cm^{-1}; ^{1}H NMR δ 7.20 (m, 1 H_{17}), 6.18 (d, 1 H, J = 2 Hz, H_{16}), 3.66 (s, 3 H, OCH_3), 1.20 (s, 3 H, H_{18}), 0.97 (d, 3 H, J = 7 Hz, H_{15}), 0.70 (s, 3 H, H_{20}); mass spectrum, m/e 330 (M^+, 41%), 315 (5%), 271 (4%), 255 (11%), 221 (4%), 161 (14%) 108 (100%). Anal. Calcd for $C_{21}H_{30}O_3$: C, 76.36; H, 9.09. Found: C, 76.34; H, 9.07.

Acknowledgment. We thank CNR for financial support.

Registry No. 1, 4614-50-0; 2, 24402-16-2; 3, 78004-32-7; 4, 78085-85-5; chloroacetyl chloride, 79-04-9.

Synthesis of Chlorinated and Brominated Biphenyl Oxides[1]

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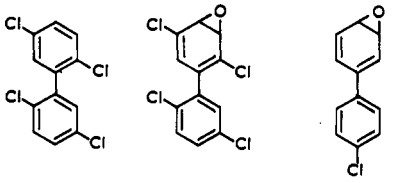
Vogel, Schubart, and Böll first reported the synthesis of the benzene oxide–oxepin valence tautomers in 1964.[2] Since then, a large number of arene oxides have been prepared and their chemistry has been studied.[2b,3,4] In recent years these substances have become of intense interest as potential intermediates in the metabolism of aromatic compounds. In fact, many of the adverse biological effects of aromatic compounds have been ascribed to the interaction of arene oxides with cell constituents. For this reason the synthesis of several chlorinated and brominated biphenyl oxides described here was undertaken, with the goal of studying their properties in relation to the toxic effects of polychlorinated and polybrominated biphenyls (PCB's, PBB's).[5] Several related compounds, including the 3- and 4-chlorobenzene oxides[4a] and biphenyl 2,3-oxide,[4b] have been prepared.

2,5,2′,5′-Tetrachlorobiphenyl (1) has been extensively

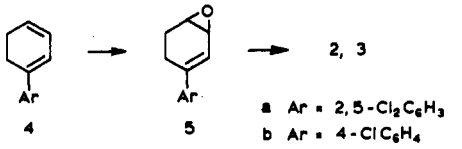


1 2 3

studied as a model for the biological effects of Arachlor mixtures,[6] and the arene oxide 2 has been implicated as an intermediate during its metabolic degradation.[6a] This compound was the primary goal of this study. We also prepared several analogues of 2 having chlorines replaced by bromines or hydrogens, as well as arene oxide 3, a possible metabolite of 4-chlorobiphenyl.[7] These compounds are the first PCB arene oxides to be prepared.

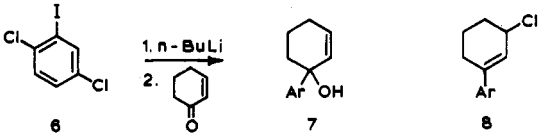
Results and Discussion

The synthetic approach is outlined below. The principal problems appeared to be regiochemical control during introduction of double bonds in 4 and the chlorines in 2.



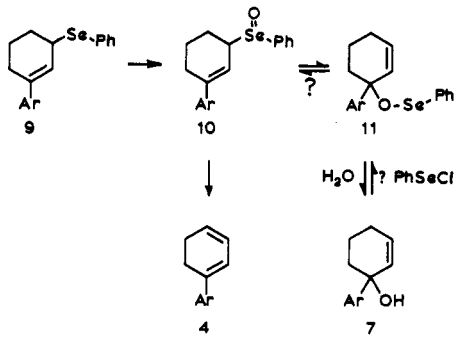
4 5

A suitable precursor for 4a was 7a, prepared by addition of the unstable 2,5-dichlorophenyllithium (6)[8] to cyclohexenone (throughout this paper the "a" series of compounds will refer to Ar = 2,5-dichlorophenyl, the "b" series to Ar = 4-chlorophenyl). However, neither direct dehydration of 7a with acid or phosphorus oxychloride or



6 7 8

dehydrohalogenation of the allylic chloride 8a under basic conditions could be carried out to give useful amounts of the diene 4a. Some success was achieved by converting 8a to the selenide 9a and oxidizing to the unstable selenoxide 10a. Although most allylic selenoxides give almost



9 10 11 4 7

exclusively products of [2,3] sigmatropic rearrangement,[9,10] several examples have been reported where syn elimination competes.[10,11] This is the case here also, although the major pathway was still rearrangement (60/40). The diene 4a was easily separated from the alcohol 7a, which could be recycled. Electron-withdrawing substituents have been

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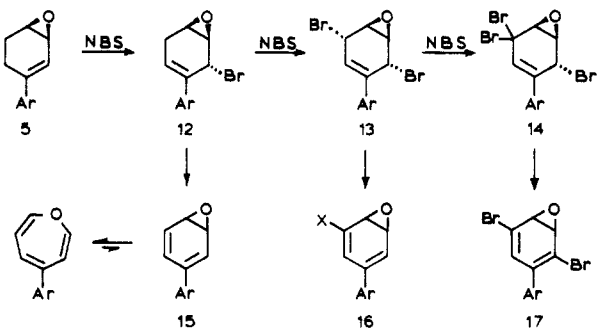
0022-3263/81/1946-3721$01.25/0

shown to dramatically accelerate selenoxide[12] and sulfoxide[13] syn eliminations. Unfortunately, [2,3] sigmatropic rearrangements are also speeded up.[14] We prepared the (2-nitro-4-methylphenyl)seleno and (4-nitrophenyl)seleno analogues of **10a** to see if these would give a more favorable ratio of elimination to rearrangement. The electron-withdrawing substituents caused the substitution reaction on the allylic chloride to be much slower and less clean and the ratio of diene to alcohol was not improved.[15]

While the procedure via **9a** provided a solution to the problem of preparing **4a**, it seemed possible to improve the process substantially by taking advantage of the reversibility of [2,3] sigmatropic rearrangements, i.e., by converting **7a** to the selenenate **11a**, which could rearrange to selenoxide **10a** and eliminate to diene **4a**. Attempts were made to carry out this process with several selenenyl (C_6H_5SeCl, $2\text{-}NO_2C_6H_4SeCl$, $2,4\text{-}(NO_2)_2C_6H_3SeBr$) and sulfenyl ($CCl_3SCl$, $2\text{-}NO_2C_6H_4SCl$, $4\text{-}NO_2C_6H_4SCl$, $2,4\text{-}(NO_2)_2C_6H_3SCl$) halides. Marginal success was attained with 2-nitrobenzeneselenenyl chloride, but the reagent of choice was 2,4-dinitrobenzenesulfenyl chloride, which is commercially available and can be used to convert a wide range of allylic alcohols to dienes by 1,4-elimination.[1,14b] When **7a** was treated with this reagent it was smoothly converted in 79–85% yield to the diene **4a**, with no trace of other regioisomers. This was the key step in the synthesis and allowed us to prepare a number of arene oxides in good yield.

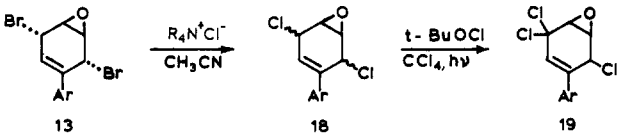
The diene **4a** was epoxidized to give **5a**, but this material could not be chlorinated in the allylic position without extensive decomposition, using either chlorine, *tert*-butyl hypochlorite, or sulfuryl chloride. It was thus necessary to proceed indirectly by NBS bromination, which could be carried out to give successively mono-, di-, and tribromo products. The monobromo (**12a**) and dibromo (**13a**)



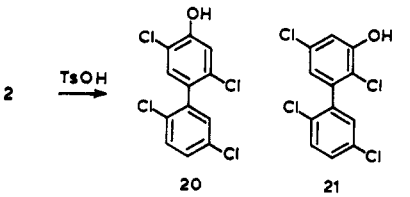
products were predominantly a single crystalline isomer. Complete stereochemical assignments of these compounds could not be made on the basis of proton–proton coupling constants, but $Eu(fod)_3$-shifted spectra allowed the assignments shown for compounds **12a** and **13a**.

