SYNTHESIS OF *p*-BENZOHYDROQUINONE-1, 3, 5-C_3^{13}

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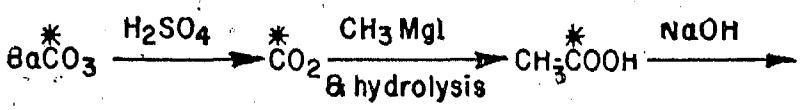
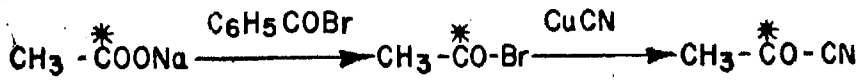
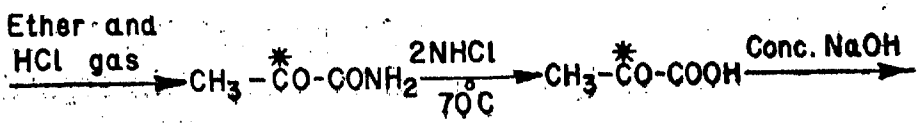
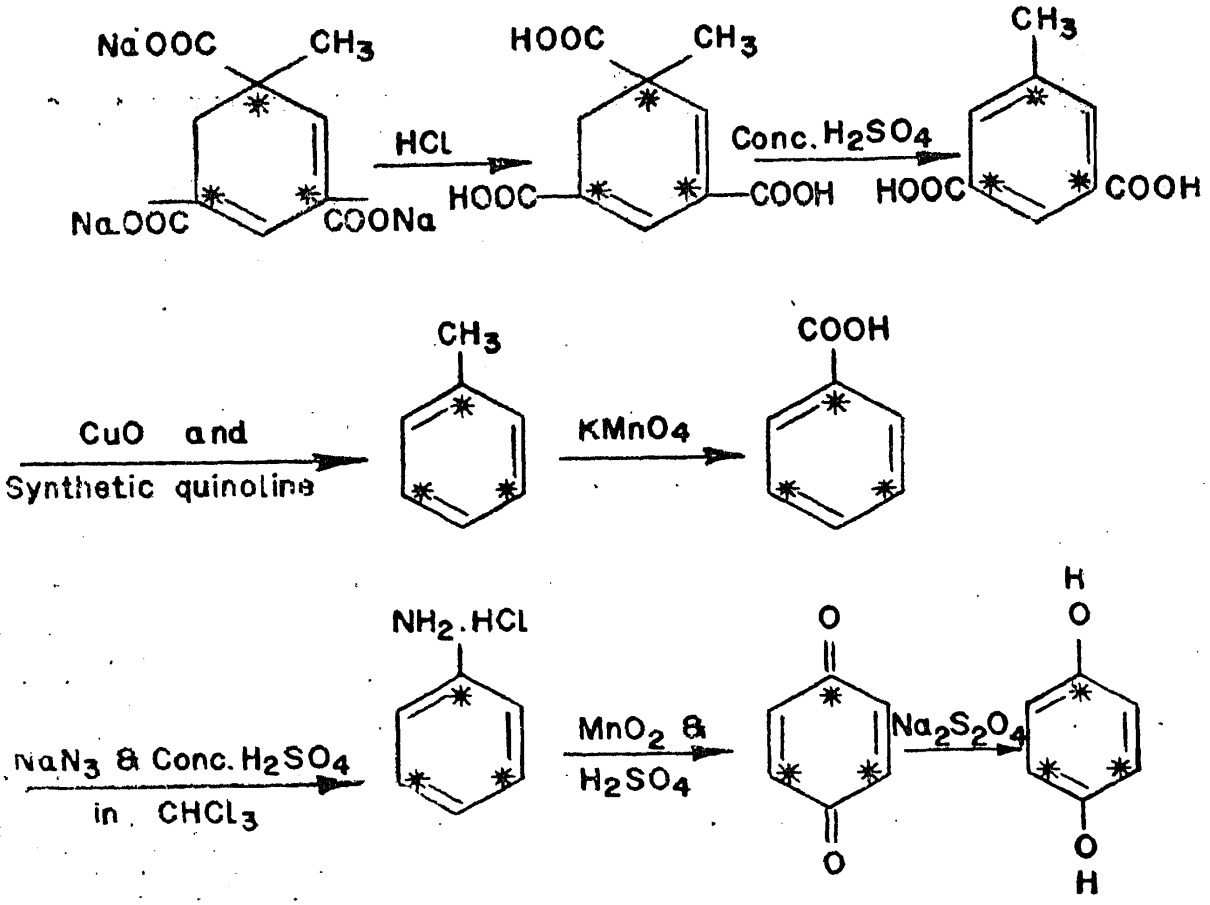
THE hyperfine splittings (hfs) produced in the electron spin resonance (ESR) spectra of aromatic free radicals by carbon-13 at specific positions give valuable information, as regards the mechanism of electron nuclear hyperfine interactions existing in such systems. The semiquinone ions, which are formed by the atmospheric oxidation of an alcoholic solution of the corresponding hydroquinones in the presence of alcoholic sodium or potassium hydroxide are suitable for the study of these interactions. The hfs due to C^{13} in natural abundance in the 2-position from *p*-benzosemiquinone ion has been observed as weak satellites by several authors,[1] and that due to C^{13} in the 1-position has also been observed[2] by using the C^{13}-labelled compound, *p*-benzosemiquinone ion 1-C^{13}. It was with a view to observe the C^{13} splittings unambiguously, from the two differently situated C-atoms in the ring that the present synthesis of *p*-benzohydroquinone-1, 3, 5-C_3^{13} was undertaken. The synthesis of *p*-benzohydroquinone-1-C^{13} was reported earlier[3]; and *p*-benzohydroquinone-1, 3, 5-C_3^{13} has been synthesised for the first time and involved the following sequence of reactions described in detail later:









