mixing. The tube was then stoppered, shaken vigorously, and plunged into a Dewar flask containing liquid nitrogen. After 1 min the tube was removed and placed in the ESR spectrometer in a liquid nitrogen bath. An ESR spectrum was then detected (gyromagnetic ratio 2.0025). The spectrum obtained in this way suffered from poor resolution, so no information about the structure of the radical was able to be obtained. Attempts to obtain a solution spectrum in dimethylformamide at room temperature were unsuccessful.

Solvent Isotope Effects. Kinetic studies in Me_2SO-D_2O (4:1 v/v) were carried out as described above except that NaOD in D_2O was substituted for $Ba(OH)_2$ in water.

Registry No. 6a, 35665-94-2; **6b**, 75993-59-8; **6c**, 21997-26-2; **6d**, 75993-60-1; **6e**, 75993-61-2; **6f**, 75993-62-3; **6g**, 53218-11-4; **6h**, 6335-82-6; **6i**, 53274-19-4; **6j**, 53218-13-6; **6k**, 75993-63-4; **7**, 75990-87-3; **9**, 75993-64-5; 4-nitrophenylacetyl chloride, 50434-36-1; *p*-nitrophenol, 100-02-7; *p*-cyanophenol, 767-00-0; *m*-nitrophenol, 554-84-7; *p*-(trifluoromethyl)phenol, 402-45-9; *m*-(trifluoromethyl)phenol, 98-17-9; *m*-chlorophenol, 108-43-0; *p*-chlorophenol, 106-48-9; phenol, 108-95-2; *p*-cresol, 106-44-5; *p*-methoxyphenol, 150-76-5; *p*-(dimethylamino)-phenol, 619-60-3.

Aromatization of Arene 1,2-Oxides. 1,2-Oxides of Methyl Phenylacetate and Methyl *trans*-Cinnamate

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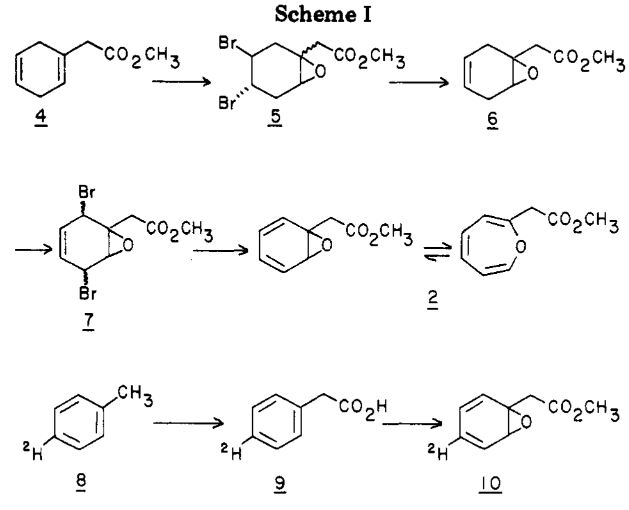
Received July 30, 1980

Substituent migration is observed only to a minor extent during aromatization of the 1,2-oxide of methyl phenylacetate to methyl (*o*-hydroxyphenyl)acetate; the major aromatization pathway does not involve substituent migration. Substituent migration is not observed during aromatization of the 1,2-oxide of methyl *trans*-cinnamate to methyl *o*-coumarate.

Our previous studies of the aromatization of arene 1,2-oxides have established the extent to which reaction occurs by C_1–O cleavage as opposed to C_2–O cleavage of the oxirane ring when the substituent is CH_3,[1] CH_2OH,[2] CHO[2], CO_2H,[2,3] CO_2CH_3,[2,3] and $Si(CH_3)_3$.[4] Whether the reaction proceeds by substituent migration or by substituent loss when C_2–O cleavage of the oxirane ring occurs was established in each case. Aromatization of toluene 1,2-oxide occurs only by the pathway involving C_1–O cleavage.[1] Although C_1–O cleavage is the predominant pathway for aromatization of the 1,2-oxide of benzyl alcohol, 8–17% of the reaction occurs by C_2–O cleavage, and substituent loss rather than migration is observed when C_2–O cleavage occurs.[2]

