

1,3,5-Tris(dialkylamino)benzenes: Model Compounds for the Electrophilic Substitution and Oxidation of Aromatic Compounds

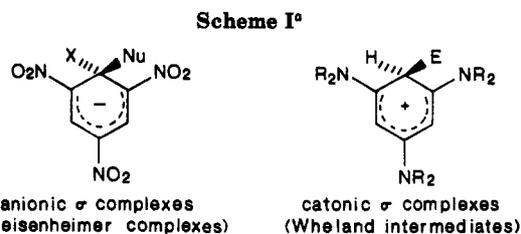
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Anionic σ complexes have been known and extensively studied as intermediates of nucleophilic aromatic substitution since the beginning of the century.¹ In a paper that still makes fascinating reading, Meisenheimer describes the formation and isolation of anionic σ complexes by reaction of picryl ethers with potassium alkoxides. Structural proof is derived from the fact that identical σ complexes are obtained from methyl 2,4,6-trinitrophenyl ether with potassium ethoxide, and from ethyl 2,4,6-trinitrophenyl ether with potassium methoxide.² Cationic σ complexes (Wheland intermediates), on the other hand, had been characterized or isolated only in a few cases,³ despite the ubiquitous implication of electrophilic aromatic substitution in synthesis. Such cationic σ complexes were expected to be stabilized best by three amino substituents, in meta positions relative to each other,⁴ in analogy to the stabilization of anionic σ complexes by three meta-oriented nitro groups (Scheme I).

Franz X. Effenberger was born in Goldenstein, Northmoravia, on April 7, 1930. He received his Ph.D. degree in 1959 and his Habilitation in 1964, both from the University of Stuttgart. He spent one year as research associate with P. A. S. Smith at the University of Michigan in Ann Arbor and was appointed full professor at the University of Stuttgart in 1972, succeeding Hellmut Brederock. In 1977 he spent five months as visiting professor at the Cornell University in Ithaca, NY. Since 1987 he is also rector (president) of the University of Stuttgart.



^aNu = nucleophile, E = electrophile.

Neither 1,3,5-triaminobenzene itself nor its N-mono-substituted derivatives can serve as model substrates for arene reactions: these compounds exist, at least in part, in the form of the nonbenzenoid tautomers,⁵ and

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(2) Meisenheimer, J. *Liebigs Ann. Chem.* **1902**, *323*, 205.
 (3) (a) Olah, G. A.; Kuhn, S. J. *J. Am. Chem. Soc.* **1958**, *80*, 6541. (b) Doering, W. von E.; Saunders, M.; Boyton, H. G.; Earhart, H. W.; Wadley, E. F.; Edwards, W. R.; Laber, G. *Tetrahedron* **1958**, *4*, 178. (c) Olah, G. A.; Tolgyesi, W. S.; Dear, R. E. A. *J. Org. Chem.* **1962**, *27*, 3441. (d) Olah, G. A.; Kuhn, S. J. *J. Am. Chem. Soc.* **1962**, *82*, 2380. (e) Brouwer, D. M.; Mackor, E. L.; MacLean, C. In *Carbonium Ions*; Olah, G. A., Schleyer, P. von R., Eds.; Wiley and Sons: New York, 1970; Vol. 2, p. 837 and references therein. (f) Koptuyug, V. A. In *Topics in Current Chemistry*, **122**; Boschke, F. L., Ed.; Springer Verlag: Berlin, 1984.

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Table I
1,3,5-Tris(dialkylamino)benzenes: Energies of Highest Occupied Orbitals, Trinitrobenzene CT Complex Band Energies,^a Polarographic Half-Wave Oxidation Potentials, and ¹H NMR Aryl Proton Chemical Shifts

-benzene	E_{HOMO}^b , β	ν_{CT}^c , cm^{-1} (TNB complex)	$E_{1/2}^{\text{ox},d}$, V (vs Ag/Ag ⁺)	¹ H NMR: ^e δ , ppm
1a, 1,3,5-tripyrrolidino-	-0.6357 ^f	16 000	0.01	5.31
1b, 1,3,5-tris(dimethylamino)-	-0.6635 ^f	17 500	0.13	5.68
1c, 1,3,5-tripiperidino-	-0.6944 ^f	18 900	0.18	6.20
1d, 1,3,5-trimorpholino-	-0.7114 ^f	20 600	0.35	6.10

^a Only longest wavelength CT band. ^b For the heteroatom parameters, the h and k values were used as described in the text and in ref 11a. ^c In CH₂Cl₂ (UVASOL Merck), determined from equimolar solutions of triamino- and trinitrobenzenes at several different concentrations (range 1–5 × 10⁻² M), rounded to the nearest 100 cm⁻¹. ^d Measured at a rotating platinum electrode in CH₃CN against Ag/Ag⁺ (10⁻² M in CH₃CN) as reference, supporting electrolyte 10⁻¹ M LiClO₄. ^e In CDCl₃, TMS internal standard. ^f Doubly degenerate HOMOs.

σ complexes, once formed, are readily deprotonated to the corresponding quinoid systems.

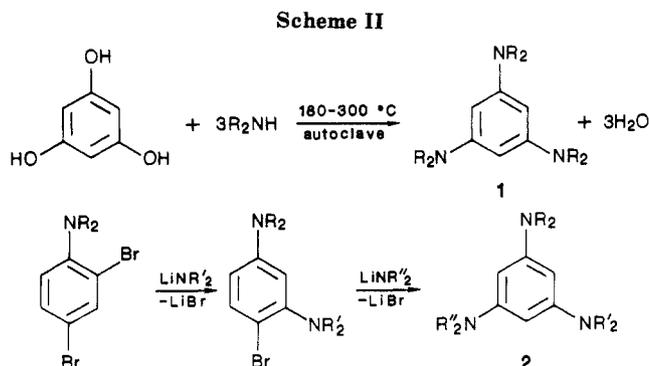
N-Peralkylated 1,3,5-triaminobenzenes would, by virtue of the high donor potential of the NR₂ substituents, represent ideal model compounds.⁴ Such compounds were not known, though, at the outset of our investigations. We have developed general synthetic routes for this class of compounds and have studied the stabilization of cationic as well as radical intermediates in the reactions of tris(dialkylamino)benzenes with electrophiles and oxidants.

