Some Aspects of Anionic σ Complexes

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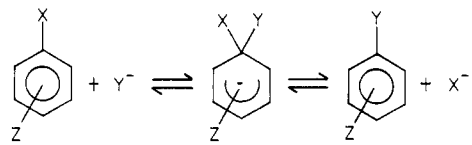
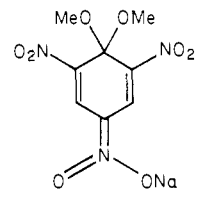
I. Introduction

Recent years saw a breakthrough in the studies on the reactions of nucleophilic aromatic substitution. The most popular mechanism for these reactions was advanced by Bunnett.[1]



Its key stage is the formation of anionic σ complexes that proved to be relatively stable in the case of substrates containing strong electron-acceptor groups. The synthesis of such σ complexes and the mechanism of their formation and decomposition, as well as their role in the reactions of nucleophilic aromatic substitution, have therefore become a subject of special concern, and the number of relevant papers is growing from year to year (see, for example, ref 2–12).

In fact, anionic σ complexes have long been known to chemists. As early as 1886 Janovsky found that treating an acetone solution of *m*-dinitrobenzene (*m*-DNB) with an alcoholic solution of an alkali gives rise to intense violet coloring.[13,14] Later it was observed that the same effect results from the action of alkaline ketones and aldehydes on *m*-DNB.[15,16] In 1895, Lobry de Bruyn isolated and analyzed a red substance that was formed by the interaction of methanolic 1,3,5-trinitrobenzene (TNB) with an equimolar amount of KOH.[17] The structure assigned to this product was $[C_6H_3(NO_2)_3 \cdot KOMe] \cdot H_2O$. Later, Jackson and Gazzolo[18] ascribed quinoid structures (**1** or **2**) to the product of the



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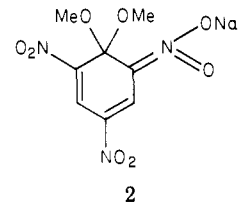

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reaction between 2,4,6-trinitroanisole (TNA) with sodium methoxide. Two years later Meisenheimer[19] obtained the first chemical evidence supporting this structure by showing that on acidification the products of the reactions between TNA and potassium ethoxide or between 2,4,6-trinitrophenetole (TNP) and potassium methoxide yield about the same amounts of TNA and TNP. Since that time the adducts of nucleophiles to polynitroaromatic compounds have been called Meisenheimer or Jackson–Meisenheimer complexes.

The present review will discuss various types of anionic σ complexes and their chemical conversions. Attention will be paid mainly to recent results. We shall confine ourselves to the σ complexes obtained from substituted benzenes, while omitting bicyclic, spirocyclic (for this information see, e.g., ref 10–12), and, for the most part, multicharge σ complexes. Since the review is not aimed at discussing the problem of nucleophilic aromatic substitution, the vast kinetic evidence on these reactions also will not be discussed, except for the fundamental results concerning the mechanism of formation of σ complexes and their stability. Special attention will be paid to the long-neglected problem of the various paths of decomposition via which σ complexes yield no products of nucleophilic aromatic substitution.

II. Types of Anionic σ Complexes

A. Anionic σ Complexes with Oxygen-Containing Nucleophiles

The anionic σ complexes of this type are formed by the reaction of alkali alcoholates with polynitro aro-

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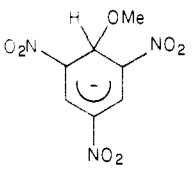
matic compounds. They were discovered long ago,[17-19] and most of them, particularly for the ethers of picric acid and TNB, were isolated. One of the major problems, i.e., the identification of the σ complexes, was partly solved as early as 1902 by Meisenheimer;[19] his chemical proof of the structure of the TNA σ complex with EtOK for decades remained the only one for σ complexes of alkyl picrates with alcoholate ions. It was not until 1964 that Crampton and Gold[20] obtained unambiguous ^1H NMR data confirming the structure of anionic δ complexes **3** and **4**. Since that time ^1H NMR



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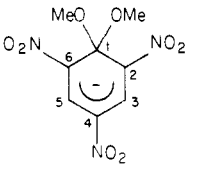

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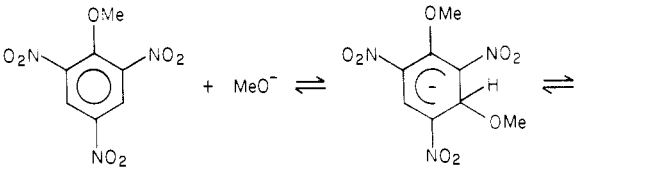
spectroscopy has become the most widely used and reliable technique for investigating the structure of anionic σ complexes. More than 300 ^1H NMR spectra of various δ complexes have been published. Most of them can be found in reviews by Strauss[7] and Gitis.[8]

Another method of direct identification, namely ^{13}C NMR spectroscopy, was applied to σ complexes rather recently. The first report was published by Olah and Mayr in 1976[21] and dealt with the spectra of 4-X-2,6-dinitroanisoles (X = Cl, F, CH_3, CF_3, NO_2) and the corresponding anionic σ complexes with methoxide ion. In addition to confirming the structure of the σ complexes, the study supplied information on the distribution of electron density in the ring. Comparison of chemical shifts in the parent nitro aromatic compounds and in their σ complexes indicated that the cyclohexadienyl carbons in the latter carry a negative charge of 0.3–0.4 e when compared with the initial substrate. This experimental finding proved the correctness of a semiempirical calculation of the charge distribution in Meisenheimer complexes[22] and refuted an earlier method of calculation[23] that predicated the charge on carbon atoms in σ complexes would decrease. All the X substituents (Cl, F, CH_3, and CF_3) except NO_2 exert virtually no influence on the negative charge in the cyclohexadienyl system. Such a remarkably strong electron acceptor as the nitro group, however, does decrease the electron density on the ring carbons; the overall upfield shift for the corresponding σ complex is 6–8 ppm less than that for the other σ complexes. Olah's pioneer investigation[21] was followed by several papers reporting the use of ^{13}C NMR in the studies of anionic σ complexes (see, for instance, ref 24–27).

