Reactor Analysis of 3-Substituted-diphenylamine Cation Radicals in Acetonitrile. Cyclization Reaction vs. Benzidine Formation

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The reactions of 3-substituted-diphenylamine cation radicals in acetonitrile were studied using an electron transfer stopped-flow method. In the reactions of the 3-chloro-diphenylamine cation radicals (mCl-DPA···), the main reaction route was the formation of the benzidine dimer, which was similar to the case of the diphenylamine cation radical (DPA···). Although the reaction of DPA··· proceeded via the cation radical - cation radical coupling as verified from the rate law of d[DPA···]/dt = k [DPA···] f, the present kinetic analysis has revealed that the decay rate of mCl-DPA··· was dependent on the concentration of the neutral molecules, i.e., the rate law was expressed as d[mCl-DPA···]/dt = k [mCl-DPA···] f [mCl-DPA]. In contrast, the reaction of the 3-methoxy-diphenylamine cation radical (mMeO-DPA···) was too fast to be observed using the stopped-flow method, which is quite in contrast to the 4-methoxy-diphenylamine cation radical (pMeO-DPA···) which was very stable in acetonitrile. In the case of mMeO-DPA···, the cyclization reaction was confirmed to proceed soon after the generation of mMeO-DPA···, which is similar to the case of the 3-methyl-diphenylamine cation radical (mMe-DPA···). Thus, it was found that the substituent on the 3-position changed the reaction pathways of DPA··· significantly, as well as their reactivity.

Key Words: 3-Substituted-Diphenylamine Cation Radicals, Dimerization Reaction, Reaction Analysis, Absorption Spectra, Stopped-Flow Analysis

1 Introduction

Reactions of aromatic amine cation radicals in aprotic solvents have been studied extensively, e.g., as recently summarized by Stechhan. 1 Because the oxidative potentials of aromatic amines are relatively negative due to the presence of the N atom in general, electrochemical oxidation is suitable for the generation of the cation radicals. On discussing the reactions of the cation radicals, a follow-up product analysis was utilized to reveal the complex reaction processes.

Among such reactions of aromatic amine cation radicals, an interesting example of the changes in reaction pathways is the case of diphenylamine derivative cation radicals. For the reactions of 4-substituted-diphenylamine and 4,4′-disubstituted-diphenylamine cation radicals, Serve and coworkers revealed different reaction pathways, i.e., the formation of four different types of dimers having benzidine, dihydridophenylphazine, p-phenylenediamine and hydrazine moieties, depending on the bases coexisting in acetonitrile solutions. 2–4 The structures are summarized below, which means that the Cp-Cp, N-Co, N-N and N-Cp couplings possibly occur (p and o indicate para-and ortho-positions of the phenyl group).

Compared with such progresses in identifying the reaction routes on the basis of the product analysis in the 1970s, the development of kinetic analysis of short-lived aromatic amine cation radicals started from the 1990s. Successful kinetic analysis could be performed using fast-scan cyclic voltammetry with ultra-microelectrodes, as well as a result, the reaction kinetics have become apparent for some diphenylamine derivative cation radicals. 5–7

On the other hand, as an alternative, or complementary, method for analyzing the reaction kinetics of short-lived cation radicals, we are proposing an electron-transfer stopped-flow (ETSF) method, in which the objective cation radicals were generated in the stopped-flow operation by mixing with stable cation radicals. 8–17 Although this method is not an electrochemical method, we can analyze the reaction process of the cation radicals, which can usually be generated using the electro-
chemical methods, in homogeneous solutions and under rigid control of the concentration of precursor molecules. The detection ability of the ETSF method is comparable to that of fast-scan cyclic voltammetry with scan rates over 1000 V s⁻¹.¹³,¹⁴

Using the ETSF method, up to now, the following conclusions have been obtained concerning the kinetics of the decay reaction of diphenylamine derivative cation radicals.

