Tetrahedron Letters No.38, pp. 3283-3286, 1969. Pergamon Press. Printed in Great Britain.

# STEREOSPECIFIC FRIEDEL-CRAFTS ALKYLATION OF BENZENE WITH 3-CHLOROBUTANOIC ACID AND 3-CHLORO-1-BUTANOL IN THE PRESENCE OF LEWIS ACID

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(Received in Japan 1 July 1969; received in UK for publication 11 July 1969)

The Friedel-Crafts alkylation of aromatic hydrocarbons with alkyl halides or alcohols has been studied extensively and reviewed in great detail(1) and several works on the alkylation with haloalcohols have been reported. Olah and Pavlath(2) showed that the alkylation of benzene with fluoromethanol in the presence of zinc chloride gave benzyl fluoride. Bachman and Hellman(3) reported that aromatic hydrocarbons were alkylated with 1-halo-2-propanol or 1-halo-2-butanol in the presence of boron fluoride to give haloalkylbenzene derivatives.

On the other hand, the reaction of benzene with 3-chlorobutanoic acid (I) or 3-chloro-1-butanol (II) in the presence of aluminum chloride afforded 3-phenylbutanoic acid (III) or 3-phenyl-1-butanol (IV) in our present work. In order to elucidate the mechanism of these alkylations, the reaction of optically active 3-chlorobutanoic acid or 3-chloro-1-butanol was investigated.

The results obtained under several reaction conditions are shown in TABLE I and II. The absolute configurations of (+)-I and (+)-II have been assigned to be S(4), while those of (-)-III and (-)-IV to be R(5,6). Thus, the alkylation of benzene with (+)-I proceeded with 43.2 % net inversion of configuration in the case of aluminum chloride catalyst at 5°. The alkylation with (+)-II proceeded also stereospecifically, although the inversion percentage was somewhat less than in the case of (+)-I.

TABLE I

Reaction of Benzene with (S)-(+)-3-Chlorobutanoic Acid in the Presence of Aluminum Chloride

| Starting (+)-I $[\alpha]_D$(C 10, toluene) | Temp, °C | Time, hr | (-)-III Yield, % | (-)-III $[\alpha]_D$(neat) | Inversion,[a] % |
|---|---|---|---|---|---|
| + 27.5° | 10 | 4.0 | 81 | - 13.7° | 37.3 |
| + 27.5° | 5 | 4.0 | 46 | - 15.8° | 43.2 |

TABLE II

Reaction of Benzene with (S)-(+)-3-Chloro-1-butanol in the Presence of Lewis Acid

| Starting (+)-II $[\alpha]_D$(neat) | Lewis acid | Temp, °C | Time, hr | (-)-IV Yield, % | (-)-IV $[\alpha]_D$(neat) | Inversion,[b] % | Recovered (+)-II Recovered, % | Recovered (+)-II $[\alpha]_D$(neat) |
|---|---|---|---|---|---|---|---|---|
| + 17.0° | $AlCl_3$ | 0 | 3.5 | 83 | - 2.54° | 13.7 | — | |
| + 23.2° | $AlCl_3$ | -10 | 4.5 | 77 | - 4.81° | 20.0 | — | |
| + 21.9° | $AlCl_3$ | -20 | 4.5 | trace | | | 52 | + 21.9° |
| + 23.4° | $AlBr_3$ | -10 | 4.5 | 92 | - 4.01° | 16.6 | — | |
| + 23.5° | $SnCl_4$ | 20 | 20 | — | | | 70 | + 23.2° |

a. Calculated from the reported rotation:(+)-I; $[\alpha]_D$ +46.6°(C 10, toluene)(7) (-)-III; $[\alpha]_D$ -62.0°(neat)(5).

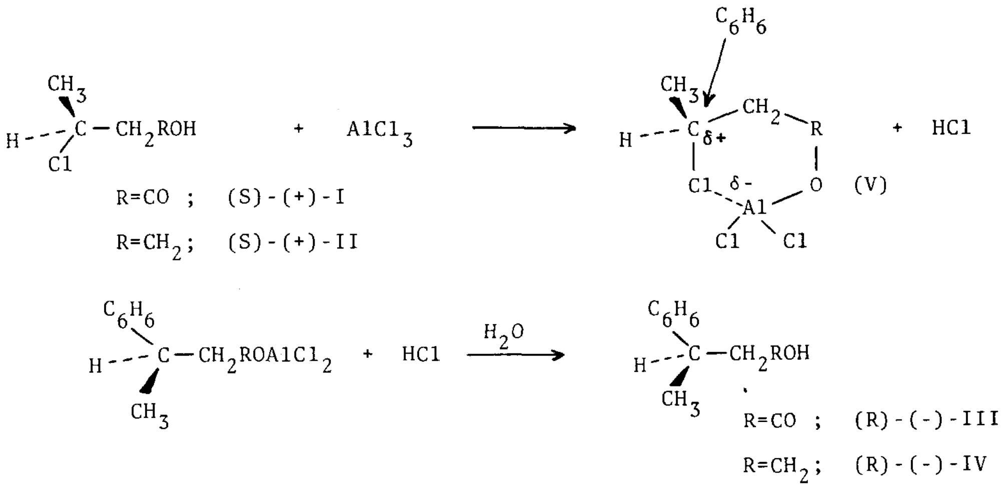
b. Although the optical rotation of (+)-II has not been reported, the optical purity of (+)-II is considered to be identical with the value of (+)-I used for the starting materials. Calculated from the reported rotation: (-)-IV; $[\alpha]_D$ -45.3°(neat)(5).

Raising the temperature resulted in increases in racemic product, and starting materials were recovered without racemization at the lower temperature. In the alkylation with (+)-II, using aluminum bromide in place of aluminum chloride increased the yield of (-)-IV and decreased the optical purity of the product. When stannic chloride was used, the alkylation did not occur and (+)-II was recovered without racemization.

Price and Lund$^{(8)}$ observed 1 % net inversion in alkylation with optically active 2-butanol and boron fluoride. Burwell and his co-workers found very small inversion in alkylation with alcohols$^{(9)}$ and ethers$^{(10)}$. Streitwieser and Stang$^{(11)}$ reported that the alkylation of benzene with 2-propanol-$d_3$ and boron fluoride proceeded with more than 93 % racemization.

Stereospecific Friedel-Crafts alkylation in the presence of aluminum chloride with such a considerable inversion as observed in our present work has not been reported, except for the alkylation with optically active cyclic compounds such as propylene oxide$^{(12)}$, 2-methyltetrahydrofuran$^{(13)}$, and γ-valero-lactone$^{(14)}$.

The stereospecificity in alkylation with 3-chlorobutanoic acid (I) and 3-chloro-1-butanol (II) may be due to the following proposed mechanism:



(+)-I or (+)-II reacts with aluminum chloride to form the quasi-ring intermediate complex (V) and hydrogen chloride. Benzene attacks the intermediate complex as a nucleophile. However, the observed optical purity of (-)-III or (-)-IV indicates that the reaction proceeds with a considerable racemization due to carbonium ion character of V.

Consequently, we believe that Friedel-Crafts reactions with such acyclic compounds are much like alkylations with cyclic ethers(12,13) or lactone(14).

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