olefin isomerization study[10] of several different strong base and acid catalysts compared to iron pentacarbonyl has indicated that iron pentacarbonyl is a faster and more complete isomerization catalyst than any of those studied. Secondly, the conditions employed with $Fe(CO)_5$ are mild and have not led to structural rearrangement or polymerization that is characteristic of acid catalysts. Thirdly, $Fe(CO)_5$ is a relatively neutral material not reacting with a variety of functional groups such as carboxylic esters, alcohols, and ketones. The results of isomerization experiments with ethers and esters will be reported in a forthcoming paper.

Experimental Section

General.—Melting and boiling points are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Model 137 spectrophotometer. The nmr spectra were obtained on a Varian HA-100 instrument. Nmr samples were dissolved in either deuterated chloroform or carbon tetrachloride with tetramethylsilane as an internal reference. All vapor phase chromatograms were obtained on an Aerograph A-90-P instrument; a 10-ft Carbowax 20 M column was employed for analysis. Mass spectra results were determined on an Atlas CH-4 spectrophotometer. The ultraviolet spectra were obtained on a Perkin-Elmer Model 202 spectrophotometer.

Materials.—Iron pentacarbonyl was purchased from Alfa Inorganics, Inc., and used as received. The unsaturated alcohols were purchased from either Aldrich Chemical Co. or Chemical Samples Co. Purity of these compounds was checked by vpc and all were found to be greater than 95% one component.

Isomerization of 1-Hepten-4-ol (Entry 1).—A solution of 10 g (0.088 mole) of 1-hepten-4-ol and 1.8 g (0.0092 mole) of iron pentacarbonyl was heated at 110° under an argon atmosphere for 4 hr. During this time the solution turned dark brown and deposits of a black solid formed on the sides of the flask. At 1-hr intervals, 0.5-ml samples were withdrawn and analyzed by infrared and vpc for appearance of 4-heptanone and disappearance of 1-hepten-4-ol. After 4 hr, the solution was cooled and 3.0 g (0.018 mole) of ferric chloride in 10 ml of 95% ethanol was added, which caused an evolution of gas (CO). This mixture was stirred for 1 hr, 50 ml of water was added, and the solution was extracted with ether. The ether layer was separated, washed with saturated sodium chloride, dried with 3A molecular sieves, and evaporated under reduced pressure. A total of 8.0 g (80% yield) of 4-heptanone was recovered. Vpc of this sample showed a major peak of 98% peak area. A 2,4-dinitrophenylhydrazone derivative was prepared, mp 70–71° (lit.[11] mp 71–72°). The mass spectrum of this product indicates a molecular ion peak at *m/e* 114 (calcd 114) with major fragment peaks at *m/e* 71 and 43 that correspond to $C_3H_7C(=O)$ and C_3H_7 groups, respectively.

Isomerization of 2-Methyl-1-hepten-3-ol (Entry 3).—A solution of 5.0 g (0.039 mole) of 2-methyl-1-hepten-3-ol and 1.5 g (0.0078 mole) of iron pentacarbonyl in 25 ml of *n*-octane solvent was refluxed at 124° for 6 hr. The solution was monitored for isomerization by infrared and vpc. After isomerization was complete, the mixture was cooled, treated with ferric chloride in 95% ethanol, diluted with ether, washed with saturated sodium chloride, and distilled to afford 3.7 g (75% yield) of 2-methyl-3-heptanone, bp 42–49° (12–15 mm) [lit.[12] bp 63–65° (25 mm)]. A vapor phase chromatogram of this product indicated a purity of 99%. The nmr spectrum of this sample has a multiplet centered at τ 7.62 (3 H, $>CHC(=O)CH_2$) and a complex band from 8.5 to 9.15 (11 H, aliphatic CH).