Each of the halides **12a**, **13a**, and **14a** could be treated with 1,5-diazabicyclo[5.4.0]undec-5-ene (DBU) to eliminate hydrogen bromide and form the corresponding arene oxide (**15a**, **16a**, and **17a**).

In order to obtain the desired tetrachloro arene oxide **2**, the allylic bromines in the epoxide **13a** were substituted by chlorines. This was accomplished by treating **13a** with benzyltriethylammonium chloride in acetonitrile. A mixture of at least three isomers of **18a** was produced. This



mixture was further chlorinated with *tert*-butyl hypochlorite in refluxing carbon tetrachloride to yield the epoxide **19a**, which was converted to **2**. Since neither the method of synthesis nor the NMR spectra provides proof for the positions of the halogens of the epoxide-containing ring of **2**, **16a** and **17a**, each of the arene oxides was aromatized with acid to a mixture of phenols or phenol acetates. Their NMR spectra, when combined with those of the arene oxide and halide precursors, allowed clearcut assignments of structure to be made. Compound **2** was converted to a 4:1 mixture of the phenols **20** and **21**, whose

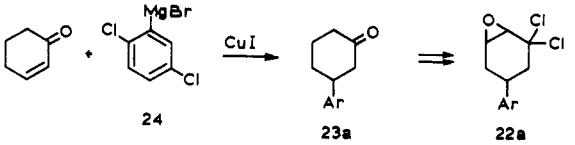


substitution pattern was unambiguously assigned by analysis of the 270-MHz NMR spectra. These phenols were converted to acetates, and the NMR spectra of pure crystalline 4-acetoxy-2,5,2′,5′-tetrachlorobiphenyl and that of the 3-acetoxy isomer in the mixture served further to confirm the structure of **2**.

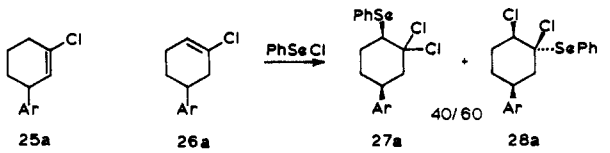
As was the case for the dibromo epoxide **13a**, the dichloro epoxide **18a** could be dehydrohalogenated with DBU to give the arene oxide **16a** (X = Cl).

The same general sequence described above was used to prepare the 4′-chlorobiphenyl oxide **3** via **7b**, **4b**, **5b**, and **12b**. Several of the synthetic intermediates (e.g., **4b**, **5b**, **12b**) were much more prone than their 2,5-dichlorophenyl analogues (**4a**, **5a**, and **12a**) to suffer from decompositions and rearrangements. The arene oxide **3** was also much less stable than any of the others we prepared.

An alternative approach to the arene oxides described above which proved unsuccessful involved as an intermediate target the epoxide **22a**. It was found that the pre-



cursor 3-(2,5-dichlorophenyl)cyclohexanone (**23a**) could be prepared under carefully controlled conditions by copper-catalyzed conjugate addition to cyclohexenone of the unstable Grignard reagent **24**, which was in turn prepared from the lithium reagent. Treatment of **23a** with phosphorus pentachloride gave a 1:3 mixture of vinyl chlorides **25a** and **26a**,[17] of which the major component was the



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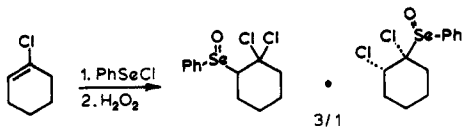
(15) Substantial changes in the ratio of allyl alcohol to diene during thermolysis of allylic sulfoxides on changing from *p*-nitro- to *p*-methoxyphenyl have been reported.[16] It is possible that the rate of cleavage of sulfenate ester was a determining factor in these systems.

(16) Isobe, M.; Iio, H.; Kitamura, M.; Goto, T. *Chem. Lett.* **1978**, 541.

desired isomer **26a**. The addition of PhSeCl to **26a** gave a 40:60 ratio of two adducts (**27a** and **28a**). Efforts to improve this ratio by varying reaction conditions or using Lewis acid catalysts or other areneselenenyl halides were not successful. The selenides **27a** and **28a**, as well as the mixture of olefins prepared from them by selenoxide syn elimination, could not be separated chromatographically because of decomposition. A chemical separation could be achieved when it was observed that partial oxidation of the selenide mixture gave principally the selenoxide of **27a** which could be thermolyzed to the olefin. Epoxidation of this olefin (mCPBA in carbon tetrachloride at 40 °C for 2 days) gave the target **22a**. Our inability to achieve further appropriate functionalization of **22a** for conversion to **2**, as well as the several difficult to separate mixtures we encountered in its preparation, led to the adoption of the alternate approach described earlier which eventually proved successful.

Model studies on the critical selenenyl chloride addition using 1-chlorocyclohexene had been somewhat more successful, giving a 75/25 ratio of two adducts which were oxidized to selenoxides **29** and **30**. Most alkyl selenoxides



29 30

fragment near room temperature, but cyclohexyl phenyl selenoxides sometimes require higher temperatures.[12a] We found that the two selenoxides **29** and **30** were stable at room temperature, and the major isomer (**29**) could be crystallized in pure form. Thermolysis gave 3,3-dichlorocyclohexene. Selenoxide **30** could also be obtained pure by taking advantage of the fact that **29** underwent syn elimination about 10 times as rapidly (1 min in refluxing CCl_4) as did **30**. The former could be selectively fragmented, leaving a solution from which pure **30** was isolated. This compound gave principally 2,3-dichlorocyclohexene after 20 min at reflux in carbon tetrachloride.

Stability of Halogenated Biphenyl Oxides. Although we have not carried out extensive studies of the decompositions of these arene oxides, we can report some qualitative observations of their reactivity. Compared to the 3- and 4-chlorobenzene oxides synthesized by Selander, Jerina, Piccolo, and Berchtold,[4a] the tetrahalogenated biphenyl oxides are much more stable to acid and base conditions. Both **17a** and **2** could be quantitatively recovered from preparative silica gel chromatography without aromatization, and solutions of these compounds in organic solvents can be washed with dilute hydrochloric acid. They appear to be indefinitely stable in crystalline form and unbuffered solutions in methanol and dimethyl sulfoxide have half-lives of 20 and 50 days, respectively, at room temperature. When there is only one halogen on the ring bearing the oxygen (**16a**, X = Br, Cl), stability goes down significantly. Chromatography without aromatization is no longer possible. Without any halogens on the oxide ring, the compounds are quite sensitive. Both **15a** and **3** decompose slowly at −20 °C. In dimethyl sulfoxide **15a** has a half-life of 2 days; **3** can decompose spontaneously to the phenol if not in contact with some base (i.e., triethylamine). The principal aromatization product in all cases is the 4-hydroxy compound, a result that parallels the isolation of 4-hydroxylated biphenyls as metabolites of appropriate PCB's.[6b,7]

Whereas the tetrachloro (**2**) and dibromodichloro (**17a**) arene oxides are white crystalline solids and exist largely in the oxide form, compounds **3** and **15**, which bear no halogen substituents on the oxygenated ring, are bright yellow and appear to be mainly in the oxepin form. This appears to fit with earlier observations[2b,3b] that substitution of any group at the 3-position in the oxide ring tends to enhance the contribution of the oxide tautomer, while 1- or 4-substitution favors the oxepin form in 1,2-oxy-3,5-cyclohexadienes.

We have made some attempts to prepare the dihydro diols formed by nucleophilic opening of the arene oxide. The parent benzene oxide has been converted to 1,2-dihydroxy-3,5-cyclohexadiene in 30% yield by treatment with excess alkaline hydrogen peroxide followed by borohydride reduction,[4d] although the procedure gives only 3% dihydro diol when applied to chlorobenzene oxide.[4e] Use of this method with compound **2** even under forcing conditions gave back starting material. Superoxide in dimethyl sulfoxide[19] or potassium hydroxide and Kryptofix 222[20] in dimethyl sulfoxide led to destruction of the arene oxide, as did attempts with various combinations of acetic acid, acetic anhydride, sodium acetate, and Lewis acid catalysts. Apparently halogenation of the arene oxide ring stabilizes the system not only against acid-catalyzed aromatization but also against nucleophilic opening of the oxirane.

