Table I

Olefin	T_R[b]	0[a]	0.5[a]	2.0[a]	5.0[a]	18[a]
12	1.0	0	1.3	4.6	6.8	9.0
29	1.5	100	0	0	0	0
13	1.7	0	32.9	30.1	29.4	27.1
14	2.0	0	65.8	59.9	58.6	56.8
15	2.2	0	1.0	3.4	5.2	7.1

[a] Time in hours. [b] Retention time.

1.86 (d, 2, J = 4.5 Hz), 5.45 (t, 1, J = 4.5 Hz); mass spectrum m/e (rel intensity) 206 (M^+, 33), 191 (100), 150 (20), 136 (28), 135 (66), 121 (62), 107 (50), 95 (47), 93 (38), 82 (38), 81 (35), 69 (48), 55 (47), 43 (34), 41 (63).

Anal. Calcd for $C_{15}H_{26}$: C, 87.30; H, 12.70. Found: C, 87.23; H, 12.87.

Acid-Catalyzed Isomerization of Octalin 29. A pure sample of octalin **29** (0.5 g, 2.5 mmol) was treated with acetic acid (4 g) containing sulfuric acid (1 g) at 40°. Samples were removed periodically for analysis by gas chromatography. Table I summarizes the results. The products were separated by preparative gas chromatography and gave ir, nmr, and mass spectra identical with those of the products previously isolated from the equilibration of olefin **12**. The octalins isolated in this experiment were optically inactive, since a racemic octalin (**29**) had been employed as the starting material.

Registry No.—**10**, 470-40-6; **11**, 50562-26-0; **12**, 32540-36-6; **13**, 50562-28-2; **14**, 50562-29-3; **15**, 50512-32-8; **16**, 50562-30-6; **17**, 50562-31-7; **18**, 50562-32-8; **19**, 50562-33-9; **20**, 50562-34-0; **21**, 50562-35-1; **22**, 51096-44-7; **23**, 51096-43-6; **24**, 50562-38-4; **25**, 50562-39-5; **26**, 50562-40-8; **27**, 50562-41-9; **28**, 50562-42-0; **29**, 50562-43-1.

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Synthesis of *cis*-1,2-Dihydroxy-1,2-dihydronaphthalene and *cis*-1,4-Dihydroxy-1,4-dihydronaphthalene

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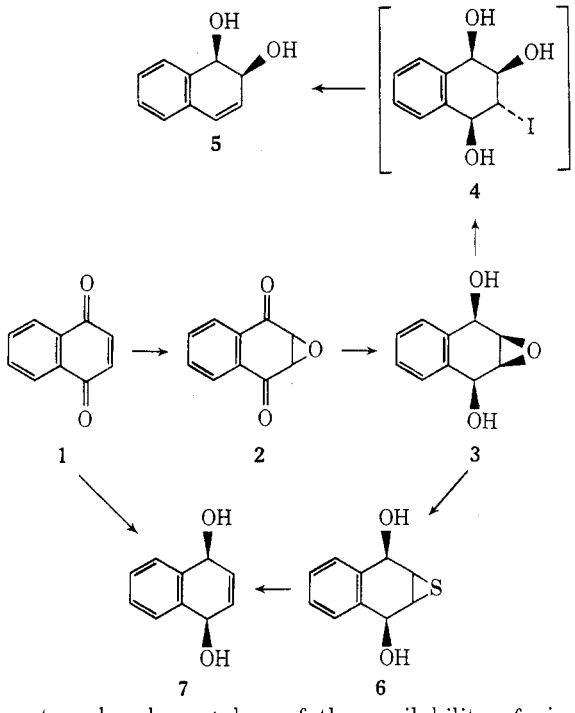
Both of title compounds were prepared from the readily accessible *cis,cis*-1,4-dihydroxy-2,3-epoxy-1,2,3,4-tetrahydronaphthalene. The 1,2-dihydrodiol, a bacterial metabolite of naphthalene, was obtained through the action of sodium iodide and zinc dust in acetic acid on the epoxide. Conversion of the epoxide to the thioepoxide and desulfurization with triphenylphosphine provided the 1,4-dihydrodiol, which was also obtained by direct reduction of *p*-naphthoquinone with diisobutylaluminum hydride.

