

SYNTHESIS OF 1-¹³C-1-INDANONE and 2-¹³C-1,2,3,4-TETRAHYDROQUINOLINE

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SUMMARY

The synthesis of 2-¹³C-1,2,3,4-tetrahydroquinoline (5) via 1-¹³C-3-phenylpropanoic acid (1), 1-¹³C-1-indanone (2), 1-¹³C-1-indanone hydrazone (3) and 2-¹³C-3,4-dihydro-2(1H)-quinolinone (4) proceeded in 78, 96, 95, 79, and 85% individual yields respectively for 1, 2, 3, 4, 5 and 61% overall yield of the latter from 1.

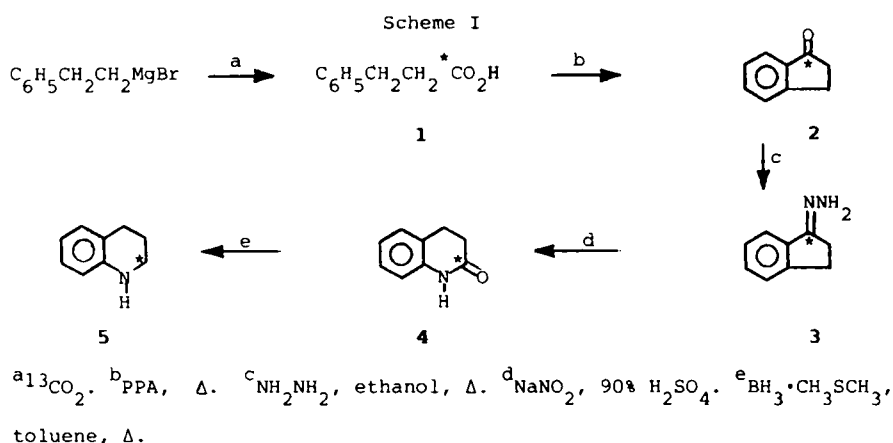
Key Words: 1-¹³C-1-indanone, 1-¹³C-1-indanone hydrazone, 2-¹³C-3,4-dihydro-2(1H)-quinolinone, 1-¹³C-3-phenylpropanoic acid, 2-¹³C-1,2,3,4-tetrahydroquinoline.

INTRODUCTION

The chemistry of coal liquefaction is of considerable current interest. One approach to gaining an understanding of the role of solvents in the liquefaction process is to study the reactions of well-defined solvents with coal at liquefaction conditions. A second is to use these solvents with model compounds which represent bond-types that are likely to be present in coal. We have prepared several solvents and related compounds bearing a specific ¹³C label (1-¹³C-sym-octahydrophenanthrene, 1-¹³C-phenanthrene, (9-¹³C-methyl)phenanthrene, 1-¹³C-1-phenol) for use in these studies (1). An all-metal apparatus, essential to this work, has been described (2). These labeled compounds were used to study solvent, solvent-solvent, and solvent-coal reactions including isomerization, cracking, adduction, and hydrogen-transfer reactions (3-6).

Because 1,2,3,4-tetrahydroquinoline has been shown to be an effective

hydrogen-transfer solvent, it was used in a series of coal liquefaction experiments (7). However, it was observed to react excessively with coal-derived intermediates (8). Therefore, to extend the study, we prepared 1-¹³C-3-phenylpropanoic acid (1) for use in a synthetic series which included 1-¹³C-1-indanone (2), its hydrazone (3), 2-¹³C-3,4-dihydro-2(1H)-quinolinone (4) and terminated with 2-¹³C-1,2,3,4-tetrahydroquinoline (5) as presented in Scheme I and described in the experimental section. Since several specifically labeled intermediates were prepared, the route obviously is adaptable to other uses.



EXPERIMENTAL

1-¹³C-3-Phenylpropanoic Acid (1) (9). In a 500 mL, 3-necked flask were placed 10.5 g (0.43 mol) of magnesium turnings (10), a Teflon-coated magnetic stirring bar, and 75 mL of anhydrous ethyl ether. To this mixture, under N₂ (11), was added approximately 5 g of 2-phenylethyl bromide. After the reaction initiated, stirring was started and the remaining 2-phenylethyl bromide (80 g, 0.43 mol diluted with an equal volume of anhydrous ethyl ether) was added dropwise over a period of 30 min. After addition was complete, reflux was maintained for 2 h.

The Grignard reagent, under N₂ pressure, was transferred to a stainless steel reactor (2). After cooling the reactor to -78 °C, using a Dry Ice/acetone bath, ¹³CO₂ (12) gas was added at 20 psi. After addition was complete at

-50 °C, the reaction mixture was allowed to warm to room temperature. The unreacted ¹³CO₂ was recovered as Ba¹³CO₃ by bubbling into a Ba(OH)₂ solution.

