Alkylbenzenes. X. The Relationship Between the Distribution of Isotopic Carbon Found in Isopropylbenzene and *n*-Propylbenzene After Treatment of *n*-Propyl-α-C^{14}-benzene with Aluminum Chloride[1]

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Received November 13, 1962

Using an isotope dilution technique, the distribution of C^{14} in the small amount of isopropylbenzene produced from *n*-propyl-α-C^{14}-benzene by reaction with aluminum chloride has been determined. Consideration of the relationships found between the isotopic distribution in the two propylbenzene isomers has led to a better understanding of the mechanisms operative in these internal rearrangements of alkylbenzene side chains

Introduction

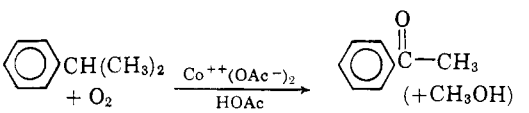
In the preceding paper[3] we reported the progressive equilibration of C^{14} between the α- and the β-positions in the side chain of *n*-propylbenzene effected by repeated treatment of *n*-propyl-α- or β-C^{14}-benzene with aluminum chloride. We have mentioned that isopropylbenzene is also produced in these reactions, but is found in only minor amounts,[3,4] presumably because of its greater susceptibility to dealkylation.[5]

Since it is possible to observe *partial* rearrangement of isotopic carbon from the α- to the β-position of the side chain (or *vice versa*), it seemed that determination of the distribution of the isotope in the isopropylbenzene produced concurrently might shed more light on the mechanism of these processes.[6] This was recognized to be a difficult task owing to the small amounts of isopropylbenzene remaining in the liquid reaction mixtures and the nearness of the boiling points of the isomeric propylbenzenes; however, a possible means of overcoming the difficulties appeared to be an isotope dilution technique.[7] This paper reports the successful application of this technique to the problem, and conclusions which have been drawn from the relationship found between the isotopic distributions in the propylbenzene isomers.

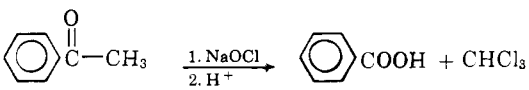
Results and Discussion

The separation problem was solved satisfactorily by diluting the propylbenzene fraction recovered by distillation of the reaction mixture with a known amount of pure isopropylbenzene and redistilling the resulting mixture through a very efficient column. It was necessary to dilute the small amount of radioactive isopropylbenzene with an amount of pure nonradioactive isopropylbenzene large enough to give approximately equal weights of the two isomers in order to allow satisfactory fractionation. The radioactive isopropylbenzene thus obtained was shown to be at least 96% pure by infrared analysis.

The degradation of isopropylbenzene was accomplished by means of the two steps outlined in equations 1 and 2:



(1)



(2)

The autoxidation of cumene (isopropylbenzene) has been studied extensively, but usually for the purpose either of determining the kinetics of the reaction or of obtaining the hydroperoxide in good yield. The decomposition of cumyl hydroperoxide in the presence of certain transition metal ion catalysts is well known; *e.g.*, Kharasch, *et al.*,[8] obtained acetophenone in 70% yield by treating an aqueous suspension of the hydroperoxide with ferrous ammonium sulfate. However, since the isolation of the hydroperoxide from a small scale autoxidation mixture would be somewhat difficult, it was desirable to effect both the autoxidation of the isopropylbenzene and the decomposition of the resulting hydroperoxide without isolation of the latter. A glacial acetic acid solution of anhydrous cobalt(II) acetate proved to be most suitable.[9] The fate of the second β-methyl group is uncertain, although it most likely was converted into methanol, which perhaps underwent further oxidation. The procedure used for the hypochlorite oxidation of acetophenone to benzoic acid was patterned after that given by Newman and Holmes.[10]

Radioassay of the two degradation products, acetophenone (as semicarbazone) and benzoic acid, permitted calculation of the distribution of C^{14} in the isopropyl side chain. The radioactivity data could also be used to calculate the percentage of isopropylbenzene in the total propylbenzene fraction, by using isotope dilution formulas. Details of these calculations are given in Experimental.

