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REARRANGEMENT STUDIES WITH ^{14}C

XXI. SIDE CHAIN REARRANGEMENT AND FRAGMENTATION FOLLOWING FRIEDEL–CRAFTS ALKYLATION OF BENZENE WITH β-^{14}C-ETHYL IODIDE

C. C. LEE, M. C. HAMBLIN, AND J. F. UTHE
Department of Chemistry, University of Saskatchewan, Saskatoon, Saskatchewan

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ABSTRACT

The aluminum chloride catalyzed reaction between β-^{14}C-ethyl iodide and benzene in 1,2,4-trichlorobenzene as solvent was studied under different conditions of temperature and reaction time. Yields of ethylbenzene were estimated by isotopic dilution. Up to 20% rearranged product, α-^{14}C-ethylbenzene, was found. The trend indicated that yield of ethylbenzene was lower and side chain rearrangement greater when the reaction mixture was heated at higher temperature for longer time. The rearrangement apparently occurred after the initial formation of β-^{14}C-ethylbenzene. After a reaction time of 5 min at 154 °C, only 0.1–0.3% unreacted and unrearranged β-^{14}C-ethyl iodide was recovered while the ethylbenzene obtained from the reaction showed about 2% rearrangement. When β-^{14}C-ethylbenzene was heated with aluminum chloride in 1,2,4-trichlorobenzene for 2 or 24 h, rearrangement to α-^{14}C-ethylbenzene was observed. In some experiments, a fragmentation product, toluene, was isolated. Its specific activity suggested that 1 mole of active ethylbenzene gave 2 moles of toluene only one of which was active. The mechanistic implications of these findings are discussed.

INTRODUCTION

The Friedel–Crafts reaction of β-^{14}C-ethyl chloride (1) or β-^{14}C-ethyl iodide (2) with excess benzene gave β-^{14}C-ethylbenzene with no isotope position rearrangement in the side chain. This observation is consistent with the proposed mechanism of Brown and co-workers (3) that Friedel–Crafts alkylations may be analogous to other substitutions on saturated carbon, with primary alkyl halides reacting by a direct displacement process. Since the Friedel–Crafts catalyst can, by itself, induce rearrangements in alkyl halides, it has been suggested (4, 5) that rearranged products could have arisen from reactions with alkylating agents that have undergone rearrangement prior to the alkylation step. Treatment of β-^{14}C-ethyl chloride or β-^{14}C-ethyl iodide with aluminum chloride (1, 2), or of β-^{14}C-ethyl bromide with aluminum bromide (6), has been shown to cause extensive rearrangement of the ^{14}C-label. However, consideration of reaction rates indicated that no rearrangement of the ethylating agent could take place prior to alkylation when the Friedel–Crafts reaction was effected in excess benzene (2). In the present work, the aluminum chloride catalyzed alkylation of benzene with β-^{14}C-ethyl iodide was carried out in 1,2,4-trichlorobenzene under various conditions. It might then be ascertained if the use of an inert solvent would decrease the alkylation rate sufficiently to allow the aluminum chloride induced rearrangement of the β-^{14}C-ethyl iodide to take place, so that isotopically rearranged ethylbenzene would result. Significant extents of rearrangement were observed only in reactions effected at relatively high temperatures. Experiments were then carried out to show that these rearrangements occurred subsequent to the formation of ethylbenzene. In addition, a fragmentation product, toluene, was isolated in certain cases and its ^{14}C-contents determined.

RESULTS AND DISCUSSION

The molar ratio of the reactants was 1.0:3.0:3.2 for $AlCl_3$:C_6H_6:C_2H_5I. The solvent, 1,2,4-trichlorobenzene, has previously been used by Brown and co-workers (3). The reaction mixture was heated at different temperatures for various lengths of time. A known amount of ordinary ethylbenzene was then added as carrier, and the crude product was isolated by distillation. Pure ethylbenzene was finally separated by preparative vapor-phase chromatography (v.p.c.). The ethylbenzene recovered was oxidized to benzoic acid, whose activity, relative to that of ethylbenzene, measured the extent of rearrangement of the ^{14}C-label from the β- to the α-positions in the ethyl side chain. The results are summarized in Table I.

