

Synthesis of O-Ethyl-S-Phenyl-¹⁴C(U)- Ethylphosphonodithioate

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SUMMARY

O-Ethyl-S-phenyl-ethylphosphonodithioate ⁽¹⁾ a broad spectrum soil insecticide ⁽²⁾ was uniformly labeled in the benzene ring with Carbon-14 to expand the residue and metabolism information ⁽³⁾ gained from previous labelings of this compound ⁽⁴⁾.

INTRODUCTION.

The synthesis of O-ethyl-S-phenyl-¹⁴C(U)-ethylphosphonodithioate was initiated with benzene-¹⁴C(U) which was sulfonated with a large excess of 100 % sulfuric acid. The benzene sulfonic acid thus formed was reacted with thionyl chloride to produce benzene sulfonyl chloride. This route to benzene sulfonyl chloride was chosen over direct chlorosulfonation with chlorosulfonic acid because the latter route produced varying amounts of diphenyl sulfone whereas the former route produced none of this impurity.

The benzene sulfonyl chloride was reacted with lithium aluminum hydride, and the resultant dithiophenyl lithium aluminum dichloride complex ⁽⁵⁾ reacted directly with O-ethyl-ethylphosphonochloridodithioate to yield O-ethyl-S-phenyl-¹⁴C(U)-ethylphosphonodithioate. The reaction scheme is illustrated in Figure 1.

EXPERIMENTAL.

Benzene sulfonyl chloride-¹⁴C(U).

Benzene sulfonic acid was prepared by the addition, at 0° C, of 0.68 ml (1,250 mg or 12.8 mmole) of 100 % sulfuric acid to 166 mg (2.13 mmole) of benzene-¹⁴C(U), having a specific activity of 4.7 mC per mmole. The reaction mixture was subsequently stirred at 55° C for one hour. The benzene sulfonic acid solution was chilled to 0° C, 0.925 ml (1,520 mg or 12.8 mmole)

of thionyl chloride added, and the mixture heated at 55° C until the initial turbidity cleared and gas evolution ceased. The reactor was chilled to -5° C and, with good mixing, 2 ml of water added as rapidly as possible while keeping foaming at a minimum. The product was extracted from the reaction medium with two 3 ml washings of diethyl ether. The combined ether extracts were washed repeatedly with 1 ml portions of 15% aqueous sodium carbonate solution until the pH of the wash solution remained unchanged. The ether solution was dried over powdered anhydrous magnesium sulfate and filtered into a 25 ml pearshaped flask. The ether was evaporated to yield 364.9 mg benzene sulfonyl chloride (97% of theory).

A sample was prepared for gas chromatographic analysis by dissolving 1 λ of the product in 100 λ of carbon disulfide. A 1 λ portion of this solution was injected into a Varian Aerograph 204-1B gas chromatography instrument which was fitted with a six foot by 1/4 inch Pyrex column, packed with 3% OV-1 (100% methyl silicone polymer) on 60/80 mesh Gas Chrom Q (silicated diatomaceous earth), a hydrogen flame ionization detector (mass purity) and a Cary Ion Chamber and vibrating reed electrometer (radiochemical purity). The injection port was at 225° C. The column was programmed from 100 to 250° C at 10° C per minute. The hydrogen flame ionization detector and splitter were at 275° C. The ion chamber had a volume of 275 ml and was