The degradation applied to disclose the isotopic distribution in *n*-propylbenzene was permanganate oxidation to benzoic acid, as in previous work.[4]

(1) A preliminary report of some of these results was given in *Chem. Ind* (London), 926 (1959).

(2) Taken from the Ph.D. thesis of J. E. D., The University of Texas, 1959; Procter and Gamble Co. Fellow, 1957–58. Present address, University of Kentucky, Lexington, Ky.

(3) R. M. Roberts and J. E. Douglass, Part IX, *J. Org. Chem.*, **28**, 1225 (1963).

(4) R. M. Roberts and S. G. Brandenberger, *J. Am. Chem. Soc.*, **79**, 5484 (1957).

(5) R. M. Roberts, paper presented at the Symposium on Carbonium Ions of the Organic Division, 139th National Meeting of the American Chemical Society, March 27, 1961, St. Louis, Mo.

(6) This was originally suggested by Professor C. D. Nenitzescu in a personal communication.

(7) We are indebted to Dr. S. G. Brandenberger for suggesting this approach.

(8) M. S. Kharasch, A. Fono, and W. Nudenburg, *J. Org. Chem.*, **15**, 763 (1950).

(9) A. E. Woodward and R. B. Mesrobian, *J. Am. Chem. Soc.*, **75**, 6189 (1953).

(10) M. S. Newman and H. L. Holmes, *Org. Syn.*, **2**, 428 (1943).

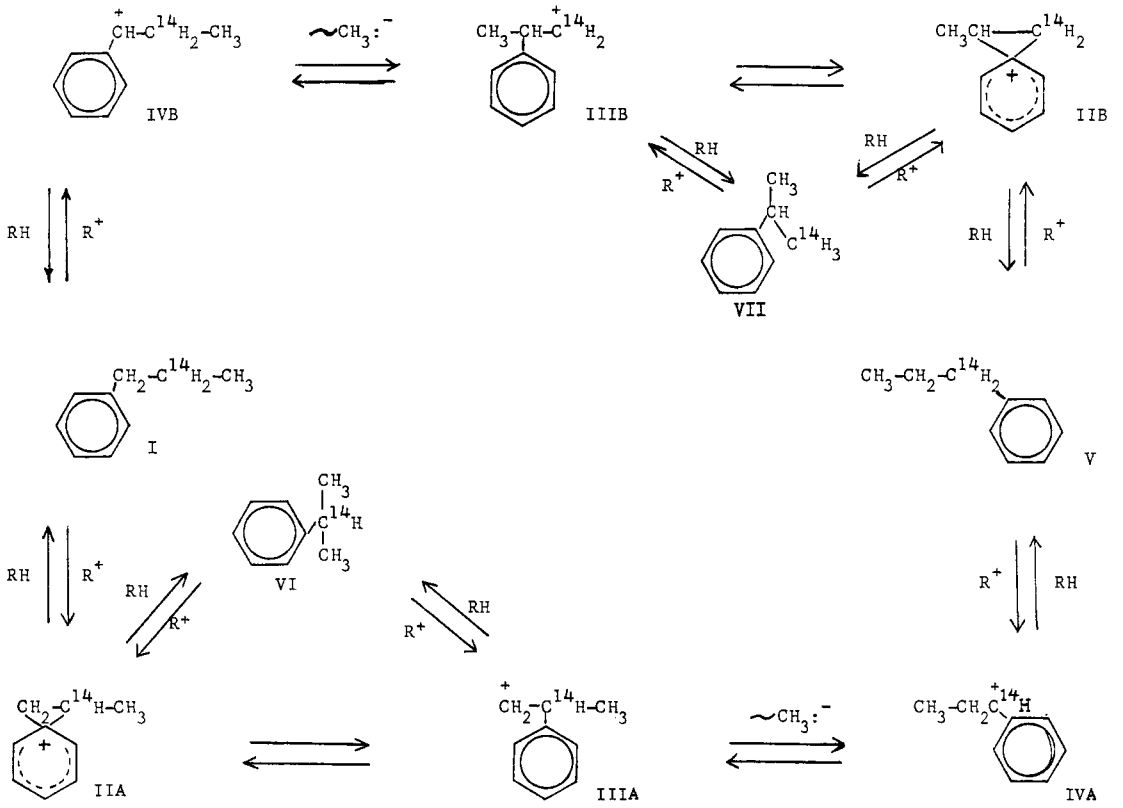


Fig. 1.—Propylbenzene rearrangement mechanisms.