Summary. A synthetic route suitable for the preparation of 4′-chloro-, 2′,5′-dichloro-, 5,2′,5′-trichloro-, 2,5,2′,5′-tetrachloro-, 5-bromo-2′,5′-dichloro-, and 2,5-dibromo-2′,5′-dichlorobiphenyl 3,4-epoxides[21] has been developed. The nonepoxide ring is introduced by addition of the appropriate halogenated aryllithium reagent to cyclohexenone, and thus the synthesis should be applicable to the preparation of many analogues with different substitution there. On the 3,4-epoxide-containing ring, the procedure permits placement of chlorine or bromine at the 5- or at 2- and 5-positions. The stability of the halogenated biphenyl oxides prepared increases dramatically with increased halogen substitution on the epoxide ring.

Experimental Section

General Procedures. Nuclear magnetic resonance spectra were obtained on a JEOL MH-100 spectrometer unless otherwise indicated. The 270-MHz spectra were obtained on a Brucker WH-270 spectrometer. Infrared spectra were obtained on a Beckman Acculab 7 spectrophotometer and mass spectra on an AEI MS-902 spectrometer. Unless specified otherwise, NMR and IR spectra were recorded in CCl_4 solution. Elemental analyses were performed by Spang or Galbraith Laboratories. Preparative thin-layer chromatography (TLC) was carried out with Brinkman MN silica gel P/UV 254.

Diphenyl diselenide (Ph_2Se_2),[22] benzeneselenenyl chloride (PhSeCl),[22] and *tert*-butyl hypochlorite (*t*-BuOCl)[23] were prepared according to published procedures. The following reagents were purchased from Aldrich Chemical Co. and used without further purification: 1-chloro-4-iodobenzene, *m*-chloroperbenzoic acid (mCPBA), *N*-bromosuccinimide (NBS), 1,5-diazabicyclo[5.4.0]-

(17) This ratio was not improved when catechylphosphorus trichloride[18] or the 3,6-diisopropyl derivative was used instead of PCl_5.
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(20) Dietrich, B.; Lehn, J. M. *Tetrahedron Lett.* **1973**, 1225.
(21) The numbering employed is that of the parent biphenyl. In the Experimental Section the arene oxides are named as derivatives of 1,2-epoxy-3,5-cyclohexadiene.
(22) Reich, H. J.; Cohen, M. L.; Clark, P. S. *Org. Synth.* **1979**, *59*, 141.
(23) Mintz, M. J.; Walling, C. "Organic Syntheses"; Wiley: New York, 1973; Collect Vol. 5, p 184.

undec-5-ene (DBU), 2,4-dinitrobenzenesulfenyl chloride, and benzyltriethylammonium chloride. 2-Cyclohexen-1-one (Aldrich) was distilled before use. Ether and tetrahydrofuran (THF) were freshly distilled from sodium benzophenone ketyl.

2,5-Dichloro-1-iodobenzene was prepared on 0.74-mol scale from 2,5-dichloroaniline according to the procedure of DeCrauw.[24] Instead of steam distillation to purify the product, the reaction mixture was heated on the steam bath for 0.5 h, ether was added, and the organic layer was extracted with 10% $NaHSO_3$, 5% NaOH, 5% HCl, H_2O, and saturated NaCl solutions. The solvent was removed and the product was distilled at 0.6 mm: bp 82–85 °C; 70% yield; solidifies in refrigerator; NMR δ 7.18 (dd, J = 8.5, 2.0 Hz, 1 H), 7.25 (d, J = 8.5 Hz, 1 H), 7.78 (d, J = 2.0 Hz, 1 H).

1-(2,5-Dichlorophenyl)cyclohex-2-en-1-ol (7a). To a three-necked round-bottom flask under N_2, equipped with a dropping funnel, a thermometer, and a magnetic stirrer were added 4.02 mL of 1-iodo-2,5-dichlorobenzene (**30** mmol), 15 mL of THF, and 30 mL of ether. The solution was cooled to −90 °C in a MeOH–liquid N_2 bath and 18.7 mL of 1.6 M n-BuLi solution (30 mmol) in 10 mL of ether was added dropwise over a 0.5-h period, keeping the temperature in the flask below −75 °C. 2-Cyclohexen-1-one (3.0 mL, 30 mmol) in 20 mL of ether was added dropwise so that the temperature did not exceed −75 °C. The flask was then warmed to −50 °C and poured into 1 N HCl solution and ice. Ether and pentane (1:1) were added and the HCl solution was removed. The organic layer was washed with H_2O, saturated $NaHCO_3$, and NaCl solutions. Each aqueous layer was reextracted with ether–pentane. The organic layers were combined and dried (Na_2SO_4), and the solvent was removed. The n-butyl iodide was distilled (Kugelrohr, 60 °C, 0.2 mm) and the solid residue was crystallized from CH_2Cl_2–hexane, yielding 5.79 g (80%) of **7a**: mp 79–80 °C; NMR δ 1.6–2.5 (m, 7 H), 5.65 (dt, J = 10.0, 1.5 Hz, 1 H), 5.95 (dt, J = 10.0, 3.6 Hz, 1 H), 7.07 (dd, J = 8.2, 2.2 Hz, 1 H), 7.17 (d, J = 8.2 Hz, 1 H), 7.75 (d, J = 2.2 Hz, 1 H); IR 3615, 3470 (br), 2945, 1462, 1224, 1113, 978 cm^{-1}. A sample was recrystallized for analysis.

Anal. Calcd for $C_{12}H_{12}Cl_2O$: C, 59.28; H, 4.98. Found: C, 59.27; H, 4.82.

1-(2,5-Dichlorophenyl)-1,3-cyclohexadiene (4a). To a well-stirred flask containing 2.43 g of **7a** (10 mmol) and 7.0 mL of NEt_3 (50 mmol) in 25 mL of CH_2Cl_2 under N_2 was added in one portion 5.88 g of 2,4-dinitrobenzenesulfenyl chloride (25 mmol). The contents of the flask warmed up, and the CH_2Cl_2 was refluxed. This mixture was stirred for 45 min after which 100 mL of pentane was added dropwise. The mixture was filtered through Celite on a sintered glass funnel and the precipitate was washed with pentane. The pentane solution was washed with 0.5 N HCl (2×), water, and saturated NaCl solutions. Each aqueous wash was extracted with 20 mL of pentane. The pentane solutions were combined, dried (Na_2SO_4), and evaporated. The product was filtered through a 40-g column of silica gel with pentane to remove the residual aryl disulfide. The yield was 1.77 g (79%): NMR (270 MHz, $CDCl_3$) δ 2.29 (m, 2 H), 2.48 (tt, J = 10.2, 1.2 Hz, 2 H), 5.90 (dtd, J = 9.2, 4.2, 1.0 Hz, 1 H), 5.99 (dd, J = 5.3, 1.0 Hz, 1 H), 6.05 (ddt, J = 9.2, 5.3, 1.7 Hz, 1 H), 7.13 (dd, J = 8.5, 2.5 Hz, 1 H), 7.22 (d, J = 2.5 Hz, 1 H), 7.25 (d, J = 8.5 Hz, 1 H); IR 3050, 2940, 1466, 1395, 1103, 890, 705 cm^{-1}; mass spectrum, m/e 224.0160 (M^+, calcd 224.0160). A sample was collected by GLC for analysis on a 0.25 in. × 5 ft column of 20% SE-30 on 60/80 Chromosorb W AW DMCS at 175 °C.

Anal. Calcd for $C_{12}H_{10}Cl_2$: C, 64.02; H, 4.48. Found: C, 64.00; H, 4.31.