Synthesis and Physical Properties of 1,3,5-Tris(dialkylamino)benzenes

N-Alkylation of aminobenzenes provides the usual access to (*N,N*-dialkylamino)benzenes. This synthetic procedure is not applicable to 1,3,5-triaminobenzene because of its instability⁶ and competitive C-alkylation. We have prepared N-peralkylated triaminobenzenes in good yield by two alternative routes. When phloroglucinol is simply heated with secondary amines at 180–300 °C in an autoclave, triaminobenzenes 1 are obtained⁷ with three identical NR₂ substituents. Reaction of (dialkylamino)halobenzenes with lithium dialkylamides allows for the stepwise introduction, via aryne intermediates, of various dialkylamino groups, affording triaminobenzenes 2 with different NR₂ substituents⁸ (Scheme II).

The extent to which NR₂ substituents influence the electronic state and the reactivity of an arene π system strongly depends on the relative π -donor potential of the individual dialkylamino group and on the hybridization of its N atom. The graduated effect of dialkylamino groups on π systems is well-known from the chemistry of enamines.⁹ A quantification of the resonance interaction between individual NR₂ groups and a C=C π system appeared highly desirable, considering the widespread preparative employment of enamines.

The relative donor potential of NR₂ substituents with respect to an acceptor π system in the uncharged ground state should be reflected in the different π -electron density at the β -carbon. The chemical shift of β -protons in enamines has indeed been employed successfully for probing C _{β} π -electron density.¹⁰ In the



case of enamines of cyclic ketones, however, it is difficult to assess the influence of conformational and buttressing effects on chemical shifts. The 1,3,5-tris(dialkylamino)benzenes, in contrast, have a rigid planar structure. This makes them better suited for a quantification of the donor potential of the different NR₂ moieties on the basis of aromatic ring proton chemical shifts.

We have derived a consistent set of HMO parameters for the dimethylamino and pyrrolidino groups by correlating HMO π -electron densities with aryl proton chemical shifts for a series of methoxy-, (dimethylamino)-, and pyrrolidinobenzenes.^{11a} In this procedure, it was essential to scrupulously account for specific steric and/or anisotropic effects on protons in ortho positions to the substituents, which are different for each group, and also to exclude protons in meta positions which may principally not be incorporated into a Hückel-type correlation.^{11a} The parameters $k_{\text{C-N}}$ thus derived describe, in a quantitative manner, the different overlap integral ($\beta = k_{\text{C-N}}\beta_0$) of the lone electron pairs of the respective NR₂ moieties with the sp²-carbon $p\pi$ orbitals. For the piperidino and morpholino groups, the respective $k_{\text{C-N}}$ values were determined from a comparative study of the C(1)–NO rotation barriers in 2,4,6-tris(dialkylamino)-1-nitrosobenzenes.^{11b}

amino group	$k_{\text{C-N}}$
pyrrolidino	0.90
dimethylamino	0.84
piperidino	0.775
morpholino	0.74

Chemical shifts, however, reflect upon the electronic properties of the (neutral) ground state. The (positively charged) transition state for electrophilic attack of the aromatic π system is better approximated by charge-transfer (CT) complexes with strong electron acceptors,

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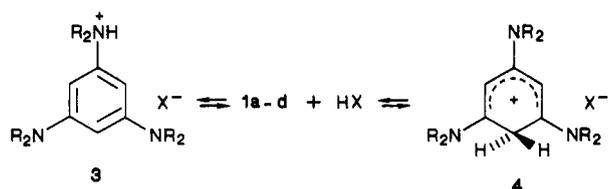
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Scheme III^a

^aX = Cl, Br, BF₄, ClO₄.

or by the relative stability of the radical cations formed in oxidation. Still, the CT transition energies for complexes of 1a-d with trinitrobenzene are well correlated with the HOMO energies, calculated with the chemical shift derived k_{C-N} parameters. For the first polarographic oxidation potentials, the correlation likewise holds. The physical properties of the symmetrical tris(dialkylamino)benzenes 1a-d are collected in Table I.

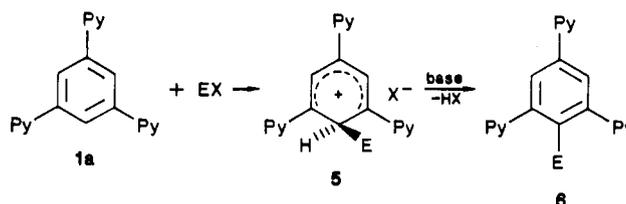
Formation, Structure, and Reactivity of Aromatic σ Complexes

Aminobenzenes, as ambident nucleophiles, may be attacked by electrophiles both at the amino group and at the aromatic ring. Attack at the amino function, though kinetically more favorable, is often reversible. Reaction at a ring position, on the other hand, may be followed by irreversible deprotonation, i.e., re-aromatization. So, C-substitution products are as a rule isolated from the reactions of aminobenzenes with electrophiles.

A mixture of C- and N-monoprotonation products has been established spectroscopically for the protonation of 1,3,5-triaminobenzene itself.^{12a,b} Protonation of the triaminobenzenes 1a-d likewise affords C- and N-protonation products 3 and 4, depending on the NR₂ substituent, which in this case are stable and isolable^{7a,12c} (Scheme III).