In most of the experiments, the specific activity of the original β-^{14}C-ethyl iodide was also determined. Since the amount of added ethylbenzene carrier and the specific activity of the diluted product were known, the yields of ethylbenzene for various runs were estimated by isotope dilution calculations. The basis of these calculations is as follows.

For every experiment, the theoretical yield of ethylbenzene was 3.18 g and the amount of carrier added was 1.73 g (2.0 ml).

Let x = g of ethylbenzene formed; if no carrier had been used, the specific activity of the ethylbenzene would have been the same as that of the β-^{14}C-ethyl iodide.

(Specific activity of $C_2H_5I)x$ = (observed specific activity of $C_6H_5C_2H_5)(1.73 + x)$. Solving for x, % yield = $(x/3.18) \times 100$. The yields calculated in this way are also included in Table I.

The data in Table I show that both yield of ethylbenzene and ^{14}C-rearrangement in the side chain are dependent on reaction temperature and reaction time. Under the relatively milder conditions of lower temperature and shorter reaction time, reproducibilities in yields and extents of rearrangement were fair. When the reaction mixtures were heated at higher temperatures for 24 h, results with much greater deviations were obtained. The general trend indicated by the data of Table I is that higher temperature and longer reaction time could cause greater amounts of rearrangement and lower yields of ethylbenzene. These observations strongly suggest the occurrence of processes which destroyed part of the ethylbenzene subsequent to its formation, and gave rise to side chain rearrangements in the ethylbenzene that remained.

To show more definitely that rearrangement did occur after ethylbenzene formation, first of all it was demonstrated that rearrangement did not arise prior to alkylation. In expt. 7 and 8 (Table I), which involved heating the reaction mixture at 154 °C for 5 min, besides the usual inactive ethylbenzene carrier, 2.0 ml of inactive ethyl iodide carrier was also added. The ethyl iodide fraction obtained by distillation would then contain unreacted β-^{14}C-ethyl iodide. This fraction was used for a Friedel–Crafts alkylation of an excess of benzene to give ethylbenzene, a process which does not cause appreciable rearrangement (2). From the activities of the ethylbenzene so obtained, calculations based on isotope dilution showed that only 0.1% and 0.3% of unreacted β-^{14}C-ethyl iodide were recovered in expt. 7 and 8. Moreover, oxidation of the ethylbenzene derived from the recovered ethyl iodide gave inactive benzoic acid, indicating no rearrangement of the β-^{14}C-ethyl iodide during the course of expt. 7 and 8. Thus the possibility of slowing down the alkylation by inert solvent to allow β-^{14}C-ethyl iodide to rearrange before alkylation was not realized.

TABLE I

Yields of ethylbenzene and rearrangements to α-^{14}C-ethylbenzene from aluminum chloride catalyzed reaction of benzene with β-^{14}C-ethyl iodide

Expt.	Reaction temp. (°C)*	Reaction time (h)	Specific activities (c.p.m./mmole)			Yield of $C_6H_5C_2H_5$(%)‖	Rearrangement (%)
			C_2H_5I†	$C_6H_5C_2H_5$‡	C_6H_5COOH§		
1	80	24	251 000	121 000	1 010	51	0.8
2	110	2	—	231 000	2 080	—	0.9
3	110	2	—	226 000	2 820	—	1.2
4	110	24	570 000	212 000	5 770	32	2.7
5	110	24	570 000	217 000	4 210	33	1.9
6	154	1/12	—	725 000	14 900	—	2.1
7	154	1/12	925 000	389 000	7 270	40	1.9
8	154	1/12	925 000	396 000	7 390	41	1.9
9	154	2	—	218 000	8 060	—	3.7
10	154	2	612 000	206 000	10 200	28	4.9
11	154	24	—	173 000	20 900	—	12.0
12	154	24	—	138 000	11 700	—	8.5
13	154	24	612 000	80 200	14 100	8	17.6
14	154	24	570 000	172 000	11 300	24	6.6
15	190	2	295 000	114 000	5 290	34	4.6
16	190	2	438 000	126 000	17 700	22	14.0
17	190	2	438 000	120 000	13 400	21	11.2
18	190	24	438 000	87 800	13 700	14	15.6
19	190	24	438 000	71 500	14 500	11	20.2
20	208	2	—	173 000	6 210	—	3.9
21	208	2	612 000	283 000	11 000	47	3.6
22	208	24	295 000	29 300	6 000	6	20.5
23	208	24	295 000	50 300	8 120	11	16.1