The 1,2-oxides of phenylacetic acid and *trans*-cinnamic acid are of interest since they, or the arene 2,3-oxides, may be intermediates in the ortho hydroxylation of the corresponding aromatic substrates in biological systems. Feeding studies with *A. chinensis* by Kindl[5] have shown that formation of (*o*-hydroxyphenyl)acetic acid (1) from phenylalanine involves substituent migration; phenylpyruvic acid is probably an intermediate and the substituent migration during hydroxylation is analogous to that observed in the transformation of tyrosine to homogentisic acid via (*p*-hydroxyphenyl)pyruvic acid.[6] On the other hand, substituent migration was not observed by Kindl in the formation of 1 by hydroxylation of phenylacetic acid.[5] Similarly, the results of Ellis and Amrhein indicate that formation of *o*-coumaric acid in plants by hydroxylation of *trans*-cinnamic acid does not involve substituent migration.[7]

Scheme I

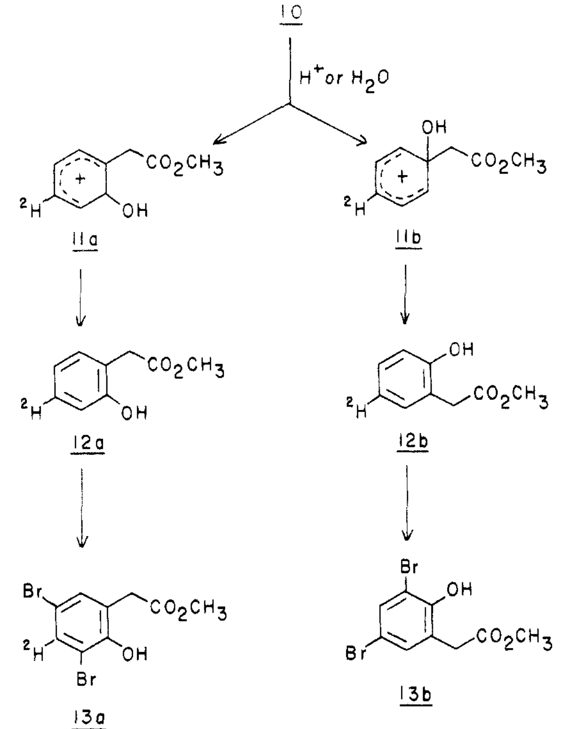


Our interest in these biological transformations derives from the question of whether arene 1,2-oxides are likely intermediates in such ortho-hydroxylation reactions. Described herein are the preparation and aromatization reactions of the arene 1,2-oxides of methyl phenylacetate (2) and methyl *trans*-cinnamate (3). The 1,2-oxide of phenylacetic acid was too unstable for isolation by the synthetic route investigated. The 1,2-oxide of *trans*-cinnamic acid could be isolated only in impure form for aromatization studies.

Arene oxide 2 was prepared as indicated in Scheme I. Birch reduction of phenylacetic acid by a modification of the literature procedure followed by esterification afforded

(1) Chao, H. S.-I.; Boyd, D. R.; Berchtold, G. A.; Jerina, D. M.; Yagi, H.; Dynak, J., submitted for publication.
(2) Chao, H. S.-I.; Berchtold, G. A. *J. Am. Chem. Soc.*, in press.
(3) Boyd, D. R.; Berchtold, G. A. *J. Am. Chem. Soc.* **1979**, *101*, 2470–2474.
(4) Van Epp, J. E.; Boyd, D. R.; Berchtold, G. A., submitted for publication.
(5) Kindl, H. *Eur. J. Biochem.* **1969**, *7*, 340–347.
(6) Daly, J. W.; Jerina, D. M.; Witkop, B. *Experientia* **1972**, *28*, 1129–1149 and references cited therein.
(7) Ellis, B. E.; Amrhein, N. *Phytochemistry* **1971**, *10*, 3069–3072.

Scheme II



4. Since the disubstituted olefinic group of **4** was more reactive to electrophilic reagents, **4** was treated with Br_2 to effect bromination at C_3–C_4 and subsequently oxidized with *m*-chloroperbenzoic acid (mCPBA) to give **5**. Intermediate **5** could not be converted to **2** with base due to base-catalyzed opening of the oxirane ring initiated by proton abstraction from the side-chain methylene group. Consequently, **5** was debrominated with NaI/acetone to afford **6**. Allylic bromination of **6** with *N*-bromosuccinimide (NBS) yielded **7** that was dehalogenated (NaI/acetone) to afford **2**. Arene oxide **2** was a relatively unstable substance that readily aromatized to methyl (*o*-hydroxyphenyl)acetate in quantitative yield.