4-(2,5-Dichlorophenyl)-1,2-epoxy-3-cyclohexene (5a). To a round-bottomed flask equipped with an addition funnel and thermometer were added 35 mL of CCl_4 and 4.80 g of mCPBA (85%, 23.6 mmol). The slurry was stirred magnetically and 5.07 g of **4a** (22.5 mmol) was added dropwise rapidly in 12 mL of CCl_4. An ice bath was used to keep the temperature of the reaction mixture between 20 and 30 °C. After the addition the stirring was continued without the ice bath for 10 min. The reaction mixture was poured into a separatory funnel containing 5% NaOH solution, ice, and enough ether (~100 mL) so that the organic layer floats. The organic layer was extracted with 5% NaOH (2×), saturated $NaHCO_3$, and saturated NaCl solutions. Each aqueous layer was extracted again with 25 mL of ether–pentane. The organic layers were combined, dried (Na_2SO_4), and evaporated. The product was ~90% pure by NMR (270 MHz, $CDCl_3$) δ 1.70–1.88 (m, 1 H), 2.20–2.47 (m, 3 H), 3.41 (t, J = 4.2 Hz, 1 H), 3.60 (distorted ddd, J = 4.2, 2.4, 1.3 Hz, 1 H), 5.98 (dd, J = 4.2, 2.8 Hz, 1 H), 7.15–7.20 (m, 2 H), 7.27 (distorted d, $J \simeq 9$ Hz, 1 H); IR 3020, 2945, 1463, 1251, 1103, 1005, 905, 888 cm^{-1}; mass spectrum, m/e 240.0109 (M^+, calcd 240.0107).

3-Bromo-4-(2,5-dichlorophenyl)-1,2-epoxy-4-cyclohexene (12a). The epoxide **5a** (6.5 mmol) was treated with 1.16 g (6.5 mmol) of NBS in 50 mL of CCl_4. The mixture was refluxed for 3 h. NMR showed a mixture of starting epoxide, monobrominated product and dibrominated product. Preparative TLC (5% ether–pentane, R_f 0.18) gave 0.450 g of white solid in 22% yield from diene **4a**. Crystallization from hexane-CH_2Cl_2 gave 0.287 g of **12a**: mp 145–146 °C; NMR (270 MHz, $CDCl_3$) δ 2.69 (dq, J = 21, 2.2 Hz, 1 H), 2.87 (ddq, J = 21, 5.6, 1.6 Hz, 1 H), 3.50 (ddd, J = 3.6, 1.6, 0.7 Hz, 1 H), 3.73 (ddd, J = 3.6, 2.2, 0.9 Hz, 1 H), 5.22 (d, J = 1.6 Hz, 1 H), 5.58 (ddd, J = 5.6, 2.5, 1.6 Hz, 1 H), 7.23–7.26 (m, 2 H), 7.31 (distorted d, $J \simeq 9$ Hz, 1 H); IR ($CHCl_3$) 3020, 2900, 1462, 1101, 996, 916, 835, 821 cm^{-1}; mass spectrum, m/e 317.9206 (M^+, calcd 317.9214).

3,6-Dibromo-4-(2,5-dichlorophenyl)-1,2-epoxy-4-cyclohexene (13a). To 5.4 g (22.5 mmol) of **5a** in 125 mL of CCl_4 was added 12 g (67.5 mmol) of NBS and 58 mg of dibenzoyl peroxide. The mixture was refluxed for 3 h. The reaction mixture was checked by NMR and found to consist of 25% starting material **5a**, 50% monobrominated material **12a**, and 25% dibrominated product. More NBS (6 g, 34 mmol) and dibenzoyl peroxide (54 mg) were added to the reaction mixture and the reflux was continued for 2 h (20% monobromo and 80% dibromo). More NBS (3 g, 11 mmol) and dibenzoyl peroxide (53 mg) were added to the reaction mixture and the reflux was continued for 2 h (complete reaction). It was necessary to check the extent of reaction by NMR because the amount of material reacting in a given amount of time with a given amount of NBS was not always reproducible. The reaction mixture was filtered (Celite) and the solids were washed with ether. The organic filtrate was washed with 10% $NaHSO_3$, 5% NaOH (2×), saturated $NaHCO_3$, and saturated NaCl solutions. Each aqueous wash was extracted again with ether. The organic solutions were dried (Na_2SO_4) and evaporated. The partially solidified oil was divided into two parts. One-third (7.5 mmol) was carried on without purification. Two-thirds (15 mmol) was dissolved in ~25 mL of hexane containing a small amount of CH_2Cl_2 and allowed to crystallize: yield 2.98 g (50%); mp 146–147 °C; NMR (270 MHz, acetone-d_6) δ 3.87 (m, 1 H), 3.95 (ddd, J = 3.7, 2.0, 1.1 Hz, 1 H), 5.29 (~dq, J = 5.8, 1.5 Hz, 1 H), 5.45 (m, 1 H), 6.00 (dd, J 5.8, 1.7 Hz, 1 H), 7.34 (dd, J = 2.4, 0.4 Hz, 1 H), 7.47 (dd, J = 8.5, 2.4 Hz, 1 H), 7.52 (dd, J = 8.5, 0.4 Hz, 1 H); IR ($CHCl_3$) 3025, 1465, 1155, 1105, 886, 830 cm^{-1}.

Anal. Calcd for $C_{12}H_8Br_2Cl_2O$: C, 36.13; H, 2.02. Found: C, 36.47; H, 1.81.

This appears to be a single pure isomer. An NMR spectrum of the mother liquor shows evidence of other isomers.

3,6,6-Tribromo-4-(2,5-dichlorophenyl)-1,2-epoxy-4-cyclohexene (14a). To 3.7 mmol of the epoxide **5a** in 25 mL of CCl_4 was added 3.6 g (20 mmol) of NBS and the mixture was refluxed under a sunlamp for 1 h. NMR analysis showed formation of dibromide **13a** and ~15% of tribromide **14a**. More NBS (0.71 g, 4 mmol) was added and the reaction was continued for 2 h. NMR showed peaks for tribromide **14a** with ~15% dibromide left. The product at this point was a mixture possibly containing several tribromo isomers. The NMR resonances at δ 4.04 (d, J = 3 Hz), 4.11 (m), 5.18 (br s), and 6.10 (d, J = 2 Hz) were assigned to the main tribromo isomer.

4-(2,5-Dichlorophenyl)-1,2-epoxy-3,5-cyclohexadiene (15a).[25] To a solution of 46 mg (0.14 mmol) of monobromide **12a** was added 22 μL (0.15 mmol) of DBU in 1 g of CD_2Cl_2 in an NMR tube. After 1 h at 30–40 °C, the elimination was essentially complete (~15% starting material left). Pentane was added and the organic layer was washed with dilute NH_4Cl solution, dried

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(25) This compound is predominantly in the oxepin form.

(Na_2SO_4), and evaporated. NMR (270 MHz, Me_2SO-d_6) showed ~80% pure product, 34 mg, existing mostly in the oxepin form: NMR δ 5.12 (dm, J = 4.7 Hz, 2 H), 6.11 (dm, J = 4.7 Hz, 1 H), 6.17 (ddm, J = 7.7, 4.7 Hz, 1 H), 6.34 (dt, J = 7.7, 1.0 Hz, 1 H), 7.40 (dd, J = 2.6, 0.6 Hz, ~1 H), 7.44 (dd, J = 8.5, 2.6 Hz, ~1 H), 7.53 (dd, J = 8.5, 0.6 Hz, ~1 H); mass spectrum, m/e 237.9953 (M^+, calcd 237.9953). The sample was allowed to stand in Me_2SO solution at room temperature. After 1 day 15% phenol was formed; after 3 days, 85% of the oxepin had been converted to phenol. The phenol product consisted mainly of 2,5-dichloro-4'-hydroxybiphenyl (~80%); NMR (270 MHz, Me_2SO-d_6) δ 3.51 (br s), 6.86, 7.28 (AA'BB'), 7.38–7.42 (m), 7.56 (distorted d, $J \simeq$ 9 Hz).

