BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 52 (6), 1873—1874 (1979)

Friedel-Crafts Reaction of Anisole with 2-*t*-Butyloxirane

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(Received November 2, 1978)

Synopsis. The title reaction in excess anisole gave a mixture composed of 3-(methoxyphenyl)-2,3-dimethyl-1-butanols (**2**) (a mixture of ortho and para isomers), 2-(*p*-methoxyphenyl)-2-methybutane (**3**), and oligomer of 2-*t*-butyloxirane, while the same reaction in nitromethane gave a product composed of **2** (only the para isomer) and hexylanisoles, but not **3**. The reaction sequences to give the products are discussed in terms of step-by-step and concerted alkylation mechanisms.

A recent paper has described that epoxides react competitively with the aromatic substance under Friedel-Crafts conditions *via* two different paths:[1] Path a; a nucleophilic attack of aromatics on epoxide to yield 2-aryl-1-alkanols,[2] and Path b; a rearrangement of the epoxide to a carbonyl compound, followed by condensation with aromatics. It was also found that the alkylation of anisole with epoxides in a nitromethane solvent takes place preferentially through Path b. In the course of our study of Friedel-Crafts reactions with epoxides, we found a curious behavior of 2-*t*-butyloxirane (**1**) under Friedel-Crafts conditions.

When **1** was allowed to react with an excess of anisole in the presence of aluminum chloride, 3-(methoxyphenyl)-2,3-dimethyl-1-butanols (**2**) (21% yield;[3] ortho isomer 50% and para isomer 50%) and 2-(methoxyphenyl)-2-methylbutane (**3**) (14% yield; only para isomer) were found, together with the oligomer (**4**).

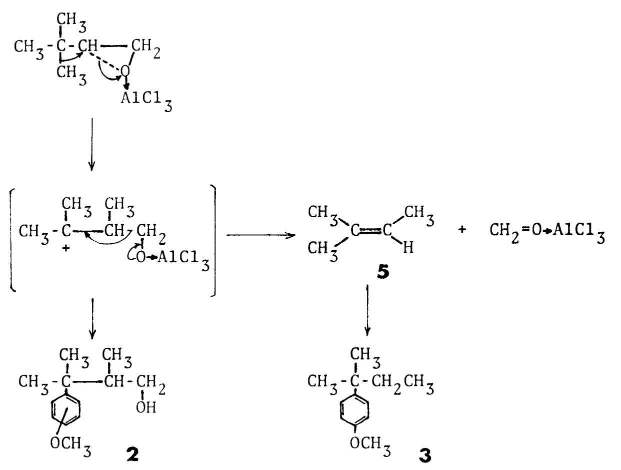
The retention volumes on GLC suggested that **4** was a mixture of dimer (8 wt% on the basis of the weight of the **1** used) and trimer (8 wt%) of **1**. When the reaction was carried out in nitromethane, a 14% yield of **2** (only para isomer) and a 30% yield of a mixture of isomer of hexylanisole were obtained, but no formation of **3** was observed.

As the ring-opening and the rearrangement of simple epoxide are widely accepted as proceeding without the formation of a fully developed carbonium ion,[4] the formation of **2**, which appears to be derived from a neopentyl rearrangement, is interesting. Although the base-catalyzed ring-opening and polymerization of **1** have been well established,[5] no report concerning a reaction under acidic conditions has appeared to our knowledge. Therefore, several kinds of acid-catalyzed ring-openings of **1** were carried out in order to examine the possibility of such a rearrangement.

As is shown in Table 1, the products are those which are formed by the direct attack on the epoxide carbon of **1**; no product could be detected which is to be expected from the neopentyl rearrangement, followed by nucleophilic attack. The results of the alkylation reported here are the first example of this kind of rearrangement in a simple aliphatic epoxide.[6]

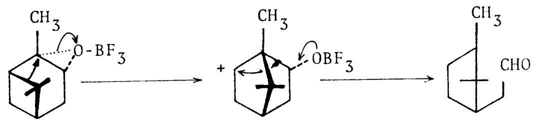
TABLE 1. ACID-CATALYZED RING-OPENING OF *t*-BUTYLOXIRANE (**1**)

Reaction condition	Product (isolated yield)
35% HCl, dioxane, 10 °C, 3 h.	1-Chloro-3,3-dimethyl-2-butanol (**10**) (90%)
$\mathrm{AlCl_3}$, 1,2-dichloroethane, ice bath, 2.5 h.	**10** (8.4%)
Acetic acid, 70 °C, 48 h, then 10% NaOH.	3,3-Dimethyl-1,2-butanediol (**11**) (92%)
Formic acid, ice bath, 24 h.	*t*-Butylethylene diformate (18%), 2-hydroxy-3,3-dimethyl formate (19%), 1-(hydroxymethyl)-2,2-dimethylpropyl formate (8%), and **11** (8%)
Ethanol, a drop of $\mathrm{H_2SO_4}$, room temp, 8 days.	1-Ethoxy-3,3-dimethyl-2-butanol (89%)



Scheme 1. Proposed reaction sequences for the reaction of **1** in excess anisole.