Isomerization of *cis*-3-Hexen-1-ol (Entry 7).—To 5.0 g (0.05 mole) of *cis*-3-hexen-1-ol was added 1.0 g (0.005 mole) of iron pentacarbonyl which caused an immediate evolution of gas (CO) and a 5° rise in temperature. Within 3 min the solution turned dark brown; however, infrared analysis indicated that the starting alcohol had not changed. The solution was heated to 110° for 6 hr and analyzed by vpc and infrared. The mixture has vpc peaks (170°) at retention times of 1.1, 2.0, 2.5, and 7.8 min. Peak 1 (1.1 min) was identical in retention time with hexanal, and peak 3 corresponded to *cis*-3-hexen-1-ol. Peak 2 probably corresponds to partially isomerized *cis*-3-hexen-1-ol. An infrared spectrum of the product mixture showed two bands at 5.8 (aldehyde C=O) and 5.95 (conjugated C=O) as well as peaks at 6.1 (conjugated C=C) and 10.35 μ (*trans* olefin). Peak 4 was collected from the gas chromatograph and analyzed by mass, ultraviolet, and nmr spectra and elemental analysis. The collected sample has a λ_{max} in 95% EtOH at 232 mμ (ϵ 13,500); nmr peaks at τ 0.62 (1 H, singlet, >CHO), 3.1 (1 H, triplet, CH=CC=O), 7.75 (4 H, multiplet, allylic CH_2), and a broad peak from 8.6 to 9.05 (16 H, aliphatic CH). The mass spectrum of the product has a molecular ion peak at 182. This data accommodates structure **1** for the product.

Anal. Calcd for $C_{12}H_{22}O$: C, 79.1; H, 12.1. Found: C, 79.2; H, 11.8.

Reaction of Hexanal with Iron Pentacarbonyl.—A solution of 20 g (0.20 mole) of freshly distilled hexanal and 3.9 g (0.02 mole) of iron pentacarbonyl was heated at 110° for 6 hr. An infrared spectrum of the mixture after this time had peaks at 5.8 (aldehyde C=O) and 5.95 μ (conjugated C=O). Vpc analysis (170°) of the mixture showed three peaks with the major component (~85%) having a retention time of 7.8 min, identical with that of **1** isolated from the reaction of *cis*-3-hexen-1-ol with iron pentacarbonyl. The major peak was collected from the gas chromatograph. An nmr spectrum of this material was found to be identical with the nmr spectrum of **1**.

Isomerization of 9-Decen-1-ol with Iron Pentacarbonyl and Ultraviolet Light (Entry 9).—A 200-w high-pressure mercury lamp in a quartz reactor was used in this irradiation procedure. A solution of 5.0 g (0.032 mole) of 9-decen-1-ol and 0.31 g (0.0016 mole) of iron pentacarbonyl in 125 ml of pentane was irradiated at ~20°. Samples of 5 ml were withdrawn at 1-hr periods for 5 hr and analyzed by infrared and vpc for the appearance of decanal and loss of 9-decen-1-ol. Within 1 hr, terminal olefin peaks (10.1 and 10.95 μ) and aldehyde C=O (5.8 μ) had formed. No other carbonyl peaks were present. The solution turned a dark green but a precipitate did not form during this reaction. The vpc analysis of this reaction mixture and subsequent experiments indicated that a maximum amount of decanal had formed at a 5-hr reaction time. The reaction was stopped at this time and filtered to remove insoluble iron carbonyls, pentane was evaporated under reduced pressure, and the crude product, which showed 54% decanal by vpc, was recovered. A 2,4-dinitrophenylhydrazone derivative of the decanal in the mixture was prepared, mp 100–101° (lit.[13] mp 104.2–104.8°). A total of 7.2 g (54% yield) of 2,4-dinitrophenylhydrazone derivative was obtained.

Registry No.—**1**, 13019-16-4; 4-heptanone 2,4-dinitrophenylhydrazone, 1655-41-0; 2-methyl-3-heptanone, 13019-20-0. Table I: 1, 3521-91-3; 2, 4048-42-4; 3, 13019-19-7; 4, 3391-86-4; 5, 822-67-3; 7, 1708-81-2; 8, 13019-22-2.

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The *ortho* Bromination of Phenols

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One of our objectives in research work has been to manipulate orientation in various ways to obtain any isomer desired.[1] The bromination of phenol serves as one example. *para* substitution is predominant by bromination in carbon bisulfide,[2] almost exclusive in

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ethylene chloride,[3] and highly exclusive using dioxane dibromide as the brominator.[4] *meta* substitution has been brought about indirectly by rearrangement of *p*-bromo- to *m*-bromophenol (77% yield containing 12% *p*-bromophenol) with large excesses of aluminum chloride and liquefied hydrogen bromide under autogenous pressure.[5] There remains the problem of searching for exclusive *ortho* bromination of phenol. We were guided initially by the general principle that, to obtain maximum *ortho* substitution, the attack of the electrophile must be made from the position of the substituent (in this case, the hydroxyl group) whether the electrophile be held by coordination or hydrogen-bonding forces or whether it be covalently bonded to the oxygen atom.[1]