In the first experiment, *n*-propyl-α-C^{14}-benzene was treated with water-activated aluminum chloride at 100°—conditions which previous experiments indicated should give about 30% isotopic rearrangement. Of the propylbenzene fraction recovered after the usual decomposition and distillation, a small sample was oxidized directly to benzoic acid, while the major part was diluted with pure (nonradioactive) isopropylbenzene and distilled through an efficient column in order to obtain a sample of radioactive isopropylbenzene. This material was then degraded to acetophenone and benzoic acid as described above. The results of the radioassays are given in Table I. The distribution of isotopic carbon calculated as described in the Experimental section is presented in Table II. The proportion of isopropylbenzene in the propylbenzene fraction before dilution calculated from the isotope dilution formula was 3.55%, which was in good agreement with the value from infrared analysis, 3.6%.

TABLE I

RADIOACTIVITIES OF STARTING MATERIALS AND DEGRADATION PRODUCTS[a]

Expt.	*n*-Pr-α-C^{14}-Ph[b]	Benzoic acid[c]	Acetophenone[d]	Benzoic Acid[e]
1	1.83	1.30	0.0565	0.0200
2.1	2.12	1.42	0.0610	0.0291
2.2[f]	...	1.11	0.0194	0.0128

[a] Radioactivities in microcuries per millimole (μc./mmole). [b] *n*-Propyl-α-C^{14}-benzene assayed as sulforamide. [c] From *n*-propylbenzene. [d] As semicarbazone (A_a; *cf.* Experimental section). [e] From acetophenone (A_b; *cf.* Experimental section). [f] The propylbenzene fraction recovered from experiment 2.1 was treated with fresh $AlCl_3 + H_2O$.

TABLE II

DISTRIBUTION OF C^{14} IN *n*-PROPYL- AND ISOPROPYLBENZENE

	Percent C^{14} in			
	n-PrC_6H_5		*i*-PrC_6H_5	
Expt.	α-C	β-C	α-C	β-C's
1	71	29	22	78
2.1	67	33	31	69
2.2	52	48	49	51

In a second experiment, a larger amount of *n*-propyl-α-C^{14}-benzene was subjected to reaction so that enough propylbenzene could be recovered to allow a second treatment with fresh catalyst.[3] The results of the consecutive treatments with catalyst are tabulated under experiments 2.1 and 2.2 in Tables I and II. In experiments 1 and 2.1, the distribution of isotopic carbon between the α- and β-positions of the side chains of *n*-propyl- and isopropylbenzene exhibited an inverse relationship. After two catalyst treatments (experiment 2.2), the isotopic carbon was almost equally distributed between the α- and β-positions in both propylbenzene isomers. These results are not at variance with the mechanism which was first suggested for the isotopic rearrangement of *n*-propylbenzene,[4] but information accumulated since that time leads us to favor now a more orthodox mechanism which is outlined in Fig. 1.[11] This mechanism also allows a more plausible explanation of the presently reported results.

Since all of the steps outlined in Fig. 1 are expected to be reversible, conversion of *n*-propyl-α-C^{14}-benzene (V) to *n*-propyl-β-C^{14}-benzene (I) may occur *via* either clockwise or counterclockwise routes. However, before equilibrium is reached, any isopropylbenzene

(11) The guiding principle in the formulation of the first mechanism was to account for the apparently insignificant amount of rearrangement to isopropylbenzene. We now know that there is more rearrangement to isopropylbenzene than is indicated by the amount of this isomer found in the liquid reaction mixture, owing to the greater susceptibility of isopropylbenzene to dealkylation[4]; thus there is no necessity of avoiding a mechanism which would be expected to lead to isopropylbenzene as well as to isotopically rearranged *n*-propylbenzene.