Although *cis*- and *trans*-1,2-dihydroxy-1,2-dihydroarenes have been known as oxidative metabolites of the aromatic ring for many years,[1] relatively little has been reported on the synthesis of this important class of metabolites. Both *cis*- and *trans*-1,2-dihydroxy-1,2-dihydrobenzene have been prepared by dehalogenation of the corresponding tetrachlorocyclohexanediols.[2] While *cis*-1,2-dihydrodiols at the K regions of polycyclic aromatic hydrocarbons are available through the action of osmium tetroxide,[3] the procedure fails with naphthalene. *trans*-1,2-Dihydrodiols have been prepared by reduction of K region *o*-quinones with lithium aluminum hydride.[4,5] The hydride reduction produces only pyrocatechol from *o*-benzoquinone[4] and a mixture of cis and trans isomers is formed from 7,12-dimethylbenz[*a*]anthracene-5,6-quinone.[5] Reduction of certain *p*-quinones such as 1,4-naphthoquinone results in conjugate addition of hydride.[6] The only 1,4-dihydrodiols without substitution at the carbinol position prepared thus far have been by lead tetraacetate oxidation[7] of the 9,10 positions of anthracene and by the lithium aluminum

hydride reduction of 9,10-anthraquinone.[6] An attempt to prepare the 1,4-dihydrodiol of naphthalene from 1,4-dihydronaphthalene *endo*-1,4-oxide was unsuccessful.[8]

Metabolism of naphthalene by bacteria produces the *cis*-1,2-dihydrodiol.[9] Evidence for the 1,4-dihydrodiol has been obtained with mammalian systems.[8] The first chemical syntheses of *cis*-1,2- and 1,4-dihydrodiols of naphthalene (**5** and **7**), the title compounds, are reported here.



Advantage has been taken of the availability of *cis,cis*-1,4-dihydroxy-2,3-epoxy-1,2,3,4-tetrahydronaphthalene (**3**), through epoxidation of **1** to **2** and subsequent reduction with sodium borohydride to **3**,[10] for the synthesis of both compounds. Treatment of **3** with Cornforth's reagent[11] gives an intermediate iodohydrin **4** which potentially could form either **5** or **7**. Only **5** was isolated in 85% yield. The 1*R*,2*S* dihydrodiol, which results from bacterial metabolism of naphthalene,[9] showed the same nmr and mass spectra as **5**. Only the 1*R*,2*S* isomer of **5** is metabolized by microorganisms, thus affording a satisfactory method of obtaining pure 1*S*,2*R* isomer.[12]

Attempted deoxygenation of **3** to **7** with triphenylphosphine, in the presence of hydroquinone at room temperature, was unsuccessful. When the mixture was heated, the only detectable product was α-naphthol. The thioepoxide **6**, however, is readily desulfurized to give a 70% yield of **7** along with 14% of **5**. At first the formation of **5** in this reaction seemed quite unusual. However, careful examination of the nmr spectrum of the sample of **6** used in this preparation revealed signals consistent with the presence of *cis*-1,2-dihydroxy-3,4-thioepoxy-1,2,3,4-tetrahydronaphthalene, which had formed in a competing reaction during preparation of **6** from **3** with potassium thiocyanate.

The previous attempt to prepare **7** by the reduction of **1** with lithium aluminum hydride failed[6] because of the propensity of this reagent to undergo 1,4 addition. Diisobutylaluminum hydride, in contrast, causes 1,2 reductions of similar systems.[13] Treatment of **1** with this reagent produces **7**, although in low yield. Acid-catalyzed dehydration of **7** gives only α-naphthol, at a rate 52 times faster than **5**, which in turn is more unstable than the trans isomer of **5**.[9]

Catalytic hydrogenation of **7**, prepared from **3**, to *cis*-1,4-dihydroxy-1,2,3,4-tetrahydronaphthalene (**8**) gave a product indistinguishable from a sample obtained by catalytic reduction of **1** with copper chromite to which the trans stereochemistry has been assigned.[14] The stereochemistry of **7** was established by reducing the diacetate of **7** with deuterium in the presence of Wilkinson's catalyst, which catalyzes cis addition.[15] Analysis of the nmr spectrum of the 8-*cis*-2,3-d_2, in the presence of shift reagents, showed a single broadened resonance band corresponding to the 2,3 hydrogens. In comparison, **8** showed two bands under similar conditions. These results are only compatible with a stereospecific addition of deuterium to one face of **7**, which must have had cis stereochemistry. Thus, the original assignment of **3**[10] would seem correct, and the diol (**8**) isolated from the catalytic reduction of **1** is possibly the cis isomer.