The structural parameters of the Meisenheimer complex were established by X-ray diffraction analysis.[28,29] The C(4)–N bond proved much shorter than the C-(2)–N bond, which means the *p*-nitro group carries a greater negative charge. The cyclohexadiene ring is largely planar; the plane containing two alkoxy groups is perpendicular to that of the ring. The length of the C–O bonds is close to the lengths in aliphatic ethers and far greater than those in TNP. The nitro groups attached to the C-2 and C-6 carbons are approximately coplanar with the ring, whereas in TNP the dihedral angle between the ring and the *o*-nitro group is equal to 62°. Despite all its advantages, this method failed to gain wide recognition, since it is difficult indeed to obtain single crystals of σ complexes.

As it has been mentioned, Crampton and Gold argued that the adduct of methoxide ion to TNA has the structure **4**.[20] Soon, however, Servis reported that the



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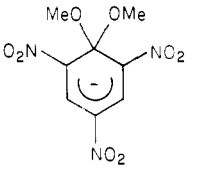

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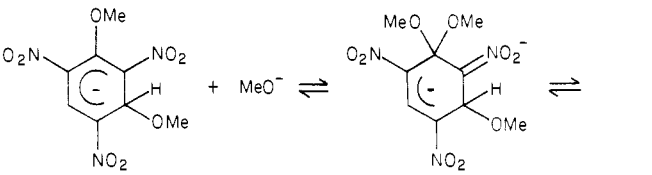
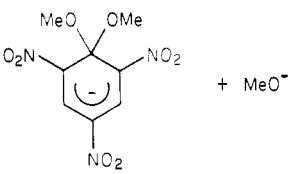
initial product was an isomeric σ complex, **5**, in which the MeO^- ion adds to the unsubstituted C-3 carbon atom.[30,31a] Since then the anionic σ complexes obtained from other 1-X-2,4,6-trinitrobenzenes and containing a bond between the nucleophile and C-3 carbon have often been referred to as Servis complexes. The 1,3 σ complex **5** is extremely labile and in 15 min gives rise to a more stable 1,1 σ complex **4** (rate constant = 4×10^{-3} s^{-1}[30]). It is believed that the **5** → **4** transformation may be an inter- as well as an intramolecular process, but no convincing evidence favoring either path has been obtained so far. Addition of MeOH or MeO^- to Me_2SO solutions of **5** was found to avidly catalyze the **5** → **4** transformation; the methoxide ion supposedly promotes the formation of an intermediate dianionic σ complex, **6**.[30,31a]



5 **6**



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The first solid Servis complex to be isolated was a product of the reaction between 1-carbomethoxy-2,4,6-trinitrobenzene and KOH.[32] In the solid phase and in the solution alike, it takes but a few h at room temperature for the complex **7** to convert into the 1,1 σ complex **8** (which also was isolated). The greater stability of **4** with regard to **5** is explained by the fact that the coplanar 1-methoxy and 2,6-dinitro groups suffer steric compression, while in **4** the 4-methoxy groups are situated in the plane perpendicular to that of the ring.[33]

The formation of the σ complexes **4** and **5** is also essentially dependent on solvation, charge delocalization, and steric factors both in the complexes and in the corresponding transition states.[7] Bernasconi, for in-

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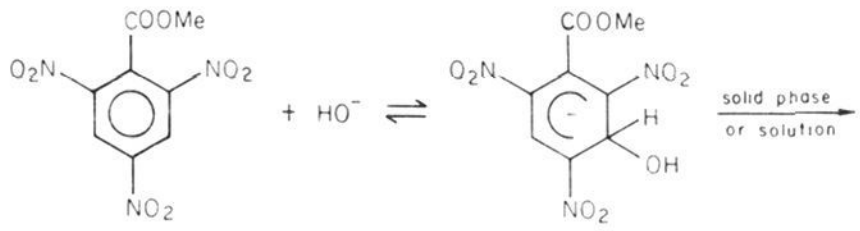
stance, maintains that the better charge delocalization in the 1,3 σ complex due to the contribution of resonance structures **9** and **10** accounts for its preferential formation at the kinetically controlled stage. However, the formation of an energetically advantageous *gem*-dimethoxy group gives rise to isomerization of the forming 1,3 σ complex into the 1,1 σ complex.[34]



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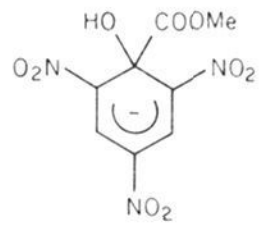

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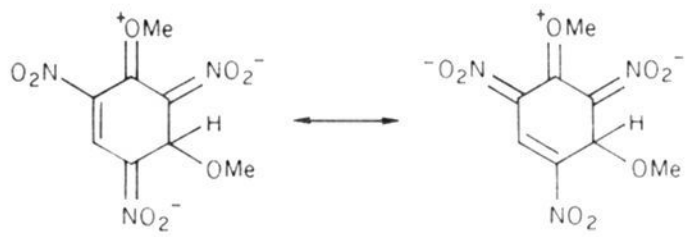