In order to establish the extent of substituent migration during aromatization of **2**, deuterated arene oxide **10** was prepared (Scheme I). Decomposition of the Grignard reagent of *p*-bromotoluene gave **8**[8] that was converted to **9** by benzylic bromination, displacement with cyanide, and hydrolysis as described in the Experimental Section. The low-voltage (7.5 eV) mass spectrum of the benzyl cyanide[9] indicated 83% deuterium incorporation. That all of the deuterium was at C_4 and none was at the α-carbon atom due to exchange of the Grignard reagent was established from integration of the ^1H NMR spectra of **8**, **9**, and the bromide and cyanide precursors of **9**. All spectra were consistent with 83% ^2H at C_4. Labeled arene oxide **10** was prepared from **9** by the same procedure for preparation of **2** from phenylacetic acid.

Aromatization of **10** may occur by initial cleavage of the C_1–O bond to afford cation **11a** that subsequently gives labeled methyl (*o*-hydroxyphenyl)acetate (**12a**) or by cleavage of the C_2–O bond to afford cation **11b** followed by substituent migration and enolization to **12b** (Scheme II). The dibromide derivative of the aromatization product retains the deuterium label at C_4 (**13a**) if substituent migration has not occurred, and deuterium label is lost at C_5 (**13b**) if substituent migration has occurred.[10] Integration of the relative intensity for H_4 (7.45 ppm) and H_6 (7.25 ppm) in the ^1H NMR spectrum of **13** and correction for 83% deuterium incorporation thus provides a measure of the extent of reaction by each pathway.

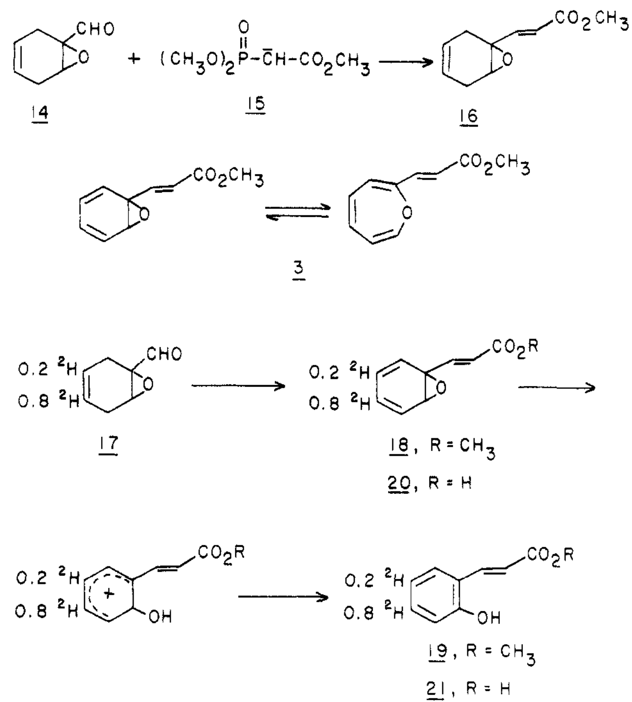
The conditions under which aromatization of **10** was investigated and the extent to which substituent migration has occurred during product formation are listed in Table I. Aromatization occurs predominantly by initial cleavage of the C_1–O bond of the arene oxide, but a small amount of the reaction proceeds through C_2–O cleavage and subsequent migration of the substituent with somewhat more C_2–O cleavage at high and low pH as compared to the intermediate pH range. A similar trend in C_1–O vs. C_2–O cleavage as a function of pH was observed in the aromatization of the 1,2-oxide of benzyl alcohol.[2]

Attempts to prepare the 1,2-oxide of phenylacetic acid by hydrolysis of **2** with aqueous base resulted in complete aromatization. Although hydrolysis of the ester group probably occurs prior to aromatization, the reaction was not pursued. Undoubtedly, aromatization of the 1,2-oxide of phenylacetic acid occurs predominantly or entirely by initial C_1–O cleavage of the oxirane ring. No products suggesting carboxyl participation during aromatization were observed, but such substances might be expected to be transformed to (*o*-hydroxyphenyl)acetic acid during the

Table I. Aromatization of 10

conditions	pH	% C_1–O cleavage (substituent retention)	% C_2–O cleavage (substituent migration)
CF_3CO_2H		84	16
dioxane/H_2O (2:1)	1.1	88	12
	4.0	93	7
	7.0	94	6
	10.0	89	11

Scheme III



(8) Boyd, D. R.; Campbell, R. M.; Craig, H. C.; Watson, C. G.; Daly, J. W.; Jerina, D. M. *J. Chem. Soc., Perkin Trans. 1* 1976, 2438–2443.