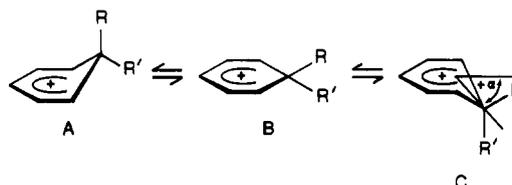
N-Protonation to 3 is favored by high basicity of the amino nitrogen, which may be approximated by the basicity of the respective secondary amines. Increasingly higher donor potential of the NR₂ substituent toward the aromatic π system tips the scale in favor of C-protonation to 4. The donor potential of the pyrrolidino group is significantly higher than that of the piperidino group ($k_{C-N} = 0.90$ vs 0.775, see above) while pyrrolidine and piperidine have similar basicity ($pK_a = 11.27$ and 11.12, respectively).¹³ Indeed, 4a is formed exclusively from 1a, and 3c only from 1c. The donor strength of the piperidino and morpholino groups, on the other hand, is of the same order. Since morpholine is definitely less basic than piperidine ($pK_a = 8.33$),¹³ trimorpholinobenzene (1d) upon protonation gives both 3d and 4d.^{12c}

The problem of competitive N- and/or C-reaction arises for the reaction of 1a-d with all electrophiles. For model investigations, the pyrrolidino compound 1a represents the most suitable substrate since it reacts with electrophiles preferentially at a ring carbon, and since well-established σ complexes 5 are isolated from the alkylation,^{14,15} sulfonation,¹⁶ acylation,¹⁶ and halo-

Scheme IV^a

^aPy = 1-pyrrolidinyl-, EX = HX, alkyl halide, R¹COCl, R²SO₂Cl, Br₂, Cl₂.

Scheme V



genation^{17,18} of 1a. The halo σ complexes are much less stable, though, and will be discussed separately (see below) (Scheme IV).

The activation of 1a, by three pyrrolidino groups, is sufficient to allow for reactions with a wide variety of electrophiles in inert organic solvents without the addition of catalysts. The ionic σ complexes 5 crystallize directly from the reaction mixture. Especially stable σ complexes with nonnucleophilic anions, e.g., BF₄⁻ and ClO₄⁻, are obtained by straightforward anion exchange. As a rule, re-aromatization of Wheland intermediates occurs spontaneously. Deprotonation of the σ complexes 5, i.e., formation of the substituted tris(dialkylamino)benzenes 6, requires base.

The stability of the σ complexes 5 allows for a facile crystal structure determination. By combining such experimentally determined geometries with MO calculations, a deeper understanding may be obtained of how electronic and steric influences combine to affect the stability and reaction behavior of Wheland intermediates in general.¹⁹ One planar (B) and two bent conformations (A, C) are theoretically possible for Wheland intermediates. Earlier CNDO calculations had predicted a planar structure for σ complexes with R = R' = H and a bent one for R = H, R' = CH₃.²⁰ σ complexes with unlike substituents indeed are bent, as determined spectroscopically in solution;²¹ heptamethylcyclohexadienylum tetrachloroaluminate, on the other hand, has been found by X-ray crystallography to be more or less planar²² (Scheme V).

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Table II
Bonding Geometries^a and Relative Energies for Different Conformations of Selected σ Complexes (Cyclohexadienylum Ions) 5 and 7^b

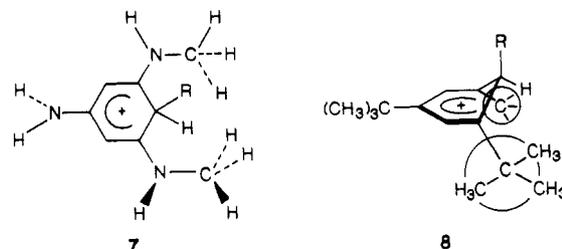
compound	α^d	C(1)-E, C(1)-R	E^c (α)			ΔE^e
			20°	0°	-20°	
5a: E = H, X = Br (X-ray) (A) ^f	0.8					
(X-ray) (B)	1.0					
5b: E = CH ₃ , X = ClO ₄ (X-ray)	15.4	1.561				
5c: E = X = Br (X-ray)	15.0	2.000				
7a: R = H (MNDO)	0.1	1.117	1.66	0.00	1.66	0.00
7b: R = CH ₃ (MNDO)	21.6	1.559	0.08	3.98	12.38	12.35
7c: R = Br (MNDO)	15.5		0.17	1.87	8.87	8.60

^a Bond angles α and bond distances C(1)-E and C(1)-R, obtained from MNDO calculations and X-ray crystal structure determinations. ^b Energies (kcal/mol) are given relative to the most stable conformer of each compound. ^c Relative energies calculated for the indicated α values (all 3-21G energies and all MNDO energies and structures are the result of optimization in which the atoms C _{α} , C _{α s}, C _{β} , C _{β s}, and C _{γ} and the bonds C _{β} -H, C _{γ} -H, and C _{β s}-H were maintained in a plane. A mirror plane was assumed to pass through atoms C(1) and C _{γ} . ^d The α value (deg) for the most stable conformation. ^e The energy difference between the two nonplanar conformers ($\alpha = \pm 20^\circ$). ^f The bond angle α is listed separately for the three independent observations. Bond distances have been averaged.

We have determined the crystal structure of 2,4,6-tripyrrolidinocyclohexadienylum bromide (5a: E = H, X = Br), 1-methyl-2,4,6-tripyrrolidinocyclohexadienylum perchlorate (5b: E = CH₃, X = ClO₄), and 1-bromo-2,4,6-tripyrrolidinocyclohexadienylum bromide (5c: E = X = Br).¹⁹ The protonated σ complex 5a in fact is basically planar, but 5b and 5c are definitely bent, with the CH₃ and Br substituents in axial positions. The deviation from planarity, as given by the experimentally determined dihedral angle α , is 15.4° for 5b and 15.0° for 5c (Table II). This dihedral angle, in conjunction with the length of the bond between C(1) and the incoming substituent E, plays a crucial role in correlating the stability and reactivity of σ complexes with theoretical calculations.