1. *Sodium acetate*-1-C^{13} (CH_3–$\dot{C}OONa$)

The labelled sodium acetate was synthesised from $Ba\dot{C}O_3$ (enriched with C^{13} to about 51%) through the Grignard reaction and the method has been described earlier.[3]

2. *Acetyl*-1-C^{13} *bromide* (CH_3–$\dot{C}O$–*Br*)

An excess of benzoyl bromide[4] (3·25 moles of bromide for 1 mole of the fused acetate) was added to the fused sodium acetate contained in a round-bottomed flask. The flask was connected to a distilling assembly with provision for circulating ice-cold water; the contents of the flask were slowly heated using an oil-bath. When the temperature of the bath comes to 180° C. distillation starts and the distillate is collected while the temperature of the bath is maintained between 180 and 185° C. A typical yield from 20 gm. of the acetate is 24·9 gm. (83%).

3. *Pyruvonitrile*-2-C^{13} (CH_3–$\dot{C}O$–*CN*)

The acetyl-1-C^{13} bromide was converted to pyruvonitrile using a modified version of the method used by Calvin and Lemmon.[5] The apparatus con-

sisted of a 250 c.c. round-bottomed flask with two necks, to one of which is attached a reflux condenser protected from moisture by a fused $CaCl_2$ tube. To the other neck is attached a small separating funnel containing 22 gm. of acetyl bromide. A slight excess of dry cuprous cyanide (5 moles for 4 moles of acetyl bromide) was taken in the flask and the bromide was added slowly in the course of 35–40 min. The flask was shaken vigorously during the addition. The pyruvonitrile was isolated as described by Calvin and Lemmon[5]; yield 7·3 gm. (59·4%); b.p. 93° C.