(9) Nibbering, N. M. M.; De Boer, Th. J. *Tetrahedron* 1968, 24, 1435–1440.

(10) Procedure used by Kindl[5] to determine tritium labeling in (*o*-hydroxyphenyl)acetic acid.

reaction. Participation in the C_2–O oxirane cleavage of the 1,2-oxide of (3,5-dibromo-4-methoxyphenyl)acetic acid or amide is the proposed pathway for formation of a natural product from marine sponges.[11,12]

Arene oxide 3 was prepared by the sequence outlined in Scheme III. Reaction of **14**[2] with **15**[13] afforded **16**. Treatment of **16** with 1 equiv of Br_2 and subsequent elimination of HBr with 1,5-diazabicyclo[4.3.0]non-5-ene (DBN) yielded **3**. Arene oxide **3** is a stable orange crystalline material that exists predominantly as the oxepin valence tautomer in solution. Aromatization of **3** in 2:1 tetrahydrofuran/H_2O at pH 0.1 or 1.1 requires several days for completion, and at pH 4.0 or 7.0 only partial aromatization is observed after a period of 1 month. The aromatization product is methyl *o*-coumarate.

Deuterium-labeled **3** (**18**, 80% ^2H at C_4 and 20% ^2H at C_5) was prepared from **17**[2] by the same procedure for preparation of unlabeled **3**. Aromatization of **18** in ether containing CF_3CO_2H or in 2:1 tetrahydrofuran/H_2O at pH 0.1, 1.1, 4.0, 7.0, or 10.0 gave methyl *o*-coumarate with the deuterium distribution indicated for **19** (analysis by integration of the ^1H NMR spectrum—see Experimental Section), and therefore aromatization must occur exclusively by C_1–O cleavage of the oxirane ring and no migration of substituent occurs.

Hydrolysis of the ester group of **18** with cold 4% aqueous NaOH, acidification with NaH_2PO_4, and extraction with ether gave a product mixture containing 30% **20** and 70% **21**. Attempts to purify **20** resulted in further aromatization. Considering the stability of **3**, **21** formed during the preparation of **20** undoubtedly is formed from aromatization of **20** and not from aromatization of **18**. Treatment of the 30:70 hydrolysis mixture with acid to effect complete aromatization gave *o*-coumaric acid with the deuterium distribution indicated by **21**, and this result indicates that aromatization of **20** occurs without any substituent migration. Coumarin was not formed during the aromatization of **20**; consequently, no cis → trans isomerization of the side-chain olefinic bond occurs under the reaction conditions.

In conclusion, aromatization of **2** occurs predominantly by a pathway involving C_1–O cleavage of the oxirane ring and relatively little C_2–O cleavage with subsequent migration of the substituent, and the arene 1,2-oxide of phenylacetic acid undoubtedly aromatizes with little or no side-chain migration. The 1,2-oxides of cinnamic acid and its methyl ester aromatize solely by C_1–O cleavage of the oxirane ring, and no migration of substituent is observed. Since substituent migration is not observed in the ortho hydroxylation of phenylacetic acid and *trans*-cinnamic acid in biological systems, the arene 1,2-oxides, as well as the arene 2,3-oxides, must be considered plausible intermediates.

Experimental Section

Melting points were determined with a Thomas-Hoover Unimelt and are corrected. ^1H NMR spectra were obtained at 60 or 250 MHz with Varian T-60, Perkin-Elmer R24B, and Brücker FT spectrometers, respectively. Unless otherwise indicated, spectra were obtained at 60 MHz. Chemical shift values (δ) are reported in parts per million downfield from tetramethylsilane. Mass spectra were determined with a Varian MAT 44 instrument. Infrared spectra were obtained with a Perkin-Elmer Model 238B spectrophotometer. Ultraviolet spectra were obtained with a Perkin-Elmer Model 552 spectrophotometer. Microanalyses were performed by Galbraith Laboratories, Knoxville, TN.