For σ complexes with identical ligands, R = R', and hence equivalent C-R and C-R' bonds, the planar conformation is expected to be electronically most stable since the cyclohexadienylum π system favors a planar geometry, and hyperconjugative stabilization is at a maximum in this conformation. With unlike ligands, R \neq R', conformations A and C no longer are energetically degenerate, and the conformation that has the ligand with the better donor σ orbital in the axial position is better stabilized. This electronic effect is expected to be reinforced if the ligand with the better σ donor bond also is the sterically more demanding one. The markedly different degree of hyperconjugation weakens the axial and strengthens the equatorial bond in the bent conformation. MNDO results show that σ complexes that are unsubstituted in the pentadienyl moiety are not very susceptible to steric effects of the ligands R and R' at C(1) and that hyperconjugation effects dominate for these σ complexes. To test the validity of the MNDO calculations, the σ complexes 7 with unlike ligands were optimized with MNDO methods. The geometries thus obtained are in reasonable agreement with the crystal structures determined for 5a-c (see Table II). The MNDO results in particular confirm the planar conformation to be more stable for σ complexes with identical ligands, and a nonplanar conformation to be more stable for σ complexes with unlike ligands. Due to the above-mentioned steric and hyperconjugative effects, a big energy difference results between the stable conformation with R = CH₃ or Br in a quasi-axial position ($\alpha = +20^\circ$, see Table II) and the inverted conformation with a quasi-axial hydrogen

Scheme VI



($\alpha = 20^\circ$). Population of this inverted conformation consequently is likely to be very low indeed.

Two limiting situations may be envisaged on the basis of the theoretical and experimental results outlined so far for the reactivity of nonplanar σ complex intermediates: (i) the most stable conformation of the σ complex has the potential leaving group R' in a quasi-axial position; (ii) the most stable conformation is that with R' in a quasi-equatorial position (see C and A, respectively, in Scheme V). Re-aromatization via elimination of R'⁺ is kinetically favored for i. In the case of ii, an energetically highly unfavorable conformation, close to C with quasi-axial R', has to be adopted prior to dissociation.

Figure 1 illustrates this concept graphically. The circle at the reaction coordinate represents, in comparison to C, the less stable conformation A, which as a result of calculations is not a minimum in the energy profile. It follows that if the attacking electrophile prefers the axial position in a nonplanar σ complex, the second energy barrier represents the rate-determining step (Figure 1: reaction from left to right). If, under otherwise constant conditions, the entering group goes preferentially into the equatorial position, the leaving group is needed in an axial position, and the first activation barrier is rate-determining (Figure 1: reaction from right to left). These results also suggest that a σ complex may be stabilized with respect to re-aromatization by purely steric effects in addition to the well-known electronic stabilization. The 2,4,6-tri-*tert*-butyl σ complex 8²³ (Scheme VI), with a poor leaving group R in an axial position, may well represent an example for this situation.

Experimental results that were hitherto hard to understand now became explicable in terms of the out-

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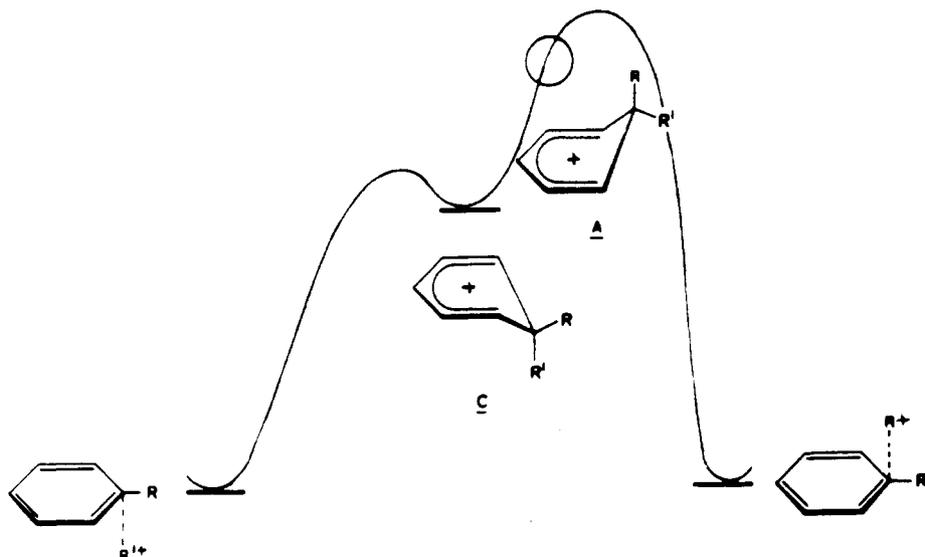
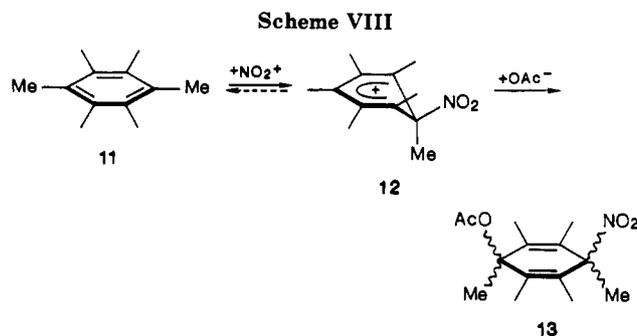
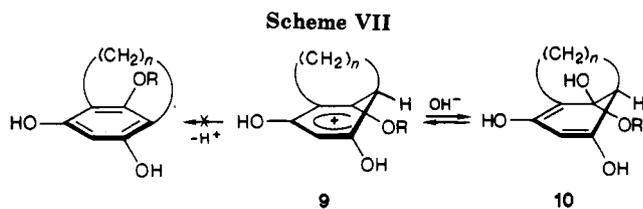


Figure 1. Simplified hypersurface of the electrophilic substitution on aromatics with nonplanar intermediate σ -complexes.



