The Mechanism of the Rearrangement Reaction of 3-Phenyl-4-methoxy-5-bromotropone to 3-Phenyl-4-methoxybenzoic Acid[1]

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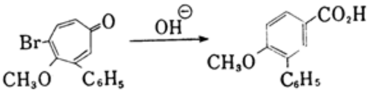
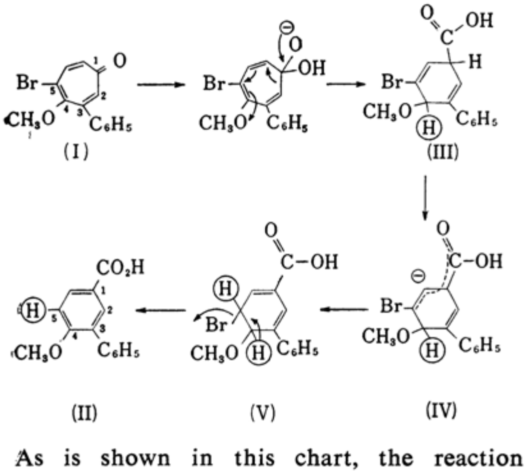
An examination of the reaction mechanism of the rearrangement of 2-phenyl-4-bromotropone to 2-phenylbenzoic acid by using heavy water was described in a preceding paper.[2] A similar reaction has recently been found by one of the present authors (T. M.)[3] in the rearrangement of 3-phenyl-4-methoxy-5-bromotropone (I) to 3-phenyl-4-methoxybenzoic acid (II), a reaction which cannot be explained by the known mechanism of the rearrangement reaction of tropoids.



(I) (II)

The reaction mechanism depicted below has been assumed for the rearrangement of I to II; this hypothesis was examined, using deuterium as the tracer element.



As is shown in this chart, the reaction begins with the attack on the carbonyl carbon in I by a hydroxyl ion, which causes a ring contraction, and then the carbon atom carrying the methoxyl group undergoes protonization to form III. III forms the anion IV by the action of a base and, through the formation of V by protonization to the carbon atom in the 5-position or by an intramolecular proton 1, 3-transfer,[4] forms II by dehydrobromination.

If this rearrangement is carried out in a system containing deuterium, the position marked with Ⓗ in the above chart will be occupied by deuterium atoms. If, on the other hand, the formation of the intermediate V is due to protonization, the deuterium content at the 5-position in the rearrangement product should be close to the theoretical value (8.33 atom.%), while the value will be far smaller than the theoretical if the 1, 3-transfer of the proton has occurred. In any case, if the foregoing reaction mechanism is correct, the position of the deuterium ion in II should be 5 and not any other position.

A solution of I dissolved in a system of deuterium oxide,[5] sodium hydroxide-*d*, and methanol-O-*d*[6] was refluxed for 30 min.; the rearrangement product so obtained was converted to the methyl ester with diazomethane, and the ester was hydrolyzed with alkali,[2] thus affording deuterated 3-phenyl-4-methoxybonzoic acid (II) with a m. p. of 214—215°C.[7]

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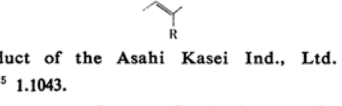
[1] Paper read at the 13th Annual Meeting of the Chemical Society of Japan, Tokyo, April, 1960.

[2] Y. Kitahara, I. Murata and T. Muroi, This Bulletin, 34, 1359 (1961).

[3] T. Muroi, This Bulletin, 34, 178 (1961).

[4] The relative rates of the double-bond migration and of deuterium exchange of perdeuterio-1-pentene with unlabeled 2-methyl-1-pentene and solvent have been determined at 55°C in the system of potassium *t*-butoxide in dimethyl sulfoxide by S. Bank, C. A. Rowe, Jr., and A. Schriesheim, *J. Am. Chem. Soc.*, 85, 2115 (1963). They found that the isomerization is 16 times faster than the exchange. Thus they concluded that the isomerization reaction involves an intramolecular proton transfer. A reasonable mechanism can be developed on the basis of a tightly-bound ion pair.



[5] Product of the Asahi Kasei Ind., Ltd. Purity, 99.80%, d_4^{25} 1.1043.

[6] D. H. Hill, B. Stewart, S. W. Kantor, W. A. Judge and C. R. Hauser, *J. Am. Chem. Soc.*, 76, 5129 (1954).

[7] It was confirmed through infrared spectral identification that 3-phenyl-4-methoxybenzoic acid does not undergo secondary deuteration under these rearrangement reaction conditions.