Previous studies on *ortho* bromination of phenols are summarized in de la Mare and Ridd,[6] but the most important are documented here. As early as 1927, Skraup made the interesting observation that the absence of strong acids led to higher *ortho* to *para* ratios in the bromination of phenol.[7] He used the weak base, pyridine, to absorb the generated acid and obtained a monobrominated product containing 64% *o*-bromophenol.[8] He also obtained the same *ortho* to *para* ratio in bromination of aqueous sodium phenoxide with sodium hypobromite. We can substantiate the futility of seeking exclusive *ortho* bromination using metal phenoxides. The best of some 40 odd experiments was bromination of silver phenoxide with N-bromosuccinimide in methylene chloride giving 46% monobrominated phenol containing 61% *o*-bromophenol. Similar *o*-bromo contents could be realized using ammoniacol silver nitrate and bromine. In a doctoral thesis,[9,10] Dukker and Havinga have undertaken an extensive study of *ortho* bromination in aprotic solvents. N-Bromoacetamide and N-bromosuccinimide gave monobromophenol fractions containing 40 and 74% *o*-bromophenol, respectively, but, of greater interest, they found that acetyl hypobromite, generated from silver acetate and bromine, in benzene, gave a monobromophenol fraction containing 90% *o*-bromophenol, the highest *ortho* to *para* ratio reported in bromination of phenol. In most other solvents, the *ortho* content was about 70%. The yield of monobromophenol fraction was not high enough in our opinion to consider the problem of *ortho* bromination solved. Dukker and Havinga proposed that the high *ortho* to *para* ratio was accounted for by one of two mechanisms: (1) hydrogen bonding of the phenolic hydrogen with the carbonyl oxygen of the acetyl hypobromite, followed by a cyclic shift to *o*-bromophenol; (2) phenyl hypobromite formation followed by *ortho* substitution through the *ortho*-quinoid structure.

Simultaneous with the work of Dukker and Havinga, we were investigating metal phenoxides and N-bromoamines as likely systems for *ortho* bromination. Our studies culminated in the discovery of a simple, efficient process for exclusive *ortho* bromination free from *para* bromination. The essential features of the process are as follows. (1) The system must contain a strong basic aliphatic amine to react with liberated hydrogen bromide. It is desirable that the amine hydrobromide salt be insoluble in the reaction medium. Both *t*-butylamine and triethylenediamine form hydrobromide salts which precipitate out as the reaction proceeds. (2) N-bromo compounds, such as N-bromosuccinimide and particularly N-bromo-*t*-butylamine,[11] are useful reagents but not essential. Tertiary amines, such as triethylenediamine (Dabco) and triethylamine, serve as media for substitution with bromine. (3) The reagents should be mixed at low temperature (*ca.* −70°). The halogenation evidently takes place at a slightly higher temperature than −70°, but this point must be approached slowly. The behavior suggests that the intermediate (or complex) leading to *ortho* bromination is susceptible to competitive reactions giving brominating species which substitute in the *para* position of phenol. Low temperature also favors the precipitation of the amine hydrobromide.

The best procedure is to add bromine to a cold solution of *t*-butylamine in toluene. The mixture is then cooled to *ca.* −70° and phenol is added dropwise over a short period of time. Using this procedure on large scale, 2,6-dibromophenol was obtained in 87% yield using 2 equiv of bromine and 2-bromophenol in 60% yield using 1 equiv of bromine. As with most aromatic halogenations, small amounts of unwanted polyhalophenols and unreacted phenol accompany the product. No difficulty was encountered in the preparation of 2,6-dibromophenol as it could be recrystallized cleanly. But the preparation of 2-bromophenol had to be run with excess phenol to prevent the formation of 2,6-dibromophenol which was most difficult to separate. Unreacted phenol could be removed by extraction of a hexane solution of the crude 2-bromophenol with water.

In smaller scale preparations, *o*-bromothymol was obtained in 80%, 7-bromo-8-hydroxyquinoline in 92%, and 2-bromo-1-naphthol in 61% yields, all in high purity. In regard to the latter preparation, an intermediate of deep purple coloration can be discerned, the color of which disappears as the reaction terminates.