6-Bromo-4-(2,5-dichlorophenyl)-1,2-epoxy-3,5-cyclohexadiene (16a, X = Br). To a solution of 0.399 g (1.0 mmol) of dibromide **13a** in 2 mL of CH_2Cl_2 was added 0.300 mL of DBU and the solution was stirred under positive N_2 pressure for 2 h. The reaction mixture was diluted with ether–pentane and extracted with dilute NH_4Cl and saturated NaCl solutions. The organic extract was dried (Na_2SO_4) and concentrated. The crude product was essentially pure **16a**. It was crystallized from Et_2O to yield 0.238 g (75% yield): mp 95–96 °C (decomposition to phenol); NMR (270 MHz, $CDCl_3$, 1 μL of NEt_3 added to prevent decomposition to phenol) δ 4.32 (t, J = 3.8 Hz, 1 H), 4.42 (dd, J = 3.8, 2.2 Hz, 1 H), 6.41 (dd, J = 3.8, 1.0 Hz, 1 H), 6.72 (dd, J = 2.2, 1.0 Hz, 1 H), 7.23–7.27 (m, 2 H), 7.33 (distorted d, $J \simeq$ 9 Hz, 1 H); IR 3025, 1547, 1463, 1104, 1033, 997, 949, 863 cm^{-1}.

Attempted preparative TLC on silica gel or alumina resulted in decomposition to phenol. A sample of **16a** (150 mg) was stirred in 2 mL of CH_2Cl_2 with 10 mg of TsOH for 0.5 h. The solution was filtered through 2 g of silica gel, and the solvent was evaporated. NMR (270 MHz, $CDCl_3$) showed the presence of one hydroxy isomer, 3-bromo-4-hydroxy-2',5'-dichlorobiphenyl: NMR δ 5.65 (s, 1 H), 7.07 (d, J = 8.4 Hz, 1 H), 7.22 (dd, J = 8.5, 2.4 Hz, 1 H), 7.279 (dd, J = 8.4, 2.0 Hz, 1 H), 7.282 (d, J = 2.4 Hz, 1 H), 7.36 (d, J = 8.5 Hz, 1 H), 7.53 (d, J = 2.0 Hz, 1 H); IR ($CHCl_3$) 3515, 3230 (br), 3030, 1506, 1465, 1193, 1107, 1034, 823 cm^{-1}. Crystallization from Et_2O yielded 92 mg, mp 95–96 °C.

Anal. Calcd for $C_{12}H_7BrCl_2O$: C, 45.32; H, 2.22. Found: C, 45.28; H, 2.33.

3,6-Dibromo-4-(2,5-dichlorophenyl)-1,2-epoxy-3,5-cyclohexadiene (17a). To a solution of 3.7 mmol of tribromide **14a** in 15 mL of CH_2Cl_2 was added 2.4 mL (16 mmol) of DBU. The solution was stirred for 2 h at 25 °C and then filtered through 40 g of silica gel, eluting with CH_2Cl_2 (50-mL fractions taken). The product was eluted in fractions 2 and 3 and was further purified by preparative TLC, eluting with 5% ether–pentane–1% Et_3N. The total yield was 0.50 g (34% yield) of **17a**, from diene **4a**, as an oil which solidified in the freezer: NMR (270 MHz, $CDCl_3$) δ 4.29 (dd, J = 3.7, 2.6 Hz, 1 H), 4.41 (d, J = 3.7 Hz, 1 H), 6.52 (d, J = 2.6 Hz, 1 H), 7.19 (d, J = 2.4 Hz, 1 H), 7.29 (dd, J = 8.6, 2.4 Hz, 1 H), 7.38 (d, J = 8.6 Hz, 1 H); IR 1630, 1462, 1100, 1040, 995, 876 cm^{-1}. A portion was crystallized from hexane: mp 80–82 °C; mass spectrum, m/e 393.8171 (M^+, calcd 393.8164).

A sample (52 mg) of **17a** was treated with 5 mg of p-TsOH in 1 mL of CH_2Cl_2 for 1 h. The mixture was filtered through 1 g of silica gel to remove the acid. NMR (270 MHz, acetone-d_6) shows the presence of 2,5-dibromo-4-hydroxy-2',5'-dichlorobiphenyl and the 3-hydroxy isomer in a 75:25 ratio: NMR of 4-hydroxy isomer in mixture δ 3.23 (br s), 7.36 (s), 7.38 (d, J = 2.3 Hz), 7.47 (dd, J = 8.6, 2.3 Hz), 7.51 (s), 7.55 (d, J = 8.6 Hz); NMR of 3-hydroxy isomer in mixture δ 3.23 (br s), 7.00 (d, J = 2.2 Hz), 7.27 (d, J = 2.2 Hz), 7.37 (d, J = 2.6 Hz), 7.49 (dd, J = 8.6, 2.6 Hz), 7.56 (d, J = 8.6 Hz); IR of mixture ($CHCl_3$) 3515, 3200 (br), 1493, 1462, 1293, 1190, 1103, 1063, 822 cm^{-1}.

3,6-Dichloro-4-(2,5-dichlorophenyl)-1,2-epoxy-4-cyclohexene (18a). To a flask containing 3.50 g of crystalline **13a** (8.8 mmol) was added 30 mL of CH_3CN followed by 8.0 g of benzyltriethylammonium chloride (35 mmol). The mixture was stirred on a magnetic stirrer (~30 °C). After 2 h a homogeneous solution was formed. After 22 h the reaction mixture was poured into 200 mL of 1:1 ether–pentane. The organic layer was washed with 200 mL of water (2×) and 50 mL of saturated NaCl. The aqueous layers were reextracted with 30 mL of ether–pentane. The organic layers were combined and dried (Na_2SO_4), and the solvent was removed. The residual oil was subjected to two more exchanges with benzyltriethylammonium chloride under the same conditions as described above. This was done to ensure that all the bromine was exchanged. The final product oil, crude weight 2.8 g, appears to be a mixture of at least three isomers; NMR δ 3.73 (m, 2 H), 4.90 (m, 0.70 H), 5.08 (m, 0.74 H), 5.36 (m, 0.35 H), 5.50 (m, 0.17 H), 5.68 (m, 0.74 H), 5.79 (m, 0.30 H), 7.1–7.4 (m, 3 H).

3,6,6-Trichloro-4-(2,5-dichlorophenyl)-1,2-epoxy-4-cyclohexene (19a). The crude dichloride **18a** from the preceding experiment (~8.8 mmol) was dissolved in 40 mL of CCl_4 and treated with 10.5 mL of t-BuOCl (88 mmol). The solution was refluxed under a sunlamp for 2 h. More t-BuOCl (3.5 mL, 29 mmol) was added and reflux under light was continued for 2 more h. The reaction mixture was cooled, poured into ether, and washed with 10% $NaHSO_3$, water, and saturated NaCl solutions. Each aqueous layer was reextracted with 30 mL of ether–pentane. The organic layers were combined, dried (Na_2SO_4), and evaporated to yield an oil containing one main trichloro isomer and some chlorinated *tert*-butoxylated products which could not be pumped off under vacuum. This mixture was used in the next experiment to prepare the arene oxide **2**.

In a different experiment 4.46 mmol of the trichloro mixture **19a** was submitted to preparative TLC on four plates (20 × 20 cm), elution with 10% ether–pentane. Fraction 1, R_f 0.52, was the main trichloro isomer essentially pure: 0.544 g (35% yield); NMR δ 3.86 (dd, $J \simeq$ 4, 2 Hz, 1 H), 3.94 (dd, $J \simeq$ 3, 2 Hz, 1 H), 5.05 (dd, J = 2.2, 1.1 Hz, 1 H), 5.96 (d, J = 2.2 Hz, 1 H), 7.2–7.4 (m, 3 H). Fraction 2, R_f 0.43 (0.484 g), was mainly a 2:1 mixture of another trichloro isomer and a dichloro isomer. The trichloro isomer could be crystallized from the mixture in pentane: 0.238 g; mp 98–107 °C; ~80% pure; NMR δ 3.91 (dd, J = 3.4, 2.6 Hz, 1 H), 4.07 (dd, J = 3.4, 2.4 Hz, 1 H), 5.43 (t, J = 2.2 Hz, 1 H), 6.05 (t, J = 2.1 Hz, 1 H), 7.3–7.5 (m, 3 H). NMR of dichloro isomer in 2:1 mixture: δ 3.5–3.8 (m, 2 H), 4.89 (dd, $J \simeq$ 4, 2 Hz, 1 H), 5.04 (d, $J \simeq$ 2 Hz, 1 H), 5.72 (dd, J = 6.0, 2.5 Hz, 1 H).