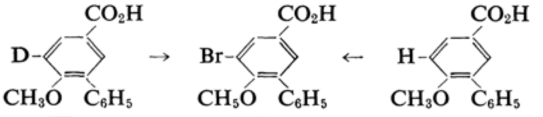
The infrared absorption spectrum of II (cf. Table I) was somewhat different from that of the 3-phenyl-4-methoxybenzoic acid[8] (II′) prepared from anisic acid from the out-of-plane to the finger-print region and indicated the presence of deuterium. The deuterium content was found to be 0.28 atom.% by mass analysis; this is far smaller than the theoretical value. This result shows that the base-catalysed protropic migration is intramolecular.

TABLE I. INFRARED ABSORPTION MAXIMA OF II AND II′*

II	II′
665 (w)	665 (w)
695 (s)	694 (s)
700 (s)	—
728 (s)	723 (s)
772 (s)	772 (s)
824 (m)	824 (m)
832 (m)	—
870 (w)	870 (w)
907 (w)	907 (w)
920 (m)	—
—	930 (m)
957 (w)	—
1023 (s)	1023 (s)
1043 (s)	1044 (s)
1078 (w)	1077 (w)
1120 (m)	1121 (m)
1139 (s)	1139 (s)
1146 (m)	—
—	1177 (m)
1185 (w)	1186 (w)
1245 (s)	—
1260 (s)	1260 (s)
1270 (s)	—
1312 (s)	1307 (s)
1400 (m)	1404 (m)
1440 (s)	1440 (s)
—	1450 (s)

* IR spectra are measured using a Perkin-Elmer Model 21 double beam spectrophotometer in KBr pellet.

The position of the deuterium atom in II should be 5 (the position meta to the carboxyl carbon), according to the hypothetical mechanism, and this atom should be replaced by the bromine atom upon the bromination of II. The bromination of II with 1 mol. of bromine in glacial acetic acid afforded a monobrominated compound (VI) with a m. p. of 231—232°C, the infrared absorption spectrum of which was identical with that of the brominated product of II′.



(II) (VI) (II′)

It follows, therefore, that the deuterium atom in II is at the 5-position and that there are none in other positions. This fact supports the mechanism described above.

Experimental[9]

The Rearrangement Reaction of 3-Phenyl-4-methoxy-5-bromotropone (I) in a Heavy Water System.—Sodium (0.11 g.) was dissolved in methanol-O-*d* (8 ml.); deuterium oxide (8 ml.) and I (0.4 g.) were added to it, and the mixture was refluxed on a water bath for 25 minutes, protected with a calcium chloride tube. Methanol was evaporated under reduced pressure, and the residue was diluted with 10 ml. of water and extracted with chloroform in order to remove a neutral portion. The aqueous layer was acidified to Congo red with hydrochloric acid; the crystals that separated out were collected, and the filtrate was extracted with chloroform. The crystals obtained were combined and suspended in ether, and an ether solution of diazomethane was added to it in order to effect esterification. The crystal obtained by the evaporation of ether were dissolved in a mixture of methanol (4 ml.) and 2 N sodium hydroxide (1.5 ml.), and the mixture was refluxed for 4 hr. Methanol was evaporated under reduced pressure, and the residue was diluted with water and acidified. The crystals that separated out were collected by filtration to crude crystals (0.25 g.) of II, m. p. 202—206°C. This was purified by sublimation under reduced pressure, and the sublimate was recrystallized from methanol to II as colorless prisms, m. p. 214—215°C.

Found: C, 73.48; H, 5.49; D, 8.33. Calcd. for $C_{14}H_{14}DO_3$: C, 73.67; H, 5.30%; D, 0.23 atom.%.

3-Phenyl-4-methoxy-5-bromobenzoic Acid (VI).—Bromine (70 mg.) was added to a solution of II (80 mg.) dissolved in glacial acetic acid (0.5 ml.) by heating, and then the mixture was heated on a water bath at 45—55°C for 4 more hours. The crystals that separated out were collected by filtration to 70 mg. of crude crystals with a m. p. of 217—222°C. Recrystallization from ethanol gave VI melting at 231—232°C.

VI was similarly obtained from II′.

Found: C, 54.55; H, 3.37. Calcd. for $C_{14}H_{11}O_3Br$: C, 54.74; H, 3.61%.

The determination of deuterium by mass analysis was carried out by Dr. Sumio Horibe, Faculty of Science, Tokyo Metropolitan University, while the infrared spectral measurement was made by Mr. Hideji Aono of this Institute, to both of whom the authors wish

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[8] K. H. Slotta and A. E. Nold, *Ber.*, **68**, 2226 (1935).

[9] All melting points are uncorrected.

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