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The Jacobsen Reaction and the Acid-Catalyzed *Ortho-para* Interconversion of Iodoanisoles and Iodophenetoles

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o-Iodoanisole and *p*-iodoanisole are unstable when brought into contact with sulfuric acid and readily undergo disproportionation to yield 2,4-diiodoanisole.[1] Similarly behave both *o*- and *p*-iodophenetoles, giving 2,4-diiodophenetole in a high yield. Such intermolecular iodo migration is usually referred to as the Jacobsen reaction. When a small amount of *o*- or *p*-iodoanisole is dissolved in sulfuric acid, an intense dark brown color develops, which persists over a period of many days. Dilution of the solution with acetic acid or water, however, causes disappearance of this color and the formation of the iodoanisolesulfonic acid. The deep-colored solution has the iodinating power, but the diluted colorless solution has not. In contrast, *m*-iodoanisole is merely sulfonated to give *m*-iodoanisolesulfonic acid, and the solution neither becomes colored nor possesses the iodinating property.

Several inorganic iodo compounds are known, when dissolved in sulfuric acid, to give deep-colored solutions which contain stable positive iodine (I_3^+ or I_5^+) or multivalent iodine (IO^+ or IO_2^+), and possess the strong iodinating power.[2] In this connection, it seems interesting to examine the intermediate species which is responsible for such an easy intermolecular transfer of the iodine atom in the Jacobsen reaction of iodoanisoles. Being brought into solution, *o*- or *p*-iodoanisole develops at first green, then yellow color, which gradually deepens to yellow brown, and finally to dark brown or black. Within several hours after preparation, both solutions from *o*- and *p*-iodoanisole showed the same ultraviolet absorption (λ_{max}, 205, 227, 238—239 *sh*,[3] 281, 410 *sh*, and 438 nm), and this spectral pattern remained unchanged for days. When a bsaic hydrocarbon such as mesitylene was added to these systems, decoloration soon took place and the formation of iodomesitylene was observed at the time of the disappearance of characteristic color. With a weaker base such as *o*-dichlorobenzene or sterically crowded 1,2,4,5-tetraisopropylbenzene, however, such decoloration was not observed. The solution diluted with acetic acid or water contained neither elementary iodine nor iodic acid, so the possible role of the positive iodine or the multivalent iodine for these coloration was ruled out. The spectral pattern of the above solutions differs from the spectra of the any known inorganic iodo compounds dissolved in sulfuric acid,[2] but resembles the spectrum which is superposition of the spectra of anisolesulfonic acid and the benzenonium complex[4] (Fig. 1). Thus the absorption band in the visible region is thought to be due to the stable σ-complex (for example, I) formed by the addition of sulfur trioxide and stabilized through the conjugative delocalization of positive charge by methoxyl group. Then, the intermolecular transfer of iodine atom would probably proceed through the nucleophilic attack of a more basic substrate upon the iodine atom of this intermediate (Scheme 1).

