SYNTHESIS OF CYCLOPENTADIENYL-X-^{13}C THALLIUM

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SUMMARY

Cyclopentadienyl thallium has been prepared with one carbon position labeled at a concentration greater than 90 atom % carbon-13. A new method for incorporating a carbon-13 label into cyclopentadiene is reported which relies on the reaction of the di-Grignard reagent of 1,4-dibromobutane with isopropyl formate-^{13}C. The product of this reaction, cyclopentanol-1-^{13}C, is converted to cyclopentadienyl-X-^{13}C thallium.

INTRODUCTION

The potential for obtaining high resolution carbon-13 nuclear magnetic resonance spectra of organometallic compounds containing cyclopentadiene remains relatively unexplored. For highly soluble compounds, the use of natural abundance carbon-13 materials may well be suitable. However, the low solubility of many cyclopentadienyl-containing organometallic compounds, as well as the presence of line broadening effects in paramagnetic species, could easily drive signal averaging times to prohibitive levels. For this reason, a method was devised for synthesizing cyclopentadiene enriched in carbon-13. Preparative routes to cyclopentadiene-X-^{14}C [1,2] have not been applied to date for the labeling of carbon-13 analogs. The conversion of cyanide-^{14}C to doubly labeled adipic acid has been described by Pajaro and Baldi [1]. Carbon-14 methods involve the transformation of adipic-1,6-$^{14}C_2$ acid to

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cyclopentanone-1-^{14}C and necessarily involve the loss and recovery of one-half of the label. In contrast, a more direct method of isotope incorporation is outlined here and involves a two-step conversion of carbon-^{13}C monoxide to cyclopentanol-1-^{13}C as an intermediate in the preparation of cyclopentadienyl-X-^{13}C thallium.

RESULTS

The reaction sequence in Fig. 1 represents the overall conversion of carbon-^{13}C monoxide to cyclopentadienyl-X-^{13}C thallium. The reaction of carbon-^{13}C monoxide with isopropyl alcohol in the presence of sodium isopropoxide affords good yields of isopropyl formate-^{13}C. This represents an attractive route to this compound, since the reaction can be carried out under moderate pressures and the unreacted carbon-^{13}C monoxide can be recovered. Slightly less than two equivalents of magnesium are consumed when allowed to react with 1,4-dibromobutane, indicating that a di-Grignard reagent is present prior to addition of the formate ester. Upon hydrolysis, a crude product is obtained which contains cycloopentanol and other unidentified

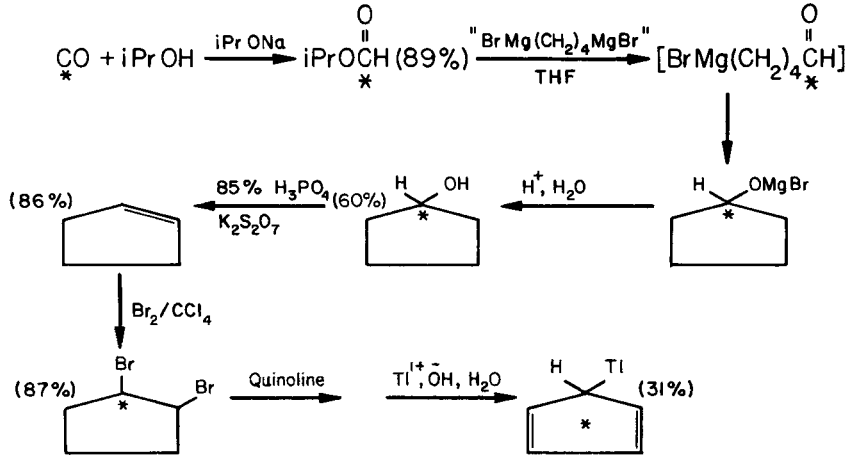

Figure I. The reaction sequence for the overall conversion of carbon-^{13}C monoxide to cyclopentadienyl-X-^{13}C thallium.

higher boiling materials. Based on a 1:1 stoichiometry, yields are approximately 30%. When the ratio of the di-Grignard reagent to ester is changed to ca. 3:1, the yield of cyclopentanol increases to 55-60%.

The conversion of cyclopentanol to cyclopentadiene has been described elsewhere [1-3]. We obtained cyclopentene in 70-75% yield from cyclopentanol in 85% phosphoric acid. We have found that the yields of this reaction could be increased to 80-85% by employing potassium pyrosulfate in 85% phosphoric acid.

