo\text{-}gem}$ (Hz)
5	-109.93	0.30	-	0	9	3
7	-121.72	0.22	22	0	-	14
8	-129.16	0.25 [a]		-	9	10
12	-131.79	0.27	20	6	8	10
13	-129.19	0.25 [a]		6	8	-
15	-135.06	0.20	20	6	8	10
16	-134.61	0.22		6	8	14

[a] values measured as an average for two different fluorines, because of signal overlap.

Table 3-6 NMR data for the aliphatic fluorines in compound **112a** in acetone-*d6*

Position	δ (ppm)	δ C_6D_6	^2J (Hz)	^3J (Hz)	$^4J_{syn}$ (Hz)	$^5J_{syn}$ (Hz)	other ^nJ (Hz)
1S	-101.16	-102.27	249		63	-	3 (F16)
1A	-98.33	-99.06		11 (F1A-F2A)	28	0	3 (F13)
2S	-97.96	-98.92	244		-	0	3 (F8)
2A	-103.56	-103.56			77	19	3 (F5)
9S	-99.47	-100.14	249	11 (F9A-F10A)	30	0	3 (F7)
9A	-104.85	-104.79			69	14	
10S	-105.03	-105.04	252	8 (F9S-F10S)	67	17	3 (F15)
10A	-99.92	-100.29			31	0	3 (F12)

Table 3-7**.** NMR data for the aromatic fluorines in compound **112a** in acetone-*d6*

Position	δ (ppm)	δ C_6D_6	$^3J_{ortho}$ (Hz)	$^4J_{meta}$ (Hz)	$^5J_{para}$ (Hz)	$^7J_{pseudo-gem}$ (Hz)
5	-130.26	-131.90	-	10	10	15
7	-156.64	-148.56	20	10	-	10
8	-141.28	-138.67		-	9	10
12	-136.74	-136.48	20	8	5	15
13	-134.49	-134.91		10	8	-
15	-133.14	-132.12	20	10	5	10
16	-135.90	-133.96		8	8	10

Table 3-8 NMR data for the aliphatic fluorines in compound **112b** in benzene-*d6*

Position	δ (ppm)	T1 (s)	^2J (Hz)	^3J (Hz)	$^4J_{syn}$ (Hz)	$^5J_{syn}$ (Hz)	other ^nJ (Hz)
1S	-104.39	1.58[b]	249		62	-	5 (F16)
1A	-99.14	1.45		5 (F1S-F2S)	30	0	<3 (F13)
2S	-101.09	1.52		12 (F1A-F2A)	-	0	5 (F8)
2A	-104.40	1.58[b]	249		76	15	4 (F5)
9S	-100.15	1.49[a]	251	10 (9S-10S)	33	0	<3 (F7)
9A	-105.06	1.66[c]			66	15	
10S	-105.16	1.66[c]	252	11 (F10A-F9A)	66	17	<3 (F15)
10A	-100.08	1.49[a]			32	0	<3 (F12)

[a, b, c] values measured as an average for two different fluorines, because of signal overlap.

Table 3-9 NMR data for the aromatic fluorines in compound **112b** in benzene-*d6*

Position	δ (ppm)	T1 (s)	$^3J_{ortho}$ (Hz)	$^4J_{meta}$ (Hz)	$^5J_{para}$ (Hz)	$^7J_{pseudo-gem}$ (Hz)
5	-126.68	0.87	-	6	7	12
7	-136.94	0.73	20	6	-	9
8	-135.84	0.72		-	7	7
12	-136.33	0.73	21	7	10	12

Table 3-9. Continued

13	-133.42	0.69		7	12	-
15	-132.00	0.75	20	7	10	7
16	-132.66	0.77		7	12	9

Table 3-10 NMR data for the aliphatic fluorines in compound **112g** in benzene-*d6*

Position	δ (ppm)	T1 (s) [a]	^{2}J (Hz)	^{3}J (Hz)	$^{4}J_{syn}$ (Hz)	$^{5}J_{syn}$ (Hz)	other ^{n}J (Hz)
1S	-98.69	1.41	252	4 (F1S-F2A)	22	-	4 (F15)
1A	-105.21	1.49		8 (F1S-F2S)	69	36	4 (F12)
2S	-102.98	1.71	251		-	37	5 (F7)
2A	-97.84	1.45			20	5	
9S	-105.21	1.51	251	10 (F9A-F10A)	73	10	3 (F7) 4 (F8)
9A	-99.61	1.65			43	5	5 (F5)
10S	-100.92	1.69	251	10 (F9S-F10S)	41	5	5 (F16)
10A	-105.40	1.80			59	10	2 (F13)

[a] In benzene-*d6* : acetone-*d6*, 1:1.

Table 3-11 NMR data for the aromatic fluorines in compound **112g** in benzene-*d6*

Position	δ (ppm)	T1 (s) [a]	$^{3}J_{ortho}$ (Hz)	$^{4}J_{meta}$ (Hz)	$^{5}J_{para}$ (Hz)	$^{7}J_{pseudo-gem}$ (Hz)
5	-129.24	1.03	-	6	10	10
7	-144.26	1.12	22	6	-	10
8	-130.60	0.97		-	10	10
12	-133.54	0.91	20	0	10	10
13	-131.92	0.94		5	10	-
15	-135.14	0.76	20	5	10	10
16	-134.80	0.83		0	10	10

[a] In benzene-*d6* : acetone-*d6*, 1:1.

Table 3-12 NMR data for the aliphatic fluorines in compound **116b** in benzene-*d6*

Position	δ (ppm)	T1 (s)	^{2}J (Hz)	^{3}J (Hz)
1S	-98.10	0.87	251	
1A	-105.65	0.94		9 (F1S-F2S)
2S	-104.31	0.92	248	3 (F1A-F2A)
2A	-94.81	0.79		

Table 3-13 NMR data for the aromatic fluorines in compound **116b** in benzene-*d6*

Position	δ (ppm)	T1 (s)	$^{3}J_{ortho}$ (Hz)	$^{4}J_{meta}$ (Hz)	$^{5}J_{para}$ (Hz)	$^{7}J_{pseudo-gem}$ (Hz)	$^{4}J_{syn}$ (Hz)	$^{5}J_{syn}$ (Hz)	other ^{n}J (Hz)
8	-139.26	0.61	20	-	-	10	10	22	5 (F2S)
13	-133.35	0.52	20	6	10	-	10	12	4 (F1A)
15	-136.17	0.44	20	6	10	10	68	0	

3.6 Experimental Section

All chemicals were purchased from Sigma-Aldrich and used directly without further purification. All reactions were done under a nitrogen atmosphere. Column chromatography was carried out on silica gel. All melting points are uncorrected. ^{1}H and ^{19}F NMR were recorded in $CDCl_3$ at 300 MHz and 282MHz, respectively (unless designated otherwise). Because of the perfluoro nature of the compounds synthesized in this chapter, which results in multiple one-, two-, and three-bond F-C couplings for each signal with little difference in chemical shift, the respective ^{13}C spectra do not provide useful observable structural information.

Perfluoro[2.2]paracyclophan-4-ol (112a): To a solution of sodium hydroxide (128 mg, 3.2 mmol) in water (0.5 mL) was added tetrahydrofuran (THF) (8 mL) and perfluoro[2.2]paracyclophane (F8) (198.4 mg, 0.4 mmol). The reaction mixture was homogenous and stirred at room temperature (RT) for 44 h, and then it was concentrated to dryness. The residue was purified by column chromatography (ethyl acetate) to give **112a** (196 mg, 99.2%) as a yellow solid: mp 192-193 ^{o}C; ^{1}H NMR (acetone-d_6) δ 3.75 (br. S, 1H); ^{19}F NMR (acetone-d_6) δ -98.15 (d, J = 255.0 Hz, 1F), -99.36 (ddm, J_1 = 255.2 Hz, J_2 = 25.1 Hz, 1F), -100.79 (dd, J_1 = 247.0 Hz, J_2 = 27.1 Hz, 1F), -101.27 (ddd, J_1 = 251.0 Hz, J_2 = 26.8 Hz, J_3 = 10.4 Hz, 1F), -102.24 (J_1 = 249.0 Hz, J_2 = 62.3 Hz, 1F), -105.20 (dddd, J_1 = 244.8 Hz, J_2 = 72.7 Hz, J_3 = 16.6 Hz, J_4 = 10.4 Hz, 1F), -106.54 (dddd, J_1 = 247.0 Hz, J_2 = 68.5 Hz, J_3 = 16.6 Hz, J_4 = 10.2 Hz, 1F), -106.82 (dddd, J_1 = 251.0 Hz, J_2 = 68.5 Hz, J_3 = 18.6 Hz, J_4 = 6.5 Hz, 1F), -131.96 (m, 1F), -134.80 (d, J = 22.1 Hz, 1F), -136.44 (m, 1F), -137.98 (d, J = 8.7 Hz, 1F), -138.82 (d, J = 72.7 Hz, 1F), -144.13 (d, J = 78.9 Hz, 1F), -162.58 (br. S, 1F); HRMS (CI), Calcd for $C_{16}H_1F_{15}O$, 493.9788; found, 493.9774.

4-Methoxyperfluoro[2.2]paracyclophane (112b) and 4,16-dimethoxy-perfluoro[2.2]paracyclophane (113): A solution of sodium methoxide (43.2 mg, 0.8 mmol) and F8 (198.4 mg, 0.4 mmol) in anhydrous THF (12 mL) was stirred at RT for 48 h, and the mixture then concentrated to dryness. The residue was purified by column chromatography (silica gel, hexanes) to give **112b** (100 mg, 49%) as a white solid and **113** (30 mg, 14%) as a white solid. **112b**: mp 121-122 ^{o}C; ^{1}H NMR, δ 3.25 (d, J = 1.2 Hz, 3H); ^{19}F NMR, δ -99.48 (ddd, J_1 = 249.4 Hz, J_2 = 29.7 Hz, J_3 = 12.2 Hz, 1F), -100.04 (ddd, J_1 = 251.1 Hz, J_2 = 32.0 Hz, J_3 = 12.0 Hz, 1F), -101.45 (ddd, J_1 = 256.4 Hz, J_2 = 32.0 Hz, J_3 = 11.7 Hz, 1F), -101.39 (dd, J_1 = 248.2 Hz, J_2 = 4.8 Hz, 1F), -104.68 (dd, J_1 = 248.7 Hz, J_2 = 59.4 Hz, 1F), -104.69 (dd, J_1 = 248.5 Hz, J_2 = 59.4 Hz, 1F), -105.36 (dddd, J_1 = 251.3 Hz, J_2 = 74.6 Hz, J_3 = 14.8 Hz, J_4 = 11.3 Hz, 1F), -105.46 (dddd, J_1 = 252.3 Hz, J_2 = 65.8 Hz, J_3 = 15.4 Hz, J_4 = 10.4 Hz, 1F), -126.98 (ddd, J_1 = 19.5 Hz, J_2 = 16.5 Hz, J_3 = 3.6 Hz, 1F), -132.30 (ddd, J_1 = 29.9 Hz, J_2 = 15.8 Hz, J_3 = 2.8 Hz, 1F), -132.96 (dddd, J_1 = 18.5 Hz, J_2 = 21.7 Hz, J_3 = 15.4 Hz, J_4 = 4.1Hz, 1F), -133.68 (m, 1F), -136.13, (m, 1F), -136.59 (m, 1F), -137.2 (m, 1F); Anal. Calcd for $C_{17}H_3F_{15}O$: C 40.18, H 0.60; Found: C 40.47, H 0.49. **113**: ^{1}H NMR, δ 3.85 (d, J = 1.2 Hz, 6H); ^{19}F NMR, δ -99.08 (ddd, J_1 = 244.8 Hz, J_2 = 31.0 Hz, J_3 = 14.7 Hz, 2F), -100.89 (d, J = 251.0 Hz, 2F), -105.27 (ddd, J_1 = 246.8 Hz, J_2 = 64.3 Hz, J_3 = 6.2 Hz, 2F), -105.49 (m, 2F), -127.06 (m, 2F), -135.87 (dd, J_1 = 66.6 Hz, J_2 = 20.6 Hz, 2F); Anal. Calcd for $C_{18}H_6F_{15}O_2$: C 41.56, H 1.16; Found: C 41.77, H 1.00.

4,7-bis-Phenylthio-perfluoro[2.2]paracyclophane (114): A mixture of sodium benzenethioxide (29.4 mg, 0.2 mmol) and perfluoro[2.2]paracyclophane (99.2 mg, 0.2 mmol) in anhydrous tetrahydrofuran (4 mL) was stirred at room temperature for 48 h.

The reaction mixture was concentrated to dryness. The residue was purified by column chromatography (silica gel, hexanes) to obtain 4,7-bis-phenylthio-perfluoro[2.2]para-cyclophane (40 mg, yield: 29.6% based on sodium thiophenolate) as a yellow solid. mp 122-124 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (m, 10H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -100.24 (dd, J_1 = 245.4 Hz, J_2 = 11.5 Hz, 2F), -100.72 (dd, J_1 = 250.5 Hz, J_2 = 42.6 Hz, 2F), -100.98 (d, J = 63.0 Hz, 2F), -102.22 (ddd, J_1 = 245.2 Hz, J_2 = 66.3 Hz, J_3 = 6.4 Hz, 2F), -103.33 (dddd, J_1 = 251.7 Hz, J_2 = 54.9 Hz, J_3 = 15 Hz, J_4 = 6.4 Hz, 2F), -128.49 (dd, J_1 = 42.7 Hz, J_2 = 10.5 Hz, 2F), -134.26 (dddd, J_1 = 54.4 Hz, J_2 = 19.8 Hz, J_3 = 6.4 Hz, J_4 = 4.0 Hz, 2F). Anal. Calcd for $C_{28}H_{10}F_{14}S_2$ C 49.71, H 1.49. Found: C 49.84, H 1.64. Note: F8 : PhSNa = 1:1.

4-(4-Fluorophenoxy)-perfluoro[2.2]paracyclophane (112c): A mixture of 4-fluorophenol (28 mg, 0.25 mmol) in anhydrous THF (10 mL) was added 60% sodium hydride (11 mg, 0.275 mmol). The resulting reaction mixture was stirred for 30 minutes, after which F8 (124 mg, 0.25 mmol) was added. The mixture was stirred at RT overnight, and then it was concentrated to dryness. The residue was purified by column chromatography (hexanes) to give **112c** (110 mg, 76.9%) as white solid: mp 98-99 ^{o}C; ^{1}H NMR, δ 7.01 (m, 2H), 6.81 (m, 2H); ^{19}F NMR, δ -99.46 (ddd, J_1 = 249.0 Hz, J_2 = 29.1 Hz, J_3 = 10.4 Hz, 1F), -100.39 (ddd, J_1 = 253.2 Hz, J_2 = 31.0 Hz, J_3 = 10.2 Hz, 1F), -100.59 (ddd, J_1 = 251.0 Hz, J_2 = 29.1 Hz, J_3 = 10.4 Hz, 1F), -100,98 (d, J = 251.0Hz, 1F), -104.54 (dd, J_1 = 244.8 Hz, J_2 = 62.3 Hz, 1F), -104.87 (ddt, J_1 = 249.0 Hz, J_2 = 72.5 Hz, J_3 = 14.7 Hz, 1F), -105.40 (ddt, J_1 = 251.0 Hz, J_2 = 62.3 Hz, J_3 = 14.4 Hz, 2F), -118.98 (m, 1F), -122.02 (m, 1F), -131.74 (m, 2F), -132.32 (dd, J_1 = 55.8 Hz, J_2 = 10.4

Hz, 1F), -133.19 (dt, J_1 = 64.3 Hz, J_2 = 16.6 Hz, 1F), -134.59 (m, 1F), -135.27 (m, 1F); Anal. Calcd for $C_{22}H_4F_{16}O$ C 44.92, H 0.69. Found: C 45.24, H 0.72.

4-(Bis(carbomethoxyl)methyl)perfluoro[2.2]paracyclophane (1d): To a solution of dimethyl malonate (161.7 mg, 1.2 mmol) in anhydrous THF (10 mL) was added 60% sodium hydride (48 mg, 1.2 mmol) and the mixture stirred at RT for 10 minutes. Then F8 (148.8 mg, 0.3 mmol) was added and the reaction mixture stirred at RT for 2 days, after which it was concentrated to dryness. The residue was purified by column chromatography (chloroform) to give **112d** (80 mg, 73% based on 60% conversion) as a white solid: mp 148-149 ^{o}C; ^{1}H NMR, δ 5.14 (s, 1H), 3.88 (s, 3H), 3.78 (s, 3H); ^{19}F NMR, δ -98.72 (ddd, J_1 = 251.0 Hz, J_2 = 24.8 Hz, J_3 = 12.4 Hz, 1F), -99.31 (ddd, J_1 = 251.0 Hz, J_2 = 20.8 Hz, J_3 = 8.2 Hz, 1F), -100.01 (ddd, , J_1 = 249.0 Hz, J_2 = 24.8 Hz, J_3 = 8.2 Hz, 1F), -100.14 (ddd, J_1 = 248.7 Hz, J_2 = 33.0 Hz, J_3 = 8.2 Hz, 1F), -104.60 (dt, J_1 = 251.0 Hz, J_2 = 16.6 Hz, 1F), -105.41 (dddd, J_1 = 251.0 Hz, J_2 = 68.5 Hz, J_3 = 35.2 Hz, J_4 = 8.4 Hz, 1F), -105.73 (ddt, J_1 = 257.2 Hz, J_2 = 68.5 Hz, J_3 = 12.4 Hz, 1F), -106.61 (ddt, J_1 = 252.9 Hz, J_2 = 74.5 Hz, J_3 = 12.4 Hz, -109.52 (dd, J_1 = 72.5 Hz, J_2 = 10.4 Hz, 1F), -122.07 (m, 1F), -129.04 (m, 2F), -131.83 (m, 1F), -134.13 (m, 1F), -134.54 (m, 1F); Anal. Calcd for $C_{21}H_7F_{15}O_4$ C 41.47, H 1.16. Found: C 41.76, H 1.06.