lined stereoelectronic concept. A pK_a value of 9.6 has been determined for the planar σ complex **5a**; the value for the nonplanar complex **5b**, in contrast, is 13.3.²⁴ Converting planar **5a** to a nonplanar conformation with a quasi-axial C-H bond requires but little energy.¹⁹ Conversion of the nonplanar, nonacidic complex **5b**, on the other hand, into the inverted, acidic conformer with a quasi-axial C-H bond requires considerable energy. The far-higher pK_a value of **5b** as compared with **5a** is thus mainly attributed to the highly unfavorable equilibrium situation between the two conformations of **5b**. In the phloroglucinophane σ complexes **9**, the bridged structure rigidly holds the crucial C-H bond in an equatorial position. Deprotonation, though thermodynamically desirable, is kinetically hindered to such a degree that the cyclohexadienylium system rather adds the nucleophile/base with exclusive formation of the hemiacetals **10** (Scheme VII).²⁵

Nitration of various methylbenzenes, e.g., **11**, with nitryl acetate results in the formation of σ complexes **12**, with the electropositive CH_3 ligand preferentially in the quasi-axial position. The negligible leaving tendency of the CH_3^+ group forestalls re-aromatization, and the 1,4-cyclohexadiene **13** is formed instead by addition of the nucleophile (Scheme VIII).²⁶

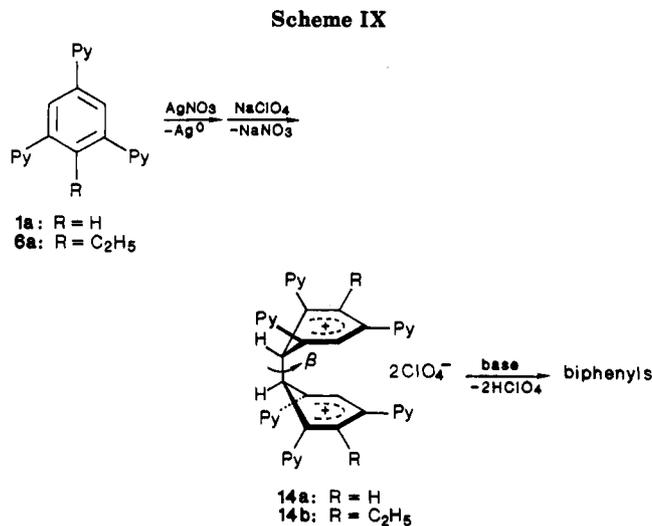
Dimeric σ Complexes as Intermediates in the Oxidative Dimerization of Arenes

Several alternative mechanisms have been discussed for the oxidative dimerization of aromatic compounds.²⁷

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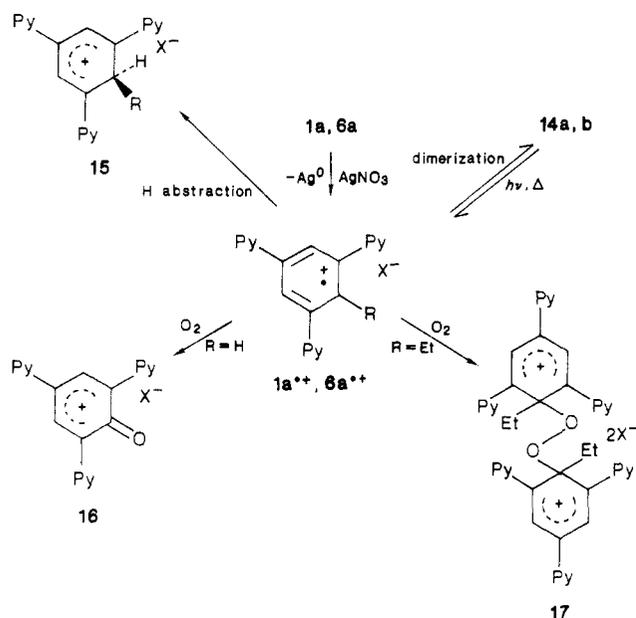
(26) (a) Fischer, A.; Ramsey, J. N. *Can. J. Chem.* 1974, 52, 3960. (b) Suzuki, H. *Synthesis* 1977, 217. (c) Moodie, R. B.; Schofield, K. *Acc. Chem. Res.* 1976, 9, 287.



There is general consent that the first step is the formation of a radical cation. Dimeric σ complexes likewise are intermediates common to all the mechanisms proposed, their deprotonation giving the biaryls as the first oxidation products isolated. It remains undecided, though,²⁷ whether the dimeric σ complexes arise from direct dimerization of radical cations, from electrophilic attack upon unreacted arene by dicationic species formed in a secondary oxidation step from the radical cations, or

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Scheme X



from oxidation of the 1:1 adducts of radical cation and arene.

Dimeric σ complexes 14 were isolated for the first time, as stable products, from the oxidation of tris(dialkylamino)benzenes.²⁸ Of the wealth of complexes 14 that could thus be obtained in crystalline form, the two σ complexes that are formed by oxidation of 1a and of 1-ethyl-2,4,6-tripyrrolidinobenzene (6a, $R = \text{C}_2\text{H}_5$) were selected for an X-ray structure determination, and for an in-depth study of the mechanism of their formation and their follow-up reactions^{29,30} (Scheme IX).

While the monomeric σ complexes 5 are characterized by simple three-band electron spectra, the longest wavelength absorption of the dimers 14 is split and/or shifted,³¹ due to through-space as well as through-bond interaction. The relative orientation of the two cyclohexadienylium rings in 14a and 14b differs widely; the torsional angle β is 65° in 14a and 163.3° in 14b. The crystal structures provide some insight into the probable arrangement of the two arene moieties which combine in the transition state of the oxidative dimerization. The endo conformation found for the dimer 14a is very similar to the geometry derived from calculations.³² This orientation is favored by considerable charge-transfer interaction between the two π systems.³² Severe steric interaction in the endo arrangement, on the other hand, between the ethyl group of one and a pyrrolidino group of the other arene ring makes the exo approach more favorable for the dimerization of 6a. This closely resembles the structure determined for the final product 14b.

Dimeric σ complexes 14 are obtained as sole products from the oxidation of 1a and 6a only if the oxidant is

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added rapidly, and if light and atmospheric oxygen have been painstakingly excluded. Without these precautions, the complexes 14 are formed together with the σ complexes 15, arising from hydrogen abstraction of the solvent, and the quinone immonium compounds 16 and diaryl peroxides 17, respectively, arising from reaction with O_2 (Scheme X).

