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Abstract

Full Text

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A METHOD FOR CLEAVING TOLUENE-C^{14} IN ORDER TO DETERMINE THE POSITION OF THE LABEL IN THE RING

In studying the processes of isomerization of aromatic compounds, the migration of the migrating group is usually determined with respect to another substituent present in the same molecule. Thus, the mechanism of migration of an alkyl group in benzene derivatives has been studied using the isomerization of dialkylbenzenes and, in particular, xylenes as an example. It should be borne in mind, however, that the presence of a second substituent in an aromatic molecule may substantially affect the character and direction of migration of the migrating group, and therefore conclusions about the mechanism drawn on the basis of such investigations must be treated with a certain caution.

In this connection, in investigating isomerization processes it seems advisable to evaluate the paths of migration of the migrating group not with respect to a second substituent, but with respect to one of the atoms of the ring labeled with radioactive carbon C^{14}. This method was used by us, in particular, in studying the mechanisms of migration of substituents (Cl, CH_3, HO_3S) in naphthalene derivatives ([1–3]). The theoretical conclusions drawn in the course of these works cannot, however, be unconditionally extended to isomerization processes of compounds of the benzene series, since the naphthalene nucleus differs from the benzene nucleus by a considerable localization of double bonds ([4]). This latter circumstance prompted us to undertake a study of the isomerization of monosubstituted benzene derivatives labeled with radiocarbon, and first of all of toluene-1-C^{14}, which is presently commercially available ([5]).

To carry out the planned investigation it was necessary to develop a method for cleaving toluene-C^{14} that would permit separate determination of the radioactivity of each atom of the benzene ring. When this part of the work had already been completed, a report appeared by Dutch investigators ([6]), who had also developed a method for cleaving toluene-C^{14}. This original method is based on converting toluene, by nitration and oxidation, into a mixture of nitrobenzoic acids. From this mixture the individual *o*- and *p*-nitrobenzoic acids are isolated, reduced to the corresponding aminobenzoic acids, and then converted by the Skraup reaction into isomeric quinolinecarboxylic acids (I and II). Oxidation of

reaction scheme: toluene with ring positions 2, 3, and 4 converted through quinolinecarboxylic acids (I) and (II) to quinolinedicarboxylic acids (IIIa) and (IIIb)

Figure 1: reaction scheme: toluene with ring positions 2, 3, and 4 converted through quinolinecarboxylic acids (I) and (II) to quinolinedicarboxylic acids (IIIa) and (IIIb)

the latter and stepwise decarboxylation of the resulting quinolinedicarboxylic acids (IIIa and IIIb) make it possible to isolate, in the form of carbon dioxide, each atom of the benzene ring of toluene:

The reliability of the results obtained in determining the distribution of radiocarbon in the benzene ring by means of this method depends on the completeness of separation of the nitrobenzoic acids and on the selectivity of the decarboxylation of quinoline acid.

In the method we propose for the cleavage of toluene-C^{14}, use was made of the data of B. A. Kazanskii and N. F. Glushnev, who showed that, on reduction with $Ca(NH_3)_6$, toluene is converted predominantly into 1-methylcyclohexene (IV) ([7]) (see also ([8–10])). 1-Methylcyclohexene is then oxidized with permanganate ([11]), and the keto acid obtained (V) is reduced to enanthic acid (VI):

$$CH_3 \longrightarrow \text{(IV)} \longrightarrow CH_3CO(CH_2)_4COOH \longrightarrow CH_3CH_2CH_2CH_2CH_2CH_2COOH$$

(V) (VI)

The successive removal of carbon atoms from the molecule of enanthic acid is readily accomplished by means of procedures described in the literature ([12,13]). For this purpose we used the following scheme:

$$RCH_2COOH \longrightarrow HCH_2COC_6H_5 \longrightarrow RCCOC_6H_5 \longrightarrow RCN + C_6H_5COOH$$

(VII) (VIII) (IX)

$$RCONH_2 \longrightarrow RCOOH$$

(X) (XI)