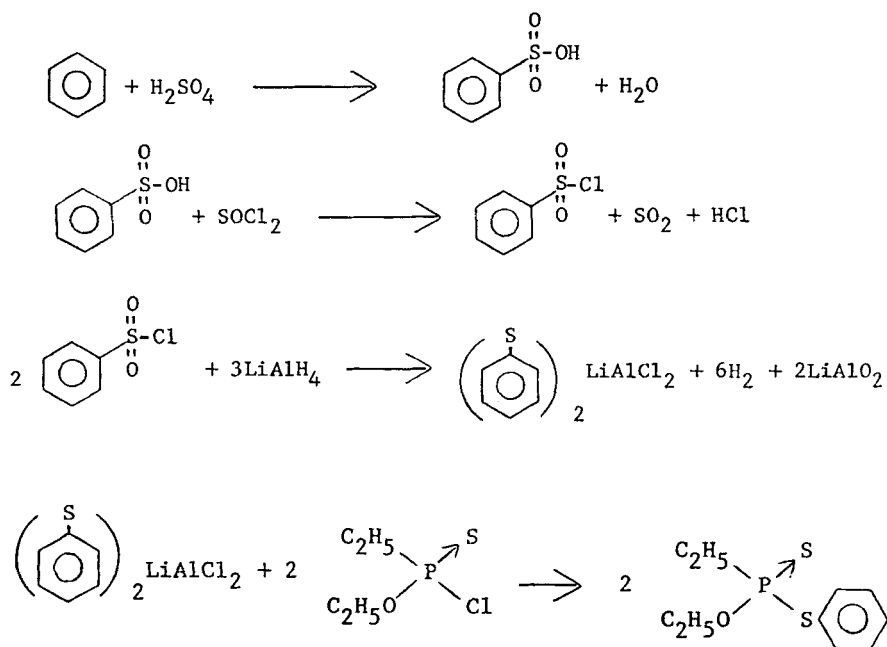


Fig. 1.

held at 290° C. Argon was used as a carrier gas and as an ion chamber purge gas. The resulting chromatogram and radiochromatogram each showed only one peak, that corresponding in retention time to benzene sulfonyl chloride.

The benzene sulfonyl chloride was diluted with tetrahydrofuran to a total volume of 3 ml to form a stock solution for this and other related syntheses.

O-Ethyl-S-phenyl-¹⁴C(U)-ethylphosphonodithioate.

A 2 ml portion of the benzene sulfonyl chloride-¹⁴C(U) stock solution (243.2 mg or 1.38 mmole) was charged to a reactor which was subsequently purged with argon and kept under that atmosphere until completion of the reaction. Lithium aluminum hydride as a five molar solution in diethyl ether (0.85 ml or 4.26 mmole) was added drop-wise with stirring over a period of 30 minutes. The mixture was stirred at reflux for one hour, cooled to room temperature, and the excess lithium aluminum hydride decomposed by the drop-wise addition of methanol until gas evolution ceased. Excess methanol was removed by stripping the mixture to a dry powder using a 40° C water bath and a gentle stream of argon. The powder was suspended in 3 ml of tetrahydrofuran and a solution of O-ethyl-ethylphosphonochloridithioate (309.5 mg, 1.79 mmole) in 0.5 ml of THF was added at 0° C. The mixture was stirred at reflux for 30 minutes after which the tetrahydrofuran was removed and replaced with diethyl ether. The mixture was washed with dilute hydrochloric acid to dissolve the heavy LaAlO₂ precipitate. The ether solution was neutralized by washing with 15 % sodium carbonate solution, dried over magnesium sulfate, filtered into a pear-shaped flask and stripped of solvent to yield 266.5 mg (1.08 mmole or 79 % of theory) of O-ethyl-S-phenyl-¹⁴C(U)-ethylphosphonodithioate. The product had a total activity of 5.2 mC and a specific activity of 4.65 mC per mmole.

A 1 λ portion of the product was diluted with 100 λ of carbon disulfide and 1 λ of this solution was charged each to a gas chromatograph and a thin layer chromatographic plate. The gas chromatograph was run on the same instrument described above, using the same column, detectors, temperatures, carrier gas and purge gas. The gas chromatogram and radiochromatogram showed the radiochemical purity to be 95 %. The thin layer chromatogram was run on a 50 cm by 100 cm Merck plate, precoated with a 250 micron layer of Silica Gel F₂₅₄. Authentic O-ethyl-S-phenyl-ethylphosphonodithioate was spotted on the same plate and the co-chromatogram developed with hexane-chloroform 60/40 for a distance of 5 cm. Visualization with iodine showed one dark spot corresponding to the product and one faint spot corresponding to diphenyl disulfide. The plate was exposed to Kodak no screen medical X-ray film for 30 minutes. Development of the radioautograph disclosed the one dark spot corresponding to the product, one faint spot corresponding to diphenyl disulfide and three unknown lesser impurities.

A subsequent preparative thin layer chromatogram of this product followed by counting of the bands in a liquid scintillation counter disclosed that 93.5 % of the radioactivity was contained in the product band.

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