Electron Beam-Induced Fries Rearrangement of Sulfonamide and Sulfonate Crystals

Jun Kato,*[†,††] Yasunari Maekawa,*[††] and Masaru Yoshida[††]
[†]*Department of Pure and Applied Chemistry, Tokyo University of Science, 2641 Yamazaki, Noda 278-8510*
[††]*Department of Material Development, Japan Atomic Energy Research Institute, 1233 Watanuki, Takasaki 370-1292*

(Received November 22, 2004; CL-041399)

The electron beam (EB) sensitivity of sulfonic acid derivatives in the crystalline state was much higher than that of the corresponding carboxylic acid derivatives, which was distinct from the results using other energy sources such as heat and UV; especially, sulfonamide derivatives could undergo the chemoselective Fries rearrangement to give *ortho* and *para* products in the ratio of ca. 7/3 without the *meta* isomer.

Ionizing radiation such as ion and electron beams possesses high energy and narrow beam size enough to modify the structures and properties of organic molecules and polymeric materials on atomic and molecular levels.[1] Because of rapid nanoscale scanning, the electron beam (EB) irradiation has attracted much attention in recent years as a promising technique for nanolithography and fabrication of future nanodevices in a variety of fields such as electronics, photonics, biologics, and mechanics.[2] Nevertheless, there have been few reports on the useful EB induced reactions of organic compounds,[3] which are required to design materials for these applications, although a number of studies on radiation-induced reactions of simple organic compounds, such as alkanes, alcohols, and stilbenes, have been conducted.[4]

Recently, we investigated the EB induced reactions of either cinnamic acid derivatives[5] or sulfonium salts[6] in the crystalline state, together with comparison with the corresponding photoreactions. These reactions proceeded via direct ionization and excitation of target molecules without any influence of a reaction medium. In addition, the crystalline lattice restrictions simplified the EB induced reactions, which generally lead to many products in complex mechanism. The Fries rearrangement of both carboxylic and sulfonic acid derivatives is known to proceed using various energy sources such as heat[7] or microwave[8] with catalyst, and UV light.[9] It is notable that these reactions are accompanied by the transformation of ester and amide linkages to hydrophilic phenol and aniline moieties, respectively; especially, an acidic sulfonamide can be converted to the corresponding basic aniline derivatives. Thus, we report herein the novel EB induced Fries rearrangement of amide and ester derivatives in the crystalline state, which has the potential of utilization in nanolithography.[10]

The EB induced reactions of the amide and ester derivatives in the crystalline state were carried out as follows. Finely powdered crystals recrystallized from alcohol were placed in a hollow (10 mm in diameter, 1 mm in depth) of a glass plate, and were covered with a Kapton film. The samples, which were placed on a water-cooled copper plate, were irradiated with EB (1 MeV, 1 mA) at a dose rate of 2.9 kGy·s^{-1}, using a cascade type electron accelerator (Dynamitron). The crystals of benzenesulfonanilide (**1a**), benzanilide (**2**), phenyl *p*-toluenesulfonate (**3**), and phenyl benzoate (**4**) were irradiated with doses of 1–20 MGy (0.54–10.8 mC·cm^{-2}); then, these conversions were determined by GC and HPLC. As shown in Figure 1, with the irradiation dose of 10 MGy (irradiation for 57.5 min), the conversions of **2** and **4** were only 2 and 7%. Whereas, those of **1a** and **3** reached to 50 and 44%, and then went up to 75 and 84% with the dose of 20 MGy. It was noted that the sensitivity of sulfonic acid derivatives to EB was much higher than that of the corresponding carboxylic acid derivatives. This was distinct from the results using other energy sources such as heat and UV.[7–9]

The EB irradiation of sulfonamide **1a** with the dose of 10 MGy gave three main products, which were observed in GC and HPLC. These products were isolated from each other by a reversed phase preparative HPLC. Then, the isolated products were assigned to *o*- and *p*-aminophenyl phenyl sulfones (**5a** and **6a**), and aniline (**7**) by IR, ^{1}H and ^{13}C NMR, and MS (Scheme 1). Namely, the EB irradiation of **1a** in the crystalline state induced Fries rearrangement to give two regio isomers (**5a** and **6a**) in 24 and 10% yields with a radiolytic product **7** in an 8.0% yield (Table 1). The *ortho*/*para* ratio was approximately 7:3 throughout the reaction. Likewise, the EB irradiation with 10 MGy of sulfonate **3** in the crystalline state induced Fries rearrangement to give *o*-hydroxyphenyl *p*-tolyl sulfone **8** and the *para* isomer **9** in yields of 6.0 and 2.3% along with the scission product, phenol (**10**) in a yield of 5.6% (Scheme 1). In the EB induced reactions of both sulfonamide and sulfonate derivatives, other degradation products could not be detected in GC and HPLC. It is noteworthy that the reactions of sulfonamide and sulfonate derivatives shown in Scheme 1 are the first example of radiation-induced Fries rearrangement via direct excitation and/or ionization.

