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A Remarkable Difference of the Positional Selectivity in Electrophilic Aromatic Substitution of Dibenzofuran between the Classical σ-Complex and Charge-Transfer Mechanisms

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Electrophilic nitration of dibenzofuran with nitric acid by a charge-transfer mechanism occurs exclusively at the 3-position and on the other hand, substitution at the 2-position predominates in the acylation, in which a classical σ-complex mechanism is important.

The idea that a charge-transfer (CT) mechanism may play a key role in electrophilic aromatic substitutions, has attracted much attention. Despite notable elaborations by Perrin,1) Kochi,2) and many others, 3) this mechanism has not yet been widely accepted. This is because in the substrates hitherto investigated, i.e., toluene, anisole, and naphthalene, the positional reactivity expected for the CT mechanism would be much the same as that for the classical σ-complex mechanism and consequently, it would be difficult to differenciate the mechanistic alternatives by the observed positional reactivities.4) We report herein that in the case of dibenzofuran (DBF) the two mechanisms certainly participate, the product distributions being quite different between the mechanistic alternatives.

Friedel-Crafts acetylation of DBF with acetyl chloride and aluminium chloride was carried out in dichloromethane under controlled conditions in low conversion to determine the isomer distribution.5) The result is shown in Table 1 together with the isomer distributions for the nitration by nitric acid.6) The 2- and 3-isomers of DBF represented more than 94% of the total reactivity of these reactions. These positions have no complexity due to ipso-attack and steric hindrance as encountered in substituted benzenes and naphthalenes.7) The positional reactivity order of DBF for Friedel-Crafts acetylation was found to be $2 \gg 3 > 4 > 1$, which is in good agreement with that observed for proton-exchange reaction8) and also the relative stability of the protonated dibenzofuranonium ions estimated by CNDO/2 calculations.9) The MNDO calculations of optimized structure for the protonated and acetylated dibenzofuranonium ions also indicated the 2-σ-complexes were ca. 3 kcal/mol more stable than the corresponding 3-isomers.10) Thus, the positional reactivity for protodetritiation and Friedel-Crafts acetylation seems to be controlled by the thermodynamic stability of the σ-complexes (Scheme 1-a).

Table 1. The isomer distributions of electrophilic reactions and charge-transfer nitration of dibenzofuran

Reaction	Conditions	Conversion %	Isomer distributions/%[a)] 1-	2-	3-	4-
Acetylation	$AcCl/AlCl_3/CH_2Cl_2$/0 °C	10>	0.8	88	10	1.2
Nitration[b)]	99% HNO_3/TFA[c)]/0 °C	10>	3	4	92	1>
Nitration[b)]	99% HNO_3/CH_2Cl_2/-45 °C	3>	2	3	95	1>
CT-Nitration	$C(NO_2)_4$/TFA/light/0 °C/10 h	99	6	11	83	1>
CT-Nitration	$C(NO_2)_4$/TFA/dark/0 °C/10 h	no reaction				

a) Determined from peak areas obtained by HPLC or GLC after calibrating for each authentic compound. The reproducible accuracy are within ± 1%.

b) Quoted from Ref. 6. c) Trifluoroacetic acid.

In remarkable contrast, the positional reactivity in nitration of DBF with nitric acid follows the sequence: 3 ≫ 2 > 1 > 4 (Table 1). This order seems to be inconsistent with that expected for the classical σ-complex mechanism, since the MNDO calculations suggest that 2-nitrated dibenzofuranonium ion is 1.73 kcal/mol more stable than the 3-nitrated isomer. As previously reported, the high regioselectivity observed in the nitration appears not to be responsible for the protonation at the oxygen atom of DBF, because the isomer ratio of 2- and 3-nitrodibenzofurans is not directly related to the acidity of the medium used and in addition, the calculations indicate that the O-protonation would be the least possibility to occur.[6)]

