Boron Trifluoride Hydrate-catalyzed Ethylation of Benzene with Ethyl-1-^{13}C Fluoride and Ethyl-1,1-d_2 Fluoride

Toshiyuki OYAMA, Toshio HAMANO,* Katsuyuki NAGUMO,* and Ryohei NAKANE
The Institute of Physical and Chemical Research, Wako, Saitama 351
**Department of Applied Chemistry, Waseda University, Shinjuku-ku, Tokyo 160*

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In the ethylation of benzene with ethyl-1-^{13}C fluoride and ethyl-1,1-d_2 fluoride in boron trifluoride hydrate, almost a 50% isotope position rearrangement in the ethyl group of ethylbenzene was found, whereas in the boron trifluoride-catalyzed ethylation in excess benzene no rearrangement was observed. Based on these results, it was suggested that an electrophile is an ethyl cation in the ethylation of benzene in excess boron trifluoride hydrate and a nonionized polar complex in the boron trifluoride-catalyzed ethylation in excess benzene.

The ethylation of benzene with ethyl fluoride in donor solvents using boron trifluoride as the catalyst proceeds through the formation of a nonionized polar complex, $C_2\overset{\delta^+}{H}_5F\cdot\overset{\delta^+}{B}F_3$, and the relative rates of toluene to benzene, k_T/k_B, were found to be 2.7 in nitromethane and 2.3 in excess aromatics.1) On the other hand, in the boron trifluoride-catalyzed ethylation carried out in a nonpolar solvent such as hexane or cyclohexane, the electrophile is an ethyl carbocation, since the ethylation with ethyl fluoride-2-^{14}C indicated the migration of radioactivity from the β- to the α-carbon atom of the ethyl group.2) In ethylation and isopropylation in hexane, an anomalous substrate selectivity was found ($k_T/k_B=0.61$ and 0.70 respectively).3) The nonpolar solvents in which the alkylations are carried out contain a trace of water. Therefore, an alkylation catalyst in nonpolar solvents would be a hydrate of boron trifluoride, which is a strong proton-acid catalyst.3)

In the present investigation, the ethylation of benzene with ethyl-1-^{13}C fluoride and ethyl-1,1-d_2 fluoride in boron trifluoride monohydrate has been carried out to obtain evidence of the incipient ethyl carbocation as an ethylation agent.

Experimental

Materials. The benzene was dried over calcium hydride. The boron trifluoride was obtained from the Hashimoto Kasei Co., Ltd. The ethyl-1-^{13}C fluoride was prepared from ethyl-1-^{13}C iodide (*ca.* 20 ^{13}C atom%. Prochem, The British oxygen Co., Ltd.) by reaction with mercuric fluoride4), which had itself been prepared from mercuric chloride with elemental fluorine (Daikin Kogyo Co.) and purified by distillation at low temperatures. The ethyl-1,1-d_2 fluoride was prepared from ethyl-1,1-d_2 alcohol,5) which had itself been obtained by the reduction of phenyl acetate with lithium aluminium deuteride6) (99 D atom%. Merck Sharp and Dohme Co., Ltd.); yield: 80.6%, IR(gas): $\nu_{\max}$ 2240, 2140 (C–D) 1180, 1170, 1155, 970, 960, and 955 (C–F) cm^{-1}; NMR (-40 °C): δ 1.05 (m of d, $J_{\mathrm{CH-CF}}=25.8$ Hz, $J_{\mathrm{CH-CD}}=1.02$ Hz). The ethylbenzene-2,2-d_2 was prepared by the hydrolysis of 2-phenylethyl-1,1-d_2 magnesium bromide prepared from the bromide and magnesium turnings in dry ether at the reflux temperature for 1.5 hours. IR(neat): $\nu_{\max}$ 2955, 2880, 2220, and 2130 cm^{-1}; MS:*m/e* 108 (M$^+$), 91 (base peak). The 2-phenylethyl-1,1-d_2 bromide was prepared from 2-phenylethyl-1,1-d_2 alcohol and a 47% solution of hydrogen bromide by the method in the literature.7) IR: $\nu_{\max}$ 2280, 2240, and 2160 cm^{-1}. The alcohol was obtained by the reduction of ethyl phenylacetate with lithium aluminium deuteride in an ether solution.