4-*tert*-Butylperfluoro[2.2]paracyclophane (112e): To a mixture of tert-butyl lithium (0.32 mL, 1.7 M, 0.55 mmol) in anhydrous THF (10 mL) was added F8 (248 mg, 0.5 mmol). The reaction mixture was stirred at RT overnight, after which it was concentrated to dryness. The residue was purified by column chromatography (hexanes) to give **112e** (140 mg, 54.4%) as a white solid: mp 104-105 ^{o}C; ^{1}H NMR, δ

1.35 (m, 9H); ^{19}F NMR, δ -97.12 (d, J = 246.8 Hz, 1F), -99.55 (ddd, J_1 = 251.0 Hz, J_2 = 29.0 Hz, J_3 = 10.4 Hz, 1F), -100.42 (ddd, J_1 = 253.0 Hz, J_2 = 24.8 Hz, J_3 = 10.2 Hz, 1F), -100.53 (ddd, J_1 = 248.7 Hz, J_2 = 24.8 Hz, J_3 = 8.2 Hz, 1F), -103.05 (dd, J_1 = 248.7 Hz, J_2 = 60.1 Hz, 1F), -104.19 (dddd, J_1 = 251.3 Hz, J_2 = 76.6 Hz, J_3 = 16.9 Hz, J_4 = 8.2 Hz, 1F), -105.59 (dddd, J_1 = 253 Hz, J_2 = 66.5 Hz, J_3 = 24.8 Hz, J_4 = 11.5 Hz, 2F), -117.49 (m, 1F), -131.06 (ddd, J_1 = 60.3 Hz, J_2 = 16.6 Hz, J_3 = 6.5 Hz, 1F), -132.89 (m, 2F), -136.21 (m, 2F), -137.09 (m, 1F); Anal. Calcd for $C_{20}H_9F_{15}$ C 44.96, H 1.70. Found: C 44.62, H 1.59.

4-(N,N-Diethylamino)perfluoro[2.2]paracyclophane (112f): To a solution of diethylamine (80 mg, 1.1 mmol) in anhydrous THF (8 mL) was added F8 (124 mg, 0.25 mmol). The reaction mixture was stirred at RT for 20 h and then concentrated to dryness. The residue was purified by column chromatography (hexanes) to give **112f** (125 mg, 91.2%) as a yellow solid: mp 121-122 ^{o}C; ^{1}H NMR, δ 3.47 (m, 2H), 3.24 (m, 2H), 1.12 (t, J = 6.9 Hz, 6H); ^{19}F NMR, δ -97.78 (dd, J_1 = 249.0 Hz, J_2 = 20.6 Hz, 1F), -98.66 (ddd, J_1 = 251.0 Hz, J_2 = 26.8 Hz, J_3 = 10.2 Hz, 1F), -99.48 (ddd, J_1 = 236.6 Hz, J_2 = 39.5 Hz, J_3 = 10.4 Hz, 1F), -100.37 (ddd, J_1 = 238.6 Hz, J_2 = 35.3 Hz, J_3 = 10.4 Hz, 1F), -104.60- -107.20 (m, 4F), -127.75 (d, J = 74.7 Hz, 1F), -128.91 (m, 1F), -130.81 (q, J = 24.8 Hz, 1F), -132.53 (t, J = 24.8 Hz, 1F), -135.17 (m, 2F), -138.69 (m, 1F); Anal. Calcd for $C_{20}H_{10}F_{15}N$ C 43.73, H 1.84, N 2.55. Found: C 43.82, H 1.59, N 2.49.

4-(Pyrrolidin-1-yl)perfluoro[2.2]paracyclophane (112g): To a solution of pyrrolidine (39 mg, 0.55 mmol) in anhydrous THF (8 mL) was added F8 (124 mg, 0.25 mmol). The resulting mixture was stirred at RT for 24 h, and then concentrated to dryness. The residue was purified by column chromatography (hexanes) to give **112g**

(115 mg, 83.9%) as a yellow solid: mp 120-122 ^{o}C; ^{1}H NMR, δ 3.71 (m, 2H), 3.35 (m, 2H), 2.00 (m, 2H), 1.87 (m, 2H); ^{19}F NMR, δ -98.48 (dd, J_1 = 251.0 Hz, J_2 = 18.6 Hz, 1F), -99.17 (dd, J_1 = 249.0 Hz, J_2 = 20.6 Hz, 1F), -100.09 (ddt, J_1 = 251.0 Hz, J_2 = 37.5 Hz, J_3 = 4.2 Hz, 1F), -101.25 (dd, J_1 = 257.2 Hz, J_2 = 39.2 Hz, 1F), -103.59 (ddt, J_1 = 246.8 Hz, J_2 = 37.5 Hz, J_3 = 4.0 Hz, 1F), -105.00- -106.70 (m, 3F), -129.40 (d, J = 72.5 Hz, 1F), -130.63 (m, 1F), -131.33 (q, J = 27.1 Hz, 1F), -133.01 (m, 1F), -134.83 (m, 2F), -144.30 (m, 1F); Anal. Calcd for $C_{20}H_8F_{15}N$: C 43.89, H 1.47, N 2.56; Found: C 43.53, H 1.24, N 2.42.

4-(N-Benzyl-N-methylamino)perfluoro[2.2]paracyclophane (112h): To a solution of N-benzyl-N-methylamine (66 mg, 0.55 mmol) in anhydrous THF (8 mL) was added F8 (124 mg, 0.25 mmol). The resulting mixture was stirred at RT for 24 h and then concentrated to dryness. The residue was purified by column chromatography (hexanes) to give **112h** (101 mg, 67.8%) as a yellow solid: mp 105-107 ^{o}C; ^{1}H NMR, δ 7.31 (m, 3H), 7.18 (d, J = 6.9 Hz, 2H), 4.42 (s, 2H), 2.92 (d, J = 2.7 Hz, 3H); ^{19}F NMR, δ -97.80- 101.00 (m, 4F), -104.80- -107.20 (m, 4F), -127.49 (d, J = 76.9 Hz, 1F), -128.62 (m, 1F), -130.45 (q, J = 22.8 Hz, 1F), -132.32 (m, 1F), -134.91 (m, 2F), -138.42 (m, 1F); Anal. Calcd for $C_{24}H_{10}F_{15}N$ C 48.26, H 1.69, N 2.34. Found: C 47.88, H 1.45, N 2.12.

4-(*N,N*-Dimethylamino)perfluoro[2.2]paracyclophane (112i): To a solution of dimethylamine (62 mg, 40% aqueous solution, 0.55 mmol) in anhydrous THF (8 mL) was added F8 (124 mg, 0.25 mmol). The reaction mixture was stirred at RT for 1 h and then concentrated to dryness. The residue was purified by column chromatography (hexanes) to give **112i** (91.2 mg, 70%) as a yellow solid: mp 150-152 ^{o}C; ^{1}H NMR, δ

3.04 (s, 6H); ^{19}F NMR, δ -98.28 (dd, J_1 = 251.0 Hz, J_2 = 18.6 Hz, 1F), -99.07 (ddd, J_1 = 224.2 Hz, J_2 = 37,2 Hz, J_3 = 10.2 Hz, 1F), -99.92 (dd, J_1 = 213.8 Hz, J_2 = 10.4 Hz, 1F), -100.67 (ddd, J_1 = 211.8 Hz, J_2 = 35.3 Hz, J_3 = 10.4 Hz, 1F), -104.80- -107.20 (m, 4F), -128.93 (d, J = 78.7 Hz, 1F), -129.19 (m, 1F), -131.03 (q, J = 22.8 Hz, 1F), -132.53 (t, J = 31.3 Hz, 1F), -135.13 (m, 2F), -140.43 (m, 1F); HRMS (APPI), Calcd for $C_{18}H_6F_{15}N$: 522.0333 ($M+H^+$), Found: 522.0356; Anal. Calcd for $C_{18}H_6F_{15}N$: C 41.48, H 1.16, N 2.69; Found: C 43.82, H 1.59, N 2.49.

4-(2-Hydroxyethoxy)perfluoro[2.2]paracyclophane (112j): A mixture of ethylene glycol (31 mg, 0.5 mmol) in anhydrous THF (10 mL) was added 60% sodium hydride (44 mg, 1.1 mmol). The resulting reaction mixture was stirred for 30 minutes, after which F8 (248 mg, 0.5 mmol) was added. The mixture was stirred at RT overnight, and then it was concentrated to dryness. The residue was purified by column chromatography (hexanes : methylene chloride = 1:1) to give **112j** (130 mg, 50%) as a white solid: mp 106-107 ^{o}C; ^{1}H NMR, δ 4.17 (m, 1H), 4.07 (m, 1H), 3.93 (m, 2H), 1.99 (t, J = 6.3 Hz, 1H); ^{19}F NMR, δ -99.48 (ddd, J_1 = 251.0 Hz, J_2 = 29.1 Hz, J_3 = 12.4 Hz, 1F), -100.39 (dd, J_1 = 249.0 Hz, J_2 = 29.0 Hz, 2F), -101.22 (d, J = 248.7 Hz, 1F), -104.10--106.40 (m, 4F), -125.39 (m, 1F), -131.59 (s, 1F), -132.12 (s, 1F), -133.83 (dd, J_1 = 62.3 Hz, J_2 = 10.4 Hz, 1F), -135.70 (m, 2F), -136.47 (d, J = 66.3 Hz, 1F); Anal. Calcd for $C_{15}H_5F_{15}O_2$ C 40.17, H 0.94. Found: C 39.95, H 0.73.

4-(2-Benzylaminoethylamino)perfluoro[2.2]perfluorocyclophane (112k): To a solution of N-benzylethylenediamine (82 mg, 0.55 mmol) in anhydrous THF (8 mL) was added F8 (124 mg, 0.25 mmol). The resulting mixture was stirred at RT for 24 h,

and then it was concentrated to dryness. The residue was purified by column chromatography (hexanes) to give **112k** (90 mg, 57.5%) as a yellow solid: mp 113-114 ^{o}C; ^{1}H NMR, δ 7.32 (m, 5H), 5.84 (br. S, 1H), 3.79 (s, 2H), 3.39 (m, 1H), 3.30 (m, 1H), 2.92 (m, 2H), 1.59 (br. S, 1H); ^{19}F NMR, δ -94.63 (d, J = 254.9 Hz, 1F), -97.80 (dd, J_1 = 252.9 Hz, J_2 = 55.8 Hz, 1F), -98.75 (dd, J_1 = 259.2 Hz, J_2 = 32.9 Hz, 1F), -99.80--102.20 (m, 3F), -104.39 (ddt, J_1 = 249.0 Hz, J_2 = 64.3 Hz, J_3 = 12.4 Hz, 1F), -105.32 (m, 1F), -132.06 (m, 1F), -132.94 (m, 1F), -133.40 (m, 1F), -136.68 (m, 3F), -150.41 (m, 1F); HRMS (APPI), Calcd for $C_{25}H_{13}F_{15}N_2$: 627.0912 ($M+H^+$); Found: 627.0906; Anal. Calcd for $C_{25}H_{13}F_{15}N_2$: C 47.94, H 2.09, N 4.47; Found: C 47.98, H 2.19, N 4.37.

Catechol adduct of F8 (115a): To a solution of catechol (110 mg, 1 mmol) in anhydrous THF (10 mL) was added 60% sodium hydride (88 mg, 2.2 mmol). The resulting reaction mixture was stirred at room temperature for 10 minutes, after which F8 (248 mg, 0.5 mmol) was added. The mixture was stirred at RT overnight, and then it was concentrated to dryness. The residue was purified by column chromatography (hexanes) to give the **115a** (220 mg, 77.5%) as a light yellow solid: mp 162-163 ^{o}C; ^{1}H NMR, δ 7.06 (dd, J_1 = 6.6 Hz, J_2 = 3.6 Hz, 2H), 6.93 (dd, J_1 = 6.6 Hz, J_2 = 3.6 Hz, 2H); ^{19}F NMR, δ -99.62 (d, J = 249.0 Hz, 2F), -100.21 (ddd, J_1 = 253.2 Hz, J_2 = 24.8 Hz, J_3 = 6.2 Hz, 2F), -103.84 (ddq, J_1 = 248.7 Hz, J_2 = 74.7 Hz, J_3 = 10.4 Hz, 2F), -104.57 (dd, J_1 = 252.9 Hz, J_2 = 62.3 Hz, 2F), -131.29 (m, 2F), -136.58 (d, J = 62.0 Hz, 2F), -139.24 (d, J = 70.5 Hz, 2F); Anal. Calcd for $C_{22}H_4F_{14}O_2$ C 46.66, H 0.71. Found: C 46.35, H 0.51.

4-Nitrocatechol adduct of F8 (115b): To a solution of 4-nitrocatechol (44 mg, 0.275 mmol) in anhydrous THF (10 mL) was added 60% sodium hydride (22 mg, 0.55

mmol). The resulting reaction mixture was stirred at RT for 10 minutes after which F8 (124 mg, 0.25 mmol) was added. The mixture was stirred at RT overnight and then was concentrated to dryness. The residue was purified by column chromatography (hexanes:dichloromethane = 7:3) to give **115b** (85 mg, 55.7%) as a slight yellow solid: mp 201-202 ^{o}C; ^{1}H NMR, δ 8.01 (dd, J_1 = 8.7 Hz, J_2 = 2.4 Hz, 1H), 7.86 (d, J = 2.4 Hz, 1H), 7.11 (d, J = 8.7 Hz, 1H); ^{19}F NMR, δ -100.05 (dd, J_1 = 251.0 Hz, J_2 = 22.8 Hz, 2F), -100.77 (dd, J_1 = 253.2 Hz, J_2 = 22.8 Hz, 2F), -103.21 (ddt, J_1 = 251.0 Hz, J_2 = 68.5 Hz, J_3 = 12.4 Hz, 2F), -104.10 (ddt, J_1 = 252.9 Hz, J_2 = 6.2 Hz, J_3 = 53.9 Hz, 2F), -130.68 (m, 2F), -135.84 (m, 4F); Anal. Calcd for $C_{22}H_3F_{14}NO_4$: C 43.23, H 0.49, N 2.29; Found: C 43.57, H 0.41, N 2.31.

1,2-Benzenedithiol adduct of F8 (115c): To a solution of 1,2-benzenedithiol (90.6 mg, 0.61 mmol) in anhydrous THF (10 mL) was added 60% sodium hydride (48.9 mg, 1.22 mmol). The resulting reaction mixture was stirred at RT for 10 minutes after which F8 (276 mg, 0.55 mmol) was added. The mixture was stirred at RT overnight and then concentrated to dryness. The residue was purified by column chromatography (hexanes) to obtain the **115c** (250 mg, 75.1%) as a yellow solid along with a tetrakis-substituted compound (50 mg, 12.8%) as a brownish solid. **115c**: mp 170-172 ^{o}C; ^{1}H NMR, δ 7.64 (dd, J_1 = 6.0 Hz, J_2 = 3.3 Hz, 2H), 7.45 (dd, J_1 = 6.0 Hz, J_2 = 3.3 Hz, 2H); ^{19}F NMR, δ -94.99(d, J = 244.8, 2F), -98.21 (ddt, J_1 = 246.8 Hz, J_2 = 54.1 Hz, J_3 = 6.2 Hz, 2F), -100.37 (dd, J_1 = 253.2 Hz, J_2 = 41.5 Hz, 2F), -104.11 (dd, J_1 = 248.7 Hz, J_2 = 60.3 Hz, 2F), -124.59 (m, 2F), -131.49 (d, J = 41.4 Hz, 2F), -134.15 (d, J = 53.9 Hz, 2F); Anal. Calcd for $C_{22}H_4F_{14}S_2$: C 44.16, H 0.67; Found: C 44.49, H 0.63.

Ethylenediamine adduct with F8 (116a): A mixture of F8 (124 mg, 0.25 mmol) and ethylenediamine (33 mg, 0.55 mmol) was stirred at RT for 16 h, after which the mixture was concentrated to dryness. The residue was purified by column chromatography (CH_2Cl_2) to obtain the **116a** (90 mg, 69.5%) as a red solid: mp 210-211 ^oC; ^1H NMR, δ 4.87 (br.s, 1H), 4.83 (br.s, 1H), 3.39 (m, 2H), 3.29 (m, 2H); ^{19}F NMR, δ -97.06 (dd, J_1 = 252.9 Hz, J_2 = 10.4 Hz, 2F), -99.69 (m, 4F), -100.95 (ddd, J_1 = 257.2 Hz, J_2 = 76.7 Hz, J_3 = 8.5 Hz, 2F), -132.87 (m, 2F), -137.73 (m, 2F), -151.85 (d, J = 68.2 Hz, 2F); Anal. Calcd for $C_{18}H_6F_{14}N_2$ C 41.88, H 1.17, N 5.43. Found: C 42.12, H 0.89, N 5.36.

***N, N'*-Diethyl-ethylenediamine adduct with F8 (116b):** A mixture of F8 (124 mg, 0.25 mmol) and *N*, *N*'-diethylethylenediamine (61 mg, 0.55 mmol) was stirred at RT for 16 h, after which the mixture was concentrated to dryness. The residue was purified by column chromatography (hexanes) to give the **116b** (120 mg, 62.1%) as a red solid: mp 158 ^oC (dec); ^1H NMR, δ 3.18 (m, 8H), 1.20 (t, J = 7.2 Hz, 3H), 1.19 (t, J = 7.2 Hz, 3H); ^{19}F NMR, δ -95.44 (dd, J_1 = 249.0 Hz, J_2 = 16.1 Hz, 2F), -98.67 (dm, J = 250.9 Hz, 2F), -104.84 (dq, J_1 = 249.0 Hz, J_2 = 10.2 Hz, 2F), -106.32 (ddd, J_1 = 253.2 Hz, J_2 = 68.5 Hz, J_3 = 22.6 Hz, 2F), -132.92 (m, 2F), -136.53 (d, J = 66.5 Hz, 2F), -140.07 (m, 2F); Anal. Calcd for $C_{22}H_{10}F_{14}N_2$ C 46.17, H 2.47, N 4.89. Found: C 46.24, H 2.18, N 4.73.

Electrochemistry. The cyclic voltammetry (CV) experiments were performed on a Bioanalytical Systems CW50 electrochemical analyzer at a sweep rate of 100 mV/s using a platinum disc working electrode, a platinum wire auxiliary electrode, and a silver wire pseudo reference electrode. At the end of each scan, ferrocene was added as

internal standard and potentials are referenced to the potential of ferrocene/ferrocenium redox couple. The differential pulse voltammetry experiments were performed with the same setup at scan rate of 20 mV/s, pulse amplitude of 50 mV, and pulse period of 200 msec. Sample and pulse width were 17 msec and 50 msec respectively. Solutions of samples were prepared in acetonitrile. The supporting electrolyte was 0.10 M tetrabutylammonium hexafluorophosphate ($TBAPF_6$). The experimental potentials obtained vs ferrocene/ferrocenium redox couple were corrected to the SCE standard (correction factor of +0.328 C).