We do not wish to commit ourselves at this time as to the mechanism of the reaction, but we do favor the phenyl hypobromite mechanism of Dukker and Havinga and earlier workers.[9,12]

Lastly, chlorination under the best conditions that worked so well for *ortho* bromination did not give the high yields of *ortho*-chlorination products that we have set as a goal (see the Experimental Section). Further adaptation of conditions to achieve this goal in chlorination and iodination is under investigation.

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(6) P. B. D. de la Mare and J. H. Ridd, "Aromatic Substitution," Butterworth and Co. (Publishers) Ltd., London, 1959.

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(8) Monobromination of phenols is always plagued by polybromination. In the following discussion of literature references, we refer *only* to the monobrominated fraction. If the product is stated to be 64% *o*-bromophenol, then the rest is 36% *p*-bromophenol.

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(10) We thank Dr. E. Havinga, professor in charge of the Ph.D. research of L. J. D., University of Leiden, for making this thesis available to us.

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Experimental Section

Gas Chromatography.—All samples were analyzed by gas chromatography. The great majority of the results which were less successful than those described here is recorded elsewhere.[13] An aliquot of the crude phenolic products was converted to the methyl ethers as described previously.[14] A 5-μl sample of the methyl ethers dissolved in methylene chloride was then injected onto a column: 15% XF-1150 on Chromosorb W (100–140 mesh), 6 ft × 0.25 in., 160°, flow rate of He 70 ml/min, thermal conductivity detector. Retention times were anisole, 2:58 (minutes:seconds); *m*-bromo, 8:15; *p*-bromo, 10:20; *o*-bromo, 12:15; 2,6-dibromo, 20:40; 2,4,6-tribromoanisole, 45:40.

2,6-Dibromophenol.—In a 5-l. three-necked flask fitted with a good mechanical stirrer, low-temperature thermometer, and addition funnel protected with a drying tube was mixed 2.5 l. of dry toluene and 147 g (2 moles) of *t*-butylamine. The flask was surrounded by a suitable container to serve as an isopropyl alcohol and Dry Ice cooling bath. The contents were cooled to −20 to −30°, and 160 g (1 mole) of bromine was added dropwise over a period of 10 min. The solution was then cooled to −70 to −75° by the addition of more Dry Ice to the cooling bath at which time 47 g (0.5 mole) of anhydrous phenol dissolved in methylene chloride was added over a period of 5 min. The reaction mixture was allowed to warm to room temperature over a period of at least 5 to 6 hr at which time the contents were washed with 500 ml of water in a separatory funnel. The organic phase was then extracted with 300- and 200-ml portions of 10% aqueous sodium hydroxide. The combined alkaline extracts were cooled and carefully acidified. The oil which separated was extracted with 200- and 100-ml portions of methylene chloride, and the combined extracts were dried with anhydrous magnesium sulfate and filtered. The filtrate evaporated to dryness at room temperature gave 110 g (87%) of white crystals of 2,6-dibromophenol, mp 50–53°. The phenol can be further purified by recrystallization from 200 ml of hexane (94 g, 75%), mp 55–56°.

2-Bromophenol.—The above procedure was used but the amount of phenol was doubled and the amount of bromine and *t*-butylamine was halved. The oil which separated after reaction was dissolved in 1 l. of hexane and washed thoroughly with four 500-ml portions of water to remove unreacted phenol. The hexane fraction was then concentrated and the residue was distilled through a 20-cm Vigreux column, bp 186–195°. The yield was 52 g (60%) an aliquot of which showed better than 99% purity by gas chromatography. Both of the above preparations have been duplicated.

2-Isopropyl-5-methyl-6-bromophenol (*o*-Bromothymol).—On a 0.025-mole scale, thymol was brominated similarly to give 4.7 g (80%) of a light yellow oil: bp 83–84° (0.5 mm); nmr (τ = 0 ppm for tetramethylsilane) τ 3.43 and 3.16 (doublet of doublets, J_{AB} = 8 cps for aromatic hydrogen atoms). Also, the product was shown to be different from *p*-bromothymol by gas chromatography of the methyl ethers: 10% silicone rubber column at 150° and 15-ml/min flow rate of He; retention times, *o*-bromothymol 7:07 and *p*-bromothymol 8:47. The phenoxyacetic derivative, recrystallized from water, gave colorless needles, mp 90.5–91.5°.

Anal. Calcd for $C_{12}H_{15}BrO_3$: C, 50.19; H, 5.23; Br, 27.85. Found: C, 49.96; H, 5.22; Br, 28.03.