Procedure. The boron trifluoride monohydrate was prepared by passing anhydrous boron trifluoride gas into distilled water cooled in an ice bath. The resultant hydrate was a heavy, fuming liquid with a specific gravity of 1.77 at 25 °C; it made a clean homogeneous solution with a small amount of benzene (0.5 g benzene/1000 g BF_3-hydrate). Ethylation was carried out by bubbling ethyl fluoride gas into the solution (424 g) for 30 min at room temperature. After the introduction of ethyl fluoride (2.4 mmol), the solution was quenched in ice water. A small amount of unreacted benzene and the products were extracted with dichloromethane. The organic layer was washed with a 5% $NaHCO_3$ aq solution and then with water. The organic solution was dried over calcium chloride, and the solvent was removed by fractional distillation. The products were subjected to GLC, NMR, and GC-MS measurements. Boron trifluoride catalyzed ethylation with ethyl fluoride in excess benzene as a donor solvent was carried out according to the previously described method.2) GLC analysis was carried out on a Hitachi Perkin Elmer gas chromatograph F6-D. The ^{1}H-NMR spectra were determined on a JEOL C-60HL. apparatus. The ^{13}C-NMR spectra were measured on a JEOL JNM-FX100 Fourier-transform NMR spectrometer. Tetramethylsilane was used as an internal reference. The mass spectra were obtained on a Hitachi RMU-6M mass spectrometer. The IR spectra were taken on a Shimadzu grating Infrared Spectrophotometer IR-27G.

Results and Discussion

In the ^{13}C-NMR spectrum (shown in Fig. 1) of the products of the ethylation of benzene with ethyl-1-^{13}C fluoride in boron trifluoride hydrate, both methyl and methylene carbon signals (15.63 and 28.89 ppm respectively) appeared strongly in a ratio of 40:60 (corrected by relative sensitivity) as compared with those of the aromatic ring (para:125.55 ppm, ortho:127.81 ppm, meta:128.29 ppm). This indicates that almost equal amounts of ethyl-1-^{13}C-benzene and ethyl-2-^{13}C-benzene were produced in this reaction. In the boron trifluoride-catalyzed ethylation with ethyl-1-^{13}C fluoride in excess benzene, it was estimated from the ^{13}C-NMR spectrum (shown in Fig. 2) that about 95% of the products consisted of ethyl-1-^{13}C-benzene. The ^{1}H-NMR spectrum of the product of the same reaction with ethyl-1,1-d_2 fluoride consists only of a methyl-group proton peak at $\delta=1.23$ ppm, with a multiplicity due to H–D coupling ($J_{\mathrm{H-D}}=1.4$ Hz), as is shown in

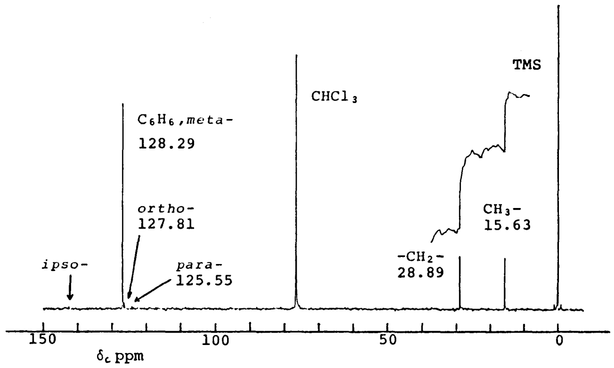


Fig. 1. ^{13}C-NMR spectrum (25 MHz FT) of ethylbenzene (in $CHCl_3$ and C_6H_6) obtained frcm the ethylation of benzene in boron trifluoride hydrate.

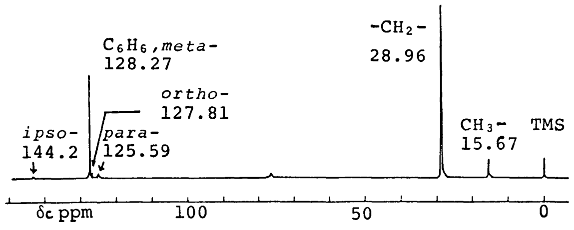


Fig. 2. ^{13}C-NMR spectrum (25 MHz FT) of ethylbenzene (in benzene) obtained from the boron trifluoride catalyzed ethylation in excess benzene.