Bulk Electrolysis of F8: Bulk electrolysis of F8 was performed on a Bioanalytical systems CV-27cyclic voltammograph, using a platinum gauze working electrode, a coiled platinum wire auxiliary electrode, and a silver wire pseudoreference electrode. Ferrocene was used as an internal standard for the reference electrode potential. F8 (200 mg, 0.4 mmol) was dissolved in 20 mL of acetonitrile containing 0.10 M tetrbutylammonium hexafluorophosphate ($TBAPF_6$) as supporting electrolyte. The solution was purged with nitrogen gas for 15 min. The potential of the working electrode was kept at -1.1 V (vs. SCE) for 4 h with continuous stirring. The solution turned darker brown as the electrolysis proceeded. The current was ca. 10 mA for the duration of the experiment. The resulting solution was concentrated to dryness, then purified by column chromatography (silica gel, hexanes) to obtain two fractions. The first fraction was recovered F8 (120 mg), whereas the second fraction was a mixture of reduced products. Both proton and fluorine NMR spectra indicated an absence of aromatic C-H bonds and the probable presence of a CH_2 group resulting from reduction of two geminal fluorines on one of the bridges of F8 to form a CH_2-CF_2 bridge.

Reaction in the presence of TEMPO: To a solution of pyridine (20.5 mg, 0.29 mmol) and 2,2,6,6-tetramethylpiperidine-1-oxyl (TEMPO, 45 mg, 0.29 mmol) in anhydrous THF was added F8 (65.4 mg, 0.13 mmol). The resulting reaction mixture was stirred for 1 h and then concentrated to dryness and purified by column chromatography (silica gel, hexanes) to provide 4-(pyrrolidin-1-yl)-perfluoro-[2.2]paracyclophane (**112g**) (100% conversion, 84% isolated yield as a yellow solid).

Competition experiments: To a mixture of pentafluoropyridine (50 mg, 0.295 mmol) and F8 (124 mg, 0.25 mmol) in anhydrous THF (6 mL) was added sodium methoxide (8 mg, 0.148 mmol). After stirring for 10 min at rt, a fluorine NMR of the mixture indicated that the methoxide anion had only reacted with the pentafluoro-pyrridine. The F8 was unreacted.

A similar experiment designed to compare the reactivities of F8 and hexafluorobenzene resulted in reaction of methoxide only with the F8.

CHAPTER 4
MULTIPLE NUCLEOPHILIC SUBSTITUTIONS OF PERFLUORO[2.2]PARACYCLOPHANE

4.1 Introduction

Studies on [2.2]paracyclophane ([2.2]PCP) demonstrate the presence of strong transannular effects in electrophilic substitutions.[95,96] The presence of one electron-withdrawing substituent in one ring deactivated both rings toward further electrophilic attack.[97,98] As an example, nitration of AF4 with nitronium tetrafluoroborate in sulfolane at room temperature afforded mononitro-AF4 in 86% isolated yield[49] with no dinitro derivatives observed. When nitration was carried out under the more forcing conditions of 5 equivalents of nitronium tetrafluoroborate and a temperature of 80 ^{o}C, the products generated were a mixture of *pseudo-meta*, *pseudo-para*, and *pseudo-ortho* dinitro-AF4 derivatives in 81% combined isolated yield[50], with the ratio of 1:1:1. Electrophilic substitution of [2.2]PCP with one electron-donating group orients *ortho* and *para* in the ring bearing the substitutent.

According to C.J. Cram's transannular directive influences study, regio-selectivity for bis-electrophilic substitution is determined by proton transfer to an acceptor site on the originally substituted ring. The geometry of [2.2]PCP is ideally suited for such proton transfer[99] and the aromatic nuclei are expected to be at least of comparable base strength to the solvent, and other bases such as bromide ion or aluminum tetrachloride ion. The proximity of the rings hinders approach by these external bases and should favor intramolecular processes. Some cases exactly follow this mechanism. For instance, bromination of 4-acetyl[2.2]PCP occurs exclusively in *pseudo-gem* position to acetyl to give the thermodynamically least stable isomer in 56% yield.[100] The reason for

the only formation of *pseudo-gem* isomer is the oxygen of acetyl group ideally positioned to accept a proton from the *pseudo-gem* position (Figure 4-1).

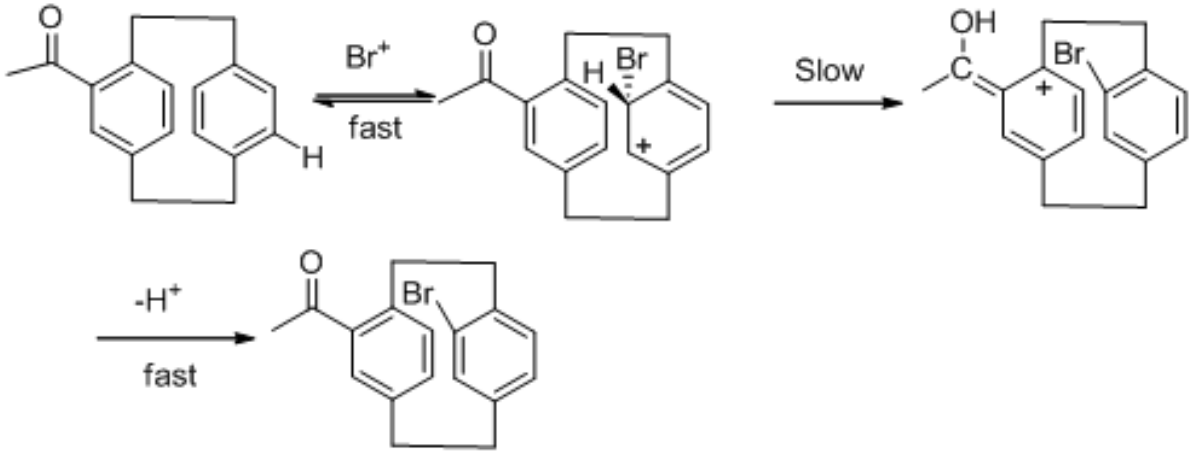


Figure 4-1 Bromination of 4-acetyl-[2.2]PCP

However, the orientations of some electrophilic substitution are hard to understand. For example, bromination of 4-nitro-[2.2]PCP provides 70% *pseudo-gem* isomer as major product, whereas nitration of 4-nitro-[2.2]PCP produces 0.7% *pseudo-gem* isomer as the minor product.

Although electrophilic substitutions of [2.2]PCP have been studied extensively, including surprising directing effects in multiple electrophilic substitution and unusual spectroscopic phenomena. Nucleophilic substitution has not been found to any extent. Nucleophilic substitution of iodo-AF4 with sodium thiophenolate and malonates in the presence of NaH provided the corresponding products in high yield via $S_{RN}1$ mechanism. When 4-nitrooctafluoro[2.2]PCP was treated with nucleophiles such as alkoxides and cyanide, a novel ring opening reaction was observed via a S_NAr mechanism. The nucleophile apparently attacks the bridgehead aryl carbon vicinal to

the nitro group, followed by subsequent aryl-CF_2 bond cleavage to form ring opening products in moderate to good yields.[56]

In the last chapter, reactions of perfluoro[2.2]paracyclophane (F8) that led mainly to mono-substitution were emphasized and factors that favor mono-substitution with a large variety of nuclophiles were discussed. This chapter will deal with multi-substitution reactions of F8, the regiochemistry of multi-substitution, and characterization of the multi-substituted products, including detailed multidimensional NMR analysis of these products.

4.2 Results and Discussion

Reaction of perfluoro[2.2]paracyclophane (F8) with sodium thiophenolate (2 equiv.) in anhydrous tetrahydrofuran provided *para*-bis-(phenylthio) product **114a** in moderate yield , together with tetrakis-(phenylthio) product **117a** and **118a** (15%) (Figure 4-2). Even when reaction of F8 with *one equivalent* of sodium thiophenolate yielded *no* mono-substituted product at all. The results obtained from the reaction of F8 with thiophenolate anion clearly indicate that the SPh substituent of the putative monoadduct must activate that ring towards addition of a second nucleophile. Such results are consistent with the previously observed formation of only *p*-bis-(phenylthio)-2,3,5,6-tetrafluorobenzene from the reaction of either one or two equivalents of thiophenolate anion with hexafluorobenzene.[81] When sodium *tert*-butyl sulfide, sodium methanethiolate, and sodium 2,3,5,6-tetrafluoro- benzenethiolate were used as nucleophilic reagents in reaction with F8, similar results were obtained. The results were shown in Table 4-1. The uv spectra of these products were displayed in Figure 4-3.

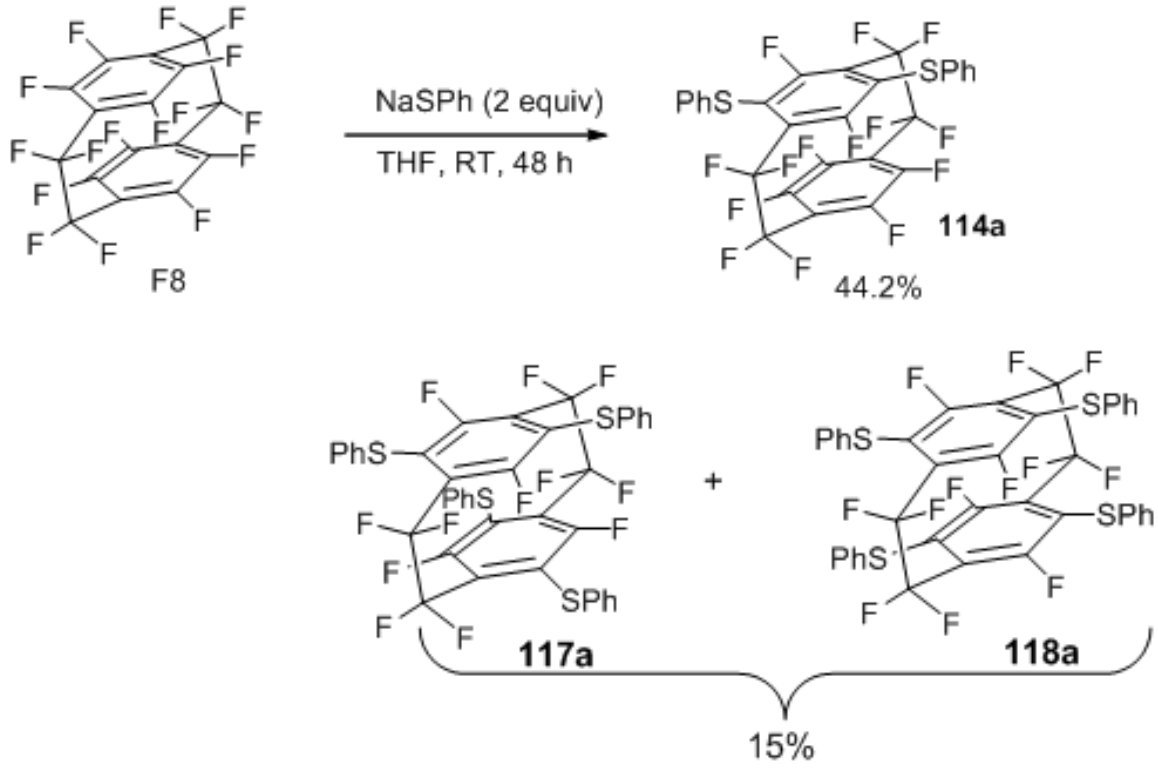


Figure 4-2 Reaction of F8 with 2 equiv. of sodium thiophenolate

Table 4-1 Reaction of sodium thiolates (2 equiv) with F8 in THF at RT

Nucleophiles	Equivalents	Reaction time h	Product No. Yield(%)	Color
PhSNa	2	48	**114a** (44.2)	Yellow
tert-BuSNa	2	24	**114b** (49.5)	Yellow
2,3,5,6-tetrafluoro -PhSNa	2	20	**114c** (47.0)	Yellow
MeSNa	2	20	**114d** (49.3)	Yellow

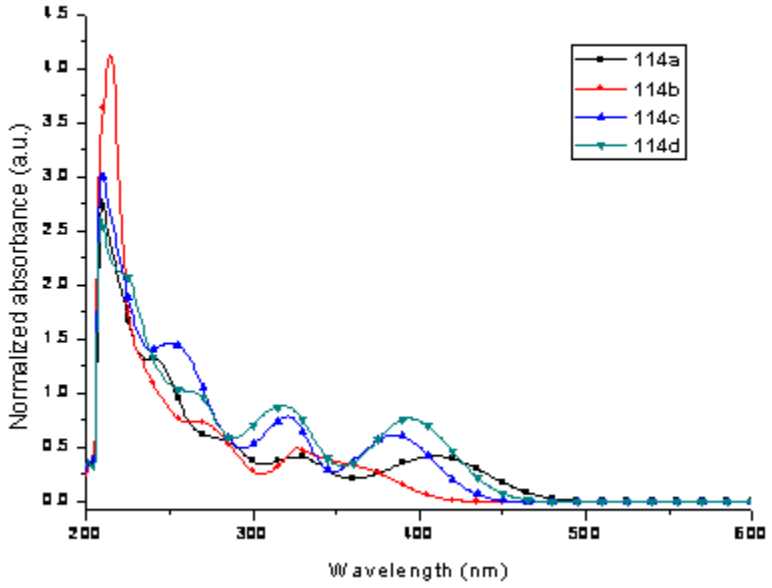


Figure 4-3 UV spectra of bis-thio-F8 derivatives

Treament of F8 with 4 equivalents of sodium thiophenolate furnished two tetrakis-phenylthio-F8 regioisomers **117a** and **118a**. Each benzene ring had two substitutents *para* to each other. Compound **117a** was the major product, whereas **118a** was the minor product (Figure 4-4). The two isomers could not be separated by column chromatography. The formation of **117a** and **118a** was via the intermediate **114a**, which the electrons of two substituents were transmitted to the *pseudo-gem* positions to result in these positions being less reactive. The other two substituents thus mainly entered the *pseudo-ortho* positions. The ratio of **117**:**118** had big variations depending on the donating or withdrawing of group which attached to sulfur. For phenyl and 2,3,5,6-tetrafluorophenyl group, due to their capable of delocalization of lone pair of sulfur to reduce donating ability of sulfur as an electron donor, the ratio of **117**:**118** is from 1.5 to 1.3. As with *tert*-butyl and methyl, because of their electron donating ability to increase donating ability of sulfur as an electron donor, the ratio of **117**:**118** is range from 7.9 to

6.5. The results were shown in Table 4-2. The reaction of F8 with 4 equivalents of sodium *p*-fluorophenolate (as a stronger donor) only isolated 4,7,12,15-tetrakis- *p*-fluorophenoxy-F8 (**119**)(Figure 4-4).

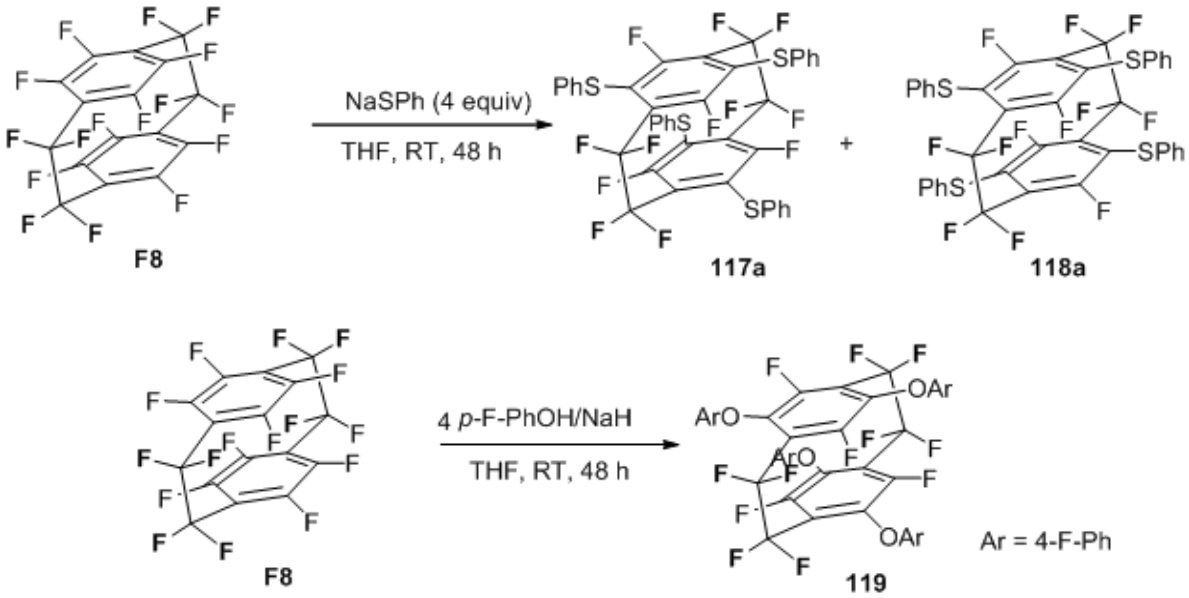


Figure 4-4 Reaction of F8 with 4 equiv. of sodium phenylthiolates

Table 4-2 Reaction of sodium thiolates (4 equiv) with F8 in THF at RT

Nucleophiles	Equivalents	Reaction time hr	Product No. ratio Yield(%)	Color
PhSNa	4	48	**117a:118a** = 1.5:1 (93.4)	Brown
tert-BuSNa	4	48	**117b:118b** = 6.5:1 (45.7)	Brown
2,3,5,6-tetrafluoro-PhSNa	4	24	**117c:118c** = 1.3:1 (37.6)	Brown
MeSNa	4	20	**117d:118d** = 7.9:1 (80.3)	Brown
4-F-PhONa	4	18	**119** (43)	White

Since the sulfur can activate the *para* position on the same benzene ring, it was predicted that the major product would be *bis*-cycloadducts on the same benzene ring if F8 reacted with 2 eguivalents of 1,2-benzene-dithiol in the presence of sodium hydride. Indeed, the reaction of F8 with 1,2-dithiol-benzene in the presence of sodium hydride

provided bis-cycloadducts (**120a**) on the same benzene ring and bis-cycloadducts (**120b**) on different benzene ring in 86% combined yield with a ratio of 49:1 for **120a**:**120b** (Figure 4-5). UV spectra of these tetrakis-substituted F8 derivatives are displayed in Figure 4-6. Compound **120** is red in color, with the UV bands extending past 450 nm.