*Temperatures of 80, 110, 154, 190, and 208 °C were maintained by the vapor of refluxing benzene, toluene, bromobenzene, benzonitrile, and 1,2,4-trichlorobenzene, respectively.
†Original reactant before dilution.
‡Diluted with carrier.
§From diluted ethylbenzene.
‖Estimated by isotope dilution calculations.

When the Friedel–Crafts alkylation was carried out at 154° for 2 or 24 h with ordinary ethyl iodide, but with some β-^{14}C-ethylbenzene added at the beginning of each trial, the ethylbenzene finally recovered gave, on oxidation, radioactive benzoic acid, indicating rearrangement of the added active ethylbenzene. Moreover, when β-^{14}C-ethylbenzene in trichlorobenzene containing aluminum chloride was heated at 154 °C for 2 or 24 h, the ethylbenzene re-isolated with the aid of carrier also showed side chain ^{14}C-rearrangement. The results are summarized in Table II. The extents of rearrangement obtained in these trials are of about the same magnitude as those observed in the corresponding experiments 9–10 and 11–14 (Table I). These findings, therefore, support the conclusion that the side chain ^{14}C-rearrangement recorded in Table I arose after the initial formation of unrearranged alkylation product, β-^{14}C-ethylbenzene.

TABLE II

Data from heating β-^{14}C-ethylbenzene at 154 °C in alkylation reaction mixture or in 1,2,4-trichlorobenzene containing aluminum chloride

		Specific activities (c.p.m./mmole)				
Expt.	Reaction time (h)	Initial $C_6H_5C_2H_5$	Recovered $C_6H_5C_2H_5$	C_6H_5COOH*	$C_6H_5C_2H_5$ recovery (%)†	Rearrangement (%)
24	2	481 000	74 400	1 880	—	2.5
25	2	481 000	251 000	8 550	36	3.4
26	24	481 000	51 900	5 350	—	10.3
27	24	481 000	124 000	13 300	23	10.7

*From recovered ethylbenzene.

†Estimated by isotope dilution calculations. In expt. 24 and 26, β-^{14}C-ethylbenzene was heated while an inactive alkylation was carried out. Besides the inactive ethylbenzene carrier added, an unknown amount of inactive ethylbenzene derived from the alkylation reaction was also present; hence no isotope dilution calculations could be made.

In the course of the v.p.c. separation of ethylbenzene from various experiments, peaks corresponding to benzene and toluene were observed (no attempt was made to identify or separate diethylbenzenes). Probably, benzene resulted from dealkylation and toluene from fragmentation. In some of the experiments with a reaction time of 24 h, sufficient amounts of toluene were present to allow its collection and determination of its specific activity. The results are shown in Table III. As expected, the yield of this fragmentation product was higher when the reaction mixture was heated at higher temperature. It may be of interest to note that under the most drastic conditions employed (expt. 22 and 23), the yields of toluene were comparable to the yields of surviving ethylbenzene.

In these experiments, the toluene was obtained without the addition of any carrier. When the specific activity of the toluene is compared with that of the corresponding ethylbenzene before any dilution of the latter by inactive carrier, the specific activity ratio is about 0.5 in all cases. This is an interesting observation, as it suggests that each mole of active ethylbenzene gave rise to 2 moles of toluene, one of which is active and the other is not. Such a situation would result if the toluene arose from 1,2-diphenyl-1-^{14}C-ethane, which could be derived from either β-^{14}C-ethylbenzene or α-^{14}C-ethylbenzene. In their studies on dealkylation and fragmentation of alkylbenzenes, Roberts, Baylis, and Fonken (7) reported the isolation of *meso*-2,3-diphenylbutane as a minor product after treatment of *sec*-butylbenzene with water-promoted aluminum chloride. A mechanism for fragmentation involving diphenylalkane as intermediate was suggested (7). Such a mechanism applied to ethylbenzene would involve 1,2-diphenylethane as intermediate, which is consistent with the observed specific activity ratio for toluene to ethylbenzene of