Fig. 3; no resonance peak due to the methylene proton was observed. Therefore, it is evident that the only ethylated product was ethyl-1,1-d_2-benzene. On the other hand, the ^{1}H-NMR spectrum of the ethylbenzene (shown in Fig. 4) produced in boron trifluoride hydrate displays a multiplet peak of a methylene proton besides a multiplet peak of a methyl group. This product was also analyzed by GC-MS. It was determined from the peak-heights ratio of the $C_6H_5CH_2^+$, $C_6H_5CDH^+$, and $C_6H_5CD_2^+$ ions that the ethylbenzene produced was a mixture of $C_6H_5CH_2CD_2H$, $C_6H_5CDHCDH_2$, and $C_6H_5CD_2CH_3$ in a ratio of 68:95:42. Therefore, the obtained ^{1}H-NMR spectrum is a superposition of the resonance peaks of the isotopic ethyl group with a multiplet due to H–H and H–D coupling.

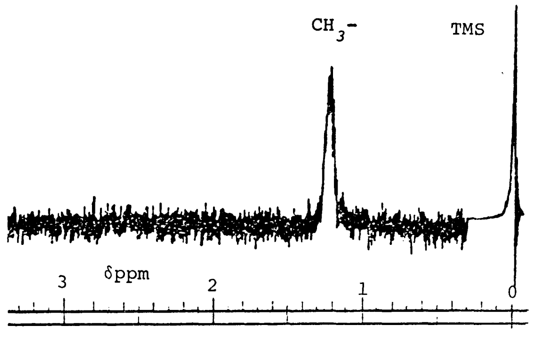


Fig. 3. ^{1}H-NMR spectrum (60 MHz methyl and methylene region) of ethylbenzene (in CCl_4) obtained from the boron trifluoride catalyzed ethylation in excess benzene.

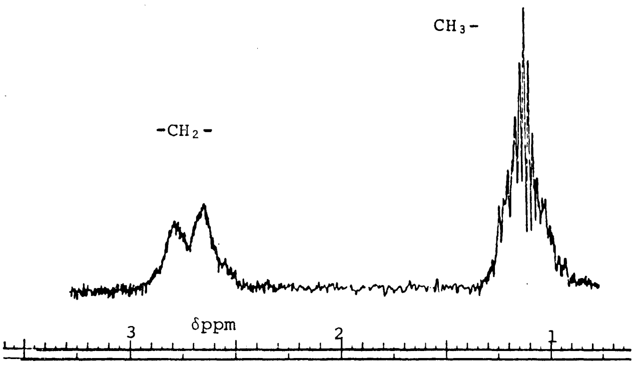


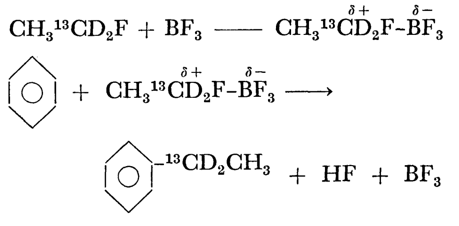
Fig. 4. ^{1}H-NMR spectrum (60 MHz methyl and methylene region) of ethylbenezene (in CCl_4) obtained from the ethylation of benzene in boron trifluoride hydrate.

In order to confirm that the rearranged ethylbenzene was obtained by the ethylation reaction in the first step, and not by the secondary isotope-position scrambling of the ethylbenzene which is formed in the first step, ethyl-1-^{13}*C*-benzene and ethyl-2,2-d_2-benzene were placed in contact with boron trifluoride hydrate under the same conditions as in the ethylation reaction. No isotope-position rearrangement in the ethyl group was observed.

It is well known that, in the consideration of primary alkyl halides with aromatics under the Friedel-Crafts condition, a rearrangement of the alkyl group usually results; this has been interpreted in terms of carbocation formation and rearrangement. All such mechanisms, however, involve primary-to-secondary carbocation conversions. Therefore, it seemed of interest to investigate the primary-to-primary rearrangement of the ethyl group. Roberts *et al.*[8] and Lee *et al.*[9] have reported that the ethylation with ethyl-2-^{14}*C* halide gave unrearranged products. One of the present authors[2] previously found that, in the boron trifluoride-catalyzed ethyaltion of benzene with ethyl-2-^{14}*C* fluoride in nitromethane, only a little isotope position rearrangement in the ethyl group took place.