Methyl (2,5-Dihydrophenyl)acetate (4). To a rapidly stirred solution of phenylacetic acid (39 g, 0.286 mol), 250 mL of ethanol, and 2.2 L of liquid ammonia was added lithium (6.56 g, 0.945 mol) in small pieces.[14] After all the lithium had been consumed, as evidenced by disappearance of the deep blue color, ammonium chloride (50.5 g, 0.945 mol) was added. The mixture was stirred for 1 h and allowed to stand overnight until the ammonia evaporated. To the residue were added 1 L of water and 700 g of ice, and the solution was acidified to pH 3 with 20% HCl to precipitate (2,5-dihydrophenyl)acetic acid. The crystalline product was collected by filtration and dried in vacuo, 36.3 g (92%). Esterification of the acid was achieved by adding 5 mL of acetyl chloride to 6 g (43 mmol) of the acid in 100 mL of methanol and heating under reflux for 6 h. The solvent was removed in vacuo, and the residue was dissolved in 100 mL of ether. The solution was washed with 5% Na_2CO_3, dried ($MgSO_4$), and concentrated. Distillation of the residue gave 5.22 g (80%) of **4**: bp 74 °C (1.9 mm); IR (neat) 1735, 1695, 1655 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.66 (s, 2 H), 5.56 (s, 1 H), 3.67 (s, 3 H), 2.99 (s, 2 H), 2.70 (s, 4 H). Anal. Calcd for $C_9H_{12}O_2$: C, 71.03; H, 7.95. Found: C, 71.03; H, 7.77.

1-[(Carbomethoxy)methyl]-4,5-dibromo-1,2-oxycyclohexane (5). Bromine (1.72 g, 10.8 mmol) in 20 mL of CCl_4 was added dropwise with stirring to a solution of **4** (1.64 g, 10.8 mmol) in 10 mL of CCl_4 at 0 °C. After addition was complete, the solvent was removed under reduced pressure, and the residue was distilled to give 2.82 g (84%) of 1-[(carbomethoxy)methyl]-*trans*-4,5-dibromo-1-cyclohexene: bp 95–97 °C (0.02 mm); IR (neat) 1738, 1680 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.68 (m, 1 H), 4.50 (m, 2 H), 3.69 (s, 3 H), 3.6–2.3 (m, 6 H). Anal. Calcd for $C_9H_{12}Br_2O_2$: C, 34.65; H, 3.88; Br, 51.22. Found: C, 34.96; H, 3.99; Br, 51.03.

To a solution of the dibromide (8.60 g, 27.7 mmol) in 80 mL of 1,2-dichloroethane was added 85% pure mCPBA (7.31 g, 36 mmol) and a few milligrams of 4,4'-thiobis(2-*tert*-butyl-5-methylphenol).[15] The solution was heated at reflux (85 °C) for 6 h, the mixture was cooled to room temperature, and unreacted peracid was destroyed by the addition of 5 mL of 10% aqueous Na_2SO_3. The precipitate was removed by filtration. The filtrate was washed with three 30-mL portions of saturated $NaHCO_3$ solution, dried ($MgSO_4$), and concentrated in vacuo. The residue was distilled to give 7.74 g (85%) of **5**: bp 105–107 °C (0.02 mm): IR (neat) 1725 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.19 (m, 2 H), 3.63 (s, 3 H), 3.10 (m, 1 H), 3.0–2.2 (m, 6 H). Anal. Calcd for $C_9H_{12}Br_2O_3$: C, 32.95; H, 3.69; Br, 48.72. Found: C, 33.18; H, 3.78; Br, 48.50.

4-[(Carbomethoxy)methyl]-4,5-oxy-1-cyclohexene (6). A mixture of **5** (2.0 g, 6 mmol) and NaI (1.83 g, 12 mmol) in 60 mL of acetone was heated under reflux overnight, cooled, and concentrated under reduced pressure. The residue was treated with 20 mL of ether, washed with two 20-mL portions of 10% aqueous Na_2SO_3 and two 20-mL portions of saturated aqueous NaCl, dried ($MgSO_4$), and concentrated in vacuo. The residue was distilled to give 0.48 g (47%) of **6**: bp 68–71 °C (0.22 mm). The product was contaminated with a trace of aromatic compound. Analytically pure **6** could be obtained by TLC (alumina, 3:1 CCl_4/CH_2Cl_2) or by VPC (3% tricresyl phosphate on 100–200-mesh Gas Chromo Q, 125 °C): IR (neat) 1738, 1664 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.38 (br s, 2 H), 3.65 (s, 3 H), 3.18 (br s, 1 H), 2.9–2.3 (m, 6 H). Anal. Calcd for $C_9H_{12}O_3$: C, 64.29; H, 7.19. Found: C, 64.59; H, 7.45.