1,2-Dibromocyclopentane is obtained from the bromination of cyclopentene in carbon tetrachloride. Cyclopentadiene is obtained in low yields from the dehydrohalogenation of 1,2-dibromocyclopentane using various reagents. In most cases, production of cyclopentadiene was facilitated by adding the dihalide dropwise to the dehydrohalogenation reagent. Reagents [4] used in this study and elsewhere for the dehydrohalogenation step are outlined in Table I.

TABLE I. Reagents for the dehydrohalogenation of 1,2-dibromocyclopentane.

Reagent(s)	Yield	Reference
Lithium bromide, lithium carbonate,) dimethylformamide)	20-25	This work
Diazobicyclo[5.4.0]undecene-5	25-30	This work
Quinoline	28-30	This work, 2,3
8-Hydroxyquinoline	30-36	This work, 2
Calcium oxide (tube furnace)	70-75	5
Barium oxide (tube furnace)	0	This work

DISCUSSION

The conversion of cyclopentadiene to cyclopentadienyl thallium affords good yields of this material [6]. The salt is only slightly air-sensitive

and can be stored under an inert atmosphere almost indefinitely. In addition, it is not subject to dimerization as is cyclopentadiene, and it is a valuable precursor in the synthesis of cyclopentadiene containing organometallic compounds.

A comparison of the efficiency of the overall conversion of cyanide-^{14}C to cyclopentanol-1-^{14}C with the method outlined here gives the respective values of 78% [1] and 53%. The adipic acid route includes recovery of the label in the form of carbon dioxide. In contrast, the label is recovered here in its original form and involves a simplified procedure.

The reaction of the di-Grignard reagent leading to a cyclized product is somewhat unique, since smaller chain analogs undergo elimination to form olefins and larger chain analogs favor intermolecular processes [7-10]. Although the ratio of the reactants in the Grignard reaction was varied, optimization of other experimental parameters (e.g., temperature, solvent, concentration) was not carried out.

Various methods for the dehydrohalogenation of 1,2-dibromocyclopentane were employed by Brooks [2], as well as by Trachuk and Lee [3]. Adequate production of cyclopentadiene from the dihalide on a micro scale has been reported by Vercier [5] using calcium oxide in a tube furnace. Modification of this method employing barium oxide under similar conditions results in no product.

EXPERIMENTAL

General -- Carbon-^{13}C monoxide was obtained from the Los Alamos Scientific Laboratory Isotope Separation Facility (Group CNC-4). Anhydrous Dowex-50 (H^+) was prepared by washing the resin (H^+ form) with absolute ethanol, followed by several successive evaporations of benzene in a rotary evaporator. Glc analyses were performed on a Varian Aerograph equipped with columns containing

Poropak Q and FFAP on chrom-W. NMR spectra were recorded on a Perkin-Elmer R-24 instrument, and proton chemical shifts are reported with respect to TMS (external standard). Infrared spectra were recorded on a Perkin-Elmer 521 instrument. All tetrahydrofuran (THF) was distilled with lithium aluminum hydride prior to use.

Isopropyl formate-^{13}C -- Sodium metal (1.0 g) was dissolved in isopropyl alcohol (380 mℓ), and this solution was placed in a dry one-liter Hastalloy autoclave. Carbon-^{13}C monoxide (91% carbon-13 containing 12% methane) was introduced to an initial total pressure of 6.0 MPa (5.3 MPa carbon monoxide, 1.3 mol). This mixture was stirred for three days at room temperature, and during this time the pressure dropped to an equilibrium value of 1.1 MPa. The residual carbon-^{13}C monoxide (0.97 MPa carbon monoxide, 0.24 mol) was recovered by venting the autoclave through a Dry Ice-acetone trap to a storage cylinder. After draining the autoclave, sodium ion was removed from the recovered solution by stirring with anhydrous Dowex-50 (H^+) (150 mℓ) for one hour. The mixture was filtered and fractionated employing a spinning band column (52-53°, 77.7 Pa) to give 93 g of material which contained ca. 90 wt % of isopropyl formate-^{13}C (89% yield based on recovered carbon monoxide) and 10 wt % isopropyl alcohol by glc. This mixture was used as such in the following step of this synthesis: NMR (neat, δ): 0.94 [d, $(CH_3)_2CH$]; 4.77 [m, $(CH_3)_2CH$]; 7.68 [d, CHO, J_{C-H} = ca. 223 Hz].