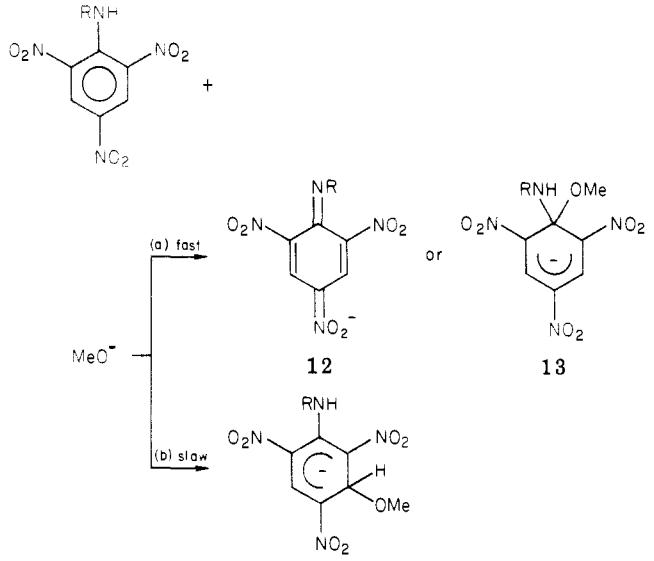
9 **10**

Another opinion, which has not become widespread, is that the formation of σ complexes **5** and **4** is independent.[35]

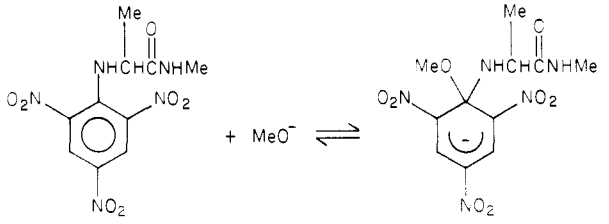
The stability of 1,3 σ complex **5** is markedly dependent on the solvent. While in Me_2SO the lifetime of the complex (15 min) permits its detection, in methanol it decayed too rapidly to be observed. The effect of an aprotic dipolar solvent (Me_2SO) on the stability of 1,3 and 1,1 σ complexes formed by the reaction between methoxide ion and 4-X-2,6-dinitroanisoles (X = SO_2CF_3, SO_2CH_3) was investigated.[36] With either substrate, the stability of both complexes increased with Me_2SO concentration, the relative thermodynamic stability remained virtually the same.

These facts are in agreement with the conclusions of Fendler et al., who suggested that the stability of anionic σ complexes in aprotic dipolar solvents is greater than in aprotic medium[37-39] and that the free energy of stabilization ($\delta\Delta G = \Delta G^{Me_2SO(DMF)} - \Delta G^{MeOH(H_2O)}$) is independent of the nature of the substrate.[37]

In general, the proportion between the products of addition to C-1 and C-3 carbon atoms in 1-X-2,4,6-trinitrobenzenes depends on the nature of both the nucleophile and the substrate. Some substrates are attacked only in an unsubstituted position. For instance, methoxide ion adds to the C-3 carbon of 2,4,6-trinitrotoluene (TNT),[40] *N*,*N*-dimethylpicramide-,[31a,31b,33,41,44] *N*-methylpicramide,[31a,31c,33] and picramide.[31a,33,42] Hence it becomes clear why the only products of acidification of picramide and *N*,*N*-dimethylpicramide σ complexes with MeONa were picramide and *N*,*N*-dimethylpicramide.[31b,43] It is of interest that the formation of 1,3 δ complex **11** is accompanied by that of a second product—a deprotonated picramide **12**[30,31,33,44] (which in excess MeONa adds methoxide ion to give the corresponding σ complex[31c]) or the 1,1 σ complex **13**.[45] However, the kinetic information obtained by means of stopped-flow and temperature-jump techniques[44] indicates that reaction a is too fast to presume the formation of 1,1 δ complex **13**. Complexes **13** are usually obtained by the action of amines on alkyl picrates (see section IIC). In an unusual case a complex of **14** was formed in the reaction between picramide **15**



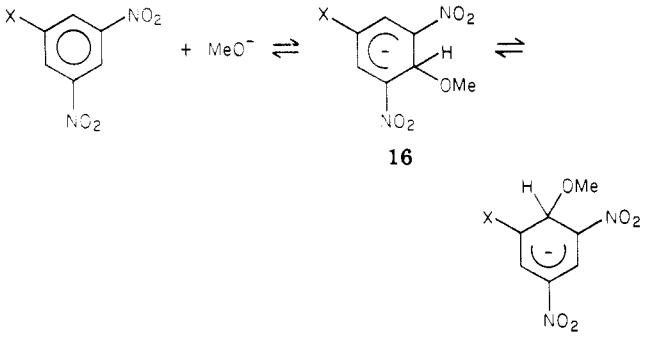
and methoxide ion.[46-48] Complex **14**, which was isolated as a solid and studied spectrally,[46] was thought to feature high stability because of its amide proton, which



was capable of forming a hydrogen bond with the *o*-nitro groups.[47,48]

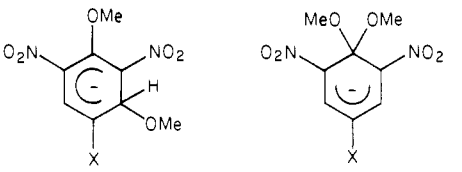
TNT and MeO^- also give rise to a 1,3 σ complex whose formation is accompanied by slow deprotonization of TNT.[40]

Two isomeric σ complexes (1,1 and 1,3) of different stability result from reactions between 1-X-3,5-dinitrobenzenes and nucleophiles. Thus, 1-X-3,5-dinitrobenzenes (X = CF_3,[49-51,53,54] COOMe,[50,51,54] Cl,[49,53,54] $CONMe_2$, SO_2Me,[51] CN[49,52-54]) with MeO^- ion rapidly yield both σ complexes **16** and **17**, but the final product is **17**, assumed to be formed from **16** at the slow stage.[49-51,54]

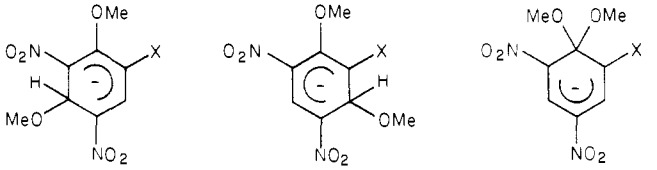


This succession of conversion was clearly demonstrated by Fyfe et al.[54] for X = CN, CF_3, COOMe, and COOEt by stopped-flow techniques with ^1H NMR spectra monitoring. As the flow is increased, i.e., as the time interval between mixing and observation is decreased, the proportion of **16** in the mixture **16** and **17** increases. When the flow is stopped, the spectrum changes almost immediately to that of the thermodynamically stable product **17** ($\tau_{1/2}$ = 0.97 s).[54]

In a similar manner methoxide ion reacts with 4-X-2,6-dinitroanisoles; unstable 1,3 σ complexes **18** (X = CN,[55,56] F,[56,57] Cl,[57] CF_3,[57] H[56,57]) observed at the initial stage afford the corresponding stable 1,1 σ complexes **19**.