Product **3** is also an abnormal product. It is well known that undesired reactions always take place as the side reactions of Friedel-Crafts reaction.[7] The reaction sequences which have thus far been proposed to explain the side reactions, however, cannot explain the formation of **3**. The most probable reaction sequence is as follows: **1** undergoes ring-opening, rearrangement of methyl group, and *β*-cleavage to yield 2-methyl-2-butene (**5**), which then reacts with anisole to give **3** (Scheme 1). A similar cleavage was reported in the $\mathrm{BF_3}$-catalyzed rearrangement of pinene oxide (**6**).[8] In the Lewis acid-catalyzed rearrangement of epoxide, the migrating groups are usually the substituents attached directly to



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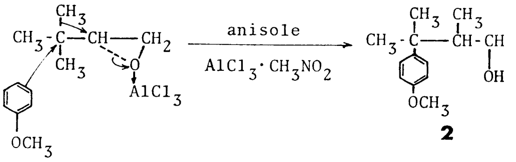
the epoxide ring. In contrast, the alkyl groups which are in the β-position to the epoxide ring shift in the reactions of **1** and **6**. As the backside of the epoxide C–O bond is shielded by the bulky *t*-butyl group in **1** or the methyl group on the bridge carbon in **6**, alkyl groups attached to the epoxide rings are prevented from approaching the carbonium-ion center.

As the reaction of anisole with 2,3-dimethyl-2-butene affords a product consisting of more than 95% para isomer (as shown by a separate control experiment), the high proportion of the ortho isomer in **2** formed in the reaction of excess anisole seems to be unusual. Kretchmer and McCloskey[9] found that ethyl allylmalonate and 5-hexen-2-one (**7**) react preferentially with anisole at the ortho position and explained the mechanism by a cyclic process, in which both anisole and the alkylating agent coordinate to an aluminum atom. A similar mechanism might be applied to the ortho alkylation of anisole with **1**. But in the reaction of **1**, the exchange of the solvent from excess anisole to nitromethane reduced the proportion of ortho alkylation from 50% to 0%, whereas the alkylation of anisole with **7** was reported to yield 65% and 55% ortho product in excess anisole and in 1-nitropropane respectively. The solvent effects of the reaction reported here seem to be too large to be explained by the ortho-alkylation mechanism.



Scheme 2.

Nakajima *et al.* reported an asymmetric induction in the reaction of benzene with optically active 1,2-epoxybutane to yield 3-phenyl-1-butanol.[10] From their results, one can consider that the hydride shift from the β to the α position occurs in concert with the alkylation step of benzene. In the reaction of **1** in nitromethane, the alkylation step seems similarly to occur in concert with the methyl migration and ring-opning of epoxide, as is shown in Scheme 2. An S_N2-like transition state favors an attack on the para position of anisole because of steric hinderance. Scheme 2 can also explain the fact that the reaction in nitromethane does not give **3**, because this reaction mechanism does not involve a fully developed carbonium ion. In the case of the anisole solvent, the reacting species have a more carbonium-ion character (Scheme 1) and the proportion of the ortho isomer increases.

Experimental

Into a mixture of aluminum chloride (2.7 g) and anisole (25 ml) held in an ice bath, a solution of **1** (1.00 g) in anisole (10 ml) was added dropwise under vigorous stirring over a period of 30 min; stirring was then continued for an additional 2 h at the ice-bath temperature. After the usual work-up, the products were separated by column chromatography on silica gel, using benzene as the elutant. The distillation of the least polar fraction by means of a ball-oven apparatus yielded 230 mg (13%) of **3**, which was identical with a sample prepared by the alkylation of anisole with **5**; NMR ($CDCl_3$): 0.6^7 (3H, t), 1.2^5 (6H, s), 1.6^0 (4H, q), 3.7^8 (3H, s), and 6.7—7.3 (4H, phenyl). MS *m/e* (rel intensity) 180 (M^+, 13), 149 (100), 121 (17), and 90 (10). IR; 830 cm^{-1}. Found: C, 81.09; H, 9.94%. From the middle fraction was obtained 170 mg of **4**; NMR ($CDCl_3$): 0.9^2 (3H, s) and 3.1—4.0 (unresolved multiplets, 1H). IR: 3600, 3450, 1480, 1365, 1120, 1095, and 1060 cm^{-1}.

The distillation of the most polar fraction by means of the ball-oven apparatus yielded 350 mg (17%) of two isomers of **2**. Para isomer of **2**: NMR ($CDCl_3$): 0.9^2 (3H, d, J=6.4 Hz), 1.7^2 (6H, s), 1.8 (2H, m, methine and OH), 3.3^5 (1H, d, d, J=7.6 and 10.6 Hz), 3.7^8 (1H, d, d, J=4.8 and 10.6 Hz), 3.7^8 (3H, s, OCH_3), and 6.7—7.3 (4H, AA′BB′ coupling, phenyl). IR: 3350, 1610, 1580, 1518, 1300, 1260, 1190, 1030, and 830 cm^{-1}.

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11) The starting material, **1**, was prepared by two different methods: the *m*-chloroperbenzoic acid oxidation of commercially available 3,3-dimethyl-1-butene, and the cyclization of 2-bromo-3,3-dimethyl-1-butanol.[12]

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