The fatty acid is converted, via the acid chloride, by the Friedel–Crafts reaction into the alkyl phenyl ketone (VII), and its α-isonitroso derivative (VIII) is subjected to a Beckmann rearrangement of the second kind under the action of concentrated sulfuric acid (see ([13])). The nitrile (IX) formed in this process is hydrolyzed under the reaction conditions to the amide (X), which is isolated and, after purification, subjected to further hydrolysis to the fatty acid (XI), containing one carbon atom fewer than the starting acid. Further shortening of the chain of the acid obtained is carried out by repeating this series of operations. The carbon atom cleaved from the fatty-acid molecule is fixed in the carboxyl group of benzoic acid. Measurement of the radioactivity of samples of this acid obtained in the course of the cleavage makes it possible to determine the distribution of radiocarbon in the molecule of toluene-C^{14}.

The proposed cleavage method is also suitable for other alkylbenzenes labeled with radiocarbon.

At present it is difficult to say which of the two methods for cleaving toluene-C^{14} is more convenient. An answer to this question can be given only after their practical use for determining the position of radiocarbon in the products of isomerization of alkylbenzenes-C^{14}.

Experimental Part

Reduction of toluene. Into a Favorskii flask of 300 ml capacity are charged 20 g of shavings of metallic calcium, and a stream of dry ammonia (desiccant–solid caustic potash) is passed through a tube reaching to the bottom of the flask until absorption ceases. The weighed amount is 80–85% of the quantity calculated for $Ca(NH_3)_6$. To the resulting solid porous mass of $Ca(NH_3)_6$, 12 g of toluene is added from a dropping funnel over 0.5 h, and the mixture is left for two days at room temperature. Upon subsequent heating of the contents of the flask on a metal bath to 300°, a colorless liquid distills over; its IR spectrum is identical with the spectrum of 1-methylcyclohexene obtained from cyclohexanone by ([14]). The yield of 1-methylcyclohexene in the reduction of toluene is 45–50%.

If half as much calcium is used for the reduction, i.e., 2 g-at. per 1 mole of toluene, as recommended in (7), then the reduction product (yield 80%) contains a considerable amount of toluene (see also (8–10)).

δ-Acetyl-*n*-valeric acid (V). Into a three-necked flask fitted with a thermometer and stirrer are charged 4.4 g of 1-methylcyclohexene, obtained by reduction of toluene, and 110 ml of water. Then, with vigorous stirring and maintaining the temperature at 0–2° by cooling, 17.8 g of finely powdered potassium permanganate is added over 6 h, and the reaction mixture is left overnight at room temperature. The precipitate of manganese dioxide is filtered off and washed with 100 ml of hot water. The combined filtrate is extracted with ether; 150 g of ammonium sulfate is dissolved in it, and it is acidified with hydrochloric acid. The keto acid that separates is extracted with ether and converted, by the usual procedure (15), into the semicarbazone. Yield 4.0 g (64%), m.p. 110–

125°; after recrystallization from water, 2.4 g, m.p. 141.5–142.5°. According to (16), the m.p. of the semicarbazone of δ-acetyl-*n*-valeric acid is 144°.

Enanthic acid (VI). 1.5 g of the semicarbazone is heated with 1.8 g of caustic potash in 9 ml of diethylene glycol for 15 h at a bath temperature of 200°. The mixture is poured into water, neutralized with 15% hydrochloric acid, and the enanthic acid that separates is extracted with ether. Yield ~100%. The IR spectrum of the acid obtained is completely identical with the spectrum of commercial enanthic acid; their S-benzylthiuronium salts also proved identical —m.p. 145.0–145.5°.

$C_{15}H_{24}N_2O_2S$.	Found, %:	N 9.53; 9.70
	Calculated, %:	N 9.46

Cleavage of enanthic acid is carried out according to (13) via enanthophenone (yield 80%) and α-isonitrosoenanthophenone (yield 32%) to caproic acid amide (yield 80%) and benzoic acid. The caproic acid amide is then hydrolyzed to the free acid and the cycle is repeated.

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Note: Figure translations are in progress. See original paper for figures.