7-Bromo-8-hydroxyquinoline.—On a 0.02-mole scale, the bromination of 8-hydroxyquinoline as above gave 4.1 g (92%) of precipitated solid, mp 137–138° (lit.[15] mp 138°). It was shown to be a single substance by tlc.

2-Bromo-1-naphthol.—On a 0.1-mole scale, the bromination of 1-naphthol as above gave a deep purple solution which on warming to room temperature turned light yellow. The resulting phenol was steam distilled to give 13.6 g (61%) of white crystals, mp 44–45° (lit.[16] mp 45°), with a single spot on tlc.

Modifications in Bromination of Phenol.—Using essentially the same procedure as above (except for the stated modification) and analyzing the total crude product by glpc gave the following results: with synthesized N-bromo-*t*-butylamine[11] in place of same reagent prepared *in situ*, 60% *o*-bromo, traces of *p*-bromo, 24% 2,6-dibromo, and 16% phenol; with no basic amine, no *o*-bromophenol, over 99% *p*-bromophenol; triethylenediamine (Dabco) in place of *t*-butylamine, 75% *o*-bromo, 2% *p*-bromo, and 21% 2,6-dibromophenol (monobromo fraction 99% *ortho*); triethylamine in place of *t*-butylamine, 27% *o*-bromo, 29% *p*-bromo, 8% phenol, the remainder being polybromophenols; N-bromosuccinimide in place of bromine and *t*-butylamine, 55% *o*-bromo, 4% *p*-bromo, 14% 2,6-dibromo, and 27% phenol (monobromo fraction 93% *ortho*); *t*-butyl hypobromite in place of bromine and *t*-butylamine, 65% *o*-bromo, 22% *p*-bromo, and 13% phenol (monobromo fraction 76% *ortho*); silver phenoxide suspended in methylene chloride to which bromine in the same solvent is added dropwise in the absence of light (the best of some 40 odd brominations of phenoxides), 29% *o*-bromo, 17% *p*-bromo, 27% 2,6-dibromo, and 27% phenol.

Attempted *ortho* Bromination of Other Substances.—Anisole gave no nuclear bromination product but rather a lachrymatory mixture indicative of methyl bromination. Anisole with *t*-butyl hypobromite gave a product consisting of 93% *p*-bromoanisole and 7% anisole. Diphenyl carbonate and phenylurethan with bromine–*t*-butylamine system gave brominated products containing no more than 10% *o*-bromophenol. *m*-Chlorophenol yielded a mixture of 2-bromo-3-chloro- and 6-bromo-3-chlorophenol which could not be separated easily. Salicylic acid gave a mixture of brominated acids which could not be separated. Catechol gave oxidation products rather than clean substitution products.

Attempted *ortho* Chlorination of Phenol.—The following reagents in toluene or methylene chloride solution at low temperature gave these results: N-chloro-*t*-butylamine, 13% phenol, 58% *o*-chloro, 29% *p*-chloro, and no polychloro; chlorine with triethylenediamine, 38% *o*-chloro, 19% *p*-chloro, and 43% polychloro; N-chlorosuccinimide gave no reaction at room temperature. These results are inferior for *ortho* chlorination as compared to *ortho* bromination. Other conditions are being investigated.

Registry No.—2,6-Dibromophenol, 608-33-3; 2-bromophenol, 95-56-7; 2-isopropyl-5-methyl-6-bromophenol, 13019-31-3; 7-bromo-8-hydroxyquinoline, 13019-32-4; 2-bromo-1-naphthol, 771-15-3.

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1,2-Diazetidinediones

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Uretidinediones, the cyclic dimers of isocyanates, are well known,[1] but no examples of 1,2-diazetidinediones have been previously established. Cyclooxalylhydrazide was claimed as a product from the pyrolysis of acetophenonesemioxamazone ($PhCCH_3$-$NNHCOCONH_2$) and similar compounds, but the product was probably polymeric oxalylhydrazide in view of its stability and insolubility.[2]

We have prepared the first examples of 1,2-diazetidinediones. The reaction of oxalyl chloride with N,N′-di-*t*-butylhydrazine afforded the yellow, crystalline di-*t*-butyl-1,2-diazetidinedione (I). This compound exhibits a carbonyl absorption in the infrared at 1813 cm^{-1} which is indicative of a strained amide carbonyl. For comparison diphenyluretidinedione absorbs at

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