1) For the decay reaction of diphenylamine cation radicals (DPA⁺⁺), the reaction rate is not affected by the presence of neutral molecules at all. The rate law was determined to be [DPA⁻⁻]/dt = k [DPA⁺⁺], where the rate constant, k, is 1.0 × 10⁶ M⁻¹s⁻¹.³

2) Compared with the results for DPA⁺⁺, the reaction of the 4-methyl-diphenylamine cation radical (pMe-DPA⁺⁺) was somewhat complex.⁵ Although the decay reaction is second order in [pMe-DPA⁺⁺] in the absence of pMe-DPA⁺⁺, a slight increase in the decay rate of pMe-DPA⁺⁺ was observed in the presence of pMe-DPA⁺⁺ together with disappearance of the absorption of the oxidation products of the benzidine dimer. This change was assigned due to the concurrent cyclization reaction promoted by pMe-DPA⁺⁺ as a coexisting base. Similar behavior was observed in the case of the 4,4'-dimethyl-diphenylamine cation radical.¹³

3) Compared with the 4-methyl derivatives, the decay reactions of 3-methyl-diphenylamine and 3,3'-dimethyl-diphenylamine cation radicals were much faster due to the cyclization reaction. This means that the 3-methyl substituent promotes the formation of the dimer having a dihydropyridinium moity, even though the benzidine formation seems to be favorable from the structure.¹³

Considering the reactivity or instability of aromatic amine cation radicals, these clarifications would be significant because it has been shown that the reaction mechanisms can be affected by the substituents even in the absence of coexisting bases in acetonitrile.

In the present paper, following the previous work on the reaction of methyl-substituted DPA⁺⁺s including the 3-methyl-diphenylamine cation radical (mMe-DPA⁺⁺),¹³ we observed the reactions of the 3-chloro-diphenylamine cation radical (mCl-DPA⁺⁺) and the 3-methoxy-diphenylamine cation radical (mMeO-DPA⁺⁺), whose structures are summarized as below.

Consequently, depending on the nature of the substituents on the 3-position of DPA⁺⁺, different routes of the reactions to form the dimer compounds, i.e., cyclization or benzidine dimer formation, were observed through electrochemical and spectroscopic measurements.

2 Experimental

The details of the ETSF method were described previously.⁸,⁹,¹⁵ In this method, unstable cation radicals (N⁺⁺) are formed via electron transfer with long-lived cation radicals (M⁺⁺), whose formal potential is positive relative to that of N⁺⁺. By mixing the solutions of N and M⁺⁺, we can form N⁺⁺ via the electron transfer, initiate the reaction of N⁺⁺, and investigate the decay reaction of N⁺⁺ spectroscopically.

For the stopped-flow measurements, a rapid-scan stopped-flow spectroscopic system, RSP-601 (Unisoku Co., Ltd., Hiranaka, Japan), was used. In this apparatus, dynamic transformation of the absorption spectra can be observed with a minimized time interval of 1.0 ms after mixing the two solutions.

All the measurements were carried out in AN as the solvent. As a substrate to form persistent cation radicals, M⁺⁺, we used the tris (p-bromophenyl) amine cation radical (TBPA⁺⁺). AN solutions of TBPA⁺⁺ were prepared by dissolving the commercially available hexachloroantimonate salt of TBPA⁺⁺ (Aldrich). In the present ETSF experiments, an AN solution of TBPA⁺⁺ was mixed with an AN solution containing DPA derivative. Because the oxidation potentials of all the derivatives are negative relative to that of TBPA, the target cation radicals were successfully formed after mixing, and the decay processes could be followed by observing the time changes in the absorption spectra.

For all of the 3-substituted-diphenylamines, the chemicals of high purity available were used as received. 4-Methoxy-diphenylamine was synthesized from iodebenzene and p-anisidine following the method reported by Nolan and coworkers⁸ and was then purified with a silica-gel chromatography and recrystallized from hexane.

For the solvent, acetonitrile dehydrated (Wako chemicals, H₂O < 50 ppm) was used as received. As supporting electrolytes in the measurements of cyclic voltammetry, tetrabutylammonium hexafluorophosphate (TBAPF₆, Fuluka, puriss. electrochem. grade) was used as received.

3 Results and Discussion

3.1 Decay reaction of 3-chloro-diphenylamine cation radical

At first, the decay reactions of mCl-DPA⁺⁺ were observed using the ETSF method by generating mCl-DPA⁺⁺ via the electron transfer reaction of Eq.1.

\[
mCl-DPA⁺⁺ + TBPA⁺⁺ \rightarrow mCl-DPA⁺⁺ + TBPA \quad (1)
\]

Figure 1A shows the time-resolved absorption spectra observed after mixing the AN solution of 0.10 mM mCl-DPA with the AN solution of 0.10 mM TBPA⁺⁺. After mixing, a decrease in the absorption maximum at 705 nm, which can be attributed to that of mCl-DPA⁺⁺, was observed in a time interval of 10 ms, together with an increase in the absorption around 580 nm. The isosbestic point observed in Fig. 1A possibly means that the decay
reaction of mCl-DPA·⁻ accompanies the conversion to the product having an absorption around 580 nm.