Continuous-flow ESR has unequivocally established the radical cations $1a^{\bullet+}$ and $6a^{\bullet+}$ as intermediates in the oxidation of 1a and 6a. Spectra simulated for these structures are in good agreement with the experimental ESR spectra.³³ The long-wavelength absorption band of the radical cations at $\lambda > 800$ nm constitutes an ideal probe for following both their formation and secondary reactions. Photochemical dissociation of the dimeric σ complexes 14 is a very fast and highly efficient process. The complexes 14 may also be thermally dissociated into two radical cations. By UV/vis-spectroscopically monitoring the different, competitive reactions of $6a^{\bullet+}$, formed from flash photolysis of 14b, the following rates have been determined for the individual processes: dimerization ($\rightarrow 14b$), $k = 2.3 \times 10^4 \text{ L M}^{-1} \text{ s}^{-1}$; H abstraction ($\rightarrow 15b$), $k = 2.5 \times 10^{-2} \text{ s}^{-1}$; reaction with O_2 ($\rightarrow 17$), $k = 9 \times 10^5 \text{ L M}^{-1} \text{ s}^{-1}$. Half-life times have been determined for the two radical cations in the same manner; surprisingly, $\tau_{1/2} \geq 1 \text{ s}$ for $6a^{\bullet+}$ and only $\approx 1 \text{ ms}$ for $1a^{\bullet+}$.

All these experimental results may be rationalized theoretically.³⁰ Qualitative arguments, which are confirmed by quantitative methods (extended Hückel, MNDO), show that interaction between the HOMOs of the two cyclohexadienylium subunits, π_2 and π_2' , respectively, in the dimeric σ complexes is confined basically to through-space interaction. The two resulting combinations, $\pi_2 \pm \pi_2'$, are energetically degenerate and nonbonding for a dimeric σ complex with a torsional angle β of 60° and almost degenerate for $\beta > 160^\circ$. For the interaction between the two lowest unoccupied orbitals, π_3 and π_3' , of the two subunits, through-bond coupling prevails over through-space coupling for all torsional angles. Hence, the combination $[\pi_3 - \pi_3' + \sigma^*]$ is energetically lower than $[\pi_3 + \pi_3' - \sigma]$ for all conformations and thus represents the LUMO of the dimeric σ complex. (The doubly occupied combination $[\pi_3 + \pi_3' + \sigma]$, corresponding to $[\pi_3 + \pi_3' - \sigma]$, connotes a significant electron transfer from the σ bond into the a priori vacant orbitals π_3 and π_3' ; this, in terms of the MO formalism, is the reason for the severe hyperconjugative weakening of the central C(1)-C(1') bond in the dimeric σ complex.)

The "photochemical dogma" demands that photo-reactivity in the condensed phase be governed, as a rule, by the first electronically excited state. This may be represented in terms of the simplest one-determinant model by promotion of one electron from the HOMO [which has no contribution from the central σ bond] into the LUMO, $[\pi_3 - \pi_3' + \sigma^*]$, which is antibonding between C(1) and C(1'). Hence, the central σ bond is weakened even more than in the ground state and thus becomes predestined for photodissociation. Both the thermal and photochemical dissociation of the dimeric σ complexes are symmetry-allowed processes, with the photoreaction being kinetically slightly more favored.

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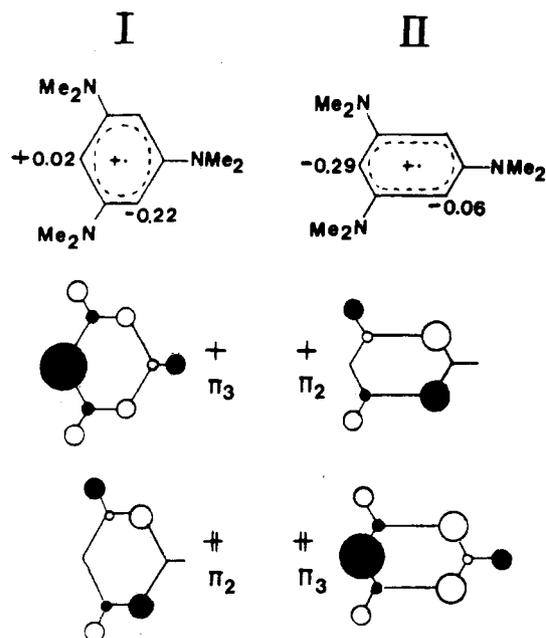
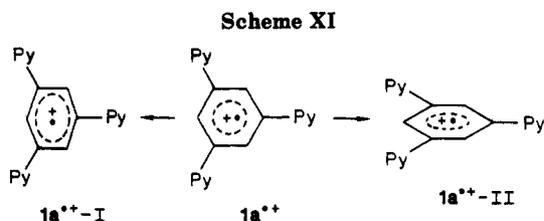


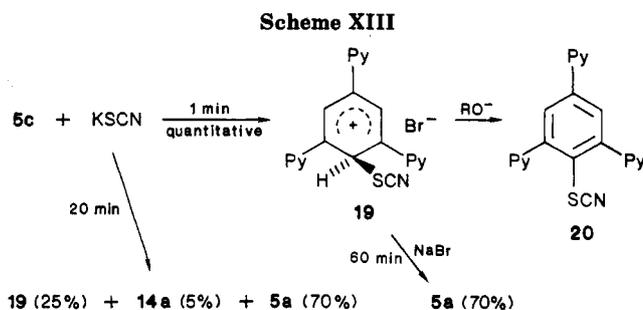
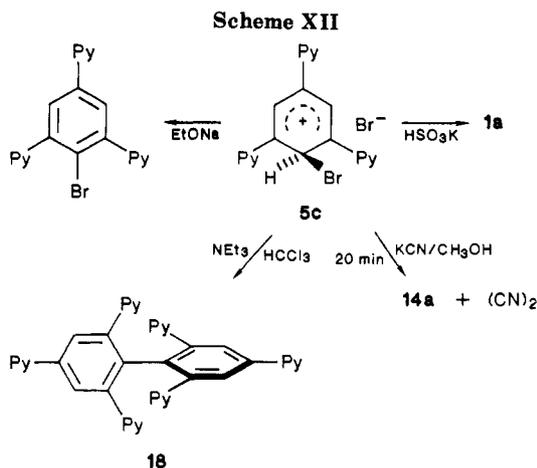
Figure 2. MNDO calculated charge densities and highest occupied π orbitals of the two Jahn-Teller distorted structures I and II for 1,3,5-tris(dimethylamino)benzene as a model for $1a^{+ \cdot}$ -I and $1a^{+ \cdot}$ -II.