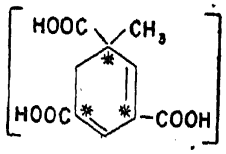
4. *Pyruvamide-2-C*^{13} (CH_3–$\overset{*}{C}O$–$CONH_2$)

As it has been found by Wood[6] that the intermediate isolation and purification of the amide increases the yield of pure pyruvic acid, compared to the direct hydrolysis of the nitrile to acid, pyruvamide-2-C^{13} was prepared from a solution of pyruvonitrile in anhydrous ether according to the method described by Anker.[7] The product was crystallised from ethyl acetate; yield: 5·3 gm. (57·6%); m.p. 127° C.

5. *Pyruvic-2-C*^{13}*-acid* (CH_3–$\overset{*}{C}O$–$COOH$)

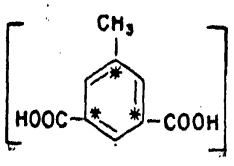
The pyruvamide was hydrolysed using an equimolecular quantity of 2 N HCl at 70° C. It was found that if the temperature of hydrolysis and the concentration of acid were higher, a good amount of the amide was hydrolysed to acetic acid. After keeping the mixture at 70° C. for an hour, the solution was cooled and was extracted a large number of times with small quantities of ether (16–18 times). The ether extract was dried with anhydrous sodium sulphate and the main bulk of the ether was distilled off using a fractionating column. The residue was processed as described by Wang *et al.*[18] Yield of pure acid: 3 gm. (56·6%).

6. *Methyl dihydro trimesic*-1, 3, 5-C_3^{13}*-acid*

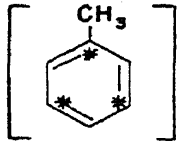


The C^{13} labelled pyruvic acid obtained as above was isotopically diluted with unlabelled pyruvic acid (pure distilled material) so that the isotopic enrichment was about 25%. This was converted to methyl dihydro trimesic-1, 3, 5-C_3^{13}-acid by the method described by Hughes and Reid.[9] Yield: 3·26 gm. (64·3%).

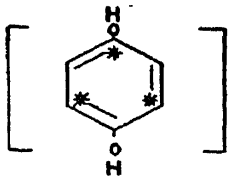
7. *Uvitic*-1, 3, 5-C_3^{13}*-acid*



The method described by Hughes and Reid[9] was followed for the synthesis of uvitic acid from methyl dihydrotrimesic acid. 3·25 gm. of the starting material gave 2·3 gm. of uvitic acid. Yield: 89·1%; m.p. 291° C.

8. *Toluene*-1, 3, 5-C_3^{13} 

The decarboxylation of the labelled uvitic acid to toluene-1, 3, 5-C_3^{13} was also accomplished by the method due to Hughes and Reid.[9] Yield of toluene from 2·3 gm. uvitic acid = 0·828 gm. (70·7%); $n_D^{25} = 1·482$.

9. *Conversions from toluene*-1, 3, 5-C_3^{13} *to* p-*Benzohydroquinone*-1, 3, 5-C_3^{13} 

From toluene-1, 3, 5-C_3^{13} to *p*-benzohydroquinone-1, 3, 5-C_3^{13}, the sequence of reactions were the same as those reported earlier by one of the authors.[3] The following modifications were found to improve the yield.

(i) From the ether extract obtained after oxidising the labelled aniline-hydrochloride, the *p*-benzoquinone-1, 3, 5-C_3^{13} was isolated by removing the ether under vacuum. The recovery is quantitative.

(ii) In the last stage, from the dried ether extract of *p*-benzohydroquinone-1, 3, 5-C_3^{13} the ether was evaporated off by a current of dry nitrogen. This makes the yield in the conversion of *p*-benzoquinone-1, 3, 5-C_3^{13} to *p*-benzohydroquinone-1, 3, 5-C_3^{13} almost quantitative.

220 mgm. of the pure final product was isolated; m.p. 170° C.

The hyperfine structures produced in the ESR spectrum of the semi-quinone ion[10] obtained from this compound has confirmed the presence of C^{13} in the 1, 3 and 5 positions.

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