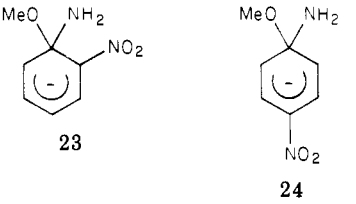


In 2-X-4,6-dinitroanisoles there are two nonequivalent positions for the addition of a nucleophile, which results in the formation of 1,3 or 1,5 σ complexes. It was shown that the immediate product is the 1,5 δ complex **20**, whose rapid conversion into the more stable 1,3 σ complexes **21** is followed by the formation of the stable 1,1 σ complexes **22** (X = Cl,[56,58,60] CN,[56,59,60] CF_3,[59,60] F[56,60]. It is likely that 1,3 σ complexes are more

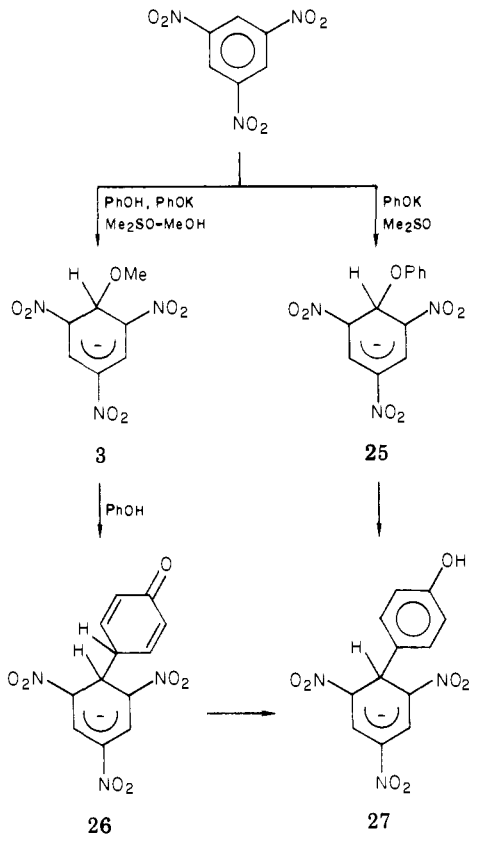


stable than the 1,5 complexes because the *p*-nitro group provides for greater delocalization of the negative charge than the X substituents.[58]

A σ complex of MeO^- with 2,4-dinitroanisole was also reported[33,61] and identified by ^1H NMR as the 1,1 σ complex.[61] In due course this complex decomposes into 2,4-dinitrophenolate.[33] Anionic σ complexes of *o*- and *p*-nitroanilines with MeO^- (σ complexes **23** and **24**) were obtained by Ohsawa and Takeda.[62,63] This is an intriguing fact when one considers that no positive information on nitrobenzene σ complexes is available.



Investigations of anionic σ complexes of another oxygen-containing nucleophile, i.e., phenoxide ion, faced peculiar problems because of its ambient nature. Indeed, this ion can give rise to both C–O and C–C σ complexes. It was originally assumed that TNB with PhO^- yields a product of structure **25**.[64,65] Later, however, Buncel[66a] demonstrated that in the reaction between TNB and PhOK in Me_2SO–MeOH the product of the first stage is a methoxy σ complex, **3**, which yields a σ complex, **26**, which in turn isomerizes into **27**. The latter was isolated from the solution on acidification. Its structure was established by means of ^1H NMR spectroscopy; the spectrum contained a quartet at 6.9 ppm characteristic of para-substituted benzenes. No formation of σ complex **25** was observed. In Me_2SO



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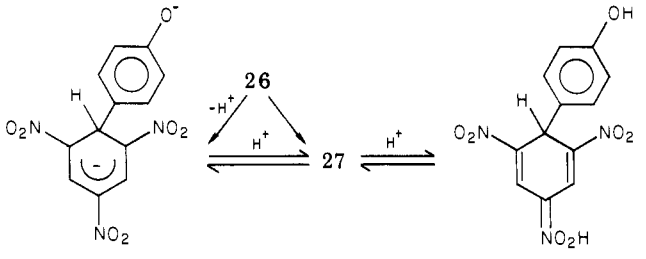
the authors[66b] found a minor amount of the o-phenoxy adduct, formed by bonding between an ortho carbon of the phenoxide ion and an unsubstituted carbon of TNB. Its structure was established by means of ^1H NMR spectroscopy. Information concerning the state of ionization of TNB–phenoxide σ complex has also been obtained.[66b] At a 2:1 molar ratio of PhOK–TNB, dianion **27a** is formed, but at a PhOK–TNB molar ratio of 1:1 the final reaction product is σ complex **27**; acidification of **27** leads to the corresponding nitronic acid **27b**.