This argument holds for **14a** ($\beta = 65^\circ$) as well as for **14b** ($\beta \approx 163^\circ$) since MO theory does not differentiate, in either the ground or the first excited state, between complexes with varying conformation about the central σ linkage. This picture changes drastically, however, when one compares the two radical cations, formed either by dissociation of **14a** and **14b** or by oxidation of **1a** and **6a**.

The radical cation $1a^{+ \cdot}$ does not exist in the highly symmetrical D_{3h} structure, but rather in two, energetically very close, Jahn-Teller distorted structures $1a^{+ \cdot}$ -I and $1a^{+ \cdot}$ -II (Scheme XI). The respective charge densities and orbital coefficients can be approximated by the MNDO data for the simplified model structure shown in Figure 2.

Both the Jahn-Teller distorted forms of $1a^{+ \cdot}$ are planar. In structure I, the overall highest coefficient and thence spin density of the SOMO π_s is located at C(1) (conjoined with a negligible charge density, not unexpected for a positively charged alternating hydrocarbon structure). Moreover, C(1) is freely accessible in structure I and, thus, the predestined point of attack in dimerization with a second radical cation, as well as in other radical reactions. Structure II is characterized by a relatively high coefficient and consequently low charge density at C(3)/C(5). These two ring positions are freely accessible and, hence, likely targets for radical attack. MNDO calculations demonstrate that, upon introduction of an alkyl substituent into the radical cation at C(1), the two neighboring dialkylamino groups are twisted almost 90° relative to the ring plane.



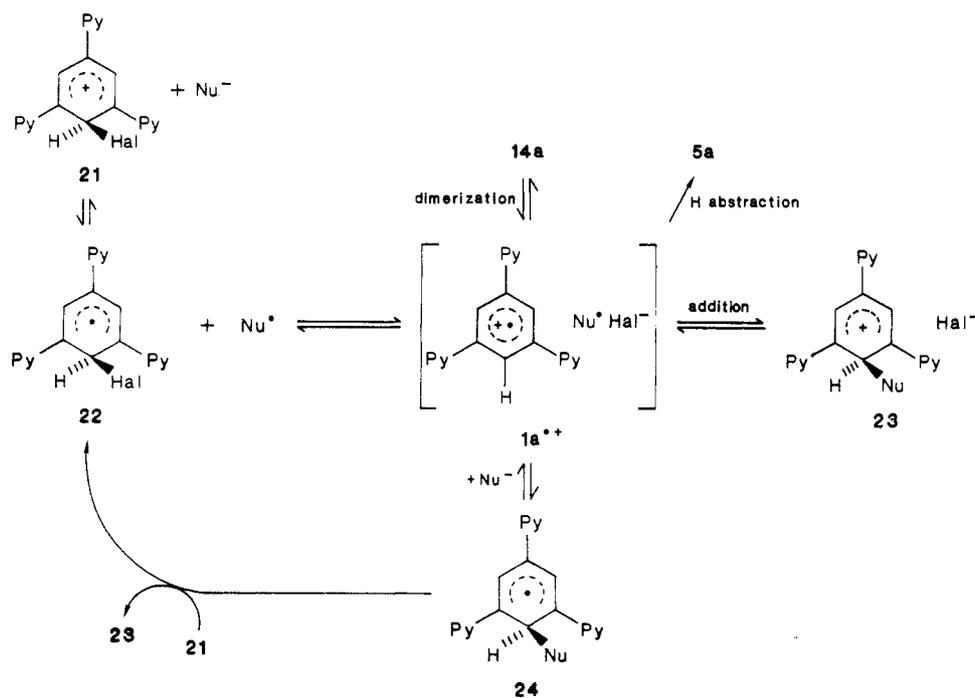
Structure $6a^{+ \cdot}$ -I thus remains as the only energy minimum for $6a^{+ \cdot}$. The electronic configuration $\pi_1^2 \pi_2^2 \pi_3$ again is characterized by an extremely high coefficient and concomitant low charge density at the alkyl-substituted ring carbon. This reactive center, though electronically favored, yet appears extremely shielded by the alkyl substituent itself as well as by the two, nearly orthogonal NR_2 groups in the α - and α' -positions.

On the basis of these theoretical arguments, and with the assumption of kinetic control, the following predictions can be made for regioselectivity and relative reactivity of the two tris(dialkylamino)benzene radical cations $1a^{+ \cdot}$ and $6a^{+ \cdot}$; all of them have been experimentally validated (see above). Reaction of $1a^{+ \cdot}$ with a sterically demanding second radical cation which would directly yield the dimeric σ complex, H abstraction from a much less bulky solvent molecule, and reaction with the sterically least demanding O_2 are all equally facilitated at either C(1) in structure $1a^{+ \cdot}$ -I or C(3)/C(5) in structure $1a^{+ \cdot}$ -II. Compound $6a^{+ \cdot}$, on the other hand, where electronic direction allows for reaction only at the extremely well shielded carbon C(1), may be attacked at this site by sufficiently small reagents only. H abstraction from the solvent and O_2 addition are still practical and indeed are observed solely at the alkyl-substituted ring carbon. Dimerization at this site is sterically impossible, however, and is thus restricted to a nonalkylated ring position. This site, though sterically much less hindered, is electronically very unfavorable. Consequently, dimerization of $6a^{+ \cdot}$ is kinetically severely impeded relative to that of $1a^{+ \cdot}$, and its half-lifetime is therefore 1000 times longer.