Although both sulfonic acid derivatives showed much higher EB sensitivity, compared with the corresponding carboxylic acid derivatives, sulfonamide **1a** could further afford the

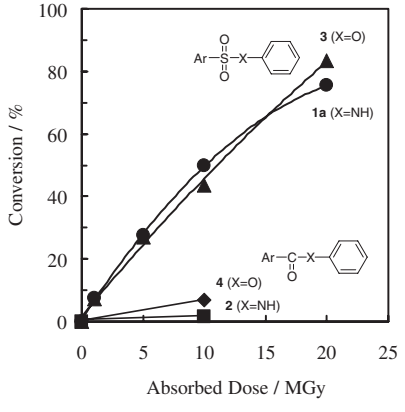
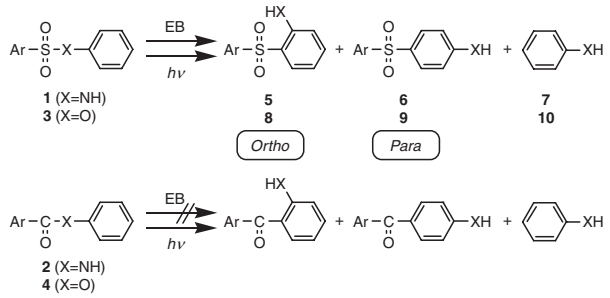
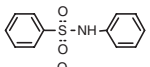
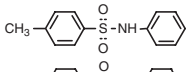
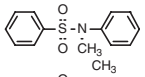
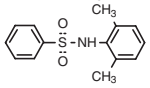


Figure 1. The conversion of the starting compounds (sulfonamide **1a**, sulfonate **3**, and their corresponding carboxylic acid derivatives, **2** and **4**) as a function of EB dose absorbed by the crystals.



Scheme 1. Fries rearrangement of amide and ester derivatives from sulfonic and carboxylic acids upon EB and UV in the crystalline state.

Table 1. Electron beam-induced Fries rearrangement of arylsulfonamides[a] (**1a**–**1d**) in the crystalline state

Reaction substrate		Conv.[b]/%	Fries rearr. products[c]/% *ortho*	*para*
	**1a**	50	24	10
	**1b**	55	16	10
	**1c**	41	(3.3 : 1)	
	**1d**	21	N.D.[d]	13

[a]Prepared according to the procedure described in Ref. 11. [b]Conversion after irradiation (10 MGy). [c]Determined by GC. All yields were calculated on the consumed sulfonamide derivatives. [d]Not detected.

Fries rearrangement products with higher selectivity than sulfonate **3**. Thus, the EB induced Fries rearrangements of the other arylsulfonamides **1b**–**1d** were examined with the dose of 10 MGy for comparison with **1a**; these results are summarized in Table 1. *p*-Toluenesulfonanilide (**1b**), which possesses one additional methyl group on the phenyl group attaching to sulfone in **1a**, showed similar conversion (55%) to give Fries rearrangement products (**5b**, **6b**) with similar *ortho*/*para* ratio (62/38) to that of **1a**. *N*-Methylbenzenesulfonanilide (**1c**), which possesses one additional methyl group on nitrogen atom in **1a**, also showed similar conversion (41%) and regioselectivity (*ortho*/*para* = **5c**/**6c** = 77/23) to those of **1a** and **1b**. Regardless of whether there is an amide proton or not, EB induced Fries rearrangement proceeded to afford *ortho* and *para* isomers in the ratio of about 7/3; in all the cases, no trace of the *meta* isomer could be detected.

The photoreaction of carbonyl compounds (amides and esters) is known to undergo Fries rearrangement through radical intermediates produced by homolytic cleavage of C(=O)–N or C(=O)–O bond via the lowest excited singlet state.[12] The photo-Fries rearrangement of sulfonamides is also thought to proceed in the similar manner to that of the corresponding carbonyl compounds to provide *ortho* and *para* isomers due to the resonance structures of phenylaminyl radicals in the intermediates. *N*-(2,6-Dimethylphenyl)benzenesulfonamide (**1d**), which has two methyl groups at both *ortho* positions of anilide moiety, showed 21% in conversion, which was lower than those of **1a**–**1c**; however, as expected, it underwent regioselective Fries rearrangement to produce only *para* isomer **6d**. The formation of **6d** ruled out the concerted mechanism for the Fries rearrangement, which gives only an *ortho* isomer. Accordingly, the EB induced Fries rearrangement of sulfonamides is inferred to proceed through radical intermediates obtained by the homolytic cleavage of the S–N bond via the lowest excited state. It is well known that radiolysis of organic molecules leads primarily to upper excited states by direct excitation or recombination of dissociated radical cation and a free electron regardless of the molecular structure. Accordingly, the upper excited state of sulfonamides produced by EB irradiation is inferred to lead to the lowest excited state, which is the same state as photoreaction, resulting in the homolytic cleavage of the S–N bond to give rise to Fries rearrangement products through radical intermediates. In contrast to sulfonic acid derivatives, the corresponding carboxylic acid derivatives undergo Fries rearrangement by photolysis but not by radiolysis under the same conditions. This difference should result from the fact that the carboxylic acid derivatives in upper excited states can not lead to the lowest excited state, from which the photo-Fries rearrangement proceeds; as the result, it should be relaxed to the ground state via the other thermal processes.

In conclusion, the EB irradiation of sulfonic acid derivatives in the crystalline state underwent the Fries rearrangement to yield the aniline and phenol derivatives, respectively; whereas, the corresponding carboxylic acid derivatives did not give rise to any rearrangement products, though both sulfonic and carboxylic acid derivatives undergo photo-Fries rearrangement. Only sulfonamide derivatives could provide the Fries rearrangement products preferentially to give *ortho* and *para* products in the ratio of ca. 7/3 without the *meta* isomer. It should be noted that this rearrangement was the first radiation-induced transformation from acid (sulfonamides) to base (anilines); thus, this EB-Fries rearrangement seems to be very useful for nanolithography and nanofabrication. Further studies on the detailed mechanism of the above rearrangement as well as other EB induced reactions in restricted matrix are underway.

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Published on the web (Advance View) January 26, 2005; DOI 10.1246/cl.2005.266