The potential curves when nitronium ion vertically approaching from above to the DBF plane have been calculated as a function of the distance between the carbon and nitrogen atoms (Fig. 1). The curves show that the oriented π-complex at the 3-position is slightly stable compared to that at the 2-position. However, the difference (0.18 kcal/mol) in energy would be too small to explain the remarkable regioselectivity. Thus, an alternative explanation would be required for the notable positional selectivity. Since nitronium ion has a high electron affinity and moreover, DBF is a good electron donor as expected from the calculated ionization potential 8.30 eV, it would be probable to consider the possibility of the CT mechanism in the nitration (Scheme 1-b). To confirm this, we undertook the nitration of DBF with tetranitromethane in trifluoroacetic acid under the irradiation by high pressure (100 W) mercury lamp,[11)] where a CT mechanism should predominate.[12)] The product was a mixture of mono-nitrated DBFs, the composition being in a similar trend to that observed for the reaction with nitric acid.
It is worth noting that the nitration with tetranitromethane did not proceed without irradiation (Table 1). These results lead us to deduce that the nitration of DBF with nitric acid is most likely to proceed by the CT pathway, the substitution at the 3-position being extremely favored. This is partly confirmed by the

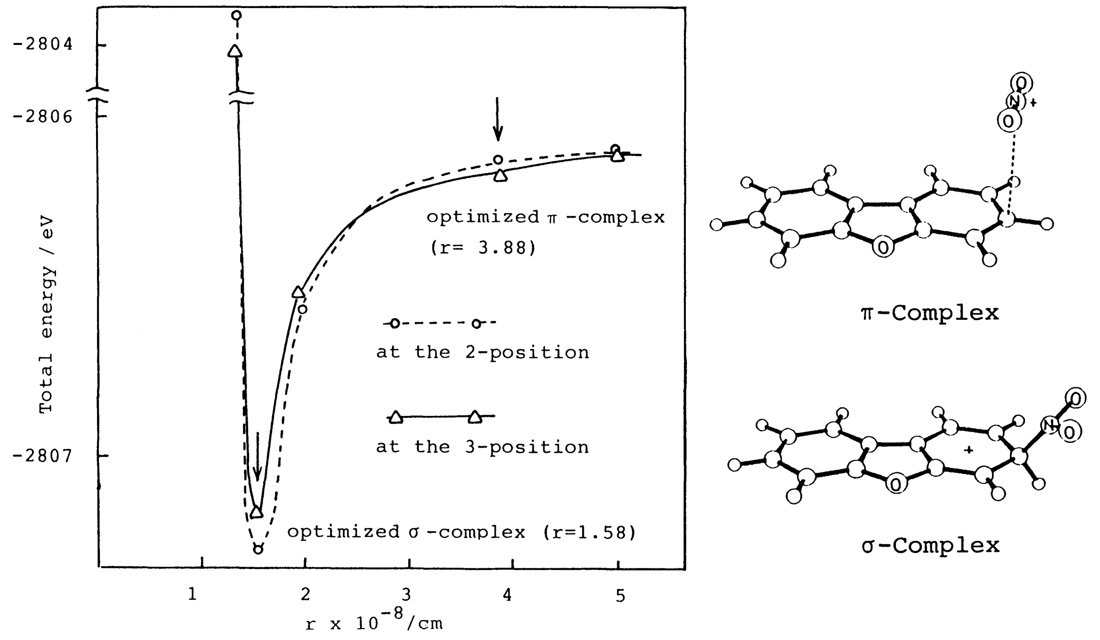
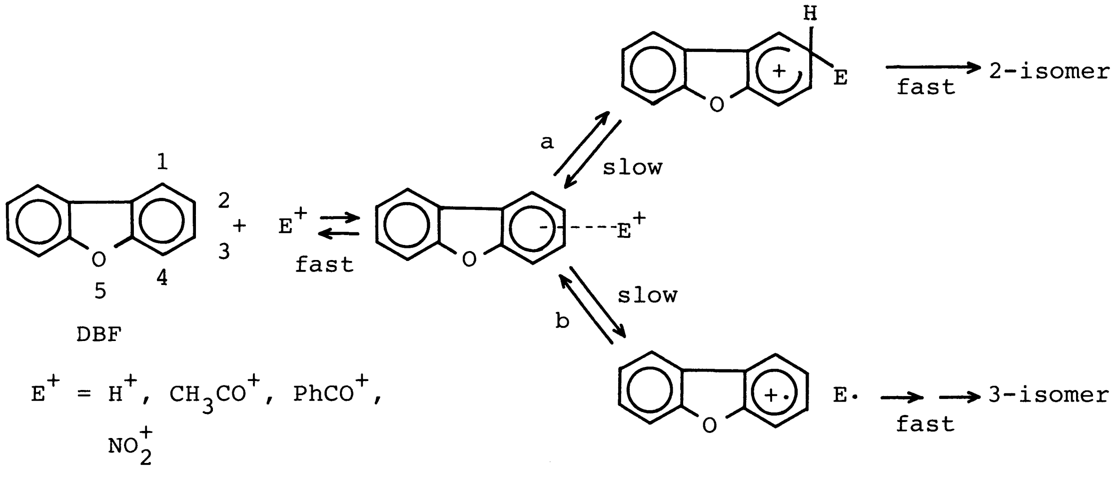