1-[(Carbomethoxy)methyl]benzene Oxide–Oxepin (2). A mixture of **6** (2.2 g, 13 mmol) and NBS (5.0 g, 28 mmol) in 45 mL of CCl_4 was stirred and heated under reflux with UV irradiation for 10 h, cooled, filtered, and concentrated to give 4.2 g of crude dibromide **7** as a viscous oil. Dibromide **7** was dissolved in 40 mL of acetone, and a solution of 3.9 g of NaI in 40 mL of acetone was added dropwise with stirring. After the addition was complete, the solution was stirred at room temperature for 1 h, concentrated in vacuo, diluted with 40 mL of ether, and washed with three 30-mL portions of 5% aqueous Na_2SO_3. The solution was dried (Na_2SO_4) and concentrated in vacuo to give a deep red

(11) Andersen, R. J.; Faulkner, D. J. *Tetrahedron Lett.* **1973**, 1175–1178.

(12) Minale, L.; Sodano, G.; Chan, W. R.; Chen, A. M. *J. Chem. Soc., Chem. Commun.* **1972**, 674–675.

(13) Wadsworth, W. S.; Emmons, W. D. *J. Am. Chem. Soc.* **1961**, *83*, 1733–1738.

(14) Modification of: Levine, S. D.; Diassi, P. A.; Wisenborn, F. L. Ger. Offen. 1,953,432, 1970; *Chem. Abstr.* **1970**, *73*, 14298.

(15) Kishi, Y.; Aratani, M.; Tanino, H.; Fukuyana, T.; Goto, T.; Inone, S.; Sugiura, S.; Kokoi, H. *J. Chem. Soc., Chem. Commun.* **1972**, 64–65.

oil that was chromatographed on neutral alumina (activity III, 1:3 ether/pentane) to give 1.60 g (74%) of 2: IR (neat) 1730, 1700, 1645, 1620, 1570 cm^{-1}; UV max (CH_3OH) 270 nm (ϵ 1330); ^{1}H NMR ($CDCl_3$) δ 6.16 (m, 2 H), 5.75 (m, 2 H), 5.46 (d, J = 5.1 Hz, 1 H), 3.72 (s, 3 H), 3.17 (s, 2 H).

Arene oxide 2 slowly decomposed to methyl (*o*-hydroxyphenyl)acetate on standing at room temperature. A crystalline Diels–Alder adduct of 2 was prepared by reaction with 4-methyl-1,2,4-triazoline-3,5-dione in $CHCl_3$: mp 161–162 °C ($CHCl_3$/pentane); IR ($CHCl_3$) 1775, 1710, 1615 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.10 (m, 2 H), 5.19 (m, 2 H), 3.70 (s, 3 H), 3.60 (d, J = 4 Hz, 1 H), 3.22 (d, J = 15 Hz, 1 H), 2.95 (s, 3 H), 2.62 (d, J = 15 Hz, 1 H). Anal. Calcd for $C_{12}H_{13}N_3O_5$: C, 51.61; H, 4.69; N, 15.04. Found: C, 51.50; H, 4.96; N, 14.82.

[4-^{2}H]Phenylacetic Acid (9). The Grignard reagent of 4-bromotoluene was quenched with ^2H_2O to obtain 8[8] that was brominated with NBS according to the literature procedure[16] for unlabeled material to afford [4-^{2}H]benzyl bromide. Reaction of the bromide with NaCN in aqueous ethanol gave [4-^{2}H]benzyl cyanide, bp 64 °C (1.3 mm) [lit.[17] bp 102–103 °C (10 mm)]. A sample of the cyanide was collected by VPC (3% tricresyl phosphate on 100–120-mesh Gas Chrom Q) for the low-voltage (7.5 eV) mass spectrum[9] that indicated 83% deuterium incorporation. Hydrolysis of the cyanide according to the literature procedure[18] for the unlabeled material gave 9, mp 77–78 °C (lit.[18] bp 72–75 °C). The ^{1}H NMR spectra of 8, 9, and the bromide and cyanide intermediates were consistent with 83% deuterium incorporation.

[4-^{2}H]-1-[(Carbomethoxy)methyl]benzene 1,2-Oxide (10). The sequence for conversion of phenylacetic acid to 2 was used to convert 9 to 10: ^{1}H NMR ($CDCl_3$) δ 6.05 (br d, 1.2 H), 5.65 (m, 2 H), 5.43 (d, J = 5 Hz, 1 H), 3.67 (s, 3 H), 3.13 (s, 2 H).