The reaction vessel was removed and its contents were poured onto ice. The mixture was acidified with conc. HCl and then extracted with ethyl ether (3 x 250 mL). The combined ether extracts were washed with 5% NaOH solution, dried (MgSO₄), filtered, and concentrated to 9.3 g of neutral products.

The alkali wash was acidified with conc. HCl and extracted with ethyl ether (3 x 250 mL). The organic layer was dried (MgSO₄), filtered, concentrated, and Kugelrohr distilled to give 52.3 g (78%) of **1** as white crystals: mp 47-48 °C (lit. (13) 46.5-48.5 °C for unlabeled acid); ¹H-NMR (CDCl₃) δ 11.76 (br s, 1H, CO₂H), 7.18-7.36 (m, 5H, ArH), 2.88-3.00 (m, 2H, CH₂CO₂H), 2.7 (q, 2H, J = 3 Hz, C₆H₅CH₂); ¹³C-NMR (CDCl₃) ppm 179.4, 140.1, 139.9, 128.4, 128.2, 126.2, 36.7, 36.5, 30.6, 30.5; IR (melt) cm⁻¹ 3030 (CO₂H), 1710 (C=O), 755, 705 (Vinyl H bend); MS m/e (relative intensity) 151.1 (M⁺, 29), 105.1 (20), 104.1 (51), 91.1 (100).

1-¹³C-1-Indanone (2). The labeled acid **1** (40.9 g, 0.27 mol) was added to 1400 g of preheated (60 °C) polyphosphoric acid. The vigorously stirred mixture was maintained at 60 °C for 1.5 h and then poured over ice with stirring to yield white crystals. These were dissolved in ether and added to the ether extract of the reaction mixture. The extracts were washed (2x) with 5% NaOH. The NaOH washings were acidified with conc. HCl and extracted with ethyl ether (3x), dried (MgSO₄), filtered, and concentrated to yield 3.1 g of recovered **1**.

The ether layer containing **2** was dried (MgSO₄), filtered, concentrated and Kugelrohr distilled to give 34.6 g (96%) of ketone **3**: mp 40-41 °C (lit. (14) 42 °C for unlabeled ketone); ¹H-NMR (CDCl₃) δ 7.72 (d, 1H, J = 3 Hz, ArH), 7.56 (t, 1H, J = 3 Hz, ArH), 7.46 (d, 1H, J = 3 Hz, ArH), 7.34 (t, 1H, J = 3 Hz, ArH), 3.1 (m, 2H, ArCOCH₂), 2.64 (m, 2H, C₆H₅CH₂); ¹³C-NMR (CDCl₃) ppm 206.2, 154.6, 154.5, 136.7, 136.0, 134.2, 127.0, 126.9, 126.5, 126.4, 126.3, 36.8, 35.2, 25.7; IR (melt) cm⁻¹ 1705 (C=O); mass spectrum m/e (relative intensity) 133.1 (M⁺, 100), 132.1 (21.1), 105.2 (11.2), 104.1

(96), 103.1 (43.7), 102.1 (8.1), 78.1 (31.5), 77.0 (23.7), 76.0 (16.4), 63.0 (7.1), 50.0 (21.5).

1-¹³C-1-Indanone Hydrazone (3). The hydrazone **3** was prepared by refluxing **2** (20 g, 0.15 mol) with a 2 mol equivalent of 85% hydrazine hydrate (17.1 g, 0.3 mol) in ethanol for 12 h. The reaction mixture was then poured into ice water and extracted 3x with ethyl ether. The ether layer was dried (MgSO₄), filtered, and concentrated to 21 g (95%) of white crystals (turned yellow on standing) of **3**: mp 86-87 °C (lit. (15) 84-86 °C for unlabeled hydrazone); ¹H-NMR (CDCl₃) δ 7.63 (m, 1H, ArH), 7.24 (m, 3H, ArH), 7.18 (d, 2H, NH₂), 3.03 (m, 2H, CH₂), 2.59 (m, 2H, CH₂); ¹³C-NMR (CDCl₃) ppm 156.4, 128.8, 126.7, 126.5, 125.1, 124.9, 120.5, 120.4, 28.3, 25.5, 24.0; IR (Nujol) cm⁻¹ 3410, 3230, 1630; mass spectrum m/e (relative intensity) 147.1 (M⁺, 100), 146.1 (40.9), 130.1 (20.9), 129.0 (12.7), 118.1 (13.6), 116.6 (26.3); exact mass (M⁺) 147.0870, required for C₈¹³CH₁₀N₂ (M⁺) 147.0877.

