Preparation of Selectively Deuterated Salen Ligands

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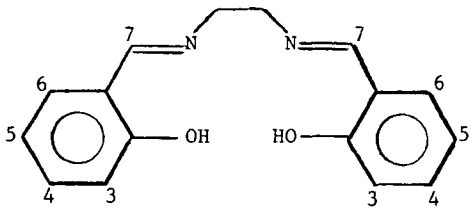
SUMMARY

A number of selectively deuterated derivatives of the common ligand N,N'-ethylenebis(salicylidenimine), salen, have been prepared. The synthesis involves preparation of selectively deuterated salicylaldehydes. Procedures necessary to carry out these syntheses are described below.

INTRODUCTION

As a part of our investigation of the nmr properties of a variety of low spin cobalt(II) Schiff base complexes,[13] it became necessary to prepare several selectively deuterated N,N'-ethylenebis(salicylidenimine), salen, ligands (7). This tetradentate ligand is used very commonly in coordination chemistry. In order to prepare the appropriately deuterated ligands it was necessary to synthesize several deuterated salicylaldehyde derivatives carrying a deuterium atom or atoms on position 3 to 6 of the aromatic ring and on the aldehyde group (6).[5]



7, salen

Deuterium labeling techniques on an aldehyde group are in general quite well known.[1-8] The most common procedure for this purpose involves activation of the aldehyde proton by converting the aldehyde group to a dithioketal. The activated proton becomes acidic enough so that the corresponding anion can be generated by treatment with a strong base such as n-butyllithium. Subsequent treatment of the anion with deuterium oxide followed by removal of the dithio-

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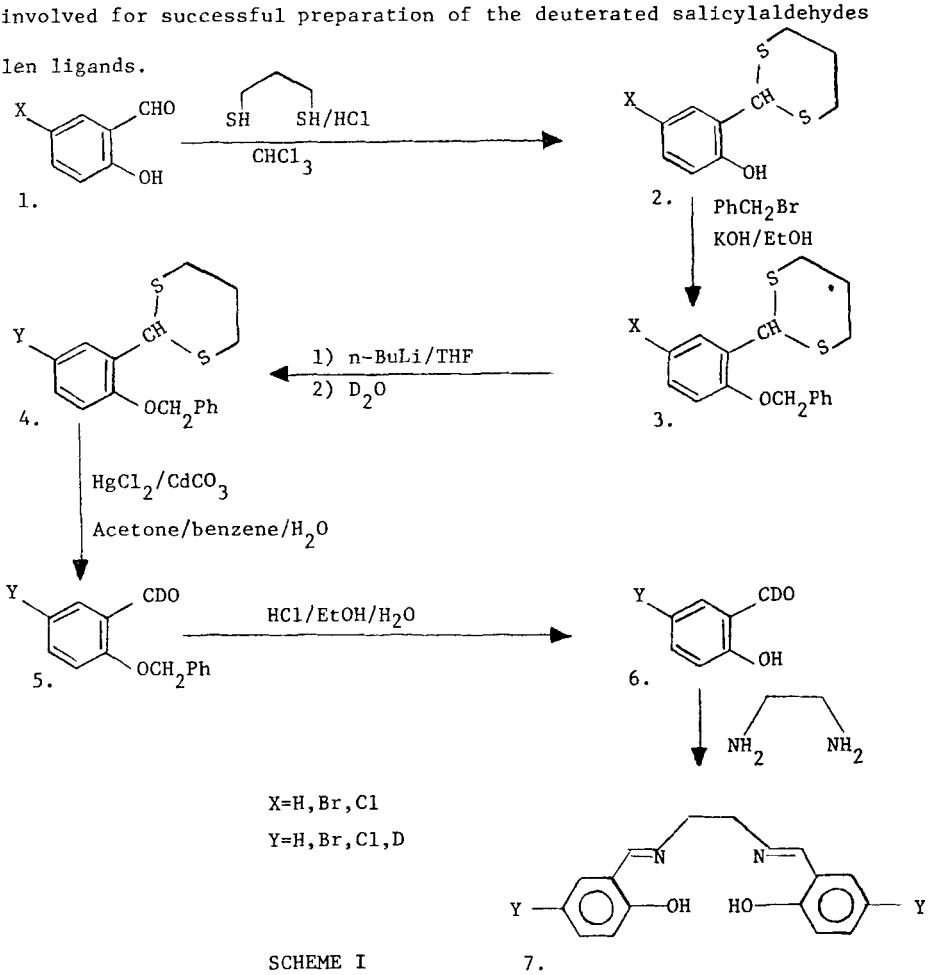
ketal group gives the deuterated aldehyde.[1,2] The general procedure has been successfully applied to the salicylaldehyde molecule. It was necessary to initially block the phenolic group by converting it to a benzylether prior to the n-butyllithium reaction. This sequence of reactions has been carried out to synthesize 1-d-salicylaldehyde and the deuterated N,N'-ethylenebis(salicylideneimine) ligand. 1-d-5-bromosalicylaldehyde and 1-d-5-chlorosalicylaldehyde and the corresponding ligand have been synthesized similarly using the corresponding halogen substituted salicylaldehyde derivatives as starting material. 1,5-di-d-salicylaldehyde can be synthesized from either 5-halosalicylaldehydes by employing excess n-buthyllithium. The reaction of aryl halides with n-butyllithium has been used previously in the synthesis of benzene 1-d.[9] Scheme I summarizes the steps involved for successful preparation of the deuterated salicylaldehydes and salen ligands.