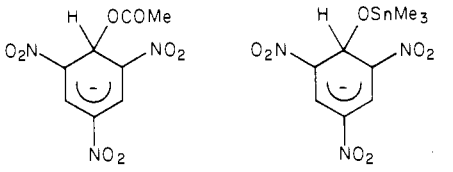
27a 27b

The formation of σ complex **25** was found by Shein et al.,[67] who demonstrated that **25** is the initial product of TNB interaction with PhOK in Me_2SO. σ complex **25** after a while yields σ complex **27**. The latter, like most δ complexes with a C–C bond, is very stable; it was oxidized by bromine to 2,4,6-trinitro-4′-hydroxybiphenyl. It is interesting to note that **25** isomerizes into **27**, i.e., only the product with the hydroxy group in the para position of phenyl ring was obtained; no isomerization was observed when a methyl group was introduced into the para position.[67] At the same time, ortho-substituted phenolates, e.g., o-chlorophenolate, again gave rise to both σ complexes **25** and **27**.[67]

In contrast to TNB, trinitroanisole and phenyl picrate (PP) react only at the oxygen atom of phenolate ion; TNA affords a 1,1 σ complex,[64,65,68] and PP affords a 1,3 σ complex that in 3–5 min converts to a 1,1 σ complex.[65]

Anionic σ complexes for the simplest oxygen-containing nucleophile, i.e., the hydroxide ion, were also reported. TNB reacts with dry NaOH solution in Me_2SO to form the TNB hydroxylic σ complex, which can be isolated by adding ether.[69] There are many other nitro aromatic substrates which also yield σ complexes with HO^- ion (see, for example, ref 70 and references therein).

Structures **28** and **29** are examples of σ complexes with other oxygen-containing nucleophiles. **28** was obtained by reaction between TNB and sodium acetate in Me_2SO[71] and **29** was formed by the action of lithium trimethylstannolate on a TNB solution in THF.[72]



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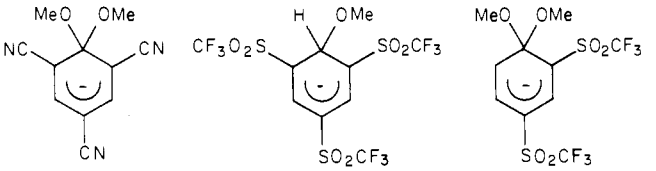
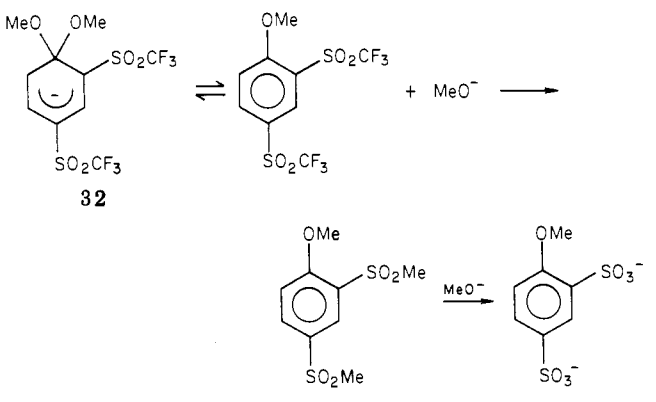
Of late, σ complexes of MeO^- with aromatic compounds containing substituents other than nitro groups have been prepared. For example, 2,4,6-tricyanoanisole and potassium methoxide yield the 1,1 σ complex **30**,[73], whose stability is 4.2×10^4 times lower than that of the corresponding TNA σ complex. No intermediate for-



30 31 32

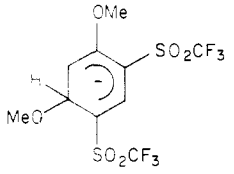
mation of a 1,3 σ complex was observed in this reaction. A remarkably stable σ complex of methoxide ion with 1,3,5-tris[(trifluoromethyl)sulfonyl]benzene (TMSB) **31** was obtained by Yagupolsky et al.[74,75] In contrast to the far less stable methoxy δ complex of TNB, this complex is formed even by simple dissolution of TMSB in MeOH;[76] it does not give rise to the acetone, trichloromethyl, and phenoxy σ complexes upon addition of acetone, $CHCl_3$, and PhOH, respectively.[75] The same authors also isolated the stable σ complex, **32**, of 2,4-bis[(trifluoromethyl)sulfonyl] anisole (BTSA) with sodium methoxide.[77] The spectral characteristics of this



32 33

complex, however, are at variance with those reported,[78] where **32** is reported to rapidly decompose into the corresponding disulfonate **33**.

A stopped-flow study of the reaction between BTSA and MeO^- indicated that the initial stage of the reaction involves the formation of an extremely unstable intermediate, which was identified as the 1,5 σ complex **34**.[79]



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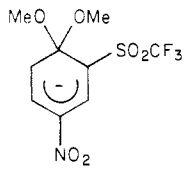

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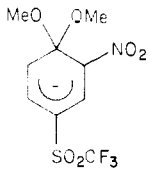

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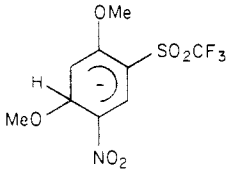
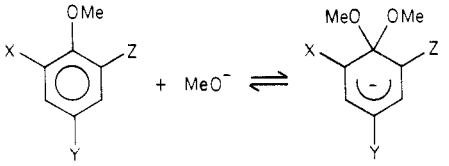


37

Labile 1,1 σ complexes were also formed by the interaction of methoxide ion with 4-nitro-2-[(trifluoromethyl)sulfonyl]anisole (**35**) and 2-nitro-4-[(trifluoromethyl)sulfonyl]anisole (**36**). With the first substrate the initial formation of the 1,5 σ complex **37** was also observed.[79] The fact that the reaction of methoxide ion with 2-nitro-4-[(trifluoromethyl)sulfonyl]anisole (and, incidentally, with 2,4-dinitroanisole as well) gives rise only to 1,5 σ complexes; this was explained by the outstanding electron-accepting capacity of the para SO_2CF_3 group.[79]

The 1,1 σ complexes **39a–e** were recently obtained by the reaction between MeO^- and anisoles **38a–e**. No