Reactions of Halo σ Complexes

As pointed out above, halo σ complexes are comparatively much less stable. In their reactions with bases, product formation strongly depends on the nature of the base, the reaction temperature, and the re-

Scheme XIV



action time.³⁴ This is exemplified in Scheme XII by the reactions of the bromo σ -complex 5c with a variety of bases/nucleophiles.

Deprotonation exclusively is effected by strong bases, e.g., alkoxides, giving 1-bromo-2,4,6-tripyrrolidino-benzene. With triethylamine in chloroform, the biphenyl 18 is obtained. Sulfides, on the other hand, and likewise hydrogen sulfite react as reducing agents only, 5c being dehalogenated to 1a. With potassium cyanide in methanol, the dimeric σ complex 14a is formed in almost quantitative yield within 20 min. The reaction of 5c with potassium rhodanide in methanol at ambient temperature illustrates most strikingly how product formation with a halobenzenium σ complex depends on the actual reaction time. If the reaction is quenched after 1 min, one finds the bromo substituent having been exchanged quantitatively, yielding the rhodano σ complex 19, which in turn may be deprotonated with alkoxide to 20. After 20 min, a mixture is obtained of the rhodano, the dimeric, and the protio σ complexes 19, 14a, and 5a, respectively (Scheme XIII).

From the reaction of 19 with sodium bromide, only the protio σ complex 5a ($\text{E} = \text{H}$, $\text{X} = \text{Br}$) is isolated after 60 min of reaction time. These reactions all show light dependence and are accompanied by drastic color changes of the reaction mixtures. The rapidity of the exchange of Br vs SCN renders a straightforward nucleophilic substitution, whether $\text{S}_{\text{N}}1$ or $\text{S}_{\text{N}}2$, highly unlikely. The formation of 14a and 15a has rather to be rationalized in terms of radical intermediates, via a one-electron charge-transfer mechanism.

The halo σ complex 21 is reduced by the nucleophile Nu^- , via electron transfer, to the radical intermediate 22 whence, by cleavage of a halide ion, the radical cation $1a^{\bullet\bullet}$ is formed. Compound $1a^{\bullet\bullet}$ now undergoes all the follow-up reactions outlined in Scheme X, e.g., dimerization to 14a and H abstraction from the solvent to 15a. The substitution product 23 may be formed by

Table III
Oxidative Potentials of Nucleophiles^a (A) and Reductive Potentials of σ Complexes (B) (vs Ag/AgNO_3 , 0.1 M)

(A)	Nu	I ⁻	SCN ⁻	Et ₃ N	Br ⁻	CN ⁻	Cl ⁻
	$E_{1/2}$, mV	-150	250	330	390	680	700
(B)	21·ClO ₄				19 ^b	14a	5a
	Hal	I	Br	Cl	SCN		
	$E_{1/2}$, mV	-100	-330	-780	-750	-1370	-1580

^aDetermined for the tetrabutylammonium salts in $\text{CH}_3\text{CN}/\text{TBAP}$, 0.1 M. ^bDetermined as the perchlorate.

radical recombination of Nu^\bullet and $1a^{\bullet\bullet}$ or by addition of the nucleophile Nu^- to $1a^{\bullet\bullet}$, and subsequent electron transfer from 24 to unreacted substrate 21 under formation of 22 in conjunction with 23. This second mechanism would constitute a radical chain process. The rate of the electron transfer depends both on the relative redox potential of the different reactive intermediates, which compete with each other in the mechanism outlined in Scheme XIV, and on the leaving tendency of the halides or other leaving groups. The experimentally determined reduction potentials of some halo σ complexes and of the σ complexes 19, 14a, and 5a are collected in Table III, together with the oxidation potentials of the respective anions (nucleophiles) and of triethylamine. The relative reactivity of the halo σ complexes 21 with rhodanide, halides, or tertiary amines shows good qualitative agreement with the gradation derived for the corresponding donor-acceptor charge-transfer interaction.³⁵ The protio σ complex 5a is formed more and more with prolonged reaction time, since it has the most negative reduction potential (see Table III) and since the negligible leaving tendency of a hydride ion makes formation of 5a virtually irreversible.

There is no stringent proof possible for the radical chain mechanism, outlined in Scheme XIV for the nucleophilic substitution of halo σ complexes, since halide

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ions set free in the course of the reaction may function as electron donors. The fact, however, that the reaction is accelerated by light and is incubated by radical inhibitors strongly argues in favor of a radical chain mechanism.

Summarizing Remarks

1,3,5-Tris(dialkylamino)benzenes are exceptionally well suited model substrates for the electronic substitution as well as the oxidation of arenes. From both types of reaction, Wheland intermediates, which still retain one hydrogen at the sp^3 carbon atom, could be isolated for the first time in crystalline form and their structure determined by X-ray crystallography. When these structural data are combined with the results of MO calculations, a deeper insight may be gained into the energy profile of electrophilic attack on aromatic substrates. Thence, experimental results that so far were inexplicable can be interpreted satisfactorily. The follow-up reactions of radical cations, formed primarily in triaminobenzene oxidation, can likewise be rationalized. Triaminobenzenes are comparable in their reaction behavior to enamines and thus can be employed

successfully as model compounds also for enamine reactions.^{14,34,36} This mechanistic parallel might prove both practically and theoretically important in future investigations.

Financial support by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie is gratefully acknowledged. To all my co-workers who have contributed to this work over the years and whose names are given in the respective references, I want to express my heartfelt thanks for their enthusiastic collaboration. Among these, I want to emphasize the names of R. Niess, who was the first to prepare N-peralkylated triaminobenzenes; W.-D. Stohrer, who did almost all the calculations on these systems; J. J. Stezowski, who determined the crucial crystal structures; and P. Fischer, who was responsible for the NMR spectroscopic part and also did the translation of this contribution.

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