Experimental Section

Diisobutylaluminum hydride and Wilkinson's catalyst [tris(triphenylphosphine)rhodium(I) chloride] were purchased from Alfa Inorganics, Beverly, Mass., and Eu(fod)$_3$ [europium(III) tris(1,1,1,-2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octanedione)] from North Chemical., Inc., Landing, N. J. Mass spectra were measured at 70 eV on a Hitachi RMU7 spectrometer. A Varian HA-100 spectrometer was used for the determinations of nmr spectra in $CDCl_3$ with TMS as internal standard. Chemical shifts are reported in δ units and coupling constants (J) in hertz. Compound **7** gave a microanalysis within 0.25% for carbon and hydrogen while the molecular ion of compound **6** was peak matched within 1 mmass unit of the expected value.

***cis,cis*-1,4-Dihydroxy-2,3-epoxy-1,2,3,4-tetrahydronaphthalene (3).** Reduction of **2**[16] to **3** with an excess of sodium borohydride in aqueous ethanol was conducted essentially as described by Rashid and Read.[10] Most of the ethanol was removed before saturation of the solution with sodium chloride and extraction with ethyl acetate. Recrystallization from chloroform gave pure **3**, mp 204° (lit.[10] mp 192–194°).

***cis*-1,2-Dihydroxy-1,2-dihydronaphthalene (5).** To 0.95 g of **3** was added 4.2 g of sodium iodide, 0.2 g of sodium acetate, 8.4 ml of acetic acid, and 4.2 g of zinc dust. The paste was stirred under nitrogen for 3 hr before adding 25 ml of water and adjusting the pH to 7.0 with sodium carbonate. The aqueous phase was extracted three times with equal volumes of ethyl acetate and the combined organic phase was dried with magnesium sulfate. Evaporation of the solvent left 0.72 g (85%) of crude diol which, by nmr, showed no trace of the 1,4 isomer (**7**). The diol was recrystallized from chloroform to give pure **5**, mp 101–102°, which was identical in all respects, except optical activity and melting point, with biosynthetic material.[9]

***cis*-1,4-Dihydroxy-2,3-thioepoxy-1,2,3,4-tetrahydronaphthalene (6).** A solution of 1 g of **3** in 10 ml of ethanol and a five-molar excess of KSCN in 1 ml of water were mixed and stored at 50° for 1 week. The ethanol was evaporated at reduced pressure and 10 ml of water was added. Products were extracted into chloroform (3 × 5 ml) and the combined extracts were dried with magnesium sulfate and concentrated to leave 0.55 g of crude **6**. A sample was purified by dissolving in chloroform, adding benzene, and allowing **6** to crystallize slowly at 4°. **6**, mp 110–113°, had a mass spectrum showing ions at m/e (rel intensity) 194 (M^+, 14), 176 (9), 161 (35), 147 (100), 144 (42), and 128 (32). The nmr spectrum of **6** ($H_{2,3}$ = 3.45, $H_{1,4}$ = 5.07 as triplets with an apparent $J_{1,2}$ = 1.8 Hz; aromatic protons δ 7.0–7.8) did not allow assignment of relative stereochemistry between the thioepoxide and the cis diol, but it was assumed to be trans.

***cis*-1,4-Dihydroxy-1,4-dihydronaphthalene (7).** A solution of 0.5 g of crude **6** in dry dimethoxyethane was treated with a three-molar excess of triphenylphosphine at 80° overnight. After removal of the solvent, nmr analysis of the residue showed the presence of **5** and **7** in a ratio of 1:5. The two isomers were separated by applying the residue in ethyl acetate–chloroform (1:1) to a 3 × 25 cm column of silica gel and eluting with the same mixed solvent. The first dihydrodiol to elute was **5**, which was followed immediately by 290 mg (70%) of **7**: mp 106–107° after crystallization from chloroform–benzene (1:1); mass spectrum m/e (rel intensity) 162 (M^+, 24), 144 (100), 128 (5), 115 (6); nmr spectrum, $H_{1,4}$ δ 5.0 and $H_{2,3}$ δ 6.12 as doublets, J (apparent) = 1.5 Hz, aromatic protons δ 7.2–7.8. Reduction of **1** (1 g) in 50 ml of benzene under nitrogen with 10 ml of 20% diisobutylaluminum hydride in hexane also gave **7** in 20% yield after purification by chromatography as described above.