SCHEME I

EXPERIMENTAL

The syntheses of all compounds 7 (Y=H,Cl,Br,D) are carried out as described below for 7,7'di-d-N,N'-ethylenebis(salicylidenimine). The intermediates except 5 and 6 were characterized by elemental analyses, mass spectroscopy, nuclear magnetic resonance, and infrared spectroscopy.

Preparation of 2-(2'-Hydroxphenyl)-1,3-Dithiane (2;X=H)[1,2,10,11]

Dry hydrogen chloride was bubbled rapidly into a solution of 1,3-propanedithiol (10.8g, 0.10 mole) and salicylaldehyde (12.2g, 0.10 mole) in chloroform (50 ml) until the mixture was saturated (5 min). The solution immediately became cloudy and was dried with anhydrous calcium sulfate. After standing 1 hour the mixture was washed with two 50 ml portions of water, filtered through anhydrous sodium sulfate, and the solvent evaporated on a rotary evaporator. The residue was treated with charcoal and crystallized from carbon tetrachloride affording 18.5g (87%) of 2(X=H), m.p. 130-131°C, NMR($CDCl_3$/TMS)δ 1.7-2.3(m, 2,CH_2), 2.7-3.2(m, 4,CH_2), 5.45 (s,1, methine), 6.44(s,1,OH), 6.7-7.5(m,4,aryl); mass spectrum (70ev) m/e(rel intensity) 212(m^+,84), 138(100).

Preparation of 2-(2'-Benzyloxyphenyl)-1,3-Dithiane(3;X=H)

2-(2'-Hydroxyphenyl)-1,3-Dithiane (2;X=H) (17.0g; 0.08 mole) was dissolved in 0.5 molar ethanolic potassium hydroxide solution (180 ml; 0.09 mole) and ethanol (220 ml) was added. The solution was treated with benzylbromide (13.7g; 0.08 mole) and then refluxed for 1 hour. The progress of the reaction is shown by the precipitation of potassium bromide. During the reaction water (50 ml) was slowly added to dissolve the potassium bromide. After 1 hour the mixture was reduced to a total volume of 100 ml on a rotary evaporator and extracted with two 100 ml portions of chloroform. The combined chloroform extract was washed with two 100 ml portions of water, filtered through anhydrous sodium sulfate and evaporated on a rotary evaporator. The residue was treated with charcoal and crystallized from a 1:1 carbon tetrachloride-high boiling petroleum ether mixture to furnish colorless crystals, 20.0g(80%) of 3(X=H), m.p. 104-105°C,NMR(CDl_3/TMS)δ 2.8-2.3(m,2,CH_2), 2.7-3.2(m,4, CH_2), 5.10(s,2,OCH_2), 5.75(s,1,methine), 6.8-7.7(m,4,aryl); mass spectrum (70ev) m/e(rel intensity) 302(m^+, 4), 212(80), 138(100), 137(90).