produced from V should have more of the isotopic carbon in the β-positions than in the α-position, since there is a route to VII *via* IIB, but VI can not be produced without passing through the highest energy intermediate ions IIIA or IIIB. This expectation is realized in experiments 1 and 2.1. After equilibrium is reached (with respect to V and I) there is equal probability of formation of VII and VI, and this is the finding in experiment 2.2. For this reason we prefer the formulation of Fig. 1 to the somewhat similar scheme of Nenitzescu,[12] in which the primary carbonium ion is a common intermediate in the formation of both isopropylbenzene and isotopically rearranged *n*-propylbenzene. As a corollary, one may also cite this inverse relationship between isotopic distribution in *n*-propyl- and isopropylbenzene as evidence for the intervention of phenonium ions in these rearrangements.[13]

Experimental

Radioassays were made by means of a liquid scintillation spectrometer (Packard "Tri-carb") as described in the preceding paper.[3]

***n*-Propyl-α-C^{14}-benzene** was synthesized from $BaC^{14}O_3$ as described in the preceding paper[3] and radioassayed in the form of its sulfonamide.

Reaction of *n*-Propyl-α-C^{14}-benzene with Aluminum Chloride–Water. Experiment 1.—A mixture of 34.4 g. (0.286 mole) of *n*-propyl-α-C^{14}-benzene, 12.7 g. (0.0952 mole) of anhydrous aluminum chloride and 0.145 g. (0.0081 mole) of water was heated with stirring at 100° for 6.5 hr. The mixture was decomposed with water, the organic layer was separated, dried, and distilled through a 45-cm. glass helices-packed column. A 10.4-g. propylbenzene fraction boiling at 148–160° was obtained; infrared analysis indicated it to contain 3.6% isopropylbenzene. Isotope dilution analysis (see below) gave 3.55% isopropylbenzene.

A 1.0-ml. portion of this fraction was oxidized to benzoic acid in the usual way[4] and recrystallized to constant melting point and radioactivity.

To the remainder of the propylbenzene fraction (8.955 g.) was added 5.941 g. of freshly distilled nonradioactive isopropylbenzene (b.p. 151–152°). The resulting mixture was distilled through a Podbielniak Series 3300 24-in. micro heli-grid column, rated at 100 plates under total reflux. A 4.7-ml. fraction, b.p. 151.3–152.0°, was shown by infrared analysis to be at least 96% isopropylbenzene.

Autoxidation of Isopropylbenzene.—A 50-ml. flask was equipped with a double-surface reflux condenser, to the top of which was attached a glass tube leading to an ice-cooled trap. Oxygen was introduced through a small side neck after having passed through a bubble-counting tube filled with silicone fluid. Glacial acetic acid used as solvent had added to it 1 ml. of acetic anhydride per 100 ml. of acetic acid to insure complete dryness. Anhydrous cobalt (II) acetate was prepared by heating the tetrahydrate in an oven at 110° for 8 hr.; it was finely ground and stored over magnesium sulfate in a desiccator.

To the reaction flask was added 16 ml. of the glacial acetic acid, 4.0 ml. of the isopropylbenzene fraction and 0.10 g. of anhydrous cobalt (II) acetate. The mixture was heated at 100 ± 1° with stirring (by means of a Telfon-covered magnet) for 24 hr., while a slow but steady stream of oxygen was passed into the flask. The contents of the flask and trap were then distilled, the acetic acid being removed at atmospheric pressure and acetophenone, 1.2 ml., at aspirator pressure.

The semicarbazone was prepared from a 0.6-ml. sample of the acetophenone by the standard procedure and the derivative was recrystallized to constant melting point and radioactivity.