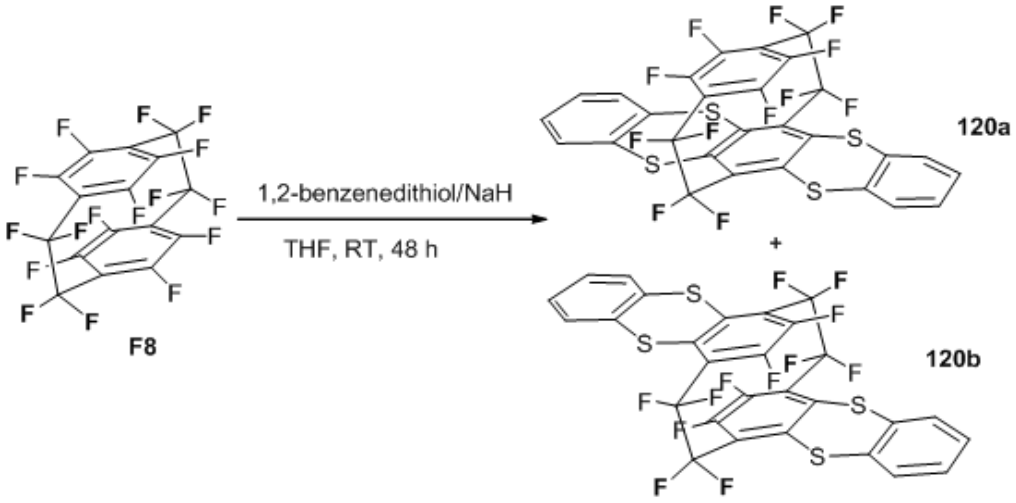


Figure 4-5 Reaction of F8 with 1,2-benzenedithiol in the presence of NaH at RT

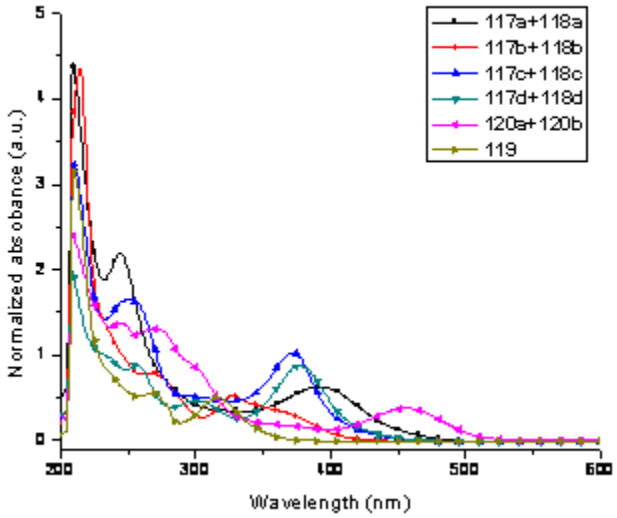


Figure 4-6 UV spectra of tetrakis-substituted F8 derivatives

Reaction of F8 with 2 equiv. of sodium *p*-fluoro-phenolate produced five regioisomers (*para*: 43%; *meta*: 10%; *pseudo-para*: 21%; *pseudo-ortho*: 15%; *pseudo-meta*: 11%) (**121**) in combined 71% yield because 4-F-PhO was a weaker electron donor that could not have strong influence upon introduction of second substituent. Interestingly, the ratio of 2 substituents in the same ring : 2 substituents in the different ring was almost 1:1 (Figure 4-7).

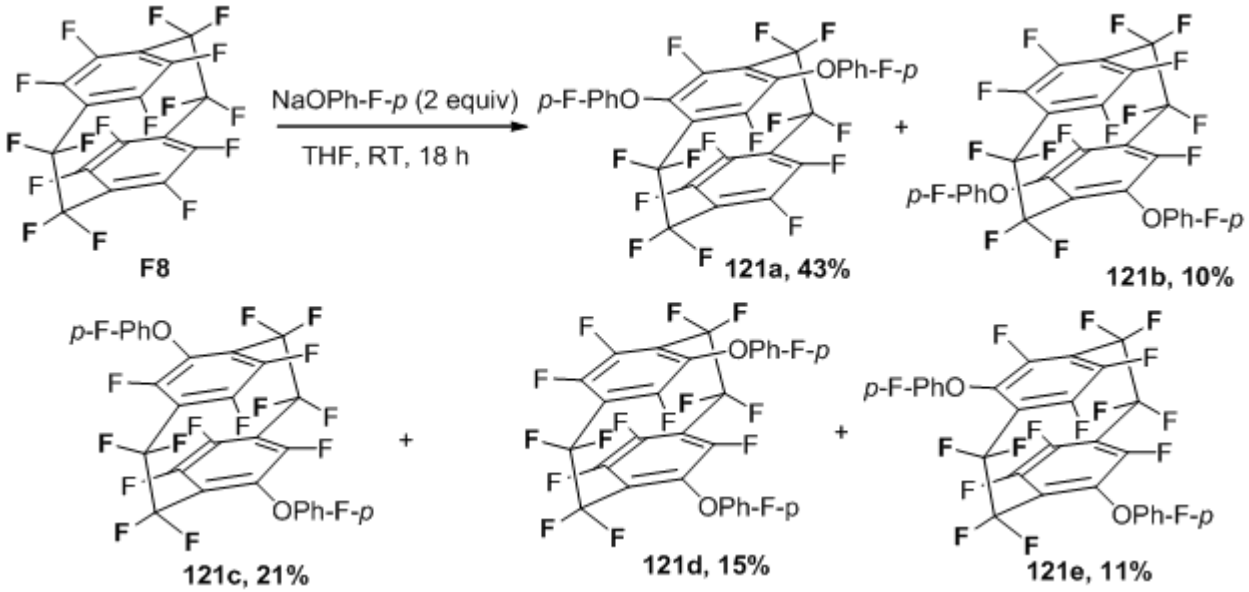


Figure 4-7 Reaction of F8 with 2 equiv of sodium 4-fluorophenolate

Reaction of F8 with catechol (1,2-benzenediol) formed the catechol adduct of F8. However, simple 1,3-benzene-diol and 1,4-benzene-diol adducts of F8 did not form when 1,3-benzenediol and 1,4-benzenediol were used as nucleophiles to react with F8 in the presence of NaH. Instead, the reaction of F8 with 1,3-benzne-diol in the presence of sodium hydride provided 4,7-bis-(3-hydroxy-phenoxy)-F8 (**123**) as a white solid, whereas 1,4-benzene-diol produced 4,16-bis-(4-hydroxy-phenoxy)-F8 (**122**) as a major product. The color of both reaction mixtures was blue (Figure 4-8). The reason for the formation of product **122** versus **123** is probably that the O^- in *para* position made

phenoxy a strong electron-donating group which deactivated the ring bearing substituent, while O^- group in *meta* position could not be as strong electron-donating as the *para* hydroxy group.

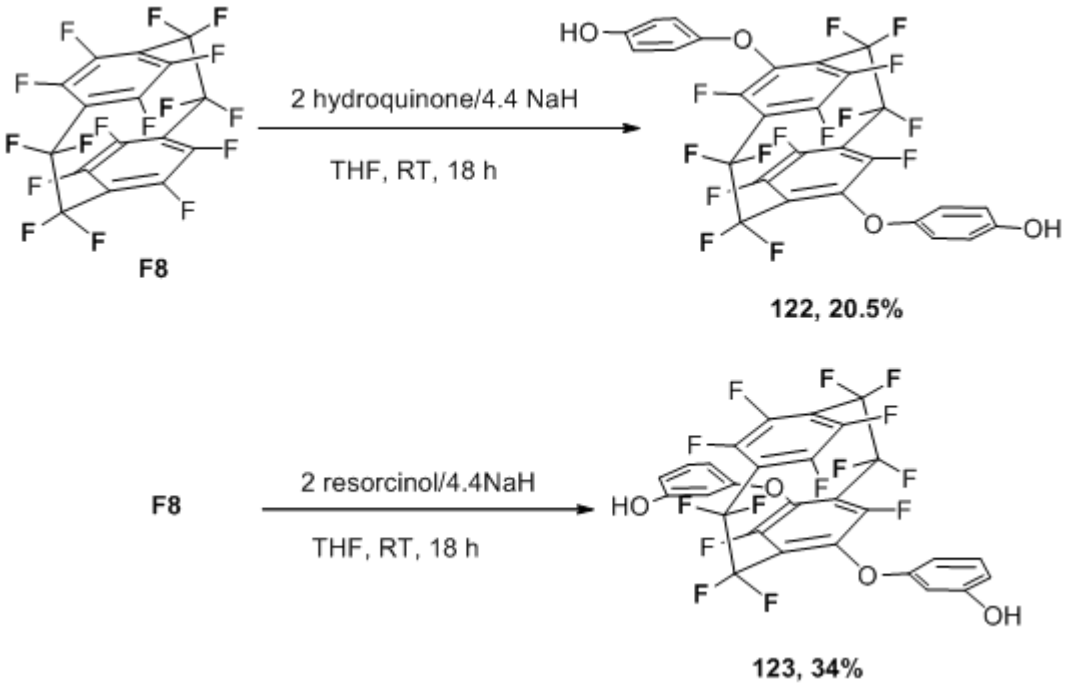


Figure 4-8 Reaction of F8 with hydroquinone/resorcinol in the presence of NaH

When 4.4 equivalents of benzylamine was used as nucleophile and base to neutralize the formed hydrogen fluoride, the formed bis-substituted products were 4,15 and 4,16-bis-benzylamino-F8 derivatives (**124**) in combined 69% yield as a yellow solid, which could not be separated by column chromatography. Since the amino group was very strong electron donating group that led the substituted ring to be electron rich and less reactive, no bis-substituted product on the same benzene ring was formed. The reaction of F8 with 4.4 equivalents of pyrrolidine produced four regioisomers, *pseudo-para* (**125**, 33%); *pseudo-ortho* (40%) as well as other two isomers (**126**) in 80% combined yield. 4,16-*bis*-pyrrolidin-1-yl-F8 (*pseudo-para* isomer) was separated from other three isomers by column chromatography (Figure 4-9). The UV spectra of these

bis-substituted products show a progression towards longer wavelength absorption as the substituent becomes increasingly electron donating (Figures 4-10 and 4-11).

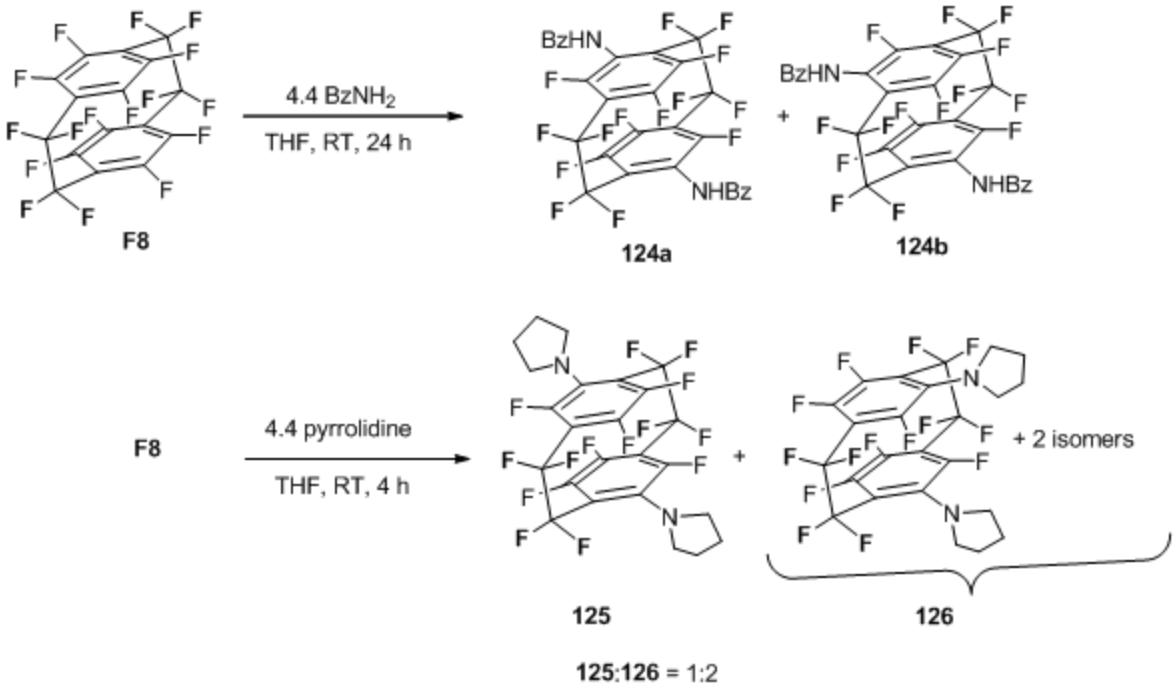


Figure 4-9 Reaction of F8 with aliphatic amines

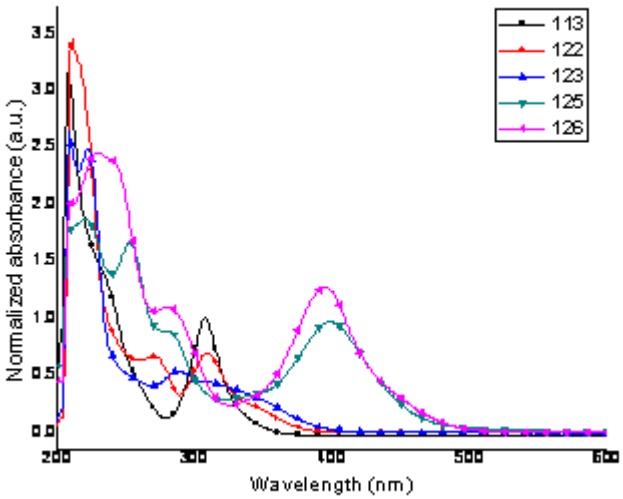


Figure 4-10 UV spectra of *bis*-substituted F8 derivatives

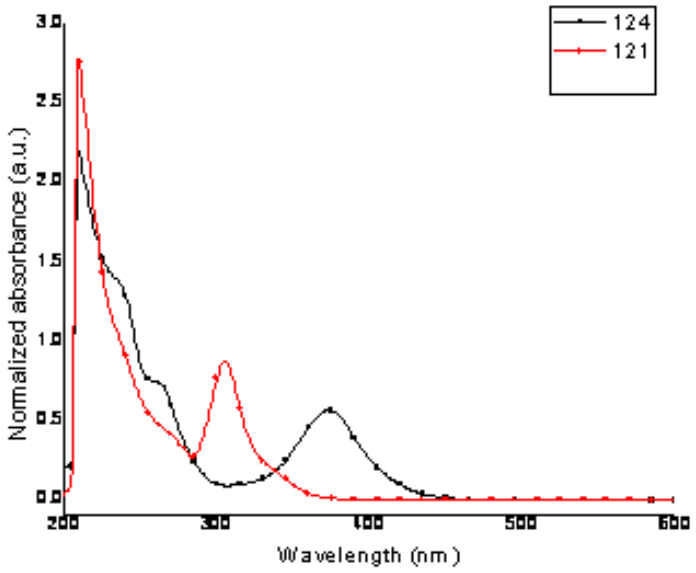


Figure 4-11 UV spectra of bis-substituted F8 derivatives

Reaction of F8 with 8.8 equivalents of pyrrolidine produced 4,7,12- (**127**) and 4,7,13-tri-pyrrolidin-1-yl-F8 (**128**) equally amount in combined 75.5%, which can be separated by column chromatography completely (Figure 4-12). The UV spectra are shown in Figure 4-13.

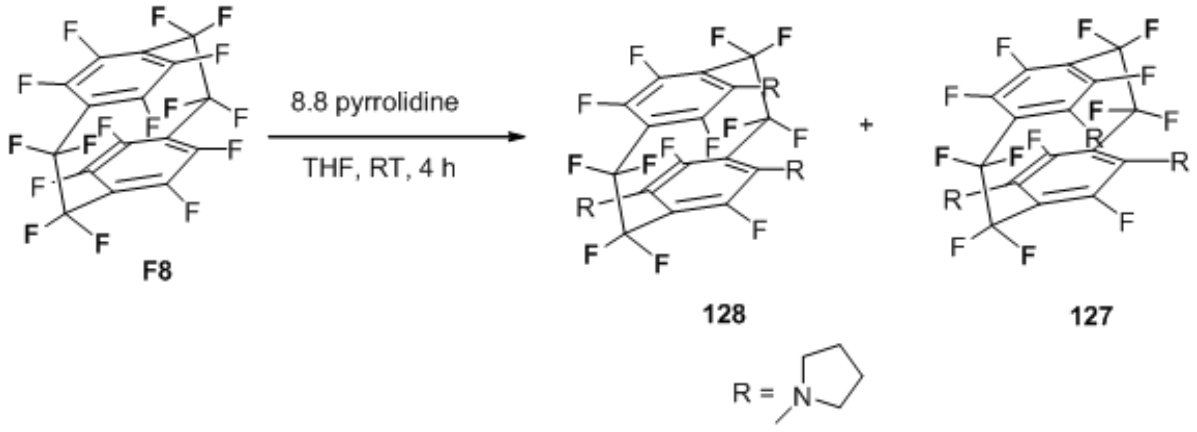


Figure 4-12 Formation of trisubstituted products by the reaction of F8 with pyrrolidines

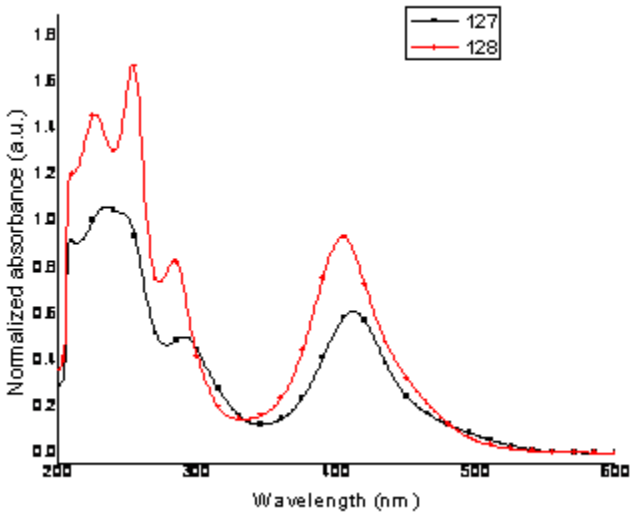


Figure 4-13 UV spectra of tri-substituted F8

4.3 Characterization

The patterns of coupling constants of mono-substituted F8 derivatives can be used for the identification of the disubstituted F8s. First, the fluorines in the half of the molecule depicted in Figure 4-14 are assigned relative to the substituent. Of the bridge fluorines, the one which doesn't display a coupling larger than 20 Hz with any aromatic fluorine is F2s. Its geminal partner is F2a. The fluorines in the other geminal pair are assigned based on the couplings F1s-F2s and F1a-F2a. The aromatic fluorines are assigned based on the largest coupling with the bridge fluorines.