Taking the equi-volume mixing in the stopped-flow operation into account, Fig. 1A is the result obtained after the quantitative completion of Eq. 1 when 0.05 mM mCl-DPA·⁻ was generated in the absence of mCl-DPA. We then observed the effect of the neutral mCl-DPA by changing the mixing ratio. Figure 1B shows the changes in absorption spectra observed after mixing the AN solution of 1.0 mM mCl-DPA with the AN solution of 0.10 M TBPA·⁻; i.e., the reaction of 0.05 mM mCl-DPA·⁻ was observed in the presence of 0.45 mM mCl-DPA. Consequently, a remarkable change in the transformation of the absorption spectra was observed in the presence of the neutral mCl-DPA as shown in this figure. Because the time interval in Fig. 1B is 2 ms, it is recognized that the decay reaction of mCl-DPA·⁻ was significantly accelerated by the presence of mCl-DPA. In addition, although an isosbestic point is seen in Fig. 1B, the wavelength became shorter compared with that in Fig. 1A. This indicates changes in the product as well as acceleration of the reaction.

To analyze the decay reactions of mCl-DPA·⁻ in detail, Figs. 2A-C show the changes in absorbance with time observed at the absorption maximum of mCl-DPA·⁻ at 705 nm. Figures 2D-F show the results of the simulation. For the decay curve of 0.05 mM mCl-DPA·⁻ in the absence of mCl-DPA (Fig. 2A), a good simulated result was observed using the rate law of Eq. 2, taking both the decrease in mCl-DPA·⁻ (curve (a) in Fig. 2D) and the increased component due to product formation (curve (b) in Fig. 2D) into consideration. The rate constant, \( k \), was determined to be 3.8 × 10⁵ M⁻¹s⁻¹.

\[
-d[mCl-DPA·⁻]/dt = k [mCl-DPA·⁻]^2
\]  

(2)

In contrast, for the decay reactions in the presence of mCl-DPA (Fig. 2B, C), the results of the simulation showed that the rate law is expressed by Eq. 3.

\[
-d[mCl-DPA·⁻]/dt = k [mCl-DPA·⁻]^2 [mCl-DPA]
\]  

(3)

Using this rate law and the identical reaction rate constant, 2.3 × 10⁶ M⁻¹s⁻¹, for Eq. 3, the simulated results of Fig. 2E and F could be obtained. This means that the decay reaction of mCl-DPA·⁻ is susceptible to the amount of mCl-DPA when the neutral molecules coexisted with the cation radical, while the cation radical -cation radical coupling proceeded in the absence of neutral mCl-DPA.

3.2 Decay reaction of 3-methoxy- and 4-methoxy-diphenylamine cation radicals

Whereas the kinetics of the decay reactions of mCl-
DPA·⁻ could be followed and analyzed clearly using the
ETSF method as in the previous section, the decay reactions of mMeO-DPA·+ were not accessible with the same approach. That is, although we actually tried the ETSF analysis with several mixing ratios of mMeO-DPA·+:TBPA·+, no absorption spectra that could be assigned to mMeO-DPA·+ were observed in the visible region at all.

This means that the reaction of mMeO-DPA·+ is too fast to follow using the stopped-flow apparatus. Namely, the decay reaction of mMeO-DPA·+ is considered to be completed within ca. 0.5 ms, which is the dead time of the present stopped-flow apparatus.

Although we have reported several results using the ETSF method successfully, very fast reactions of cation radicals are not exceptional. For instance, the reactions of aniline and N,N-dimethylaniline cation radicals in acetonitrile are also too fast to follow by the ETSF measurements.

However, in comparison with the cases of mCl-DPA·+, whose rate laws and reaction rates were determined in the present work, DPA·+ and mMeO-DPA·+ (whose reaction rates and mechanism were determined previously 9, 15), a much higher reactivity of mMeO-DPA·+ has now become apparent experimentally.

Here, it is of interest to compare the reactivity between mMeO-DPA·+ and pMeO-DPA·+. Although the precursor of the latter is not commercially available, we synthesized pMeO-DPA and carried out the ETSF measurement. As a result, the changes in absorption spectra in Fig. 3 were observed. In this result, the time interval of each spectrum was 5 sec. Thus, it was found that pMeO-DPA·+ is quite stable in AN. This means that the drastic change in reactivity is caused by the position of the substituent. Although a methoxy substituent at the para-position stabilizes the cation radical significantly, the cation radical becomes quite unstable when it is present at the meta-position.