38 **39**

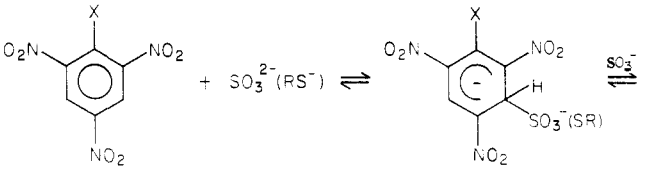
a, X = Z = NO_2; Y = SO_2CF_3
b, X = Y = NO_2; Z = SO_2CF_3
c, X = Z = SO_2CF_3; Y = NO_2
d, X = NO_2; Y = Z = SO_2CF_3
e, X = Y = Z = SO_2CF_3

data were reported on the formation of 1,3 σ complexes or on the reaction between MeO^- and $SO_2CF_3^-$ and the methoxy group of the anisoles **38a–e**[80] (see section VI).

B. Anionic σ Complexes with Sulfur-Containing Nucleophiles

The reactions between polynitro aromatic compounds and Na_2SO_3, EtSNa, and PhSNa have been investigated as well. It was established spectrophotometrically that TNB with aqueous Na_2SO_3 yields a 1:1 complex which proceeds to form a 1:2 complex upon addition of Na_2SO_3 in excess.[81] The 1:2 complex was isolated and found to correspond to the formula $TNB\cdot(Na_2SO_3)_2$.[82] Similar σ complexes were observed in absorption spectra by other authors.[83–85] The structure of mono- and diadducts as anionic σ complexes was confirmed by Crampton[42] and later by other workers[86–91,96] using ^1H NMR techniques. It was demonstrated that the ambient SO_3^{2-} anion adds to polynitro aromatic compounds to form a C–S bond.[85,91]

Along with the 1,3 σ complex **40** (X = OMe), sodium picrate was formed by the reaction between TNA and Na_2SO_3.[91]



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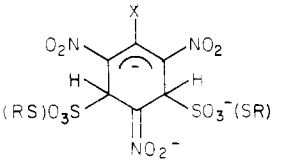


41

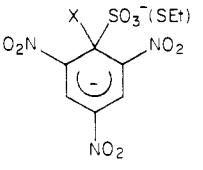
X = H, MeO, NH_2, MeNH, Me_2N, PhNH

The σ complexes **41** (X = H, MeO, OH, COOMe) with Na_2SO_3 were recently obtained by a "solid phase" reaction, i.e., by mixing the substrate with $Na_2SO_3\cdot 7H_2O$.[91] An attempt to isolate the σ complexes **41** from aqueous solutions failed.[91]

Bernasconi[85] obtained interesting data on the reaction between TNB and Na_2SO_3 using the stopped-flow technique.[85] The first (fast) stage of the reaction gave rise to the σ complex **40** (X = H), which then slowly proceeded to form two 1:2 complexes. Their absorption spectra, as well as kinetic evidence, indicated that they were cis and trans isomers of the σ complex **41**[85] a conclusion confirmed by Strauss and Taylor,[92] Crampton and Willison,[93] and Marendic and Norris.[89] Thus, assumption that all 1:2 complexes may in principle exist in cis as well as in trans forms was proved. Cis and trans isomers, however, were not found for all the 1:2 complexes; the possible reasons for this effect are discussed in ref 94a.

The σ complexes **40** also result from the reaction between EtSNa (PhSNa) and 1-X-2,4,6-trinitrobenzenes (X = NH_2, H, NHMe). The structure of the EtSNa complex was established as **40** by ^1H NMR.[95] With PhSNa the ^1H NMR spectrum contains only a broad signal of the ring protons at about 7.5 ppm, which the author ascribes to rapid exchange with free TNB.[95] Excess EtSNa converts **40** into the σ complex **41**.

In general, sulfur-containing nucleophiles form no 1,1 σ complexes in reactions with substituted trinitrobenzenes. The reaction stops at the 1,3 σ complex stage,[87,88,91] and picramides do not lose a proton, as they typically do when reacting with alcoholate ions. The exceptions are the σ complexes **42**, which were obtained in the reaction of Na_2SO_3 with picric acid (X = O^-) (from TNA)[91] and trinitrobenzaldehyde (X = CHO),[89]



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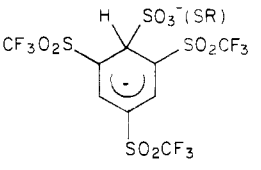


43

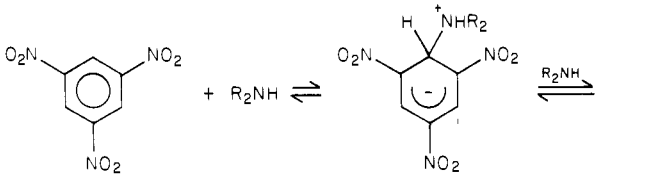
and the reaction of EtSNa with trinitrophenetole (X = EtO).[94b]

From a comparison of the constants of formation of σ complexes with sulfur-containing nucleophiles and with their oxygen counterparts Crampton[95] suggested an order of "thermodynamic affinity" to aromatic carbon: $EtS^- > MeO^- > PhS^- > PhO^-$.