The correctitude of the assignment of the fluorines in the half-molecule can be confirmed by the five-bond couplings of the bridge fluorines with the fluorines syn on the remote ring, and also by the pattern of chemical shifts of the bridge fluorines. In a monosubstituted molecule, with F15 displaying a 60-70 Hz coupling with the aromatic fluorine *ortho* and *syn*, F1s and F2a are deshielded relative to F1a and F2s. In a

disubstituted molecule, in which F13 has a coupling of 60-70 Hz with the aliphatic fluorine ortho and syn (F1s), F1a and F2s are the deshielded ones.

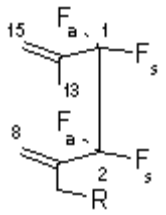


Figure 4-14 Fluorines identifiable by their position to the substituent.

Disubstituted F8 have seven isomers, depicted in Figure 4-15. Applying the numbering of the half-molecule from Figure 4-14 to these isomers is straightforward for the *ortho*, *para*, *pseudo-ortho* and *pseudo-para* isomers, and somehow confusing or inappropriate for the other three. These later isomers on the other hand are the easiest to identify. The bridge fluorines in the *meta* isomer have no geminal coupling. The *pseudo-meta* and *pseudo-gem* isomers have no couplings between fluorines from different geminal pairs. In the *pseudo-meta* isomer, fluorines in a geminal pair couple both with a 250 Hz and with a ca. 10 Hz coupling, while in the *pseudo-gem* isomer only the large coupling is present. When the coupling F1s-F8 is noticeable, in the *pseudo-meta* isomer both fluorines in the bridge pair closest to the substituent couple with the same aromatic fluorine.

The four isomers for which there is coupling between the fluorines from different geminal pairs can be then identified by the *ortho* coupling of the aromatic fluorines. Although an aromatic fluorine generally couples with the *meta*, the *para* and the *pseudo-gem* fluorines, the *ortho* coupling stands out with a coupling constant, ca. 20 Hz which is roughly double the value for the other couplings. The *ortho* isomer displays no

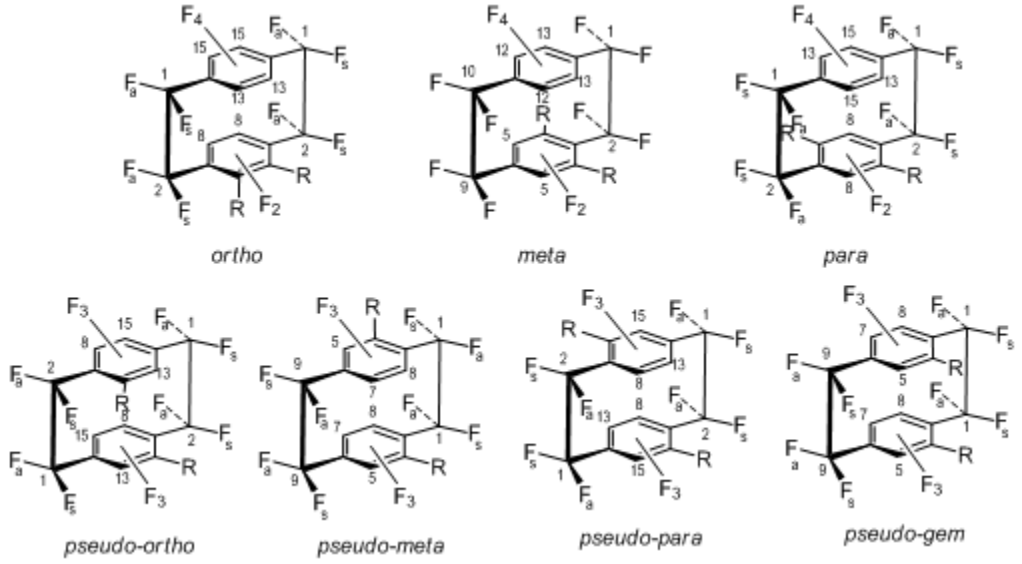
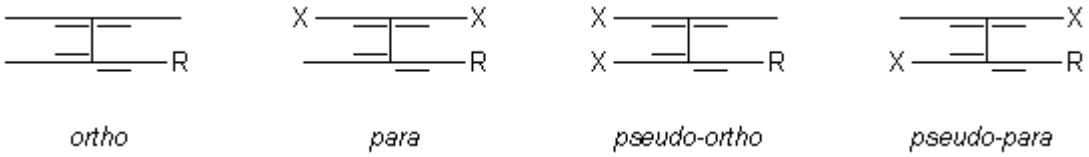


Figure 4-15 Isomers of disubstituted F8

such coupling. The *ortho* isomer also will not show a coupling between two of the aromatic fluorines, F8 and F13. In the *para* isomer, F13 and F15 display an *ortho* coupling. The *pseudo-ortho* isomer displays an *ortho* coupling between F8 and F15, while the *pseudo-para* has such a coupling between F8 and F13.



This method we established for the assignment of the regiochemistry of di-substituted F8s was applied to the examples which follow. The couplings between aliphatic fluorines were identified in a ^{19}F-^{19}F DQF-COSY spectrum in which the spectral window was restricted to the smaller region of the bridge fluorines. The couplings of the aromatic fluorines were measured from 19F spectra with selective decoupling. Both the chemical shifts and the couplings were then refined in Peter Budzelaar's gNMR program.

Table 4-3 NMR data for the aliphatic fluorines in compound **121a** (*para*) in benzene-d6

Position[a]	δ (ppm)	T1 (s)	^{2}J (Hz)	^{3}J (Hz)
1S	-101.73	[c]	250	6 (F1S-F2S)
1A	-101.77	[c]		
2S	-102.78	0.88[b]	250	8 (F1A-F2A)
2A	-101.90	[c]		

[a] the fluorine in the substituent: -118.85 ppm, tt, 8.2, 4.1 Hz. [b] In benzene-d6 : acetone-d6, 2:1. [c] Not measured, due to overlap with other signals.

Table 4-4 NMR data for the aromatic fluorines in compound **121a** (*para*) in benzene-d6

Position	δ (ppm)	T1 (s) [b]	$^3J_{ortho}$ (Hz)	$^4J_{meta}$ (Hz)	$^5J_{para}$ (Hz)	$^7J_{pseudo-gem}$ (Hz)	$^4J_{syn}$ (Hz)	$^5J_{syn}$ (Hz)	other ^nJ (Hz)
8	-123.98	0.42	-	-	-	10	58	0	
13	-131.57	0.38	20	6	-	-	35	0	
15	-134.02	0.39	20	6	-	10	35	0	

[b] In benzene-d6 : acetone-d6, 2:1.

The aliphatic fluorines in compound **121a** display two pairs with geminal coupling, and there is vicinal coupling between fluorines from different pairs. It is difficult to use the vicinal couplings to identify the *syn* fluorines in the tetrafluoroethylene bridge, because the signals of F1a and F1s are practically overlapped. In fact, these signals overlap signals from other isomers; TOCSY1D experiments with selection of each of the aromatic fluorines confirmed the position of the bridge fluorines. F13 and F15 have been assigned based on the five-bond and *syn* coupling of F15 and F2a. The 20 Hz coupling of F13 and F15 demonstrate that this is the *para* isomer. Again, the aromatic fluorine *ortho* to the substituent is the most deshielded. In fact, in all of these five isomers, these *ortho* fluorines are more deshielded, and fall in a region well separated from the rest of the signals. If one relies of the chemical shift to identify F8, then the assignment of the regiochemistry of compound **121a** is straightforward: F2s, the only aliphatic fluorine which does not have a large coupling with an aromatic one, is geminal to a fluorine which has a large coupling with F8. Therefore, **121a** is the para isomer.

Table 4-5 NMR data for the aliphatic fluorines in compound **121b** (*meta*) in benzene-d6

Position[a]	δ (ppm)	T1 (s) [b]	^{2}J (Hz)	^{3}J (Hz)
1	-101.01	0.81	-	
2	-102.10	[c]		10 (F1-F2)
9	-102.37	[c]		8 (F9-F10)
10	-102.43	[c]	-	

[a] the fluorine in the substituent: -119.05 ppm, tt, 8.2, 4.1 Hz. [b] In benzene-d6 : acetone-d6, 2:1. [c] Not measured, due to overlap with other signals.

Table 4-6 NMR data for the aromatic fluorines in compound **121b** (*meta*) in benzene-d6

Position	δ (ppm)	T1 (s) [b]	$^3J_{ortho}$ (Hz)	$^4J_{meta}$ (Hz)	$^5J_{para}$ (Hz)	$^7J_{pseudo-gem}$ (Hz)	$^4J_{syn}$ (Hz)	$^5J_{syn}$ (Hz)	other ^nJ (Hz)
5	-123.08	0.38	-	-	-	10	22	5	
12	-134.27	0.39	20	-	10	10	22	5	
13	-131.24	0.34	20	-	10	-	24	5	

[b] In benzene-d6 : acetone-d6, 2:1.

The aliphatic fluorines in compound **121b** lack the large geminal coupling, therefore this is the meta isomer. All of the couplings given in Tables 4-5 and 4-6 were determined by simulation of 14 spin system in gNMR. The vicinal couplings of the *syn* aliphatic fluorines are in the usual range, 8-10 Hz. The couplings of the aliphatic fluorines with the aromatic fluorines over four bonds and *syn* are all of comparable values, 22-24 Hz, which suggest that the differences in these couplings are due to the distortion of the PCP skeleton, not possible in the *meta* isomer.

Table 4-7 NMR data for the aliphatic fluorines in compound **121c** (*pseudo-para*) in benzene-d6

Position[a]	δ (ppm)	T1 (s)[b]	^{2}J (Hz)	^{3}J (Hz)
1S	-104.68	0.82	248	
1A	-98.14	0.75		6 (F1S-F2S)
2S	-99.84	0.89	249	11 (F1A-F2A)
2A	-104.95	0.78		

[a] the fluorine in the substituent: -119.07 ppm, tt, 8.2, 4.1 Hz. [b] In benzene-d6 : acetone-d6, 2:1.

Table 4-8 NMR data for the aromatic fluorines in compound **121c** (*pseudo-para*) in benzene-d6

Position	δ (ppm)	T1 (s) [b]	$^{3}J_{ortho}$ (Hz)	$^{4}J_{meta}$ (Hz)	$^{5}J_{para}$ (Hz)	$^{7}J_{pseudo-gem}$ (Hz)	$^{4}J_{syn}$ (Hz)	$^{5}J_{syn}$ (Hz)	other ^{n}J (Hz)
8	-136.14	0.39	20	-	10	10	77	0	5 (F2S)
13	-131.24	0.37	20	4	-	-	64	0	4 (F1A)
15	-122.25	0.41	-	4	10	10	26	17	5 (F2A)

[b] In benzene-d6 : acetone-d6, 2:1.

Compound **121c** has four different aliphatic fluorines in the tetrafluoroethylene bridge, which were positioned relative to each other based on the geminal and the *syn*-vicinal couplings. The aromatic fluorines were positioned relative to the aliphatic ones based on the large coupling over four bonds and *syn*. The coupling over five bonds and *syn* of F15 and F2a, as well as the pseudo-geminal coupling of F8 and F15, confirmed the assignments in the half-molecule. A 20 Hz coupling of F8 and F13 demonstrated that compound **121c** is the *pseudo-para* isomer. This is in agreement with F15 being the most deshielded aromatic fluorine. The couplings of the aromatic fluorines with the bridge ones follow the pattern of the monosubstituted F8s: the aromatic fluorines which have a large (60-70 Hz) $^{4}J_{syn}$ have a small (<5 Hz) $^{5}J_{syn}$ and also couple with the geminal partner of the bridge fluorine four bonds away and *syn*. These fluorines, F8 and F13, are *ortho*, as seen for the monosubstituted derivatives. The other aromatic fluorine, F15, displays a coupling with F2A similar to the one seen in monosubstituted derivatives for the aromatic fluorines which display couplings of 2-30 Hz with the bridge fluorines *syn* and four or five bonds away.

Table 4-9 NMR data for the aliphatic fluorines in compound **121e** (*pseudo-meta*) in benzene-d6

Position[a]	δ (ppm)	T1 (s) [b]	^{2}J (Hz)	^{3}J (Hz)
1S	-98.80	0.80	247	
1A	-104.02	0.76		10 (F9a-F9S)
9S	-99.28	0.77	251	7 (F1A-F1S)
9A	-105.57	0.82		

[a] the fluorine in the substituent: -118.67 ppm, tt, 8.2, 4.1 Hz. [b] In benzene-d6 : acetone-d6, 2:1.

Table 4-10 NMR data for the aromatic fluorines in compound **121e** (*pseudo-meta*) in benzene-d6

Position	δ (ppm)	T1 (s) [b]	$^{3}J_{ortho}$ (Hz)	$^{4}J_{meta}$ (Hz)	$^{5}J_{para}$ (Hz)	$^{7}J_{pseudo-gem}$ (Hz)	$^{4}J_{syn}$ (Hz)	$^{5}J_{syn}$ (Hz)	other ^{n}J (Hz)
5	-122.62	0.39	-	7	10	10	27	20	5 (F1a)
7	-134.44	0.36	20	7	-	10	70	0	8 (F9S)
8	-132.80	0.33	20	-	10	-	72	0	5 (F1S)

[b] In benzene-d6 : acetone-d6, 2:1.

121e has two pairs of aliphatic fluorines which do not display vicinal couplings between fluorines from different geminal pairs, therefore it is either the pseudo-gem or the pseudo-meta isomer. The coupling of F5 with both F9A and F9S indicates that compound **121e** is the *pseudo-meta* isomer. This is in agreement with F8 being more deshielded than F7. Smaller couplings have been noticed between the geminal bridge fluorines, which also is to be expected for the *pseudo-meta* isomer, and not for the pseudo-gem. Also, F5 and F7 couple with more than one coupling constant. The couplings of the aromatic fluorines with the bridge ones follow the pattern seen in the monosubstituted F8s and in the *pseudo-para* isomer. Like in the later, the aromatic fluorine ortho to the substituent displays couplings of 20-30 Hz with the bridge fluorines *syn* and four or five bonds away.

Table 4-11 NMR data for the aliphatic fluorines in compound **125** (*pseudo-para*) in benzene-d6

Position	δ (ppm)	T1 (s)	^{2}J (Hz)	^{3}J (Hz)
1S	-98.83		250	9 (F1S-F2S)
1A	-105.62			
2S	-104.99		248	
2A	-105.62			

Table 4-12 NMR data for the aromatic fluorines in compound **125** (*pseudo-para*) in benzene-d6

Position	δ (ppm)	T1 (s)	$^{3}J_{ortho}$ (Hz)	$^{4}J_{meta}$ (Hz)	$^{5}J_{para}$ (Hz)	$^{7}J_{pseudo-gem}$ (Hz)	$^{4}J_{syn}$ (Hz)	$^{5}J_{syn}$ (Hz)	other ^{n}J (Hz)
8	-131.77		23	6	8	8	17	31	
13	-143.50		23	6	-	-	22	35	
15	-129.89		-	-	8	8	85	0	5 (F1A)

Table 4-13 NMR data for the aliphatic fluorines in compound **126** (*pseudo-otho*) in benzene-d6

Position[a]	δ (ppm)	T1 (s)	^{2}J (Hz)	^{3}J (Hz)
1S	-100.66	0.83	254	5 (F2A-F1S)
1A	-103.11	0.83		
2S	-100.88	0.86	250	
2A	-98.84	0.90		

Table 4-14 NMR data for the aromatic fluorines in compound **126** (*pseudo-ortho*) in benzene-d6

Position	δ (ppm)	T1 (s)	$^{3}J_{ortho}$ (Hz)	$^{4}J_{meta}$ (Hz)	$^{5}J_{para}$ (Hz)	$^{7}J_{pseudo-gem}$ (Hz)	$^{4}J_{syn}$ (Hz)	$^{5}J_{syn}$ (Hz)	other ^{n}J (Hz)
8	-131.72	0.44	23	-	10	6	38	32	
13	-129.73	0.57	-	10	10	-	45	33	
15	-145.91	0.50	23	10	-	6	62	11	7 (F1S)

Table 4-15 NMR data for the aliphatic fluorines in compound **116b** (*ortho*) in benzene-d6

Position	δ (ppm)	T1 (s)	^{2}J (Hz)	^{3}J (Hz)
1S	-98.10	0.87	251	9 (F1S-F2S) 3 (F1A-F2A)
1A	-105.65	0.94		
2S	-104.31	0.92	248	
2A	-94.81	0.79		

Table 4-16 NMR data for the aromatic fluorines in compound **116b** (*ortho*) in benzene-d6

Position	δ (ppm)	T1 (s)	$^{3}J_{ortho}$ (Hz)	$^{4}J_{meta}$ (Hz)	$^{5}J_{para}$ (Hz)	$^{7}J_{pseudo-gem}$ (Hz)	$^{4}J_{syn}$ (Hz)	$^{5}J_{syn}$ (Hz)	other ^{n}J (Hz)
8	-139.26	0.61	20	-	-	10	10	22	5 (F2S)
13	-133.35	0.52	20	6	10	-	10	12	4 (F1A)
15	-136.17	0.44	20	6	10	10	68	0	

Table 4-17 NMR data for the aliphatic fluorines in compound **114a** (*para*) in benzene-d6

Position	δ (ppm)	T1 (s)	^{2}J (Hz)	^{3}J (Hz)
1S	-100.83	[a]	252	6 (F1S-F2S)
1A	-103.27	[a]		
2S	-100.35	[a]	247	10 (F1A-F2A)
2A	-102.19	[a]		

[a] Not measured, due to overlap with other signals.