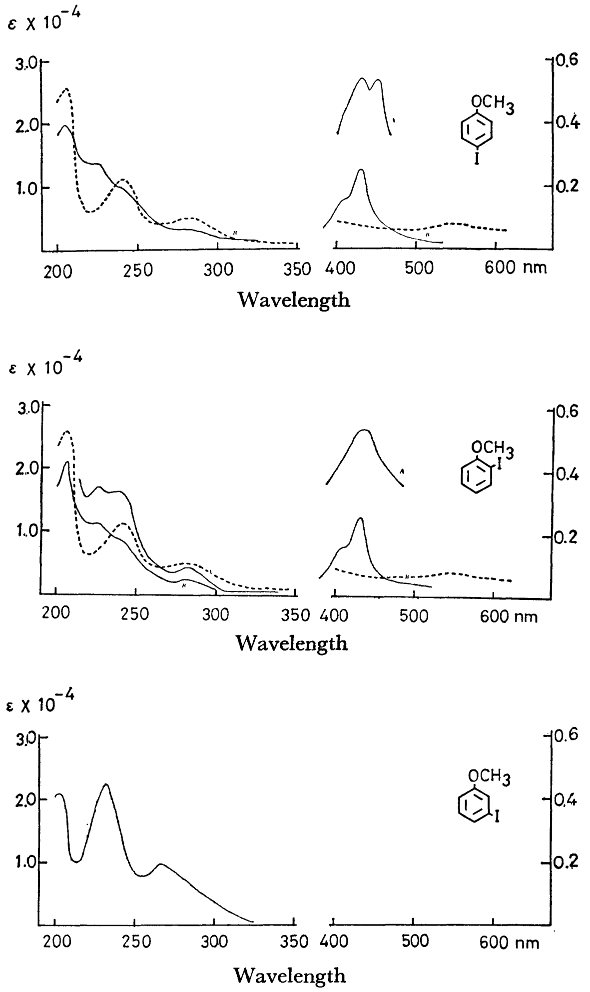

Fig. 1. Absorption curves of iodoanisoles in concentrated sulfuric acid.
Solid line: A. Immediately after dissolution.
B. Several hours later.
Dotted line: After a month's standing.

Intermolecular iodo migration is of some synthetic value. Polyalkylbenzenes can be successfully iodinated by the transfer of iodine atom from *o*-iodoanisole on

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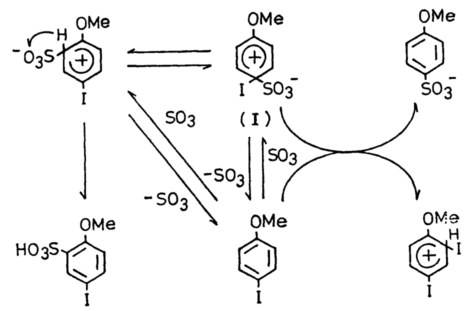
[1] H. Suzuki and R. Goto, This Bulletin, **36**, 389 (1963); *Nippon Kagaku Zasshi*, **84**, 284 (1963).

[2] J. Arotsky and M. C. R. Simons, *Quart. Rev.* (London), **16**, 282 (1962); J. Arotsky, H. C. Mishra, and M. C. R. Simons, *J. Chem. Soc.*, **1962**, 2582.

[3] The suffix *sh* denotes shoulder.

[4] G. A. Olah and P. R. Schleyer, "Carbonium Ions", Vol. 1, Interscience, London (1968), p. 180.



Scheme 1

addition of sulfuric acid.[5] Isomer distribution of the iodination products obtained by the crossed Jacobsen reaction of *o*-iodoanisole with toluene, ethylbenzene, isopropylbenzene, and *t*-butylbenzene is summarized in Table 1. The results clearly indicate the electrophilic nature and the bulkiness of the attacking species.

Table 1. Isomer distribution of the products obtained by the crossed Jacobsen reaction of *o*-iodoanisole with some alkylbenzenes

Alkylbenzene	Isomer distribution (%)			
	ortho	*meta*	*para*	1/2 *ortho*-*para* ratio
Toluene	59	a)	41	0.72
Ethylbenzene	41	1	58	0.35
Isopropylbenzene	22	2	76	0.14
t-Butylbenzene	4	0	96	0.02

a) Not determined due to ill resolution from *o*- and *p*-isomers.

Interestingly, *o*- and *p*-iodoanisoles were found to be interconversible in the presence of small amounts of sulfuric acid. This facile isomerization was carried out, agitating the light petroleum solution of each isomer with about 10% weight of sulfuric acid for several hours at room temperature. The relative amount of both isomers in the equilibrium mixture varied to some extent depending on the experimental conditions employed, but the *p*-isomer was always predominant ($o/p=0.32$—0.43). In no case, *m*-isomer was detected, which excludes the intramolecular 1,2-shift process of the isomerization. The present observation is probably the first example of the protogenic acid-catalyzed isomerization of haloanisoles.[6]

The reaction probably involves deiodination and the concurrent rapid reiodination *via* the intermediate I. The interconversion might also be formulated as the intramolecular rearrangement of iodine atom from ortho to para and *vice-versa* through the π-complex. However, the mechanism which involves the iodination of iodoanisoles to 2,4-diiodoanisole, followed by displacement of either one of iodine atoms in the latter seems less probable, since the diiodoanisole was found to be comparatively stable under the same condition.