Methyl (3,5-Dibromo-2-hydroxyphenyl)acetate. Bromination of methyl (2-hydroxyphenyl)acetate by a procedure similar to that described for bromination of (2-hydroxyphenyl)acetic acid[5] afforded methyl (3,5-dibromo-2-hydroxyphenyl)acetate in near quantitative yield: mp 119–121 °C (ethanol/water); IR ($CHCl_3$) 3520, 1730 cm^{-1}; ^{1}H NMR (acetone-d_6) δ 7.45 (d, J = 2.4 Hz, 1 H, H_4), 7.25 (d, J = 2.4 Hz, 1 H, H_6), 3.64 (s, 2 H), 3.57 (s, 3 H). Anal. Calcd for $C_9H_8Br_2O_3$: C, 33.36; H, 2.49; Br, 49.33. Found: C, 33.59; H, 2.50; Br, 49.09.

Aromatization of 10. Aromatization was studied under the conditions indicated in Table I by dissolving 10 in CF_3CO_2H or in a 2:1 dioxane–water solvent in which the pH of the aqueous portion was 1.1 (HCl), 4.0 (biphthalate buffer), 7.0 (phosphate buffer), or 10.0 (carbonate–borate buffer). The aromatization reaction was complete within a few minutes in CF_3CO_2H and at pH 1.1 and within 1 week at higher pH. The product in each reaction was isolated, purified by preparative TLC (silica, 1:1 hexane/CH_2Cl_2), and brominated as described above for unlabeled material. Deuterium content at C_4 was measured by integration of the relative intensity of H_4 vs. H_6 in the ^{1}H NMR spectrum.

Methyl 2,5-Dihydro-*trans*-cinnamate 1,2-Oxide (16). To a mixture of 3.03 g of 57% NaH (72 mmol) in 120 mL of dry 1,2-dimethoxyethane at 20 °C was added trimethyl phosphonoacetate[13] (13.1 g, 72 mmol) dropwise with stirring. The mixture was stirred at room temperature for 1 h until gas evolution ceased. Aldehyde 14[2] (9.0 g, 72 mmol) was added dropwise to the mixture while the temperature was maintained below 25 °C. The mixture was stirred for 1 h at room temperature and heated under reflux for 0.5 h. The mixture was cooled, diluted with water, and extracted with ether. The ether layer was dried ($MgSO_4$) and concentrated. The residue was chromatographed on silica gel (9:1 pentane–ether) and distilled to give 9.3 g (72%) of 16: bp 67 °C (0.15 mm); IR (neat) 1720, 1650 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.90 (d, J = 16 Hz, 1 H), 6.10 (d, J = 16 Hz, 1 H), 5.53 (br s, 2 H), 3.77 (s, 3 H), 3.20 (br s, 1 H), 2.60 (br s, 4 H). Anal. Calcd for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71. Found: C, 66.79; H, 6.68.

Methyl *trans*-Cinnamate 1,2-Oxide (3). A solution of bromine (2.67 g, 17 mmol) in 40 mL of CH_2Cl_2 was added dropwise to a solution of 16 (3.0 g, 17 mmol) in 50 mL of CH_2Cl_2 at 0 °C. The solvent was removed under reduced pressure, and the residue was chromatographed on silica gel (9:1 pentane–ether) to give 4.1 g (71%) of pure dibromide: IR (neat) 1720, 1660 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.90 (d, J = 16 Hz, 1 H), 6.17 (d, J = 16 Hz, 1 H), 4.40 (m, 2 H), 3.77 (s, 3 H), 3.4–2.3 (m, 5 H).

To the dibromide (4.0 g, 12 mmol) in 100 mL of ether under N_2 was added dropwise 3.63 g (30 mmol) of DBN. The solution was stirred for 2 h and filtered to remove DBN·HBr. The filtrate was dried ($MgSO_4$) and concentrated to yield a brown oil. Chromatography of the residue on silica gel (9:1 pentane–ether) gave 1.1 g (52%) of 3 as orange needles: mp 41–43 °C (pentane); IR (CCl_4) 1725, 1620, 1605 cm^{-1}; UV max (CH_3OH) 243 (ϵ 23400), 347 nm (ϵ 7330); ^{1}H NMR (250 MHz; $CDCl_3$) δ 7.10 (d, J = 15.4 Hz, 1 H), 6.30 (d, J = 15.4 Hz, 1 H), 6.23 (m, 2 H), 5.93 (m, 2 H), 5.62 (m, 1 H), 3.77 (s, 3 H). Anal. Calcd for $C_{10}H_{10}O_3$: C, 67.41; H, 5.65. Found: C, 67.43; H, 5.73.