3,6-Dichloro-4-(2,5-dichlorophenyl)-1,2-epoxy-3,5-cyclohexadiene (2). The crude oil (~8.8 mmol) from the preceding experiment was dissolved in 30 mL of CH_2Cl_2 under N_2. To the stirred solution was added 5.25 mL of DBU (35 mmol) dropwise. The stirring was continued for 2 h at ~30 °C. The CH_2Cl_2 solution was passed through 80 g of silica gel with CH_2Cl_2, 100 mL fractions being collected. The product **2** was collected mainly in fraction 2 with a small amount in fraction 3, crude weight 2.84 g. The crude product was purified on four 20 × 20 cm preparative TLC plates and eluted with 5% ether–pentane, containing 1% triethylamine. The main band (R_f 0.39, 1.58 g) was extracted with ether and allowed to crystallize from hexane: mp 74–76 °C; 1.06 g (39% yield from **13a**); NMR (270 MHz, $CDCl_3$) δ 4.23 (dd, J = 3.9, 2.6 Hz, 1 H), 4.31 (d, J = 3.9 Hz, 1 H), 6.34 (d, J = 2.6 Hz, 1 H), 7.21 (dd, J = 2.4, 0.4 Hz, 1 H), 7.29 (dd, J = 8.6, 2.4 Hz, 1 H), 7.37 (dd, J = 8.6, 0.4 Hz, 1 H); IR 3025, 1633, 1462, 1362, 1103, 1051 cm^{-1}; mass spectrum, m/e 305.9154 (M^+, calcd 305.9173). Recrystallization from hexane yielded an analytical sample, 0.87 g, mp 75–76 °C.

Anal. Calcd for $C_{12}H_6Cl_4O$: C, 46.79; H, 1.96, Found: C, 46.73; H, 2.06.

When 7.5 mmol of the crude dibromide **13a** without crystallization was carried on through the reaction sequence (**13a** → **18a** → **19a** → **2**), 0.65 g (28% yield from **4a**) of arene oxide **2** was obtained. This material was contaminated with 3% of an arene oxide impurity having a bromine instead of one of the chlorines.

2,5,2',5'-Tetrachloro-4-hydroxybiphenyl (20). To a solution of 86 mg of **2** in 2 mL of CH_2Cl_2 was added 6 mg of p-TsOH. The mixture was stirred at 35 °C for 0.5 h and passed through 1 g of silica gel with 20 mL of CH_2Cl_2. The solvent was evaporated, yielding 86 mg of an 83:17 mixture of the 4-hydroxy and 3-hydroxy phenols. NMR of 4-hydroxy isomer (270 MHz, acetone-d_6) δ 3.85 (br s, 1 H), 7.20 (d, J = 0.4 Hz, 1 H), 7.33 (d, J = 0.4 Hz, 1 H), 7.38 (dd, J = 2.6, 0.4 Hz, 1 H), 7.45 (dd, J = 8.5, 2.6 Hz, 1 H), 7.52 (dd, J = 8.5, 0.4 Hz, 1 H). Partial NMR of 3-hydroxy isomer in mixture (270 MHz, acetone-d_6): δ 6.87 (d, J = 2.4 Hz, 1 H), 7.15 (d, J = 2.4 Hz, 1 H), 7.47 (dd, J = 8.5, 2.6 Hz, 1 H), 7.54 (dd, J = 8.5, 0.5 Hz, 1 H); mass spectrum, m/e 305.9170 (M^+, calcd 305.9173). This mixture was put on a 10 × 20 cm preparative TLC plate and eluted 3 times with 10% ether–pentane and 2 times with 20% ether–pentane. The main band showed no separation but was cut in thirds. The faster moving fraction 1, 39 mg,

consisted of 75% 4-hydroxy isomer and 25% 3-hydroxy isomer. Fraction 2, 20 mg, was 95% 4-hydroxy isomer and 5% 3-hydroxy isomer. Fraction 3, 8 mg, was not identified. Fraction 2 was crystallized from hexane to yield 14 mg of an analytical sample of **20**: mp 101–102 °C; IR ($CHCl_3$) 3530, 3219 (br), 1496, 1465, 1297, 1193, 1103, 948, 822 cm^{-1}.

Anal. Calcd for $C_{12}H_6Cl_4O$: C, 46.79; H, 1.96. Found: C, 46.71; H, 2.09.

4-Acetoxy-2,5,2′,5′-tetrachlorobiphenyl. To 49 mg of the phenol mixture derived from **2** was added 0.2 mL of Ac_2O and 0.2 mL of pyridine. The solution was heated on the steam bath for 10 min, poured into ether, and washed with 0.5 N HCl, water, saturated $NaHCO_3$, and saturated NaCl solutions. The organic layer was dried (Na_2SO_4) and solvent was removed. The residue was crystallized from hexane to yield 31 mg of crystals, mp 110–111 °C, and 15 mg of mother liquor, a 40:60 mixture of 4-OAc to 3-OAc isomers: NMR of 4-OAc isomer (270 MHz, $CDCl_3$) δ 2.38 (s, CH_3), 7.27 (dd, J = 2.6, 0.4 Hz), 7.32 (d, J = 0.4 Hz), 7.34 (dd, J = 8.5, 2.6 Hz), 7.35 (d, J = 0.4 Hz), 7.41 (dd, J = 8.5, 0.4 Hz); IR 1790, 1465, 1193, 1103, 905 cm^{-1}; mass spectrum, m/e 347.9280 (M^+, calcd 347.9278); NMR of 3-OAc isomer in mixture (270 MHz, $CDCl_3$) δ 2.37 (s, CH_3), 7.17 (d, J = 2.5 Hz), 7.25 (d, J = 2.6 Hz), 7.28 (dd, J = 2.6, 0.4 Hz), 7.34 (dd, J = 8.6, 2.6 Hz), 7.41 (dd, J = 8.6, 0.4 Hz).

Anal. Calcd for $C_{14}H_8Cl_4O_2$: C, 48.04; H, 2.30. Found: C, 47.93; H, 2.28.

6-Chloro-4-(2,5-dichlorophenyl)-1,2-epoxy-3,5-cyclohexadiene (16a, X = Cl). A solution of dichloride mixture **18a**, 54 mg (0.174 mmol), in 0.3 mL of benzene-d_6 was treated with 0.051 mL (0.34 mmol) of DBU. After 20 min NMR showed mainly the arene oxide **16a** and ~20% of other peaks which could be assigned to the oxepin **15a**. After a total of 40 min the reaction mixture was poured into ether–pentane and dilute NH_4Cl solution. The organic layer was washed with brine and dried (Na_2SO_4); NMR (270 MHz, acetone-d_6, 1 μL of NEt_3 added to prevent decomposition to phenol) δ 4.27 (m, 2 H), 6.37 (m, 1 H), 6.50 (m, 1 H), 7.23–7.26 (m, 2 H), 7.33 (distorted d, $J \simeq 9.6$ Hz).

The sample was stirred in 1 mL of CH_2Cl_2 with 5 mg of p-TsOH for 0.5 h. The solution was filtered through 1 g of silica gel and the solvent was evaporated. NMR (270 MHz, acetone-d_6) shows that **16a** (X = Cl) rearranges to 2,5-dichloro-3′-chloro-4′-hydroxybiphenyl: NMR δ 3.17 (br s, OH), 7.12 (dd, J = 8.4, 0.3 Hz, $H_{5'}$), 7.29 (dd, J = 8.4, 2.5 Hz, $H_{6'}$), 7.39 (dd, J = 8.4, 2.5 Hz, H_4), 7.42 (dd, J = 2.5, 0.6 Hz, H_6), 7.45 (dd, J = 2.5, 0.3 Hz, $H_{2'}$), 7.52 (dd, J = 8.4, 0.6 Hz, H_3); IR ($CHCl_3$) 3510, 3270 (br), 1502, 1462, 1188, 1100, 1032, 818 cm^{-1}; mass spectrum, m/e 271.9563 (M^+, calcd 271.9562).