Table 4-18 NMR data for the aromatic fluorines in compound **114a** (*para*) in benzene-d6

Position	δ (ppm)	T1 (s) [b]	$^{3}J_{ortho}$ (Hz)	$^{4}J_{meta}$ (Hz)	$^{5}J_{para}$ (Hz)	$^{7}J_{pseudo-gem}$ (Hz)	$^{4}J_{syn}$ (Hz)	$^{5}J_{syn}$ (Hz)	other ^{n}J (Hz)
8	-100.96	0.42	-	-	-	10	66	0	
13	-128.49	0.38	20	8.1	-	-	43	0	
15	-134.26	0.39	20	8.1	-	10	54	0	

[b] In benzene-d6 : acetone-d6, 2:1

MS fragmentation data confirm the presence of a disubstituted aromatic ring (MW = 428). The chemical shift of two fluorines ortho to substituents increased from ca. -120 to -100 ppm due to deshield of sulfur (**114a**).

There are seven regiomers of trisubstituted F8, presented in Figure 4-16. In all of them the bridge fluorines are not equivalent. The geminal pairs have been identified by their large coupling in the DQF-COSY spectrum. Vicinal fluorines in the same tetrafluoroethylene unit display small couplings. Their relative position, and the position of the substituents, was established on the basis of the couplings with aromatic

fluorines. The two ‘half-molecules’ were later joined based on the ortho couplings of the aromatic protons.

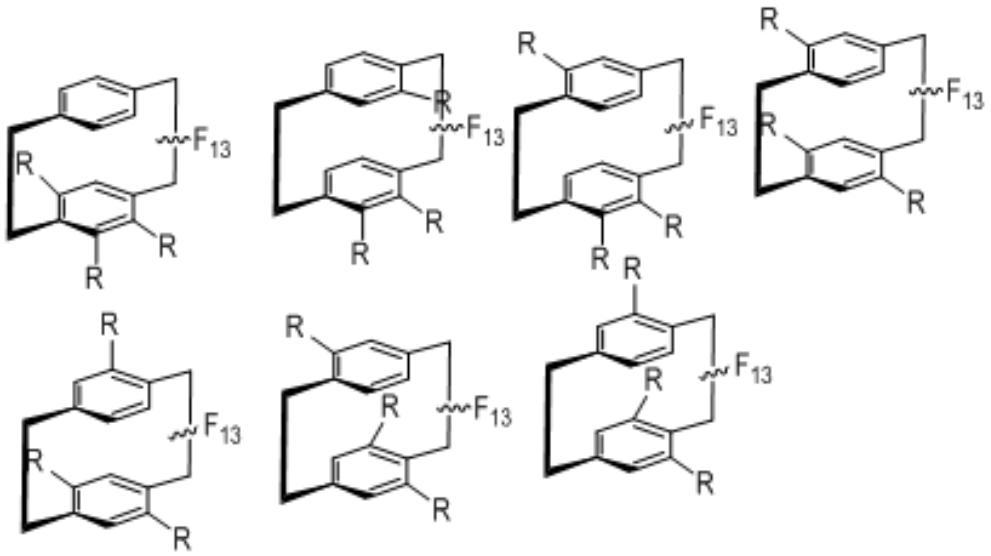


Figure 4-16 Regioisomers of trisubstituted F8

The elucidation of the structure of **128** is presented in Figure 4-17, as an example. The fluorine signals were labeled a1-a13, according to their position in the spectrum, from lower to higher field. The geminal pairs are: a1-a7, a2-a4, a3-a8, and a5-a6. Large couplings, typically around 60 Hz, identified the aromatic fluorines four bonds away and *syn* to the bridge ones: a9 to a4, a10 to a7, a11 to a6, a12 to a8, and a13 to a5. The couplings a7-a12 (10 Hz) and a8-a10 (19 Hz) placed a7 *syn* to a8 and a3 *syn* to a1. In the other tetrafluoroethylene unit, a2 is *syn* to a5 and a4 to a6, as demonstrated by the couplings a4-a11 (19 Hz), a2-a13 (21 Hz) and a6-a9 (17 Hz). The aromatic fluorines displayed only one large ortho coupling, between a12 and a13, which indicates that **128** is the 4,7,12 isomer.

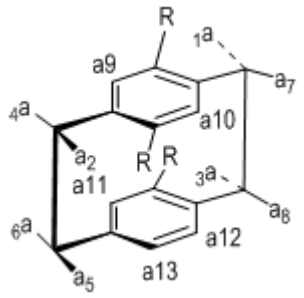


Figure 4-17 Structure of compound **128**

Table 4-19 NMR data for the aliphatic fluorines in compound **128** in benzene-d6 : acetone-d6, 2:1

Position	δ (ppm)	T1 (s)	^{2}J (Hz)	^{3}J (Hz)
1S	-102.78	0.73	251	<5 (F1S-F2S)
1A	-100.90	0.79		<5 (F1A-F2S)
2S	-97.45	0.77	247	<5 (1S-F2A)
2A	-100.57	0.79		
9S	-103.36	0.71	252	8 (F9A-F10A)
9A	-97.12	0.64		<5 (F9S-F10S)
10S	-98.37	0.60	252	<5 (F9S-F10A)
10A	-105.14	0.68		<5 (F9A-F10S)

Table 4-20 NMR data for the aromatic fluorines in compound **128** in benzene-d6; acetone-d6, 2:1

Position	δ (ppm)	T1 (s)	$^{3}J_{ortho}$ (Hz)	$^{4}J_{meta}$ (Hz)	$^{5}J_{para}$ (Hz)	$^{7}J_{pseudo-gem}$ (Hz)	$^{4}J_{syn}$ (Hz)	$^{5}J_{syn}$ (Hz)	other ^{n}J (Hz)
5	-124.68	0.48	-	-	8	-	61	20	
7									
8	-123.38	0.42			8	8	72	17	<5 (F2S)
12									
13	-131.38	0.49		0	8	-	63	19	<5 (F1A)
15	-148.56	0.50	28	0	-	8	44	21	<5 (F1A)
16	-131.96	0.40		-	8	-	62	10	

Compound **127** displays very large couplings over four bonds and *syn* F8-F2a and F12-F10s, 98 and 88 Hz, respectively. Some five bonds and *syn* couplings

between aromatic and bridge fluorines are also very large, 20-30 Hz, which made the assignment of positions 9 and 10 ambiguous. Both assignments, however, generate the same isomer. Discrimination between the two possibilities was made based on the coupling of F12 and F16, an expected *meta* coupling in one assignment, which in the other would be a coupling between F10a and F16. The structure of **127** is depicted in Figure 4-18.

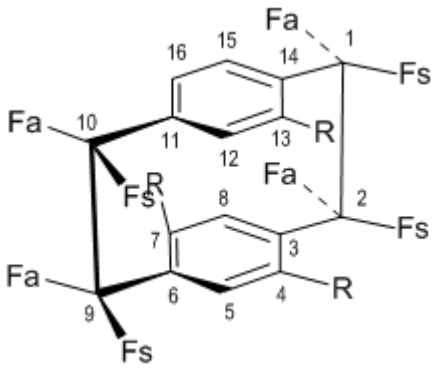


Figure 4-18 Structure of compound **127**

Table 4-21 NMR data for the aliphatic fluorines in compound **127** in benzene-d6

Position	δ (ppm)	T1 (s)	^{2}J (Hz)	^{3}J (Hz)
1S	-97.90	0.66	250	8 (F1A-F2S)
1A	-95.40	0.62		6 (F1S-F2S)
2S	-92.36	0.54	253	
2A	-99.89	0.58		
9S	-98.94	0.64	248	
9A	-105.57	0.78		5 (F9S-F10A)
10S	-106.25	0.65	250	7 (F9A-F10A)
10A	-96.65	0.64		

Table 4-22 NMR data for the aromatic fluorines in compound **127** in benzene-d6

Position	δ (ppm)	T1 (s)	$^{3}J_{ortho}$ (Hz)	$^{4}J_{meta}$ (Hz)	$^{5}J_{para}$ (Hz)	$^{7}J_{pseudo-gem}$ (Hz)	$^{4}J_{syn}$ (Hz)	$^{5}J_{syn}$ (Hz)	other ^{n}J (Hz)
5	-125.84	0.44			8	8	24	32	
7									
8	-123.79	0.35			8	0	98	51	
12	-136.62	0.47		10	6	8	88	0	
13									
15	-134.20	0.37	29		6	0	15	8	
16	-148.23	0.52		10			21	36	

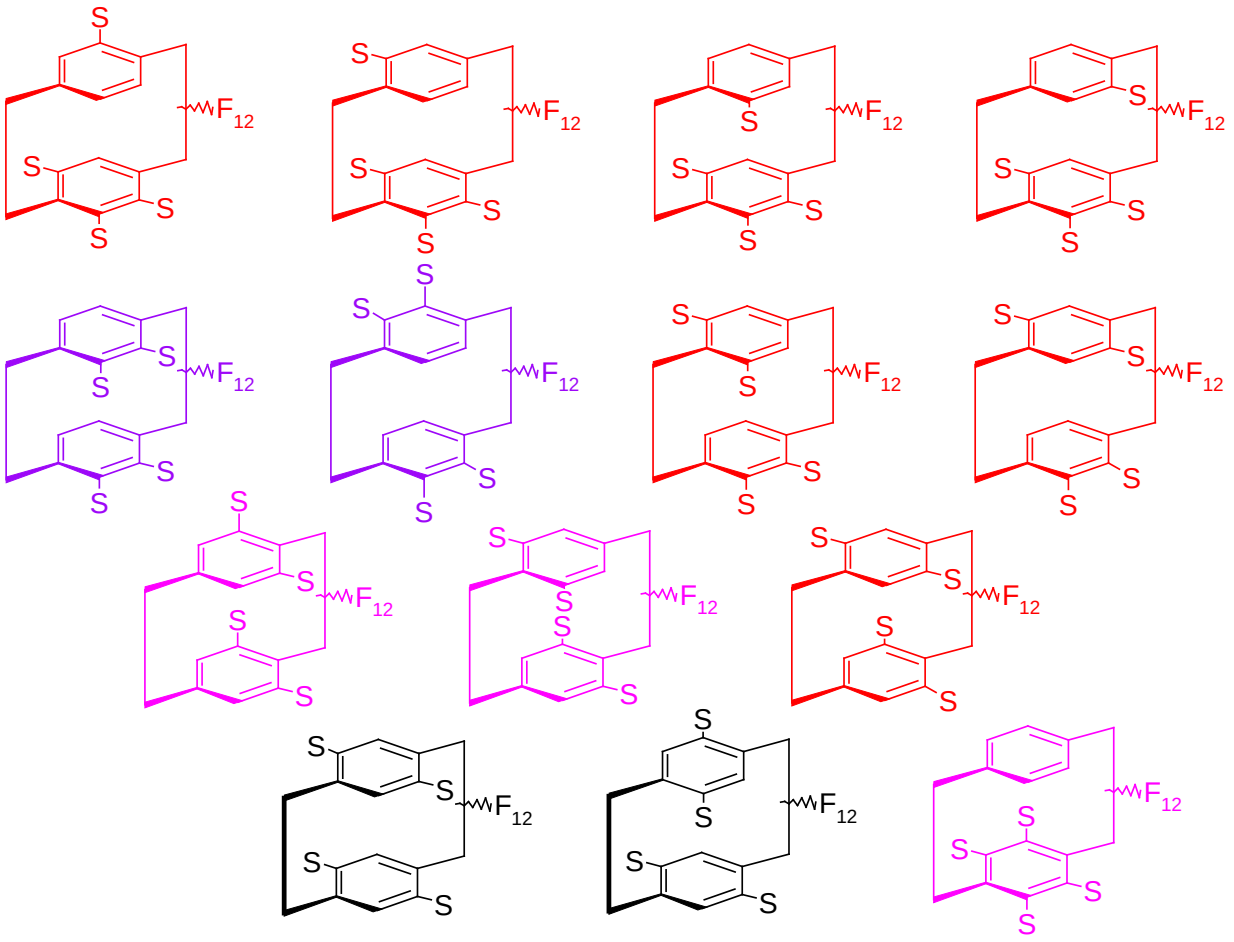


Figure 4-19 Regioisomers of tetrakis-substituted F8

There are fourteen regiomers of tetrakissubstituted F8, presented in Figure 4-19. Seven of them display more than one aromatic signal, three isomers miss the geminal coupling, and 2 do not have an aromatic fluorine ortho to the substituent (and this would produce a more shielded F19).

An attempt to assign the two isomers is made using chemical shifts increments (Figure 4-20).

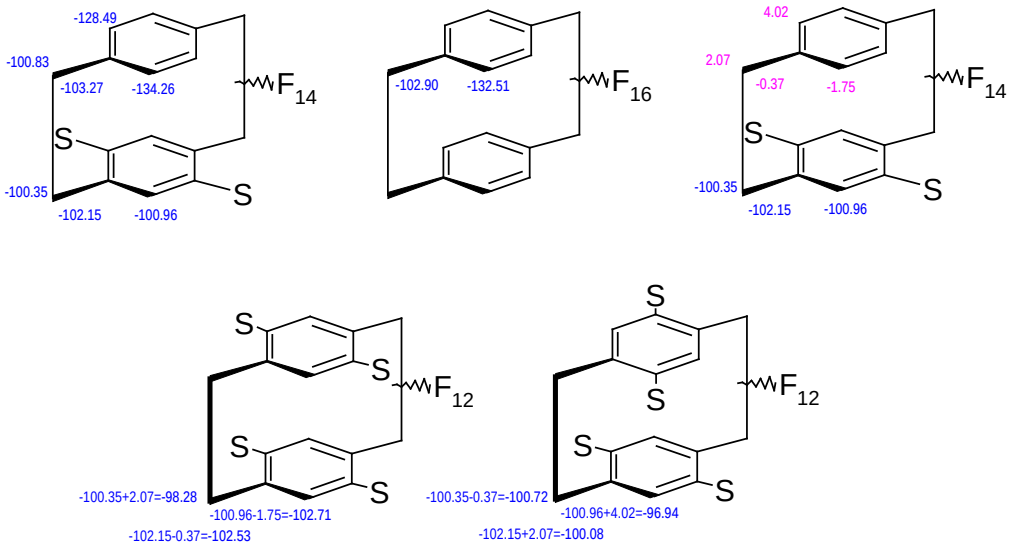


Figure 4-20 Assigning the two isomers is made using chemical shifts increments

Coupling constants in minor isomer confirm the assignment (Figure 4-21)

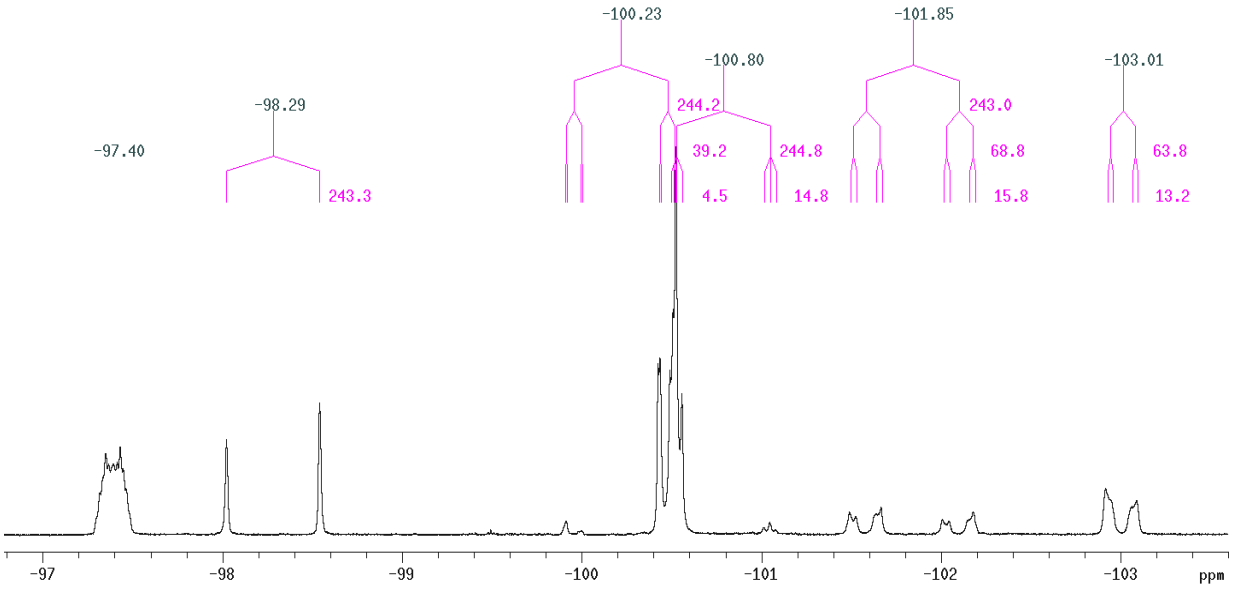


Figure 4-21 Coupling constants in minor isomer confirm the assignment

4.4 Experimental Section

All chemicals were purchased from Sigma-Aldrich and used directly without further purification. All reactions were done under a nitrogen atmosphere. Column

chromatography was carried out on silica gel. All melting points are uncorrected. ^{1}H and ^{19}F NMR were recorded in $CDCl_3$ at 300 MHz and 282 MHz, respectively (unless designated otherwise). Because of the perfluoro nature of the compounds synthesized in this chapter, which results in multiple one-, two- and three-bond F-C couplings for each signal with little difference in chemical shift, the respective ^{13}C spectra do not provide useful observable structural information.

4,7-*bis*-Phenylthioperfluoro[2.2]paracyclophane (114a): A mixture of sodium thiophenolate (29.4 mg, 0.2 mmol) and perfluoro[2.2]paracyclophane (49.6 mg, 0.1 mmol) in anhydrous tetrahydrofuran (4 mL) was stirred at room temperature for 48 h. The reaction mixture was concentrated to dryness. The residue was purified by column chromatography (silica gel, hexanes) to give 4,7-*bis*-phenylthioperfluoro[2.2]para-cyclophane (30 mg, yield: 44.2%) as a yellow solid. mp 122-124 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (m, 10H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -100.24 (dd, J_1 = 245.4 Hz, J_2 = 11.5 Hz, 2F), -100.72 (dd, J_1 = 250.5 Hz, J_2 = 42.6 Hz, 2F), -100.98 (d, J = 63.0 Hz, 2F), -102.22 (ddd, J_1 = 245.2 Hz, J_2 = 66.3 Hz, J_3 = 6.4 Hz, 2F), -103.33 (dddd, J_1 = 251.7 Hz, J_2 = 54.9 Hz, J_3 = 15 Hz, J_4 = 6.4 Hz, 2F), -128.49 (dd, J_1 = 42.7 Hz, J_2 = 10.5 Hz, 2F), -134.26 (dddd, J_1 = 54.4 Hz, J_2 = 19.8 Hz, J_3 = 6.4 Hz, J_4 = 4.0 Hz, 2F). Anal. Calcd for $C_{28}H_{10}F_{14}S_2$ C 49.71, H 1.49. Found: C 49.97, H 1.69. Note: F8 : PhSNa = 1:2.