Arene oxide 18 was prepared from 17[2] by the same procedure for the synthesis of 3 from 14.

Aromatization of 3 and 18. Aromatization was investigated in ether containing a few drops of CF_3CO_2H and in 2:1 tetrahydrofuran–water at pH 0.1, 1.1, 4.0, 7.0, and 10.0 as described for the aromatization of 10. The CF_3CO_2H-catalyzed reaction and the reactions at pH 0.1 and 1.1 required several days for completion, and product was isolated by ether extraction. The reactions at pH 4.0, 7.0, and 10.0 showed only partial aromatization after 1 month, at which time the reactions were extracted with ether, and the ether extract was dried and concentrated. The product was purified by preparative TLC (silica, 1:1 ether–pentane). The chemical shifts for the aromatic protons of the aromatization product, methyl *o*-coumarate, are δ 7.61 (H_6), 7.26 (H_4), 6.98 (H_3), 6.90 (H_5). The deuterium distribution in 19 from aromatization of 18 was determined by integration of the ^{1}H intensity for H_4 and H_5 in the 250-MHz ^{1}H NMR spectrum of 19. Results were as follows: CF_3CO_2H, 0.21 H_4, 0.79 H_5; pH 0.1, 0.20 H_4, 0.80 H_5; pH 1.1, 0.20 H_4, 0.80 H_5; pH 4.0, 0.18 H_4, 0.82 H_5; pH 7.0, 0.22 H_4, 0.78 H_5; pH 10.0, 0.19 H_4, 0.81 H_5.

Preparation and Aromatization of 20. A mixture of 18 (50 mg, 0.28 mmol) and 100 mL of 4% aqueous NaOH was stirred for 1.5 h at which time a light yellow homogeneous solution was obtained. The aqueous solution was washed with 20 mL of ether, acidified to pH 5 by dropwise addition of saturated aqueous NaH_2PO_4 at 0 °C, and extracted with ether. The ether extract was dried (Na_2SO_4) and concentrated under reduced pressure to give 30 mg of solid shown by ^{1}H NMR to be 30% 20 and 70% 21. Addition of a few drops of CF_3CO_2H in ether effected complete conversion to 21. The deuterium distribution in 21 was determined by integration of the ^{1}H intensity for the aromatic protons in the 250-MHz ^{1}H NMR spectrum: δ 7.60 (1 H, H_6), 7.26 (0.18 H, H_4), 6.99 (1 H, H_3), 6.91 (0.78 H, H_5).

Acknowledgment. We are grateful to the National Institutes of Health, Grant GM 26388, for financial support.

Registry No. 2 oxide, 76250-93-6; 2 oxepin, 76250-94-7; 3 oxide, 76250-95-8; 3 oxepin, 76250-96-9; (*E*)-4, 75996-10-0; 5, 76250-97-0; 6, 76250-98-1; 7, 76250-99-2; 8, 4409-83-0; 9, 66223-91-4; 10, 76251-00-8; 13b, 76251-01-9; 14, 75961-78-3; 15, 5927-18-4; 16, 76251-02-0; 16 dibromide, 76251-03-1; 17, 76251-04-2; 18, 76251-05-3; (*E*)-19, 76251-06-4; 20, 76251-07-5; 21, 76251-08-6; phenylacetic acid, 103-82-2; (2,5-dihydrophenyl)acetic acid, 27008-28-2; 1-[(carbomethoxy)methyl]-*trans*-4,5-dibromo-1-cyclohexene, 76251-09-7; methyl (*o*-hydroxyphenyl)acetate, 22446-37-3; 4-methyl-1,2,4-triazoline-3,5-dione, 13274-43-6; [4-^{2}H]benzyl cyanide, 13122-35-5.

(16) Qvist, W. *Acta Acad. Abo. Ser. B* **1952**, *18*, 14; *Chem. Abstr.* **1955**, *49*, 201*d*.
(17) Vogel, A. I. "A Text-Book of Practical Organic Chemistry", 3rd ed.; John Wiley and Sons: New York, 1962; p 761.
(18) Wenner, W. *J. Org. Chem.* **1950**, *15*, 548–551.