Fig. 1. Potential curves calculated as a function of the distance (r) between the carbon atom of DBF and the nitrogen atom of nitronium ion.



Scheme 1.

fact that the HOMO electron density of DBF is the highest at the 3-position, as calculated by MNDO method as 0.125, 0.061, 0.301, 0.041, and 0.000 for the 1-, 2-, 3-, 4-, and 5-positions, respectively.[13)]

Consequently, the product-determining step for the nitration of DBF with nitric acid seems to be not on the formation of σ-complex but on the CT process from DBF to nitronium ion as shown in Scheme 1-b. No giving detail isomer distributions, positive halogenations, sulfonation, and other general electrophilic reactions of DBF give the compounds substituted at the 2-position as the major product.[14)] Only the nitration with nitric acid occurs at the 3-position. This anormalous orientation has been left without any interpretations. Now, we belive the nitration of DBF with nitric acid will proceed by the CT mechanism as described above.

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5) The standard compounds of 1- and 4-acetyldibenzofurans were prepared by the reaction of corresponding dibenzofuran carboxylic acid chloride with methyl lithium; 1-acetyldibenzofuran: bp 198 °C/2 mmHg, 48% yield; 4-acetyldibenzofuran: mp 67 °C, 54% yield. The 2- and 3-acetyldibenzofurans were obtained by Friedel-Crafts acetylation of DBF.

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10) The calculations were made to the optimized geometric structures obtained by using the MOPAC-MNDO extrapolation procedure of Dewar and collaborators; J. Am. Chem. Soc., 99, 4899 (1977) and ibid., 100, 3607 (1978). The calculations for protonated ($HDBF^+$), acetylated ($AcDBF^+$), and nitrated dibenzofuranonium ions (NO_2DBF^+) at the 2- and 3-positions gave following total energies (eV); 2-$HDBF^+$ -1974.694, 3-$HDBF^+$ -1974.562, 2-$AcDBF^+$ -2580.607, 3-$AcDBF^+$ -2580.472, 2-NO_2DBF^+ -2807.273, 3-NO_2DBF^+ -2807.197.

11) A solution of 0.05 M DBF and 0.4 M tetranitromethane in trifluoroacetic acid, which is light brown-colored, was irradiated with the high pressure mercury lamp filtered through a pyrex glass at 0 °C under nitrogen stream.

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13) The spin density at the each position of DBF radical cation was also calculated from CNDO/2 method for the open shell system to give 0.088, -0.012, 0.200, -0.036, and 0.001 at the 1-, 2-, 3-, 4-, and 5-positions, respectively.

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