4,7-*bis*-*tert*-Butylthioperfluoro[2.2]paracyclophane (114b): A mixture of sodium 2-methyl-2-propanethiolate (67.3 mg, 0.6 mmol) and F8 (148.8 mg, 0.3 mmol) in anhydrous tetrahydrofuran (12 mL) was stirred at room temperature for 24 h. The reaction mixture was concentrated to dryness. The residue was purified by column chromatography (silica gel, hexanes) to give 4,7-*bis*-*tert*-butylthioperfluoro[2.2]para-

cyclophane (94.5mg, yield: 49.5%) as a yellow solid. mp 127-128 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.22 (s, 18H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -97.99 (d, J = 240.8 Hz, 2F), -98.36 (d, J = 66.3 Hz, 2F), -100.02 (ddt, J_1 = 236.3 Hz, J_2 = 76.9 Hz, J_3 = 8.2 Hz, 2F), -100.69 (dd, J_1 = 250.9 Hz, J_2 = 43.4 Hz, 2F), -103.01 (ddt, J_1 = 248.7 Hz, J_2 = 49.9 Hz, J_3 = 10.4 Hz, 2F), -128.53 (dd, J_1 = 41.5 Hz, J_2 = 29.0 Hz, 2F), -134.00 (m, 2F). Anal. Calcd for $C_{24}H_{18}F_{14}S_2$ C 45.29, H 2.85. Found: C 45.61, H 2.86.

***bis*-(2,3,5,6-Tetrafluorophenylthio)perfluoro[2.2]paracyclophane (114c):** To a solution of 2,3,5,6-tetrafluorothiophenol (100.3 mg, 0.6 mmol) in anhydrous tetrahydrofuran (10 mL) was added 60% sodium hydride (24 mg, 0.6 mmol). The resulting reaction mixture was stirred for 30 minutes. To the above mixture was added perfluoro[2.2]paracyclophane (148.8 mg, 0.3 mmol). The reaction mixture was stirred at room temperature overnight. The reaction mixture was concentrated to dryness. The residue was purified by column chromatography (silica gel, hexanes) to give 4,7-*bis*-(2,3,5,6-tetrafluorophenylthio)perfluoro[2.2]paracyclophane (110 mg, yield: 47%) as yellow solid. mp 184-186 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.12 (m, 2H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -100.62 (dd, J_1 = 252.7 Hz, J_2 = 40.9 Hz, 2F), -101.02 (d, J = 243.1 Hz, 2F), -101.82 (m, 2F), -102.74 (dd, J_1 = 245.3 Hz, J_2 = 57.8 Hz, 2F), -103.59 (dddd, J_1 = 250.1 Hz, J_2 = 55.3 Hz, J_3 = 14.4 Hz, J_4 = 7.1 Hz, 2F), -128.24 (m, 2F), -134.52 (d, J = 47.9 Hz, 2F), -134.48 (t, J = 9.6 Hz, 4F), -136.85 (m, 4F). Anal. Calcd for $C_{28}H_2F_{22}S_2$ C 40.99, H 0.25. Found: C 40.76, H 0.34.

4,7-*bis*-Methylthioperfluoro[2.2]paracyclophane (114d): A mixture of sodium methanethiolate (35 mg, 0.5 mmol) and F8 (124 mg, 0.25 mmol) in anhydrous tetrahydrofuran (10 mL) was stirred at room temperature for 20 h. The reaction mixture

was concentrated to dryness. The residue was purified by column chromatography (silica gel, hexanes) to give 4,7-*bis*-methylthioperfluoro[2.2]paracyclophane (68 mg, yield: 49.3%) as a yellow solid. mp 114-116 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.52 (d, J = 2.1 Hz, 6H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -99.62 (d, J = 244.8 Hz, 2F), -100.08 (dd, J_1 = 250.9 Hz, J_2 = 41.7 Hz, 2F), -101.24 (ddt, J_1 = 244.8 Hz, J_2 = 64.3 Hz, J_3 = 8.2 Hz, 2F), -103.03 (dddd, J_1 = 250.9 Hz, J_2 = 51.9 Hz, J_3 = 14.7 Hz, J_4 = 6.2 Hz, 2F), -104.64 (dd, J_1 = 62.0 Hz, J_2 = 6.5 Hz, 2F), -129.42 (m, 2F), -134.65 (dd, J_1 = 45.7 Hz, J_2 = 18.6 Hz, 2F). Anal. Calcd for $C_{18}H_6F_{14}S_2$ C 39.14, H 1.09. Found: C 39.30, H 0.93.

4,7,12,15-*tetrakis*-Phenylthioperfluoro[2.2]paracyclophane (117a, major) and 4,7,13,16-*tetrakis*-phenylthioperfluoro[2.2]paracyclophane (118a, minor): A mixture of sodium thiophenolate (58.8 mg, 0.2 mmol) and F8 (49.6 mg, 0.1 mmol) in anhydrous tetrahydrofuran (4 mL) was stirred at room temperature for 48 h. The reaction mixture was concentrated to dryness. The residue was purified by column chromatography (silica gel, hexanes) to give a mixture of 4,7,12,15-*tetrakis*-phenylthio-perfluoro[2.2]paracyclophane (**117a**, major) and 4,7,13,16-*tetrakis*-phenylthio-perfluoro[2.2]paracyclophane (**118a**, minor) (80 mg, yield: 93.4%) as a yellow solid. mp 145-146 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.34-7.20 (m, 20H). ^{19}F NMR (282 MHz, $CDCl_3$) **117a:** δ -97.4(dd, , J_1 = 53.9 Hz, J_2 = 12.4 Hz, 4F), -100.23 (dd, J_1 = 244.2 Hz, J_2 = 39.2 Hz, 4F), -100.80 (dt, J_1 = 244.8 Hz, J_2 = 14.8 Hz, 4F); **117b:** -98.29 (d, J = 243.3 Hz, 4F), -101.85 (ddd, J_1 = 243.0 Hz, J_2 = 68.8 Hz, J_3 = 15.8 Hz, 4F), -103.01 (dd, J_1 = 63.8 Hz, J_2 = 13.2 Hz, 4F). Anal. Calcd for $C_{40}H_{20}F_{12}S_4.CH_2Cl_2$ 52.29, H 2.35. Found: C 52.08, H 2.61.

4,7,12,15-*tetrakis*-*tert*-Butylthioperfluoro[2.2]paracyclophane (117b, major) and 4,7,13,16- *tetrakis*-*tert*-butylthioperfluoro[2.2]paracyclophane (118b, minor): A mixture of sodium 2-methyl-2-propanethiolate (149.5 mg, 1.2 mmol) and perfluoro[2.2]paracyclophane (148.8 mg, 0.3 mmol) in anhydrous tetrahydrofuran (12 mL) was stirred at room temperature for 48 h. The reaction mixture was concentrated to dryness. The residue was purified by column chromatography (silica gel, hexanes) to give 4,7,12,15-*tetrakis*-*tert*-butylthioperfluoro[2.2]paracyclophane (**117b**, major) and 4,7,13,16- *tetrakis*-*tert*-butylthioperfluoro[2.2]paracyclophane (**118b**, minor) (106.5 mg, yield: 45.7%) as a yellow solid. mp 149-150 ^{o}C; **117b:** ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.16 (s, 36H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -94.93 (dd, J_1 = 54.1 Hz, J_2 = 10.2 Hz, 4F), -97.22 (dd, J_1 = 238.6 Hz, J_2 = 58.1 Hz, 4F) -98.41 (dt, J_1 = 236.6 Hz, J_2 = 14.8 Hz, 4F); **118b:** ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.18 (s, 36H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -96.19 (dd, J_1 = 228.1 Hz, J_2 = 10.4 Hz, 4F), -99.10- -101.00 (m, 8F). Anal. Calcd for $C_{32}H_{36}F_{12}S_4$ 49.47, H 4.67. Found: C 49.77, H 4.76.

4,7,12,15-*tetrakis*-(2,3,5,6-Tetrafluorophenylthio)perfluoro[2.2]para-cyclophane (117c, major) and 4,7,13,16- *tetrakis*(2,3,5,6-tetrafluorophenylthio)-perfluoro[2.2] paracyclophane (118c, minor): To a solution of 2,3,5,6-tetrafluoro-thiophenol (200.6 mg, 1.2 mmol) in anhydrous tetrahydrofuran (10 mL) was added 60% sodium hydride (48 mg, 1.2 mmol). The resulting reaction mixture was stirred for 30 minutes. To the above mixture was added perfluoro[2.2]paracyclophane (148.8 mg, 0.3 mmol). The reaction mixture was stirred at room temperature for 24 h. The reaction mixture was concentrated to dryness. The residue was purified by column chromatography (silica gel, hexanes:dichloromethane = 4:1) to give 4,7,12,15-t*etrakis*-

(2,3,5,6-tetrafluorophenylthio)perfluoro[2.2]paracyclophane (**117c**, major) and 4,7,13,16-*tetrakis*-(2,3,5,6-tetrafluorophenylthio)perfluoro[2.2]paracyclophane (**118c**, minor) (120 mg, total yield: 37.6%) as a yellow solid. mp 200 ^{o}C decomposition; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.12 (m, 4H). ^{19}F NMR (282 MHz, $CDCl_3$) **117c:** δ -98.17 (t, J = 27.1 Hz, 4F), -101.71 (dd, J_1 = 248.7 Hz, J_2 = 37.2 Hz, 4F), -102.86 (dd, J_1 = 248.7 Hz, J_2 = 22.8 Hz, 4F); -134.33 (dt, , J_1 = 132.8 Hz, J_2 = 10.4 Hz, 8F), -136.9 (m, 8F); **118c:** -98.38 (d, J = 244.8 Hz, 4F), -102.33 (ddd, J_1 = 244.8 Hz, J_2 = 66.3 Hz, J_3 = 14.7 Hz, 4F), -103.40 (d, J = 76.7 Hz, 4F), -134.33 (dt, , J_1 = 132.8 Hz, J_2 = 10.4 Hz, 8F), -136.9 (m, 8F). Anal. Calcd for $C_{40}H_4F_{28}S_4$ C 41.97, H 0.35. Found: C 42.03, H 0.24.

4,7,12,15-*tetrakis*-Methylthioperfluoro[2.2]paracyclophane (117d, major) and 4,7,13,16- *tetrakis*-methylthioperfluoro[2.2]paracyclophane (118d, minor): A mixture of sodium methanethiolate (70 mg, 1.0 mmol) and F8 (124 mg, 0.25 mmol) in anhydrous tetrahydrofuran (10 mL) was stirred at room temperature for 20 h. The reaction mixture was concentrated to dryness. The residue was purified by column chromatography (silica gel, hexanes) to give 4,7,12,15-*tetrakis*-methylthio-perfluoro[2.2]paracyclophane (**117d**, major) and 4,7,13,16- *tetrakis*-methylthioperfluoro-[2.2]paracyclophane (**118d**, minor) (122 mg, yield: 80.3%) as a yellow solid. mp 180-182 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) **117d:** δ 2.49 (d, J = 1.2 Hz, 12H); **118d:** δ 2.44 (d, J = 1.2 Hz, 12H). ^{19}F NMR (282 MHz, $CDCl_3$) **117d:** δ -98.92 (dd, J_1 = 244.5 Hz, J_2 = 53.8 Hz, 4F), -101.03 (dd, J_1 = 242.5 Hz, J_2 = 20.6 Hz, 4F) -101.76 (d, J = 53.8 Hz, 2F), -101.83 (d, J = 49.6 Hz, 2F); **118d:** -97.09 (d, J = 242.8 Hz, 4F), -100.80 (m, 4F), -107.24 (m, 4F). HRMS (CI) Calcd for $C_{20}H_{12}F_{12}S_4$ 607.9630 (M^+), found 607.9626.

4,7,12,15-*tetrakis*-(4-Fluorophenoxy)perfluoro[2.2]paracyclophane (119):

To a solution of 4-fluorophenol (112 mg, 1 mmol) in anhydrous tetrahydrofuran (10 mL) was added 60% sodium hydride (44 mg, 1.1 mmol). The resulting reaction mixture was stirred for 30 minutes. To the above mixture was added perfluoro[2.2]paracyclophane (124 mg, 0.25 mmol). The reaction mixture was stirred at room temperature for 18 h. The reaction mixture was concentrated to dryness. The residue was purified by column chromatography (silica gel, hexanes:dichloromethane = 4:1) to give 4,7,12,15-*tetrakis*-(4-fluorophenoxy)perfluoro[2.2]paracyclophane (86 mg, yield: 43%) as a white solid. mp 248-250 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.03 (m, 8H), 6.89 (m, 8H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -101.65 (dd, J_1 = 249.0 Hz, J_2 = 49.9 Hz, 4F), -102.98 (d, J = 248.7 Hz, 4F), -119.80 (m, 4F), -123.26 (d, J = 49.9 Hz, 4F). Anal. Calcd for $C_{40}H_{16}F_{16}O_4$ C 55.57, H 1.87. Found: C 55.18, H 1.81.

***bis*-1,2-Benzenedithiol-adduct of F8 (120a, 120b):** To a solution of 1,2-benzenedithiol (69.2 mg, 0.467 mmol) in anhydrous tetrahydrofuran (10 mL) was added 60% sodium hydride (41.1 mg, 1.02 mmol). The resulting reaction mixture was stirred at room temperature for 10 minutes. To the above mixture was added F8 (98.9 mg, 0.20 mmol). The reaction mixture was stirred at room temperature overnight. The reaction mixture was concentrated to dryness. The residue was purified by column chromatography (silica gel, hexanes) to give **120a** (120 mg, yield: 86.3%) together with **120b** (ratio is 49:1) as a brownish solid. mp 296-298 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.62 (m, 4H), 7.41 (m, 4H). ^{19}F NMR (282 MHz, $CDCl_3$) **120a:** δ -88.07 (s, 4F), -100.54 (m, 4F), -133.48 (t, J = 4.2 Hz, 4F); **120b:** δ -96.05 (dm, J = 236.6 Hz, 4F), -98.1 (dd, J_1 = 244.8 Hz, J_2 = 56.1 Hz, 4F), -123.49 (dm, J = 66.3 Hz, 4F). Anal. Calcd for $C_{28}H_8F_{12}S_4$ C 48.00, H 1.15. Found: C 48.38, H 1.44.

***bis*-(4-Fluorophenoxy)perfluoro[2.2]paracyclophane (121):** To a solution of 4-fluorophenol (112.1 mg, 1 mmol) in anhydrous tetrahydrofuran (10 mL) was added 60% sodium hydride (44 mg, 1.1 mmol). The resulting reaction mixture was stirred for 15 minutes. To the above mixture was added F8 (248 mg, 0.5 mmol). The reaction mixture was stirred at room temperature for 18 h. The reaction mixture was concentrated to dryness. The residue was purified by column chromatography (silica gel, hexanes) to give *bis*-(4-fluorophenoxy)perfluoro[2.2]paracyclophane (**121**, 230 mg, yield: 71%) as a white solid. mp 98-99 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.01 (m, 4H), 6.84 (m, 4H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -103.11 (m, 8F), -119.30 (m, 2F), -122.38 (m, 1F), 124.12 (d, J = 49.9 Hz, 1F), -133.79 (m, 4F). HRMS (CI) Calcd for $C_{28}H_8F_{16}O_2$ 680.0269 (M^+), found 680.0337.

4,16-*bis*-(4-Hydroxyphenoxy)perfluoro[2.2]paracyclophane (122): To a solution of 1,4-benzenediol (110 mg, 1 mmol) in anhydrous tetrahydrofuran (10 mL) was added 60% sodium hydride (88 mg, 2.2 mmol). The resulting reaction mixture was stirred for 15 minutes. To the above mixture was added F8 (248 mg, 0.5 mmol). The reaction mixture was stirred at room temperature for 18 h. The reaction mixture was concentrated to dryness. The residue was diluted with water, extracted with diethyl ether (3 × 20 mL). The combined layers was dried over magnesium sulfate, filtered to remove magnesium sulfate and the filtrate was concentrated to dryness. The residue was purified by column chromatography (silica gel, dichloromethane) to give 4,16-*bis*-(4-hydroxyphenoxy)perfluoro [2.2]paracyclophane (**122**, 60 mg, yield: 20.5%) as a white solid. mp 256-257 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.41 (s, 2H), 6.84 (m, 8H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -99.71 (ddd, J_1 = 246.8 Hz, J_2 = 27.1 Hz, J_3 = 8.2 Hz, 2F),

-101.29 (d, J = 248.7 Hz, 2F), -105.85 (ddd, J_1 = 246.8 Hz, J_2 = 66.3 Hz, J_3 = 6.2 Hz, 2F), -106.37 (ddm, J_1 = 247.0Hz, J_2 = 78.9 Hz, 2F), -124.19 (m, 2F), -135.10 (dd, J_1 = 64.3 Hz, J_2 = 20.9 Hz, 2F), -139.37 (m, 2F). HRMS (CI) Calcd for $C_{28}H_{10}F_{14}O_4$ 676.0356 (M^+), found 676.0340.

4,7-*bis*-(3-Hydroxyphenoxy)perfluoro[2.2]paracyclophane (123): To a solution of 1,3-benzenediol (110 mg, 1 mmol) in anhydrous tetrahydrofuran (10 mL) was added 60% sodium hydride (88 mg, 2.2 mmol). The resulting reaction mixture was stirred for 15 minutes. To the above mixture was added F8 (248 mg, 0.5 mmol). The reaction mixture was stirred at room temperature for 18 h. The reaction mixture was concentrated to dryness. The residue was diluted with water, extracted with diethyl ether (3 × 20 mL). The combined layers were dried over magnesium sulfate, filtered to remove magnesium sulfate and the filtrate was concentrated to dryness. The residue was purified by column chromatography (silica gel, dichloromethane) to provide crude product, which was recrystallized from chloroform (3 mL) to give 4,7-*bis*-(3-hydroxyphenoxy)perfluoro[2.2]paracyclophane (**123**, 100 mg, yield: 34.1%) as a white solid. mp 182-183 ^oC; ^1H NMR (300 MHz, $CDCl_3$) δ 8.72 (s, 2H), 7.18 (t, J =8.1 Hz, 2H), 6.65 (m, 2H), 6.56 (m, 4H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -103.15 (dd, J_1 = 249.0 Hz, J_2 = 45.4 Hz, 2F), -103.05 (d, J = 22.8 Hz, 2F), -103.13 (d, J = 24.8 Hz, 2F) -104.21 (dd, J_1 = 246.8 Hz, J_2 = 12.4 Hz, 2F), -126.79 (d, J = 43.4 Hz, 2F), -133.39 (m, 2F), -136.23 (m, 2F). HRMS (CI) Calcd for $C_{28}H_{10}F_{14}O_4$ (M^+) 676.0356, found 676.0386.