2-¹³C-3,4-Dihydro-2(1H)-quinolinone (4). Sulfuric acid (25 mL of 90 %) was placed in a tall, narrow container and cooled (ice/water bath) to 10 °C. Sodium nitrate (2.0 g, 0.029 mol) was added slowly so that the temperature did not exceed 15 °C. Ground **3** (2.94 g, 0.02 mol) was added portionwise to the well-stirred and cooled solution of nitrosyl sulfate at such a rate that the solution did not foam out of the container. The addition was complete in 45 min and the temperature was not allowed to exceed 15 °C. The solution was stirred for 30 min and then poured onto a slurry of ice and 60 mL of conc. ammonium hydroxide. The resulting slurry was filtered and dried under vacuum to yield 1.7 g of **4**.

The filtrate was extracted twice with ethyl ether, the ether layer was dried (MgSO₄), filtered, and concentrated to an additional 0.65 g (total yield 79%) of **4**. Recrystallization gave white crystals of **4**: mp 164 °C (lit. (15) 163-164 °C for unlabeled amide); ¹H-NMR (CDCl₃) δ 9.42 (s, 1H, NH), 7.18 (t, 2H, ArH), 7.0 (t, 1H, ArH), 6.84 (d, 1H, ArH), 2.88 (m, 2H, CH₂), 2.65 (m, 2H, CH₂); ¹³C-NMR (CDCl₃) ppm 172.3, 137.2, 127.6, 127.2, 123.4, 122.8, 115.6, 31.6, 29.6, 25.3, 25.2; IR (Nujol) cm⁻¹ 3200, 1675;

mass spectrum m/e (relative intensity) 148.1 (M^+ , 100), 174.1 (10), 146.1 (8), 129.1 (17.4), 104.1 (45.1): exact mass (M^+) 148.0745, required for $C_8^{13}CH_9NO$ (M^+) 148.0718.

2-¹³C-1,2,3,4-Tetrahydroquinoline (5). A 5.6 g sample of 4 dissolved in 100 mL of dry toluene was placed in a 250 mL flask under a nitrogen atmosphere (11). Borane-methyl sulfide (50 mL, 0.04 mol, toluene, Aldrich) was then added dropwise over a period of 30 min. The dimethyl sulfide was distilled and collected. Reflux was maintained for 1.5 h after the temperature reached 100 °C. The cooled reaction product was hydrolyzed using conc. HCl, extracted twice with ethyl ether and the ether extract was dried ($MgSO_4$), filtered, and concentrated to 0.6 g of neutral material.

The aqueous layer was made basic by addition of 10% NaOH, extracted with ethyl ether (3x) and the ether extract was dried ($MgSO_4$), filtered and concentrated. Kugelrohr distillation of the crude product yielded 4.3 g (85%) of 5 as a clear liquid: bp 90 °C/0.4 torr (lit. (16) bp 251 °C/760 torr for unlabeled amine; ¹H-NMR ($CDCl_3$) δ 6.94 (t, 2H, ArH), 6.59 (t, 1H, ArH), 6.42 (d, 1H, ArH), 3.44 (t, 2H, $ArCH_2$), 2.99 (t, 1H, NH), 2.51 (m, 2H, NCH_2), 1.90 (m, 2H, $CH_2CH_2CH_2$); ¹³C-NMR ($CDCl_3$) ppm 144.4, 129.0, 126.3, 120.9, 116.4, 113.8, 41.7, 26.8, 22.1, 21.8; IR (Film) cm^{-1} 3400, 1605; mass spectrum m/e (relative intensity) 134.1 (M^+ , 89), 133.1 (100), 131.1 (22), 130.1 (54.7), 119.1 (22), 118.1 (20), 104.0 (9.3), 103.0 (10.7), 102.0 (9.0), 78.1 (12.7), 77.1 (18.1); exact mass (M^+) 134.0939, required for $C_8CH_{11}N$ (M^+) 134.0925.

ACKNOWLEDGEMENTS

The described compounds were prepared for Gulf Research and Development Company for use under DOE contract DE-FG22-82PC50782. We thank them and the Oklahoma State University Center for Energy Research for support. The help of Dr. Donald C. Cronauer and his colleagues of Gulf Research and Development Company is gratefully acknowledged.

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9. All glassware was heated overnight at 125 °C, assembled hot, and allowed to cool under a dry nitrogen flow.
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11. Nitrogen, dried by passing through molecular sieves that had been activated by heating overnight at 320 °C under vacuum.
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