Assignment of Stereochemistry to 7. Reduction of 7 in ethanol with hydrogen in the presence of 10% Pd on carbon gave 1,4-dihydroxy-1,2,3,4-tetrahydronaphthalene (8), mp 138°. This material was indistinguishable by mp, nmr, and glc (as the diacetate, 3% OV-17, 170°, retained 9.5 min) from a sample prepared by catalytic reduction of 1.[14] The diol 7 (170 mg) was acetylated with acetic anhydride in pyridine and the crude product was then reduced in 8 ml of benzene with deuterium gas in the presence of 10 mg of Wilkinson's catalyst (free diol did not reduce readily). The reaction was complete in 8 days. After removal of the solvent under reduced pressure, the product was deacetylated in 80% ethanol-water containing an excess of sodium hydroxide. The ethanol was removed, water was added, and the pH was adjusted to 7 with acetic acid. Extraction with ethyl acetate provided 8-*cis*-2,3-d_2; incorporation of two atoms of deuterium was confirmed by its mass spectrum.

Saturated $CDCl_3$ solutions (400 μl) of deuterated and normal 8 at 20° were used to determine their nmr spectra in the presence of 3 mg of Eu(fod)$_3$. Normal 8 showed the four protons at the 2 and 3 positions to be split into two separate groups at δ 2.66 and 3.16, presumably due to hydrogens cis and trans to the hydroxyl groups. The benzylic protons moved to δ 6.0 and the aromatic protons split into two groups at δ 7.5–7.6 and 8.1–8.3. The corresponding spectrum of deuterated 8 lacked the absorption at δ 2.66, and when the benzylic protons were irradiated, the signal at δ 3.16 sharpened considerably. This observation confirms the assignment of the chemical shifts in the complex and, together with the cis addition of deuterium, is consistent with the hydroxyl groups in 8 as cis.

Dehydration of the Dihydrodiols 5 and 7. Rates were measured by following the decrease in absorption at 265 nm and the increase at 295 nm for 5 and 7, respectively, in dioxane–water (1:1) which was 0.6 *M* in HCl. The rates at 25° for 5 and 7 are 5.4×10^{-4} and 2.8×10^{-2} sec^{-1}, respectively. Only α-naphthol could be detected by tlc as a product from 7.

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Registry No.—1, 130-15-4; 3, 25129-70-8; 5, 31966-70-8; 6, 50987-67-2; 7, 51096-10-7; 8, 50987-68-3.

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Formation of a Cyclohexane Ring by Condensation of a Nitro Ketone and an Aldehyde[1a]

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5-Nitro-2-pentanone (3) and furfural were used to study the feasibility of using a condensation reaction to form a cyclohexane ring. The Schiff base of furfural was condensed with the ethylene ketal of 5-nitro-2-pentanone in acetic acid to give 1-(2-furyl)-2-nitro-1-hexen-5-one 5-ethylene ketal (11). The ketal was removed and an intramolecular Michael reaction was effected using an enamine to form 3-(2-furyl)-4-nitrocyclohexanone (21). Practical syntheses of 1-methoxy-5-nitro-2-pentanone (22) and *trans*-2,6-dimethyl-2-heptenal (23) have been developed.

Earlier papers have reported experiments on the preparation and Birch reduction of 2,3-dihydrobenzofurans as possible intermediates for syntheses in the fumagillin series.[2] Corey has recently reported a synthesis of fumagillin, using a Diels–Alder reaction to form the carbocyclic ring.[3]

We considered that the cyclohexane ring of fumagillin could be formed by the condensation of a γ-nitro ketone with an aldehyde, which would allow a stereoselective synthesis. To test the feasibility of such a reaction, the condensation of furfural with 5-nitro-2-pentanone (3) was studied; these compounds are accessible and are reasonable models for the proposed syntheses.

5-Nitro-2-pentanone (3) was obtained by a modification of the published procedure.[4] An attempt to cyclize 3 with furfural according to the following scheme gave only tars, probably owing to the high reactivity of α,β-unsaturated nitro compounds.[5] A two-step condensation was therefore