TMSB was recently reported to form σ complexes with Na_2SO_3, PhSNa, and BuSNa in Me_2SO.[75,97] The σ complexes **43** with the latter two salts are very unstable (particularly in methanol[97]) and rapidly decompose by loss of the CF_3SO_2 group.[75,97] A similar exchange reaction (without, however, the formation of an anionic σ complex) occurs between TMSB and sodium thiophenolate in MeOH.[97]

C. Anionic σ Complexes with Nitrogen-Containing Nucleophiles

Ammonia and primary and secondary amines react with TNB to form the anionic σ complexes **45** which were identified by their ^1H NMR and UV spectra,[3,31a,98,99] while tertiary amines do not react with TNB.[98-100] The process involves two stages. There is



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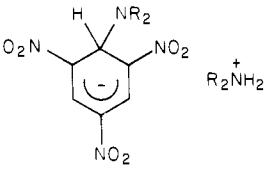
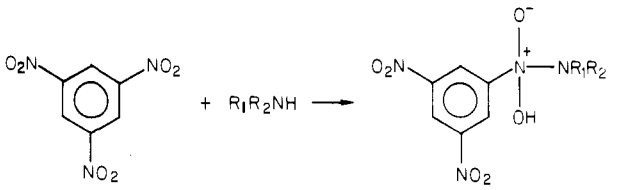


45

kinetic evidence that depending on the reaction conditions and the aromatic substrate, the rate-determining stage may be either the formation of the zwitterionic σ complex **44** or the transfer of a proton from this complex to another molecule of the amine with the σ complex **45** as the product[101] (for spiro complexes, see ref 102–104).

The alternative mechanism involving the interaction of TNB with the R_2N^- ion formed from R_2NH by autoionization seems less likely. Indeed, in this case the very low concentration of R_2N^- must have been compensated for by an extremely high rate of reaction with TNB.[98]

It was pointed out in the literature that the formation of TNB σ complexes with aliphatic amines is complicated by the reduction of the substrate to an anion radical.[105,106] Another intriguing side reaction accompanying the formation of these complexes was reported by Bernasconi.[107] In a temperature-jump study of the reaction between TNB and *n*-$BuNH_2$, piperidine, and pyrrolidine in 1:9 dioxane–water mixture, he observed a product which, according to his own kinetic evidence and borrowed data, was identified as **46**. The fact that this reaction path, i.e., the addition of the amine to the nitro group, had not been discovered earlier was attributed to the necessarily strong solvation of the ad-

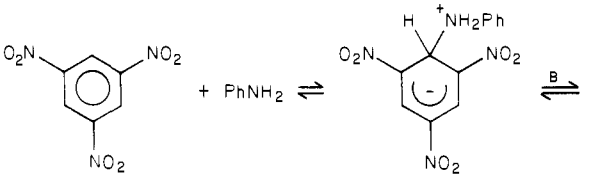


46

$R_1 = n\text{-Bu}; R_2 = H; R_1,R_2 = (CH_2)_4$

duct. In these terms, the mixture of the solvents used appears unique, since even a 50% mixture appears too rich in dioxane for the oxyhydroxylamine to be formed.

In contrast to aliphatic amines, their aromatic counterparts such as aniline yield π rather than anionic σ complexes with TNB.[108] Buncel, however, found that in the presence of a base (1,4-diazobicyclo[2.2.2]octane) the anilide σ complex **48** is formed.[109] The authors



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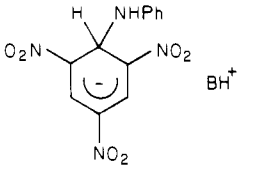
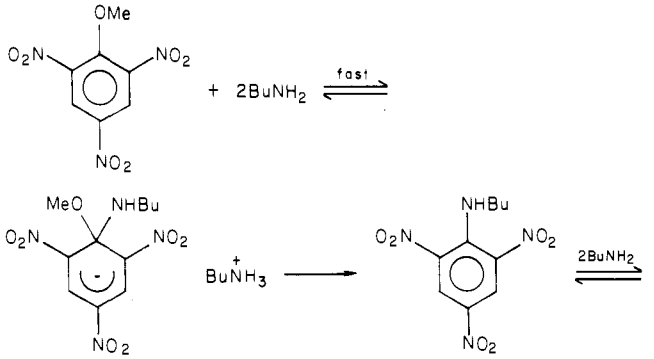


48

reached a conclusion from the kinetic evidence that the rate-determining stage of this reaction is the loss of a proton under the action of a strong enough base (e.g., 1,4-diazabicyclo[2.2.2]octane but not $PhNH_2$ itself) from the zwitterionic σ complex **47**, which was formed at the preequilibrium stage.[110,111] Buncel suggested an alternative way of obtaining **48** from TNB and PhNHK.[112] He also found that in Me_2SO–MeOH the methoxy σ complex of TNB yields the σ complex **48** on addition of aniline[113-116] (see section VA).

There are few reliable data concerning σ complexes of amines with TNA. Only recently did Fyfe and his co-workers report the formation of the 1,1 σ complex **49** from TNA and $BuNH_2$ in Me_2SO–MeOH.[117,118] A



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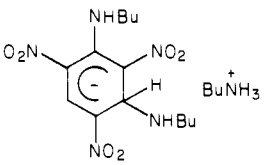
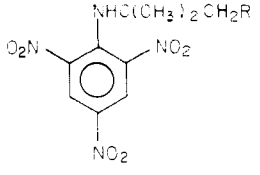


thorough low-temperature kinetic study of the reaction using the stopped-flow technique with ^1H NMR spectra measurements enabled the authors to establish that **49** is formed at the fast stage, while the slow stage is its conversion to the nucleophilic substitution product, namely *N*-butylpicramide.[117,118] It should be noted that this investigation is one of the few papers furnishing definitive evidence for the formation of a substitution product from a 1,1 σ complex.

The same authors used a similar technique to study the reaction between TNA and secondary amines in a binary mixture of Me_2SO and MeOH (1:1).[27] This process proved to stop at the first stage, i.e., the formation of a relatively stable 1,1 σ complex that does not yield a substitution product. On standing, this σ complex slowly gives rise to the methoxy σ complex of TNA which could be identified only by means of ^{13}C NMR spectroscopy (in ^1H NMR spectra the chemical shifts of both complexes were identical).[27] No mechanism was proposed for this conversion.