Preparation of 2(2'-Benzyloxyphenyl)-1,3-Dithiane-2-d(4;Y=H)[1,2]

A solution of 2-(2'-benzoyloxyphenyl)-1,3-dithiane(3;X=H) (9.06g; 0.03 mole) in anhydrous tetrahydrofuran (50ml) in a dry ice acetone bath was stirred under nitrogen while a 2.4 M solution of n-butyllithium in hexane (18.8 ml; 0.045 mole) was added in a dropwise fashion. After 1 hour the solution was warmed to 0°C and treated slowly with deuterium oxide (1g; 0.05 mole) under nitrogen. The reaction mixture was warmed to room temperature and neutralized with dilute hydrochloric acid. Tetrahydrofuran was removed on a rotary evaporator. The residue was shaken with chloroform after which the organic phase was separated and washed successively with sodium bicarbonate solution and water and then dried over anhydrous sodium sulfate. After evaporation of solvent, the residue was crystallized a 1:1 mixture of carbon tetrachloride/high boiling petroleum ether to give 7.7g(85%) of 4(Y=H), m.p. 104-105°C, NMR($CDCl_3$/TMS) δ 1.8-2.3(m, 2, CH_2), 2.7-3.2 (m,4,CH_2), 5.10(s,1,OCH_2), 6.8-7.7(m,4,aryl). NOTE: At this point if 2(2'-benzyloxy-5-halophenyl)-1,3-dithiane[2] (3;X=halide) is employed, two equivalents of n-butyllithium can be employed to produce compound 4;Y=D.

Preparation of 2-Benzyloxybenzaldehyde-1-d(5;Y=H)[10,11]

To a solution of 2-(2'-benzyloxyphenyl)-1,3-dithiane-2-d (4;Y=H)(3.03g; 0.01 mole) in a mixture of acetone (40ml), benzene (20ml), and water (4ml) was added solid cadmium carbonate (6.9g; 0.04 mole) and solid mercuric chloride (10.0g; 0.04 mole). The mixture was refluxed overnight, filtered, and the solvent removed on a rotary evaporator. Chromatography of the residue on silica gel with chloroform gave a crude product (1.1g; 52%) 5(Y=H) as a pale yellow liquid which was used in the next reaction without further purification.

Preparation of 1-d-Salicylaldehyde (6; Y=H)

2-Benzyloxybenyaldehyde-2-d(5; Y=H) (1.1g; 0.005 mole) was dissolved in absolute ethanol (5 ml) and concentrated hydrochloric acid (10 ml) was added. The solution was refluxed overnight and then neutralized with 10 percent sodium hydroxide. The mixture was washed with carbon tetrachloride to remove benzyl-chloride and the alkaline solution was acidified with dilute hydrochloric acid. The acidic solution was extracted with carbon tetrachloride and the organic

phase was washed with water, filtered through anhydrous sodium sulfate and then evaporated to give 0.55g(87%) of 6(Y=H), NMR($CDCl_3$/TMS)δ 7.3-8.2 (m,4, aryl), 11.5(s,1,OH). This compound was used directly to prepare 7 through Schiff base condensation with ethylenediamine.

Preparation of 7,7'-di-d-N,N'-ethylenebis(salicylidenimine), (7;Y=H)

This compound was prepared directly from 6 by Schiff base condensation with ethylenediamine.[12]

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