The reasonable explanation for the lack of iodine migration in *m*-iodoanisole is that the electrophilic attack could hardly occur at the *m*-position where the iodine atom occupies owing to the unfavorable positional condition relative to the methoxyl group, as a result the detachment of the iodine atom as positively-charged species is depressed and *m*-iodoanisole is merely converted to sulfonic acid. The absence of disproportionation with the iodo compounds bearing electron-attracting group[7] or bulky group[8] is probably due to either the difficulty of the formation of the intermediate ion such as I, or the steric hindrance to the S_N2 type intermolecular iodine transfer. Similar disproportionation was observed during the acid hydrolysis of some *o*-iodoacetanilides, which will be described elsewhere.

Experimental

Iodoanisoles (*o*, bp 113—114°C/14 mmHg; *m*, bp 113—114°C/16.5 mmHg; *p*, mp 50—51°C) and iodophenetoles (*o*, bp 126—127°C/16 mmHg; *p*, mp 28—29°C, bp 133—134°C/19 mmHg) were prepared from the corresponding anisidines and phenetidines, respectively. Ultraviolet spectra were measured in 98% sulfuric acid solutions on a Hitachi EPS-300 spectrophotometer and a Shimadzu QV-50 spectrophotometer. The product analysis was performed on a Hitachi Model 063 gas chromatograph using a capillary column coated with Apiezon Grease L.

Jacobsen Reaction of Iodoanisoles and Iodophenetoles. A typical procedure is as follows: A mixture of *o*-iodophenetole (12.4 g) and sulfuric acid (10 g) was stirred at room temperature for 2 hr. The dark thick mixture was diluted with excess of water and the oily precipitate was extracted with ether. The ethereal solution was evaporated and the residue was passed over a column of alumina. Elution with light petroleum, followed by recrystallization from the same solvent gave 2,4-diiodophenetole as white prisms, mp 46—47°C. Yield, 7.7 g (82%). *p*-Iodophenetole gave the same product in somewhat less yield. IR (Nujol): 799, 871, 925, 1042, 1113, 1149, 1242, and 1278 cm^{-1}: PMR (CCl_4): 8.54 (Me, t, $J=7.2$ Hz), 6.00 (CH_2O, q, $J=7.2$ Hz), 3.55 (Aromatic H, d, $J=8.8$ Hz), 2.54 (Aromatic H, q, $J=8.8$ and 1.8 Hz), and 2.03 τ (Aromatic H, d, $J=1.8$ Hz).

Found: C, 25.94; H, 2.19%. Calcd for $C_8H_8I_2O$: C, 25.70; H, 2.16%.

Similarly, *o*- and *p*-iodoanisole gave 2,4-diiodoanisole, mp 68—69°C, in 75—76% yield. IR (Nujol): 800, 872, 1037, 1146, 1187, 1245, 1263, and 1278 cm^{-1}: PMR (CCl_4): 6.14 (MeO, s), 3.48 (Aromatic H, d, $J=8.4$ Hz), 2.48 (Aromatic H, q, $J=8.4$ and 2.4 Hz), and 1.99 τ (Aromatic H, d, $J=2.4$ Hz).

Found: I, 70.73%. Calcd for $C_7H_6I_2O$: I, 70.52%.

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[5] H. Suzuki, T. Sugiyama, and R. Goto, This Bulletin, **37**, 1858 (1964).

[6] Iodophenetoles have been shown to behave similarly. There are several instances known in which the apparent intramolecular bromine shift has been observed during the demethylation of bromoanisoles in the presence of hydrobromic acid. However, these results rather belong to the well-documented isomerization of bromophenols. *Cf.* G. R. Pettit and D. M. Piatak, *J. Org. Chem.*, **25**, 721 (1960), and other papers cited therein.

[7] H. Suzuki and R. Goto, *Nippon Kagaku Zasshi*, **84**, 284 (1963).

[8] H. Suzuki, K. Nakamura, and R. Goto, This Bulletin, **39** 128 (1966).