TABLE III

Fragmentation of β-^{14}C-ethylbenzene to toluene from experiments with reaction time of 24 h

Expt.	Reaction temp. (°C)	Specific activities (c.p.m./mmole)		Specific activity ratio ($C_6H_5CH_3/C_6H_5C_2H_5$)	Yield of $C_6H_5CH_3$		Yield of $C_6H_5C_2H_5$ (%)‡
		Undiluted $C_6H_5C_2H_5$*	$C_6H_5CH_3$		(mg)	(%)†	
14	154	570 000	311 000	0.55	109	4.0	24
27	154	481 000	261 000	0.54	71	2.7	—
18	190	438 000	227 000	0.52	142	5.2	14
19	190	438 000	231 000	0.53	165	6.0	11
22	208	295 000	148 000	0.50	156	5.7	6
23	208	295 000	151 000	0.51	241	8.7	11

*In expt. 27, β-^{14}C-ethylbenzene was added as such; in the other experiments, the specific activity of the undiluted $C_6H_5C_2H_5$ was assumed to be equal to the specific activity of the C_2H_5I initially used (see Table I).

†For expt. 27, based on the β-^{14}C-ethylbenzene added; for the other experiments, based on the limiting reactant, benzene, in the Friedel–Crafts reaction mixture.

‡From Table I, also based on the benzene in the Friedel–Crafts reaction mixture.

about 0.5. The activity data of Table III may, therefore, be regarded as evidence in support of the fragmentation mechanism of Roberts, Baylis, and Fonken.

The disproportionation of ethylbenzene under conditions less severe than those used in the present experiments has been extensively investigated. The pertinent literature has been summarized in a recent paper by Ünseren and Wolf (8). The possibility of side chain rearrangements proceeding through π-complexes has been discussed by Roberts and co-workers (9, 10). It is noteworthy that in the present work, more rearrangement as well as more fragmentation were observed under conditions of higher temperature and longer reaction time. Both of these processes could result from the same intermediate. 1,2-Diphenyl-1-^{14}C-ethane might revert to equal amounts of α-^{14}C-ethylbenzene and β-^{14}C-ethylbenzene, giving rise to the side chain rearrangements observed in the surviving ethylbenzene (Tables I and II). The 1,2-diphenylethane could arise either directly from ethylbenzene or via 1,1-diphenylethane, an intermediate postulated by Streitwieser and Reif (11) for ethylbenzene disproportionation. Isotopically rearranged ethylbenzene via 1,2-diphenylethane would also be consistent with the conclusions of Ünseren and Wolf (8) and of Streitwieser and Reif (11) that disproportionation of ethylbenzene involves considerable extents of intermolecular *trans*-alkylation.

EXPERIMENTAL

The β-^{14}C-ethyl iodide was obtained from New England Nuclear Corp. The β-^{14}C-ethylbenzene was prepared by a Friedel–Crafts reaction between β-^{14}C-ethyl iodide and an excess of benzene, the product showing less than 0.3% ^{14}C rearrangement in the side chain (2). Degradation of ethylbenzene from various experiments to benzoic acid was effected by oxidation with alkaline potassium permanganate (12).

Friedel–Crafts Reactions (Expt. 1–23, Tables I and III)

All reactions were carried out in a pyrex vessel fitted with mechanical stirrer, reflux condenser, and Drierite tube. The vessel was enclosed in a pyrex jacket which was also fitted with a reflux condenser and connected to a pot of boiling liquid. The vapor from the refluxing liquid heated the reaction mixture and maintained a constant temperature.