A 0.5-ml. sample of the acetophenone was stirred with 50 ml. of a 5.25% solution of sodium hypochlorite (Clorox) at 60–70° for 45 min. Ethanol (1 ml.) was added and the mixture was stirred for another 10 min. in order to destroy any unchanged reagent. After cooling, the reaction mixture was washed with 10 ml. of ether to remove any unchanged acetophenone, the aqueous solution was evaporated on the steam cone to about one-half its original volume and then acidified to pH 1 with 6 *N* hydrochloric acid. The crystals of benzoic acid which formed on cooling amounted to 336 mg. It was recrystallized and sublimed to constant melting point and radioactivity.

Experiment 2.1—A second experiment was carried out with 172 g. (1.44 moles) of *n*-propyl-α-C^{14}-benzene, 63.7 g. (0.477 mole) of aluminum chloride and 2.16 g. (0.120 mole) of water as starting materials. The same conditions of reaction and procedures of work-up were used as in experiment 1. A 47.0-g. propylbenzene fraction was obtained by distillation. Isotope dilution analysis (see below) indicated 3.66% isopropylbenzene. A 1.0-ml. sample was oxidized to benzoic acid, which was purified and radioassayed as before. An 8.518-g. sample was diluted with 6.812 g. of isopropylbenzene. The mixture was fractionated using the Podbielniak column to give 6.0 ml. of radioactive isopropylbenzene, b.p. 150.2–151.6°. This was degraded to acetophenone and benzoic acid as before.

Experiment 2.2—The remainder of the propylbenzene fraction above, 37.7 g., 0.311 mole, was treated with 14.3 g. (0.107 mole) of aluminum chloride and 0.49 g. (0.027 mole) of water at 100° for 6.5 hr., with stirring. The products were distilled to yield 10.3 g. of propylbenzene fraction. A 1.0-ml. sample was degraded to benzoic acid. Another portion was diluted quantitatively with isopropylbenzene and the resulting mixture was distilled through the Podbielniak column. The radioactive isopropylbenzene obtained was degraded to acetophenone and benzoic acid as before.

The results of the radioassays are given in Table I. The values given are the average of at least two assays after constant activity was reached.

Calculations.—A. Distribution of C^{14} in isopropyl-α,β-C^{14}-benzene. Let

A_a = molar radioactivity of acetophenone semicarbazone from degradation of isopropylbenzene (represents the amount of C^{14} present in α-position plus one-half that in β-positions of isopropylbenzene).

A_b = molar radioactivity of benzoic acid from degradation of acetophenone (represents the amount of C^{14} present in α-position of isopropylbenzene).

Then $2(A_a - A_b)$ = amount of C^{14} in β-positions and

$$A_t = \text{amount of C}^{14} \text{ in } \alpha\text{- plus } \beta\text{-positions} = A_b + 2(A_a - A_b) = 2A_a - A_b$$

Hence

$$\%\ \text{C}^{14} \text{ in } \alpha\text{-position} = \frac{A_b}{A_t} 100 = \frac{A_b}{2A_a - A_b} 100 \quad (3)$$

$$\%\ \text{C}^{14} \text{ in } \beta\text{-positions} = \frac{2(A_a - A_b)}{A_t} 100 = \frac{2(A_a - A_b)}{2A_a - A_b} 100 \quad (4)$$

B. Amount of isopropylbenzene in the total propylbenzene distillation fraction. Let

A_0 = molar radioactivity of undiluted isopropylbenzene = initial molar radioactivity of *n*-propyl-α-C^{14}-benzene.

W_0 = weight of total propylbenzene fraction.

W_i = weight of ordinary isopropylbenzene used as diluent.

A_t = molar radioactivity of diluted isopropylbenzene = $2A_a - A_b$ (as above).

Then, the usual inverse isotope dilution formula may be derived to give

$$\%\ \text{isopropylbenzene} = \frac{W_i}{W_0 (A_0/A_t - 1)} 100 \quad (5)$$

Acknowledgment.—This research was supported in part by a grant (NSF-G5925) from the National Science Foundation, to whom we are grateful.

(12) C. D. Nenitzescu, I. Necsoiu, A. Glatz, and M. Zalman, *Chem. Ber.*, **92**, 10 (1959).

(13) A mechanism analogous to that of Fig. 1 can be written for the isobutylbenzene-*sec*-butylbenzene rearrangement.