Now, in the ethylation with ethyl-1-^{13}*C* fluoride and ethyl-1,1-d_2 fluoride in excess benzene, no isotope-position-rearranged product was obtained. These facts show that the boron trifluoride catalyst forms, with ethyl fluoride, the nonionized complex in the Friedel-Crafts ethylation in the donor solvent and that the complex attacks the aromatic ring carbon without rearrangement. The ethylation proceeds *via* an S_N2 displacement reaction on the complex.

Boron trifluoride monohydrate,[10] which is formed by introducing an equal amount of boron trifluoride into

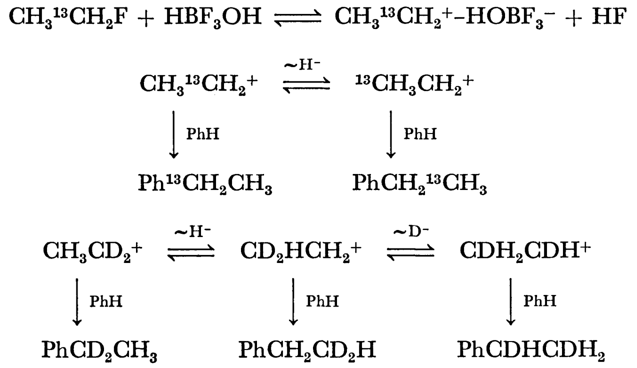


$$CH_3{}^{13}CD_2F + BF_3 —— CH_3{}^{13}\overset{\delta+}{C}D_2F\text{-}\overset{\delta-}{B}F_3$$

$$C_6H_6 + CH_3{}^{13}\overset{\delta+}{C}D_2F\text{-}\overset{\delta-}{B}F_3 \longrightarrow C_6H_5\text{-}{}^{13}CD_2CH_3 + HF + BF_3$$

Scheme 1.

water, is a heavy, fuming liquid and is a strong proton acid of the hydroxyfluoroboric-acid type. This hydrate is used as a catalyst for polymerizations and alkylations.[11] When the hydrate of boron trifluoride reacts with ethyl fluoride, an ethyl cation or its ion pair is produced, and internal 1,2-hydride and deuteride shifts occur almost completely in the ethyl group before the ethyl cation combines with the benzene ring. Thus, the ethylation with the isotope-position-rearranged ethyl cation or its ion pair gave a mixture of isotopic ethylbenzene. These facts suggest that the ethyl cation of its ion pair is the electrophile in boron trifluoride hydrate-catalyzed ethylation. In a competitive ethylation an anomalous relative rate ($k_T/k_B=0.8$), as in a nonpolar solvent, was obtained in boron trifluoride hydrate.[12] The ethylation of benzene with boron trifluoride and ethyl-2-^{14}C fluoride, carried out in a nonpolar solvent such as hexane and cyclohexane, gave isotope-position-rearranged ethylbenzene, indicating the ethyl-cation formation in the course of the reaction.[2] Therefore, it may be concluded that the ethylation catalyst in a nonpolar solvent is a boron trifluoride hydrate.



$$CH_3{}^{13}CH_2F + HBF_3OH \rightleftharpoons CH_3{}^{13}CH_2{}^{+}\text{-}HOBF_3{}^{-} + HF$$

$$\begin{tikzcd}
CH_3{}^{13}CH_2{}^{+} \arrow[r, shift left, "\sim H^-"] \arrow[d, "PhH"] & {}^{13}CH_3CH_2{}^{+} \arrow[l, shift left] \arrow[d, "PhH"] \\
Ph^{13}CH_2CH_3 & PhCH_2{}^{13}CH_3
\end{tikzcd}$$

$$\begin{tikzcd}
CH_3CD_2{}^{+} \arrow[r, shift left, "\sim H^-"] \arrow[d, "PhH"] & CD_2HCH_2{}^{+} \arrow[l, shift left] \arrow[r, shift left, "\sim D^-"] \arrow[d, "PhH"] & CDH_2CDH^{+} \arrow[l, shift left] \arrow[d, "PhH"] \\
PhCD_2CH_3 & PhCH_2CD_2H & PhCDHCDH_2
\end{tikzcd}$$

Scheme 2.

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