3.3 Cyclic voltammetry of 3-substituted-diphenylamine

As utilized previously 15 cyclic voltammetric results provided us a key information concerning the reaction products in the cases of DPA derivatives. This is because typical responses were obtained when the benzidine moiety was formed after the dimerization reaction.

Figure 4 shows the cyclic voltammograms of three 3-substituted-diphenylamines in AN together with that of DPA. In the oxidation scans, the first peak corresponds to the formation of the monomer cation radicals, and the second broad peak is the oxidation of the protonated form of the monomers. The shifts in the oxidation potentials can be attributed to the changes in electronic character caused by the substituents.

In all the derivatives, the currents observed in the reversed cathodic scans are small, which indicates the high reactivity of the monomer cation radicals. However, the characteristic responses due to the benzidine formation, which are marked by an asterisk (*), were observed only in the voltammograms of DPA and mCl-DPA (Figs. 4A and B).

In contrast, in the cases of mMe-DPA and mMeO-DPA, very small responses that cannot be attributed to the redox couple of the benzidine were observed as shown in Figs. 4C and D. In the previous paper 15 we assigned the reduction wave of mMeO-DPA to that of the dication of the cyclized dimer, referring to the previous result by Berkenkotter and Nelson. 15

Concerning the results of the cyclic voltammetry, it
can be mentioned at first that the benzidine formation is most probable for mCl-DPA·• in comparison with the CV of DPA. In the dimerization reaction of DPA derivative cation radicals (X-DPA·•) to form benzidine, the outline of the reaction can be written as Scheme I representing the diphenylbenzidine derivative as X-DPB-X.

**Scheme I**

\[
\begin{align*}
2\text{X-DPA} \cdot & + \text{mCl-DPA} \cdot \rightarrow \text{Dimer} \cdot \quad (7) \\
\text{Dimer} \cdot & + \text{mCl-DPA} \cdot \rightarrow \text{Dimer}^{\cdot \cdot} + \text{mCl-DPA} \quad (8) \\
\text{Dimer}^{\cdot \cdot} & \rightarrow \text{mCl-DPB-mCl} + 2\text{H}^{\cdot} \quad (9)
\end{align*}
\]

Here, Dimer represents a transient dimer state before H· leave.

When the initial reaction (Eq. 7) is in equilibrium and the second reaction (Eq. 8) is the rate-determining step, the rate law agrees with the obtained one (Eq. 3). Thus, the chloro-substituent effect on the 3-position can be concluded to change the reaction mechanism from that of DPA·•, though the product is similar, i.e., benzidine formation.

On the other hand, in the CVs of mMe-DPA and mMeO-DPA (Figs. 4C and D), the reduction waves of the benzidine dimer disappeared in the voltammograms. In comparison, the CV of pMeO-DPA is nearly reversible as shown in Fig. 5, which reflects the stability of pMeO-DPA·• as revealed by the ETSF measurement in the previous section (Fig. 3).

The disappearance of the reduction waves of the benzidine dimer may be the reason for the cyclization reaction referred to the previous work. However, it seems that the result is not sufficient to specify the reaction route. Thus, in the following sections, we would like to present some spectroscopic differences for distinguishing the cyclization reaction and benzidine formation.

### 3.4 Diagnostic spectroscopic measurement to distinguish the reaction route

In the benzidine formation reactions, it is characteristic that strong absorptions of the formed products, i.e., X-DPB-X·• and X-DPB-X^{••}, are observed in the visible region. In addition, because these oxidized states of benzidine are stable enough, colored solutions are obtained after the reaction of X-DPA·• when the benzidine dimer is formed. Thus, as a diagnostic measurement for distinguishing the reaction routes on the basis of the products, we would like to propose a simple UV-visible measurement after the reactions initiated by the concept of the ETST method. As the practical procedures, the UV-vis measurements after mixing the AN solutions of X-DPA and TBPA·• were carried out for this purpose.

Figure 6 shows the absorption spectra observed after 0.20 mM X-DPA was mixed with 0.20 mM TBPA·•. For DPA and mCl-DPA, whose cation radicals turns to the benzidine dimer, strong absorptions were observed as shown in Figs. 6A and B. These absorption spectra can be assigned to mainly those of the dimer cation radicals, though some dimer dications coexist. Similar absorption

![Fig. 5](image_url)  
**Fig. 5** Cyclic voltammogram of pMeO-DPA in AN. The experimental conditions are same as those in the caption pf Fig. 3.

