Analysis of α-Halophenylacetic Acids.[6] Total halogen was first determined by hydrolyzing 100 mg of the halo acid with 25 mL of 0.5 N sodium hydroxide solution on a stream bath for 30 min. The cold solution was acidified with dilute nitric acid and titrated with 0.02 N silver nitrate with two drops of saturated potassium chromate solution as indicator.

Bromine was determined by hydrolyzing a 50-mg sample as above, neutralizing with dilute hydrochloric acid, and adding 5 mL of 20% potassium dihydrogen phosphate solution buffer. Chlorox hypochlorite bleach (5 mL) was added, the solution was heated for 10 min on a steam bath, 5 mL of 50% sodium formate solution was added, and then 0.5 g of potassium iodide was added to the cold solution. The liberated iodine was determined by titration with standard sodium thiosulfate.

The analyses were shown to be reliable by analyzing authentic α-bromophenylacetic acid samples; theory is 37.2% bromine. Total halogen was found to be 37.0% and bromine was found to be 37.8%.

Registry No. Phenyl(tribromomethyl)carbinol, 38158-81-5; (dibromochloromethyl)phenylcarbinol, 74586-59-7; (bromodichloromethyl)phenylcarbinol, 74586-57-5; α-bromophenylacetic acid, 4870-65-9; α-chlorophenylacetic acid, 4755-72-0; benzaldehyde, 100-52-7; bromoform, 75-25-2; dibromochloromethane, 124-48-1; dichlorobromomethane, 75-27-4; phenyl(tribromomethyl)carbinyl acetate, 13136-09-9; (dibromochloromethyl)phenylcarbinyl acetate, 74586-58-6; (bromodichloromethyl)phenylcarbinyl acetate, 74586-56-4.

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Increased Yield of a Desired Isomer by Equilibria Displacement on Binding to Silica Gel, Applied to *meso*-Tetrakis(*o*-aminophenyl)porphyrin

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Picket-fence porphyrins have been used as model compounds to study a variety of biological processes, including heme oxygen binding,[1] porphyrin photoreactions,[2] and metallations[3,4] in organized media, and interactions of binuclear metal complexes present in enzyme active sites.[5] The fundamental building block for these syntheses has been the α,α,α,α-atropisomer of *meso*-tetrakis(*o*-aminophenyl)porphyrin, the rotational isomer with all four amino groups above the plane of the porphyrin ring. The four possible atropisomers occur at equilibrium in a 1:2:4:1 statistical mixture and are easily prepared by the method of Collman.[6] The α,α,α,α-atropisomer comprises $^1/_8$ of the mixture and is purified by silica gel chromatography. The undesired atropisomers are reequilibrated and chromatographed again; repetition of this cycle allows conversion of most of the mixture into the α,α,α,α-atropisomer. Though this method is effective, it is also quite tedious, and the quantity of α,α,α,α-atropisomer which can be easily prepared is limited. I report a facile isomerization technique which allows conversion of the random mixture of atropisomers into the α,α,α,α-atropisomer in 66% yield.

Because the interconversion of atropisomers is an equilibrium process and the α,α,α,α-atropisomer has the highest affinity for silica gel, the isomerization of atropisomers in the presence of silica gel and a suitable solvent should afford primarily the α,α,α,α-atropisomer. It is preferentially bound and thus the complex has the lowest free energy of the system. The silica gel–porphyrin slurry is then poured to form a chromatography column and eluted to obtain the α,α,α,α-atropisomer. The choice of solvent for the isomerization is crucial since it must conserve the desired most favorable binding of the α,α,α,α-atropisomer at the isomerization temperature.

When $CHCl_3$ was used as the solvent, the α,α,α,α-atropisomer was obtained in random statistical abundance. However, with benzene as the solvent, the mixture of atropisomers was converted into the α,α,α,α-atropisomer in yields of 60–70%. This is to be compared with the maximum theoretical conversion of 12.5% in each cycle of the repetitive chromatography and a maximum overall percent conversion of $100[1 - (7/8)^n]$, where n is the number of cycles performed. This technique should be of general utility for enriching mixtures of isomers in the component having the highest affinity for a given solid phase.[7]

Experimental Section

Reagent-grade benzene (85 mL) and 36 g of E. Merck SI 60 silica gel (230–400 mesh, 500 m^2/g) were added to a 250-mL three-neck round-bottom flask fitted with a nitrogen inlet and a reflux condensor. This was immersed in an oil bath maintained at 75–80 °C, with magnetic stirring and a steady flow of benzene-saturated dry nitrogen gas. After 2 h, 1 g of the mixture of atropisomers of *meso*-tetrakis(*o*-aminophenyl)porphyrin was added to the flask. After an additional 20 h, the dark slurry was cooled to room temperature and then poured into a 53-mm diameter chromatography column. The residual undesired atropisomers were eluted with benzene–anhydrous ether (1:1) until the eluant became pale red in color (about 200 mL), and then acetone–ether (1:1) was used to elute the α,α,α,α-atropisomer. The column effluent was carefully monitored by using TLC analysis (silica gel, benzene–ether (1:1)). The first fraction (215 mg) consisted primarily of the α,α,α,β-atropisomer, the final fraction (660 mg) consisted of the α,α,α,α-atropisomer, and an intermediary fraction (60 mg) consisted of both atropisomers (66% conversion, 93.5% recovery). Slight variations in the amount of benzene or silica gel used, or the duration for isomerization, caused no significant changes in the yield of the α,α,α,α-atropisomer, indicating that equilibrium has been attained. A small aliquot of the recovered α,α,α,α-atropisomer was isomerized to the expected statistical mixture of atropisomers on refluxing in toluene for 30 min. The NMR[8] and visible spectra of the recovered α,α,α,α-atropisomer were identical with those of the α,α,α,α-atropisomer obtained by repetitive chromatography: ^1H NMR (Me_2SO-d_6) δ 8.79 (s, 8 H), 7.69–6.97 (m, 16 H), 4.62 (s, 8 H), −2.78 (s, 2 H); visible spectrum (DMF), 648, 590, 553, 516, 415 nm.

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Registry No. *meso*-Tetrakis(*o*-aminophenyl)porphyrin, 52199-35-6.

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