4,16-*bis*-Benzylaminoperfluoro[2.2]paracyclophane (124a) and 4,15-*bis*-benzylamino perfluoro[2.2]paracyclophane (124b): To a solution of benzylamine (235 mg, 2.2 mmol) in anhydrous tetrahydrofuran (10 mL) was added F8 (124 mg, 0.25

mmol). The reaction mixture was stirred at room temperature for 24 h. The reaction mixture was concentrated to dryness. The residue was purified by column chromatography (silica gel, hexanes) to give a mixture of 4,16-*bis*-benzylamino-perfluoro[2.2]paracyclophane (**124a**) and 4,15-*bis*-benzylaminoperfluoro[2.2]para-cyclophane (**124b**) (115 mg, yield: 68.7%) as a yellow solid. mp 134 ^{o}C decomposition; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35 (m, 6H), 7.28 (m, 4H), 4.50 (s, 2H, 4.67 (d, J = 1.2 Hz, 4H). ^{19}F NMR (282 MHz, $CDCl_3$) **124a:** δ -93.85 (dd, J_1 = 250.3 Hz, J_2 = 51.3 Hz, 2F), -94.47 (dd, J_1 = 254.6 Hz, J_2 = 20.3 Hz, 2F), -101.65 (dd, J_1 = 250.1 Hz, J_2 = 40.6 Hz, 2F), -103.91 (dddd, J_1 = 250.4 Hz, J_2 = 63.1 Hz, J_3 = 16.9 Hz, J_4 = 7.4 Hz, 2F), -102.37 (d, J = 39.4 Hz, 2F), -136.42 (ddd, J_1 = 51.0 Hz, J_2 = 22.8 Hz, J_3 = 8.5 Hz, 2F), -149.46 (d, J = 63.8 Hz, 2F). **124b:** δ -95.37 (d, J = 253.7 Hz, 2F), -97.60 (dd, J_1 = 252.2 Hz, J_2 = 59.7 Hz, 2F), -99.69 (dd, J_1 = 252.5 Hz, J_2 = 38.2 Hz, J_3 = 5.2 Hz, 2F), -100.60 (ddddd, J_1 = 254.5 Hz, J_2 = 78.0 Hz, J_3 = 20.5 Hz, J_4 = 6.2 Hz, J_5 = 2.1 Hz, 2F), -131.62 (s, 2F), -137.86 (d, J =78.4 Hz, 2F), -148.33 (dddd, J_1 = 59.9 Hz, J_2 = 22.9 Hz, J_3 = 9.2 Hz, J_4 = 4.6 Hz, 2F). Anal. Calcd for $C_{30}H_{16}F_{14}N_2$ C 53.74, H 2.41, N 4.18. Found: C 53.81, H 2.54, N 3.89.

4,16-*bis*-(Pyrrolidin-1-yl)perfluoro[2.2]paracyclophane (125) and a mixture of 4,12-*bis*-(pyrrolidin-1-yl)perfluoro[2.2]paracyclophane (60% as well as 40% other two isomers, 126): To a solution of pyrrolidine (78 mg, 1.1 mmol) in anhydrous tetrahydrofuran (8 mL) was added F8 (124 mg, 0.25 mmol). The reaction mixture was stirred at room temperature for 4 h. The reaction mixture was concentrated to dryness. The residue was purified by column chromatography (silica gel, hexanes) to provide 4,16-*bis*-(pyrrolidin-1-yl)perfluoro[2.2]paracyclophane (**125**, 40 mg) and a mixture of

4,12-*bis*-(pyrrolidin-1-yl)perfluoro[2.2]paracyclophane (60% as well as 40% other two isomers, **126**) (total yield: 80.0%) as a yellow solid. **125:** mp 245 ^{o}C decomposition; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.72 (m, 4H), 3.36 (m, 4H), 2.00 (m, 4H), 1.85 (m, 4H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -97.72 (m, 2F), -98.49 (dd, J_1 = 246.8 Hz, J_2 = 16.6 Hz, 2F), -105.99 (ddd, J_1 = 249.0 Hz, J_2 = 35.3 Hz, J_3 = 10.4 Hz, 2F), -106.48 (ddd, J_1 = 249.0 Hz, J_2 = 85.2 Hz, J_3 = 31 Hz, 2F), -130.36 (d, J = 87.1 Hz, 2F), -131.96 (m, 2F), -143.25 (m, 2F). Anal. Calcd for $C_{24}H_{16}F_{14}N_2$ C 48.17, H 2.70, N 4.68. Found: C 48.28, H 2.88, N 4.53. **126:** mp 154 ^{o}C decomposition; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.62 (m, 4H), 3.22 (m, 4H), 1.96 (m, 4H), 1.78 (m, 4H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -94.82- -106.08 (m, 8F), -129.60- -132.20 (m, 2F), -132.20- -133.80 (m, 2F), -146.20- 147.30 (m, 2F). Anal. Calcd for $C_{24}H_{16}F_{14}N_2$ C 48.17, H 2.70, N 4.68. Found: C 48.21, H 2.62, N 4.55.

4,7,12-*tri*-(Pyrrolidin-1-yl)perfluoro[2.2]paracyclophane (127) and 4,7,13-*tri*-(pyrrolidin-1-yl)perfluoro[2.2]paracyclophane (128): To a solution of pyrrolidine (156 mg, 2.2 mmol) in anhydrous tetrahydrofuran (8 mL) was added F8 (124 mg, 0.25 mmol). The reaction mixture was stirred at room temperature for 96 h. The reaction mixture was concentrated to dryness. The residue was purified by column chromatography (silica gel, hexanes) to provide compound **127** (first fraction, 62 mg) and compound **128** (second fraction, 61 mg) (total yield: 75.5%) as a brownish solid. **127:** mp 203 ^{o}C decomposition; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.68 (m, 4H), 3.42 (m, 4H), 3.16 (m, 4H), 1.82 (m, 12H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -97.85 (dd, J_1 = 246.8 Hz, J_2 = 18.6 Hz, 1F), -98.35 (d, J = 251.0 Hz, 1F), -99.34 (dd, J_1 = 257.2 Hz, J_2 = 20.9 Hz, 1F), -101.44 (ddd, J_1 = 251.0 Hz, J_2 = 41.5 Hz, J_3 = 14.4 Hz, 1F), -101.71 (ddd, J_1 = 249.0 Hz, J_2 = 74.7 Hz, J_3 = 22.6 Hz, 1F), -103.86 (dd, J_1 = 251.0 Hz, J_2 = 62.3 Hz, 1F), -104.55 (dd, J_1

= 251.0 Hz, J_2 = 58.1 Hz, 1F), -105.98 (dd, J_1 = 252.9 Hz, J_2 = 60.1 Hz, 1F), -124.22 (d, J = 72.8 Hz, 1F), -125.97 (dd, J_1 = 58.1 Hz, J_2 = 16.6 Hz, 1F), -131.82 (dd, J_1 = 68.2 Hz, J_2 = 26.8 Hz, 1F), -132.22 (d, J = 57.8 Hz, 1F), -147.72 (m, 1F). Anal. Calcd for $C_{28}H_{24}F_{13}N_3$ C 51.78, H 3.72, N 6.47. Found: C 51.44, H 3.50, N 6.12. **128:** mp 219-220 ^{o}C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.65 (m, 4H), 3.40 (m, 4H), 3.09 (m, 4H), 1.74 (m, 12H). ^{19}F NMR (282 MHz, $CDCl_3$) δ -92.97 (d, J = 251.0 Hz, 1F), -96.14 (dt, J_1 = 248.2 Hz, J_2 = 8.2 Hz, 1F), -97.53 (dd, J_1 = 251.0 Hz, J_2 = 20.6 Hz, 1F), -98.38 (d, J = 249.0 Hz, 1F), -99.95 (dd, J_1 = 249.0 Hz, J_2 = 25.1 Hz, 1F), -100.94 (ddd, J_1 = 249.0 Hz, J_2 = 95.3 Hz, J_3 = 51.9 Hz, 1F), -106.91 (ddd, J_1 = 249.0 Hz, J_2 = 35.3 Hz, J_3 = 6.2 Hz, 1F), -107.16 (ddd, J_1 = 251.0 Hz, J_2 = 84.9 Hz, J_3 = 33.3 Hz, 1F), -124.73 (d, J = 97.6 Hz, 1F), -126.83 (m, 1F), -134.76 (m, 1F), -137.37 (d, J = 87.1 Hz, 1F), -148.73 (m, 1F). Anal. Calcd for $C_{28}H_{24}F_{13}N_3$ C 51.78, H 3.72, N 6.47. Found: C 51.47, H 3.51, N 6.29.

APPENDIX
X-RAY DATA

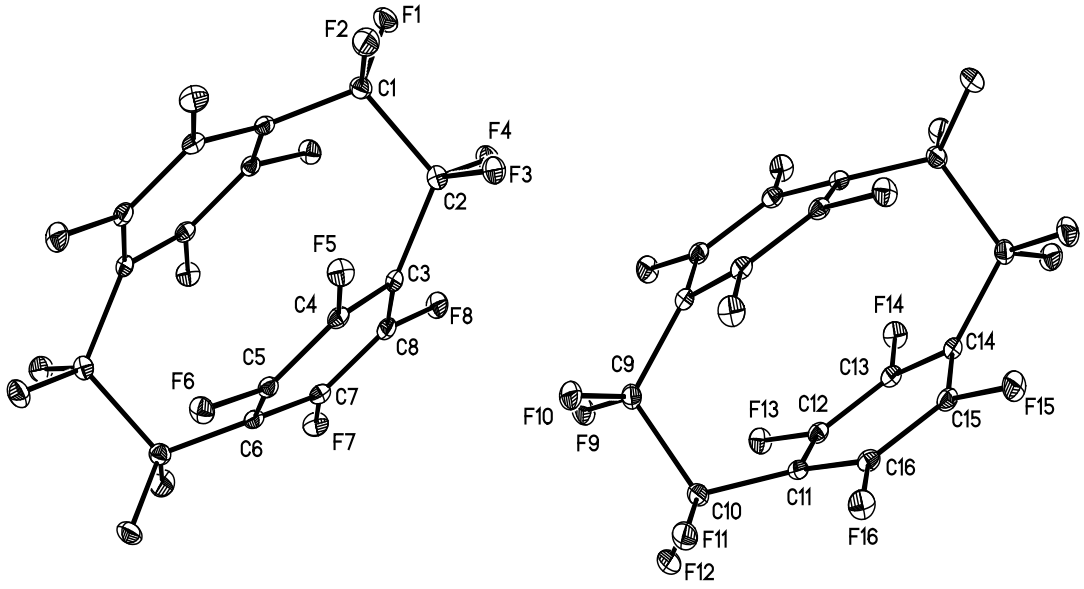


Figure A-1 X-ray structure of perfluoro[2.2]paracyclophane

Crystal Data and Structure Refinement for Perfluoro[2.2]paracyclophane

Identification code	px01	
Empirical formula	C16 F16	
Formula weight	496.16	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)/c	
Unit cell dimensions	a = 13.9870(6) Å	α= 90°.
	b = 8.8637(4) Å	β= 100.184(2)°.
	c = 11.7764(5) Å	γ = 90°.
Volume	1437.00(11) $Å^3$	
Z	4	
Density (calculated)	2.293 Mg/m^3	
Absorption coefficient	0.281 mm^{-1}	
F(000)	960	
Crystal size	0.18 x 0.14 x 0.09 mm^3	
Theta range for data collection	1.48 to 27.49°.	
Index ranges	-18≤h≤11, -11≤k≤11, -11≤l≤15	
Reflections collected	8928	
Independent reflections	3277 [R(int) = 0.0462]	
Completeness to theta = 27.49°	99.0 %	
Absorption correction	Integration	
Max. and min. transmission	0.9819 and 0.9548	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3277 / 0 / 289	
Goodness-of-fit on F^2	1.061	
Final R indices [I>2sigma(I)]	R1 = 0.0350, wR2 = 0.0905 [2654]	
R indices (all data)	R1 = 0.0464, wR2 = 0.0972	
Largest diff. peak and hole	0.407 and -0.323 e.$Å^{-3}$	

$R1 = \sum(||F_o| - |F_c||) / \sum|F_o|$

$wR2 = [\sum[w(F_o^2 - F_c^2)^2] / \sum[w(F_o^2)^2]]^{1/2}$

$S = [\sum[w(F_o^2 - F_c^2)^2] / (n-p)]^{1/2}$

$w= 1/[\sigma^2(F_o^2)+(m*p)^2+n*p]$, $p = [\max(F_o^2,0)+ 2* F_c^2]/3$, m & n are constants.

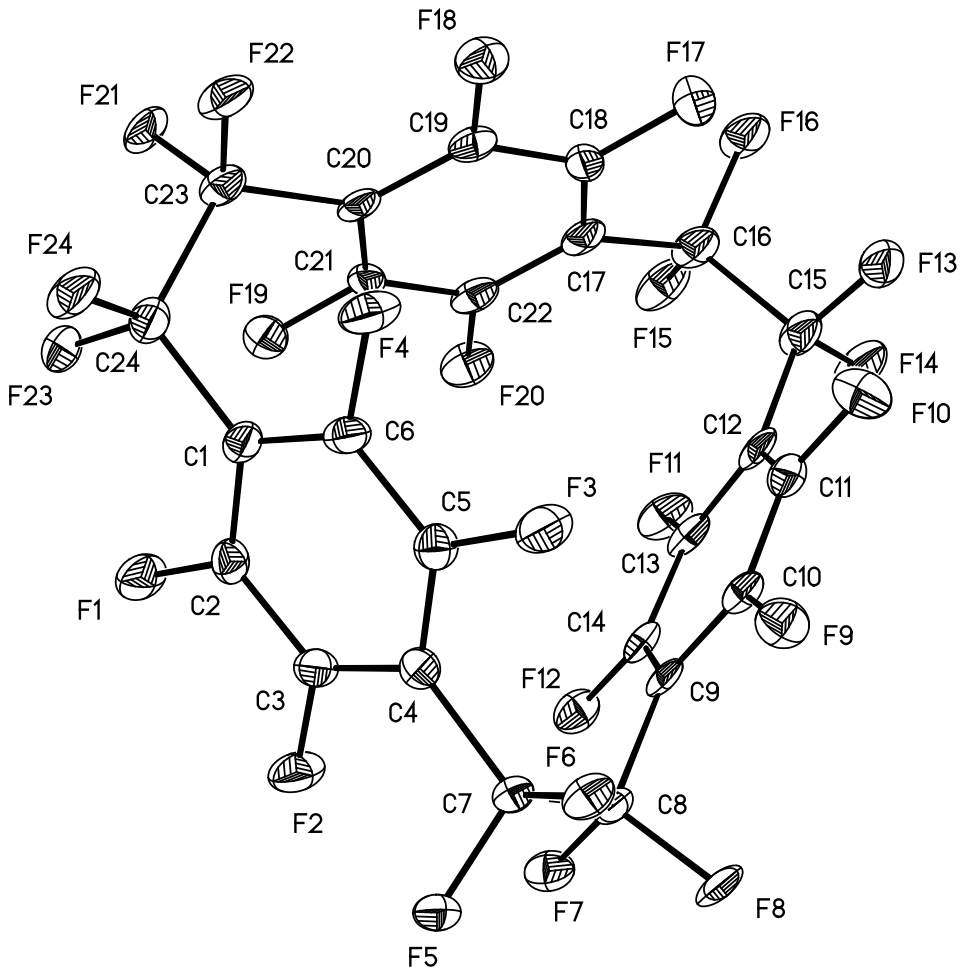


Figure A-2 X-ray structure of perfluoro[2.2.2]paracyclophane

Crystal Data and Structure Refinement for Perfluoro[2.2.2]paracyclophane

Identification code	lhz2	
Empirical formula	C24 F24	
Formula weight	744.24	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 10.056(3) Å	α= 70.809(4)°.
	b = 10.297(3) Å	β= 80.175(4)°.
	c = 13.570(4) Å	γ = 61.718(4)°.
Volume	1168.4(6) $Å^3$	
Z	2	
Density (calculated)	2.115 Mg/m^3	
Absorption coefficient	0.259 mm^{-1}	
F(000)	720	
Crystal size	0.23 x 0.08 x 0.05 mm^3	
Theta range for data collection	1.59 to 22.75°.	
Index ranges	-10≤h≤10, -11≤k≤8, -14≤l≤14	
Reflections collected	5488	
Independent reflections	3082 [R(int) = 0.0469]	
Completeness to theta = 22.75°	97.9 %	
Absorption correction	None	
Max. and min. transmission	0.9884 and 0.9433	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3082 / 0 / 433	
Goodness-of-fit on F^2	1.004	
Final R indices [I>2sigma(I)]	R1 = 0.0337, wR2 = 0.0878 [2478]	
R indices (all data)	R1 = 0.0442, wR2 = 0.0940	
Largest diff. peak and hole	0.346 and -0.281 $e.Å^{-3}$	

$R1 = \sum(||Fo| - |Fc||) / \sum|Fo|$ $wR2 = [\sum[w(Fo^2 - Fc^2)^2] / \sum[w(Fo^2)^2]]^{1/2}$
$S = [\sum[w(Fo^2 - Fc^2)^2] / (n-p)]^{1/2}$ $w= 1/[\sigma^2(Fo^2)+(m*p)^2+n*p]$, $p = [\max(Fo^2,0)+ 2*Fc^2]/3$, m & n are constants.

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BIOGRAPHICAL SKETCH

Lianhao Zhang was from Shandong, People's Republic of China. He received his B.S. degree from Shandong University in July 1987, and the M.S. degree in organic chemistry from Northwest University in July 1990. From July 1990 to January 1997, he worked in the Xi'an Modern Chemistry Research Institute as a research chemist. From January 1997 to June 2000, He worked in the University of Florida as a visiting scholar with Professors William R. Dolbier, Jr. and Alan R. Katritzky.

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