1-(4-Chlorophenyl)cyclohex-2-en-1-ol (7b). To a flask under N_2, equipped with a dropping funnel, thermometer, and magnetic stirrer was added 17.5 mL of 1.7 M n-BuLi solution (30 mmol) and 20 mL of ether. The solution was cooled to −78 °C and a solution of 1-chloro-4-iodobenzene in 10 mL of ether was added fairly rapidly while maintaining the temperature below −40 °C. 2-Cyclohexen-1-one (3.0 mL, 30 mmol) in 10 mL of ether was added without the temperature exceeding −40 °C. The reaction mixture was warmed to 0 °C and poured into 1 N HCl solution and ice. Pentane was added and the organic layer was extracted with 1 N HCl solution, H_2O, and saturated $NaHCO_3$ and NaCl solutions. All aqueous layers were reextracted with 20 mL of 1:1 ether–pentane. The organic layers were combined and dried (Na_2SO_4), and solvent was removed. The n-butyl iodide was distilled (Kugelrohr, 65 °C, 0.6 mm). The solid residue was crystallized from pentane to give 5.82 g (93% yield) of **7b**: mp 57–58 °C; NMR δ 1.2–2.2 (m, 6 H), 3.28 (s, 1 H), 5.58 (d, J = 10.1 Hz, 1 H), 5.91 (dt, J = 10.1 , 3.6 Hz, 1 H), 7.23 (AA′BB′, 4 H); IR 3600, 3450 (br), 3020, 2940, 1490, 1093, 1018 cm^{-1}. A sample was recrystallized for analysis; mass spectrum, m/e 208.0655 (M^+, calcd 208.0655).

1-(4-Chlorophenyl)-1,3-cyclohexadiene (4b). A solution of 6.26 g (30 mmol) of **7b** and 21 mL (150 mmol) of NEt_3 in 75 mL of CH_2Cl_2 was cooled in an ice bath under N_2. To this well-stirred solution was added in one portion 17.7 g (75 mmol) of 2,4-dinitrobenzenesulfenyl chloride. The ice bath was removed and the mixture was stirred at 25 °C for 1 h, after which 250 mL of pentane was added rapidly dropwise. The mixture was filtered (Celite). The precipitate was washed with pentane. The pentane solution was washed with H_2O and saturated NaCl solution. Each aqueous wash was extracted with 20 mL of pentane. The pentane solutions were combined, dried (Na_2SO_4), and evaporated. The product was passed through an 80-g column of silica gel with pentane to yield 3.96 g (69% yield) of **4b**, pure by NMR. This material could be crystallized from pentane at −20 °C to yield 3.77 g (66% yield): mp 50–51 °C; NMR (270 MHz, $CDCl_3$) δ 2.32 (tm, $J \simeq 10$ Hz, 2 H), 2.54 (tm, $J \simeq 10$ Hz, 2 H), 5.89 (dt, J = 9.3, 4.5 Hz, 1 H), 6.06 (ddt, J = 9.3, 5.4, 1.8 Hz, 1 H), 6.28 (d, J = 5.4 Hz, 1 H), 7.30 (AA′BB′, 4 H); IR 3045, 2945, 2880, 2830, 1497, 1098, 1020, 697 cm^{-1}.

Anal. Calcd for $C_{12}H_{11}Cl$: C, 75.59; H, 5.82. Found: C, 75.69; H, 6.01.

4-(4-Chlorophenyl)-1,2-epoxy-3-cyclohexene (5b). A mixture of 3.43 g (18 mmol) of **4b** in 400 mL of CCl_4 and 3.02 g (36 mmol) of $NaHCO_3$ in 70 mL of H_2O was cooled in an ice bath. To this well-stirred mixture was added 4.03 g (85%, 19.8 mmol) of mCPBA and stirring as continued at 0 °C for 1 h. Layers were separated and the organic layer was washed with 100 mL of 5% NaOH, saturated $NaHCO_3$, and saturated NaCl solutions. The aqueous layers were reextracted with 50 mL of ether–pentane. The organic layers were combined and dried (Na_2SO_4) and solvent was removed. The crude product was ~70% pure. Crystallization from ether–hexane yielded 3.13 g of **5b**, mp 60–63 °C, but did not give completely pure material: NMR (270 MHz, $CDCl_3$) δ 1.68–1.82 (m, ~1 H), 2.38–2.46 (m, ~3 H), 3.44 (t, J = 4.2 Hz, ~1 H), 3.59 (ddd, J = 4.2, 2.2, 1.1 Hz, ~1 H), 6.25 (dd, J = 4.4, 2.2 Hz, ~1 H), 7.19 (s, ~4 H); IR 3005, 2935, 1495, 1098, 1017, 896 cm^{-1}; mass spectrum, m/e 206.0492 (M^+, calcd 206.0496).

4-(4-Chlorophenyl)-1,2-epoxy-3,5-cyclohexadiene (3).[25] A solution of 3.32 g (75% pure, 12 mmol) of epoxide **5b** in 125 mL of CCl_4 was treated with 2.8 g (16 mmol) of NBS and refluxed under a sunlamp for 1 h. NMR shows disappearance of epoxide and formation of monobromide and some dibromide. The reaction is not very clean and shows considerable decomposition. Attempted purification by preparative TLC leads to aromatization.

The crude product was dissolved in 30 mL of CH_2Cl_2 and treated with 4.8 mL of DBU for 0.5 h at 25 °C. The reaction mixture was extracted with dilute NH_4Cl and saturated NaCl solutions. The dark brown oil contains ~40% of the oxepin by NMR. It was triturated with 50 mL of hexane in 5-mL portions. After solvent evaporation 0.855 g of a yellow solid was obtained. Some Et_3N (~10 μL) was added to stabilize the arene oxide against rearrangement to phenol. A portion was crystallized from hexane (1% Et_3N) to yield a seample of **3**: mp 48–50 °C, ~70% pure with the major impurity being 4-chloro-4′-hydroxybiphenyl and possibly some 4-chlorobiphenyl; NMR (270 MHz, Me_2SO-d_6, 1% Et_3N) δ 5.27 (d, J = 4.7 Hz, 1 H), 5.33 (dd, J = 5.0, 1.3 Hz, 1 H), 6.14 (dd, J = 7.6, 4.7 Hz, 1 H), 6.26 (d, J = 5.0 Hz, 1 H), 6.67 (d, J = 7.6 Hz, 1 H), 7.47 (AA′BB′, ~4 H).

Samples of **3** can rearrange spontaneously to 4-chloro-4′-hydroxybiphenyl upon standing, even in the freezer: NMR (270 MHz, acetone-d_6) δ 6.59, 7.14 (AA′BB′, 4 H), 7.05, 7.22 (AA′BB′, 4 H); IR ($CHCl_3$) 3590, 3290 (br), 3030, 1616, 1492, 1176, 1102, 828 cm^{-1}. Although there are some impurity peaks present in the NMR spectrum, there are no peaks seen which would be characteristic of the protons ortho to the hydroxy of 4-chloro-3′-hydroxybiphenyl.

