Synthesis of *p*-Methylacetophenone-1-^{14}C

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In connection with a carbon-14 isotope effect study [1] of the peracid oxidation of a series of *p*-substituted acetophenones, it became necessary to synthesize 1-ring labeled *p*-methylacetophenone. Since toluene-4-^{14}C was not available or easy to synthesize, the usual Friedel-Crafts acylation could not be used. Accordingly, the following synthesis involving reaction of dimethyl sulfate with the Grignard reagent prepared from the ethylene glycol ketal of *p*-bromoacetophenone-1-^{14}C was developed.

p-Bromoacetophenone-1-^{14}C was prepared by the Sandmeyer method [2] from *p*-aminoacetophenone-1-^{14}C, which had been prepared from the corresponding nitro compound by low pressure catalytic hydrogenation. The *p*-nitroacetophenone-1-^{14}C had been prepared from the commercially available *p*-nitrobenzoic-1-^{14}C acid by reaction of its acid chloride with ethoxymagnesiomalonic ester and subsequent cleavage by the method of Bowman [3].

The general method developed by Sulzbacher, Bergman, and Pariser [4] was adapted for the preparation of the ethylene glycol ketal of *p*-bromoacetophenone-1-^{14}C. *p*-Bromoacetophenone-1-^{14}C, 59.2 g (0.30 mole), was dissolved in 400 ml of dry benzene, and 125 ml of ethylene glycol and 0.5 g of *p*-toluenesulfonyl chloride were added. This mixture was refluxed for 24 hours with water being collected in a Dean-Stark type collector. The mixture was washed with a sodium bicarbonate solution to remove the catalyst and the excess ethylene glycol. The benzene was removed by distillation. The reaction mixture was vacuum distilled to give 69.5 g (95.9 % yield) of the ethylene glycol ketal of *p*-bromoacetophenone-1-^{14}C, b. p. 119° C (5 mm). No reported physical constants for this compound could be found. The nmr spectrum is consistent with that expected for the ketal : $\delta \overset{CDCl_3}{TMS}$, 1.61 (s, 3 H, C-$CH_3$), 3.90 (m, 4 H, C-O-$CH_2$-$CH_2$-O), 7.42 (s, 4 H, BrC_6H_4C).

Smith's method [5] for the conversion of bromomesitylene to isodurene was adapted for the conversion of the ethylene glycol ketal of *p*-bromoacetophenone-1-^{14}C to *p*-methylacetophenone-1-^{14}C. A one liter, three-necked flask was equipped with an overhead stirrer, condenser, and pressure equalized dropping funnel. Clean magnesium, 3 g (0.11 mole), was added and covered with 75 ml of freshly distilled tetrahydrofuran. A few drops of methyl iodide was added to initiate the reaction. After the reaction had been initiated, 0.1 mole of the ethylene glycol ketal of *p*-bromoacetophenone-1-^{14}C in 100 ml of tetrahydrofuran was added dropwise with stirring and heating. When

the reaction was complete, an excess of freshly distilled, dried dimethyl sulfate in 70 ml of tetrahydrofuran was added slowly to the Grignard reagent. The solution was refluxed for 2 hours, cooled, and dilute hydrochloric acid was added. The tetrahydrofuran was removed by steam distillation. The product was extracted into chloroform, the chloroform was removed, and the product was vacuum distilled to give 9.5 g (71 % yield) of *p*-methylacetophenone-1-^{14}C, b. p. 85° C (4 mm), reported [6] b. p. 93-94° C (7 mm).

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