![Fig. 6](image_url)  
**Fig. 6** UV-visible absorption spectra observed after the AN solution of 0.20 mM DPA derivative was mixed with the AN solution of 0.20 mM TBPA·•. (A) DPA, (B) mCl-DPA, (C) mMe-DPA and (D) mMeO-DPA.
spectra for both DPA and mCl-DPA imply that the reaction pathway is similar to form the benzidine.

In contrast, for mMe-DPA and mMeO-DPA, the solutions obtained after the mixing were pale colored, and the absorption spectra (Figs. 6C and D) were different from those for DPA and mCl-DPA (Figs. 6A and B). This difference indicates the change in the reaction product in solution.

As discussed previously, when the cyclized dimer is formed, the oxidation potential of the dimer to form the cation radical is comparable to that of the monomer. This is a significant difference compared with the benzidine formation, in which the oxidation potential of the monomer is positive relative to that of the dimer cation radical to the dimer dication. Therefore, in the case where the cyclized dimer is formed, it is expected that the amount of the colored species, i.e., the dimer cation radical, is much smaller than that in the case of benzidine formation (no cyclized dimer dication is formed judging from the oxidation potential). Thus, the UV-visible measurements as shown in Fig. 6 can be used as a diagnostic tool to distinguish the reaction routes between cyclization and benzidine formation.

Although the previous analysis on mMe-DPA·" was concluded to be the cyclized dimer formation, benzidine formation was expected to occur as a minor side reaction. This is because a small amount of the benzidine dimer is seen to be produced in Fig. 6C, though the amount is small. However, in the case of mMeO-DPA·", for which a very fast reaction was confirmed in the present work, such formation of the benzidine dimer was not observed at all as shown in Fig. 6D.

3.5 Further evidence of the cyclized dimer formation

Although the above UV-visible measurements were carried out within 5-10 minutes after the mixing, the transient absorption spectra measurements in the ETSF analysis also gave further support to the similarity of the reactions of mMe-DPA·" and mMeO-DPA·".

Figures 7A and B show a two-step spectral change observed after mixing 0.10 mM TBPAA·" with 10 mM mMe-DPA. In this case, the first change can be assigned to decay of mMe-DPA·" as reported previously and then a decrease in the absorbance is observed around 450 nm. The latter change can be attributed to the follow-up equilibria involving the cyclized dimer affected by the presence of a large excess of the neutral mMe-DPA. The rates of the two reactions are quite different as shown in Fig. 7C.

Similarly, Fig. 8 shows the result obtained after mixing 0.10 mM TBPAA·" with 10 mM mMeO-DPA. Although the decay process of the dimer mMeO-DPA·" was not observed as mentioned above, interestingly, a slow reaction very similar to the result for mMe-DPA·" (Fig. 7B) was observed as shown in Fig. 8A. This similarity would be further support for the same reaction route of mMe-DPA·" and mMeO-DPA·".

4 Conclusions

In the present work, we observed the effects of the substituent at the 3-position of DPA·" by following the reactions of mCl-DPA·" and mMeO-DPA·" using the ETSF method, together with some comparisons with the electrochemical and spectroscopic results for DPA·" and mMeO-DPA·". Consequently, it was clarified that the
reaction could be divided into two cases, \textit{i.e.}, the benzidine dimer formation for DPA·+ and mCl-DPA·+ and the cyclized dimer formation for mMe-DPA·+ and mMeO-DPA·+. Thus, as well as the presence of the base molecules,\textsuperscript{1–4} the nature of the substituents at the 3-position (= meta-position) was found to be very significant for promoting the cyclized reactions of DPA derivative cation radicals.

Kinetically, the change in the rate law was clarified between the cases of DPA·+ and mCl-DPA·+, so that the substituents at the 3-position are concluded to alter the reaction mechanism even though this position is remote. Although the reaction mechanism of mMeO-DPA·+ unfortunately could not be analyzed by the ETSF method, the reaction rate of mMeO-DPA·+ being much faster than that of mMe-DPA·+ would be a manifestation of the substituent effect.

The significant effect of the methoxy substituent at the \textit{meta}-position could also be confirmed by the difference in the reactivity compared with the results for pMeO-DPA·+, which is quite stable in AN.

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References