4-Acetoxy-4′-chlorobiphenyl. A sample of phenol (0.434 g) formed from crude oxepin **3** (which was ~50% pure) was treated with 2 mL of Ac_2O and 2 mL of pyridine and heated on a steam bath for 10 min. The solution was poured into ether and washed with 0.5 N HCl, H_2O, saturated $NaHCO_3$, and saturated NaCl solutions. The organic layer was dried (Na_2SO_4), solvent was removed, and the residue was purified by preparative TLC, eluting with 20% ether–pentane. Fraction 1 contained 90 mg of 4-chlorobiphenyl, mp 72–73 °C, identified by NMR and mass spectrometric peak match; mass spectrum, m/e 188.0396 (M^+, calcd 188.0393). Fraction 2, 331 mg, was 4-acetoxy-4′-chlorobiphenyl, containing 10–20% of another acetate, probably 3-bromo-4-acetoxy-4′-chlorobiphenyl formed from the dibromide **13b** present in the reaction mixture after NBS bromination of **5b**. This material was crystallized from ether–hexane to yield 137 mg: mp 111–112 °C; NMR ($CDCl_3$) δ 2.30 (s, CH_3), 7.16, 7.52 (AA′BB′), 7.36, 7.48 (AA′BB′); IR 3030, 1763, 1482, 1370, 1202, 1007 cm^{-1}.

Anal. Calcd for $C_{14}H_{11}ClO_2$: C, 68.16; H, 4.50. Found: C, 68.31; H, 4.59.

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Registry No. 2, 68099-35-4; **3**, 78143-54-1; **4a**, 68099-15-0; **4b**, 68099-22-9; **5a**, 68099-31-0; **5b**, 78143-55-2; **6**, 29682-41-5; **7a**, 68099-13-8; **7b**, 68099-16-1; **8a**, 78143-56-3; **9a**, 78163-67-4; **12a**, 78185-42-9; **13a**, 78185-84-9; **13b**, 78143-57-4; **14a**, 78143-58-5; **15a**, 68099-37-6; **16a** (X = Br), 68125-11-1; **16a** (X = Cl), 78143-59-6; **17a**, 68099-36-5; **18a**, 68099-34-3; **19a**, 78143-60-9; **20**, 51274-68-1; **21**, 51274-67-0; **23a**, 78143-61-0; **25a**, 78143-62-1; **26a**, 78143-63-2; **27a**, 78143-64-3; **28a**, 78143-65-4; **29**, 78143-66-5; **30**, 78143-67-6; 2,5-dichloroaniline, 95-82-9; 2-cyclohexen-1-one, 930-68-7; 2,5-dichloro-4'-hydroxybiphenyl, 53905-28-5; 3-bromo-4-hydroxy-2',5'-dichlorobiphenyl, 78143-68-7; 2,5-dibromo-4-hydroxy-2',5'-dichlorobiphenyl, 78143-69-8; 2,5-dibromo-3-hydroxy-2',5'-dichlorobiphenyl, 78143-70-1; 3-acetoxy-2,5,2',5'-tetrachlorobiphenyl, 78143-71-2; 4-acetoxy-2,5,2',5'-tetrachlorobiphenyl, 78143-72-3; 2,5-dichloro-3'-chloro-4'-hydroxybiphenyl, 78143-73-4; 1-chloro-4-iodobenzene, 637-87-6; 4-chloro-4'-hydroxybiphenyl, 28034-99-3; 4-chlorobiphenyl, 2051-62-9; 4-acetoxy-4'-chlorobiphenyl, 57396-87-9; 3-bromo-4-acetoxy-4'-chlorobiphenyl, 78143-74-5; 1,1-dichloro-3-(2,5-dichlorophenyl)cyclohexane, 78143-75-6; 1-chlorocyclohexene, 930-66-5; benzeneselenyl chloride, 931-59-9; 1-phenylseleno-2,2-dichlorocyclohexane, 78143-76-7; 1-phenylseleno-1,2-dichlorocyclohexane, 78143-77-8; 3,3-dichloro-1-cyclohexene, 78143-78-9; 2,3-dichlorocyclohexene, 40099-06-7; 1,2-epoxy-3,3-dichlorocyclohexane, 78143-79-0; 1,2-epoxy-1,3-dichlorocyclohexane, 78143-80-3.

Supplementary Material Available: Experimental details for the preparation of compounds **8a**, **9a**, **23a**, **26a**, **27a**, **29**, **30**, 3,3-dichlorocyclohexene, 2,3-dichlorocyclohexene, 1,2-oxy-3,3-dichlorocyclohexane, and 1,2-epoxy-1,3-dichlorocyclohexane (5 pages). Ordering information is given on any current masthead page.

Synthetic Methods and Reactions. 103.[1] Preparation of Alkyl Iodides from Alkyl Fluorides and Chlorides with Iodotrimethylsilane or Its in Situ Analogues

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We have previously exploited the strong affinity of silicon for oxygen to carry out a number of synthetic transformations with iodotrimethylsilane.[2] These reactions included the cleavage of esters[3] and ethers[4] and the reduction of sulfoxides[5] and sulfonyl halides.[6] Silicon also forms an exceptionally strong bond with fluorine. Utilizing this property, we considered it feasible that the displacement of fluorine by iodine in fluoroalkanes could be achieved with iodotrimethylsilane, despite the reverse stability of the involved carbon–halogen bond (C–F > C–I).

Table I. Synthesis of Iodoalkanes

$$RF + Me_3SiI \longrightarrow RI + Me_3SiF$$

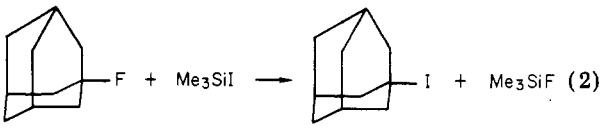
substrate R	reaction conditions: time, h	reaction conditions: temp, °C	yield,[a] %
1-hexyl	48	25	81[b]
1-decyl	24	61	*c*
benzyl	48	25	78
cyclohexyl	16	25	72
1-adamantyl	16	25	87
1-adamantyl	16	25	97[d]
1-adamantyl	16	25	92[e]
2-norbornyl	48	25	76
1-adamantyl	16	61	94[f]
2-methyl-2-propyl	16	61	90[f]

[a] Yield of the isolated, purified product. All products were >98% pure by GLC and had satisfactory physical and spectral data. [b] A mixture of 2- and 1-iodohexanes (55:45) was obtained. [c] Reaction incomplete even after 24 h in refluxing chloroform. [d] Reaction performed with $I_2/Me_3SiSiMe_3$ reagent. [e] Reaction performed with $Me_3SiCl/NaI/CH_3CN$ reagent. [f] The corresponding chlorides were the starting materials. The reaction was performed in refluxing chloroform.

Indeed, when tertiary and secondary alkyl fluorides are reacted with iodotrimethylsilane in a suitable inert solvent such as methylene chloride, the corresponding alkyl iodides are obtained in high yield (Table I, eq 1).

$$RF + Me_3SiI \rightarrow RI + Me_3SiF \quad (1)$$

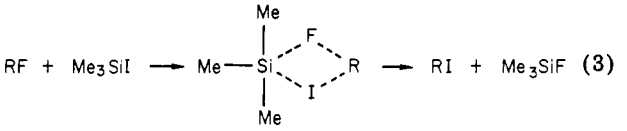
In a typical reaction, 1-fluoroadamantane was treated with iodotrimethylsilane (1.1 equiv) at room temperature under a dry nitrogen atmosphere. 1-Iodoadamantane was obtained in almost quantitative yield. An equivalent amount of fluorotrimethylsilane is formed in the reaction (eq 2).



(2)

The reaction proceeds readily for tertiary fluoroalkanes. Secondary fluoroalkanes react slower but generally without rearrangements. Thus, for example, fluorocyclohexane was transformed to iodocyclohexane without formation of any 1-iodo-1-methylcyclopentane. The reaction with primary fluoroalkanes is sluggish and generally leads to a mixture of iodoalkanes. For example, the conversion of 1-fluorohexane to 1-iodohexane is incomplete even after 24 h at room temperature.

The halogen exchange reaction probably proceeds via an intermediate pentacoordinate silicon species (eq 3).



(3)

The fluoride–iodide halogen exchange can also be accomplished with in situ reagents, such as chlorotrimethylsilane/sodium iodide or hexamethyldisilane/iodine.

It is interesting to note that tertiary chlorides such as 1-chloroadamantane and 2-chloro-2-methylpropane can also be transformed into the corresponding iodoalkanes, albiet at a much slower rate. However, secondary and primary chloroalkanes are not affected under the reaction conditions.

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