A mixture of 2.34 g (30 mmoles) of anhydrous benzene, 1.33 g (10 mmoles) of sublimed, anhydrous aluminum chloride, and 50 ml of redistilled 1,2,4-trichlorobenzene was placed in the reaction vessel and brought to the desired temperature. A solution of 5.0 g (32 mmoles) of β-^{14}C-ethyl iodide in a small amount of 1,2,4-trichlorobenzene was then added through the top of the reflux condenser. Heating was continued for the desired length of time and then the reaction stopped by the addition of 50 ml of ice water. Two ml (1.73 g) of inactive ethylbenzene was introduced as carrier. The organic layer was separated and washed successively with 50-ml portions of 5% hydrochloric acid, 2% sodium hydroxide solution containing 5 g of sodium thiosulphate, and water. The washings were extracted with ether and the extract combined with the original organic layer. After the solution was dried over anhydrous magnesium sulphate, it was fractionated. The major portion of the product distilled at 130–135 °C, but the fraction boiling over the range 100–160 °C was collected. Recoveries were of the order of 2–3 g. Final purification was effected by passage through a preparative column packed with Apiezon L on firebrick in a Beckman GC-2A gas chromatograph. Ethylbenzene was recovered in all experiments, while in some cases, toluene, in addition to ethylbenzene, was also collected. The identities of these products were confirmed by n.m.r. spectroscopy. The spectra of the recovered ethylbenzene and toluene were the same as those of corresponding authentic samples. The typical triplet–quartet splitting was shown by the ethyl protons of ethylbenzene and a singlet was observed for the methyl protons of toluene. The τ-values also agree with those given by Tiers (13) for ethylbenzene and toluene.

In expt. 7 and 8, which involved stopping the reaction after heating at 154 °C for 5 min, 2.0 ml of inactive ethyl iodide, in addition to the inactive ethylbenzene carrier, were also added before the mixture was worked up as described above. Two fractions were collected, one contained the ethylbenzene and the other, boiling over the range of 40–80 °C, contained unreacted β-^{14}C-ethyl iodide diluted by carrier. The ethyl iodide fraction was used for a Friedel–Crafts reaction with excess benzene. The ethylbenzene obtained was purified by v.p.c. Its activity measured the amount of unreacted β-^{14}C-ethyl iodide recovered and its oxidation to inactive benzoic acid indicated no rearrangement in the unreacted β-^{14}C-ethyl iodide.

Treatment of β-^{14}C-Ethylbenzene with Aluminum Chloride (Expt. 24–27, Tables II and III)

Two procedures were used. In expt. 24 and 26, a mixture of 1.70 g (22 mmoles) of anhydrous benzene, 1.33 g (10 mmoles) of sublimed, anhydrous aluminum chloride, and 50 ml of redistilled 1,2,4-trichlorobenzene was heated to 154 °C. Inactive ethyl iodide (3.64 g, 23 mmoles) and β-^{14}C-ethylbenzene (0.86 g, 8 mmoles) were introduced and the reaction mixture heated for 2 or 24 h. The reaction was stopped by addition of ice water. After the introduction of 1.0 ml of inactive ethylbenzene as carrier, the resulting material was worked up as in the Friedel–Crafts reactions to give pure ethylbenzene.

In expt. 25 and 27, 1.33 g (10 mmoles) of sublimed, anhydrous aluminum chloride and 50 ml of 1,2,4-trichlorobenzene were heated to 154 °C and then 2.60 g (24 mmoles) of β-^{14}C-ethylbenzene was introduced. Heating was continued for 2 or 24 h. Ice water was added followed by 1.0 ml of inactive ethylbenzene as carrier. The resulting material was worked up the usual way to give pure ethylbenzene. In expt. 27, which involved 24 h of heating, both ethylbenzene and toluene were recovered in the final purification by v.p.c.

Radioactivity Determination

All activities were measured by a liquid scintillation counter. Active ethyl iodide, ethylbenzene, toluene, and benzoic acid were counted in toluene solution containing PPO and POPOP. Sample concentrations were about 15 mg/20 ml. Ethyl iodide showed appreciable quenching and correction factors were determined by use of a known amount of ^{14}C-toluene as internal standard.

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