Cyclopentanol-1-^{13}C -- Magnesium metal turnings (60 g) and THF (1.0 liter) were placed in a three-liter round-bottom flask flushed with argon and equipped with a reflux condenser, addition funnel, and mechanical stirrer. 1,4-Dibromobutane (90 mℓ, 0.75 mol) was added at a rate to maintain a gentle reflux. After the reflux had ceased, stirring was continued for two hours, and an additional amount of THF (0.8 liter) was added. A solution of isopropyl formate-^{13}C (22.7 g, 0.23 mol containing ca. 10% isopropyl alcohol) in THF (250 mℓ) was

added dropwise with stirring over a period of three hours. The reaction mixture was hydrolyzed by the careful addition of small aliquots of a saturated aqueous solution of ammonium sulfate (ca. 0.2 liter). The reaction mixture was transferred to a four-liter beaker containing water (0.5 liter). The THF layer was decanted and dried over anhydrous potassium carbonate and sodium sulfate, and the excess solvent was removed with a rotary evaporator. The residue (ca. 50 mℓ) was dried over anhydrous potassium carbonate and transferred to a 100-mℓ flask where the excess solvent was removed by distillation, and the resulting residue was fractionated under reduced pressure. Cyclopentanol-1-^{13}C was obtained (41-43°, 80 Pa, n_d 1.4412-1.4507, 12.1 g, ca. 60% yield) and was used without further purification. NMR (neat, δ): 1.62 [m, ring C$\underline{H}_2$]; 4.32 [m, C$\underline{H}$OH, J_{C-H} = ca. 146 Hz]; 3.95 [s, CHO$\underline{H}$].

1,2-Dibromocyclopentane-1-^{13}C -- Cyclopentanol-1-^{13}C (9.1 g, 0.1 mol), 85% phosphoric acid (40 g), potassium pyrosulfate (24 g), and a stirring bar were placed in a 100-mℓ pear-shaped flask. The flask was fitted with a small condenser connected to a receiving vessel which was immersed in a Dry Ice-acetone bath. The contents were stirred and slowly heated to 85-90°. Cyclopentene began to distill at 37-40° (79.2 Pa), and after initial frothing had subsided the temperature of the contents was raised from 90° to 140°. The cyclopentene distillate (6.2 g, 86% yield) was dried over calcium sulfate, dissolved in carbon tetrachloride (100 mℓ), transferred to a 250-mℓ round-bottom flask, and chilled in a Dry Ice-acetone bath. A solution of bromine (16 g, 0.1mol) in carbon tetrachloride (ca. 100 mℓ) was added slowly via an addition funnel with cooling. The excess solvent and bromine were removed on a rotary evaporator, and distillation of the residue gave 17.9 g (87% yield) of 1,2-dibromocyclopentane-1-^{13}C (49-51°, 40 Pa). NMR (neat, δ): 1.6-3.1 [m, ring C$\underline{H}_2$]; 4.56 [m, C$\underline{H}$Br, J_{C-H} = ca. 165 Hz].

Cyclopentadienyl-X-^{13}C thallium -- Freshly distilled quinoline (15 mℓ),

hexamethylphosphoric triamide (20 mℓ), and a stirring bar were placed in a 50-mℓ round-bottom flask with a side arm fitted with a serum stopper. The flask was equipped with a micro condenser and receiving vessel placed in crushed ice. The temperature of the contents was raised to 185-190°. 1,2-Dibromocyclopentane-1-^{13}C (6.7 g, 0.025 mol) was introduced dropwise with rapid stirring by means of a syringe. A second syringe containing ethanol was used intermittently to flush the apparatus of any undistilled product during addition of the dihalide. The distillate was added to an aqueous solution containing potassium hydroxide (10 g) and thallous acetate (7.1 g, 0.027 mol), stoppered, and shaken vigorously. The contents were chilled in an ice bath, and the precipitate was filtered, washed with water, cold methanol, and air-dried. Upon sublimation (85-100°, 1.3 Pa), cyclopentadienyl thallium (2.1 g, 31% yield) was obtained. The sublimate can be stored under refrigeration in an inert atmosphere almost indefinitely. The overall yield based on carbon-^{13}C monoxide is 12%. Anal: Calcd. for C_5H_5Tl, C, 22.54; H, 1.86. Found: C, 22.62, H, 1.74; Ir: KBr disk, 1000 cm^{-1}, 732 cm^{-1}.

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