Tertiary amines such as Et_3N undergo only methylation by trinitroanisole to give the corresponding picrate.[119] Under more vigorous conditions (boiling in toluene), sterically hindered secondary and even primary amines are also methylated[120] (for more detail see section VIA). An interesting intermediate preceding the formation of a σ complex was observed in the reaction of phenyl and mesityl picrates with sterically hindered amines at −57 °C.[120] Under these conditions the reaction product is nitronic acid **50**, identified from ^1H NMR data. This species reacts with excess amine to give the σ complex **51** and yields the substitution product **52** when heated to room temperature.



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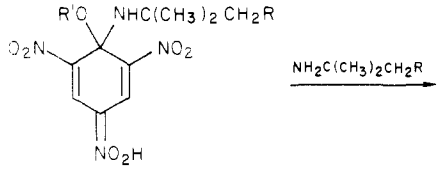

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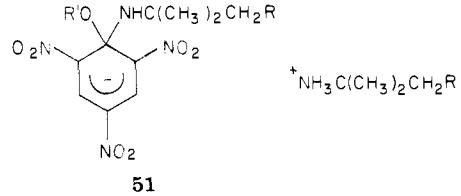
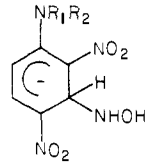


51

R = H, R′ = Ph; R = H, R′ = *s*-$Me_3C_6H_2$

Conclusive evidence against the opinion that picramides do not react with amines[31] was recently obtained by Fyfe,[117] who observed that *N*-butylpicramide with *n*-$BuNH_2$ leads to a 1,3 σ complex identified by ^1H and ^{13}C NMR spectroscopy.

Anionic σ complexes of another nitrogen-containing nucleophile, namely hydroxylamine, were reported [the complexes **53** (R_1 = H, R_2 = NHPh; R_1 = H, R_2 = Me; R_1 = R_2 = Me;[121] R_1 = R_2 = H[122]), **54**,[122] **55** (X = NMe_2,[45] H[122]]. All these species result from the addition of sodium methoxide to a solution of a nitroaromatic substrate plus hydroxylamine hydrochloride. The reactions are markedly dependent on the solvent. Thus, in Me_2SO it leads to the σ complex **54**, whereas in methanol the immediate product is the 1:2 σ complex **55** (X = H).[122] In the opinion of the authors,[122] this is due to the fact that Me_2SO better solvates the former and methanol the latter σ complex.



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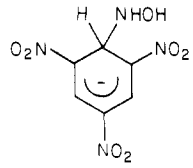

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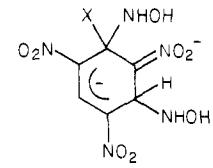


55

The mechanism for the formation of the σ complexes **53**–**55** is virtually unknown. It was suggested that **53** and **54** are formed either from the corresponding methoxy σ complexes (which, incidentally, were not observed in the reaction) through substitution of the MeO^- group by the more nucleophilic ^-NHOH

$$NH_2OH + MeO^- \rightleftharpoons {}^-NHOH + MeOH$$

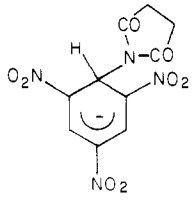
$$[TNB{\cdot}MeO]^- + {}^-NHOH \rightarrow [TNB{\cdot}NHOH]^- + MeO^-$$

or directly from the substrate and the ^-NHOH ion[122]

$$TNB + {}^-NHOH \rightleftharpoons \mathbf{53}$$

The latter reaction is believed to be more likely.[122]

TNB with lithium (potassium) succinimide in Me_2SO gives an anionic σ complex, **56**.[71] It is stable in the solution, but on addition of water this complex rapidly decomposes to recover TNB and the succinimide.[71]



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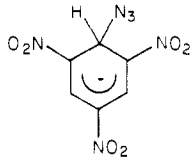
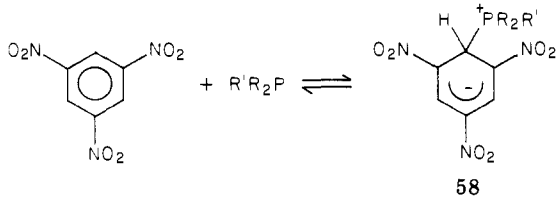


57

As far as other nitrogen-containing nucleophiles are concerned, at −45 °C the azide ion adds to TNA to form the 1,1 σ complex **57** which was identified by UV and ^1H NMR spectra.[125] The complex features very low stability and, upon heating to 0 °C, decomposes to release nitrogen.

D. Anionic σ Complexes With Phosphorus-Containing Nucleophiles

Unlike tertiary amines, trialkylphosphines (but not triphenylphosphine) and many other P(III) compounds react with TNB in Me_2SO to form zwitterionic σ complexes **58**. For *n*-Pr_3P, $Ph_2P(OEt)$, $PhP(OEt)_2$, P-

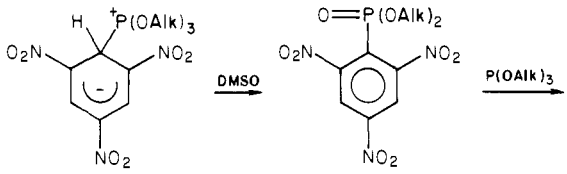


58

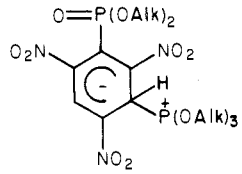
R = *n*-Pr, NMe_2, OMe, OEt; R′ = Ph

$(NMe_2)_3$, $P(OMe)_3$, and $P(OEt)_3$ these compounds have been identified in solutions by ^1H NMR and UV spectra.[126-128] In general, the formation of σ complexes occurs early in the reaction of substituted *m*-DNB (and TNB) with $(BuO)_2PH$ in the presence of NaOH.[124]

When exposed to light as well as on evaporation of solvent the σ complexes **58** decompose. In Me_2SO the σ complexes **59** (Alk = Me, Et) turn into the picrylphosphonates **60**. The authors do not consider the



59 60



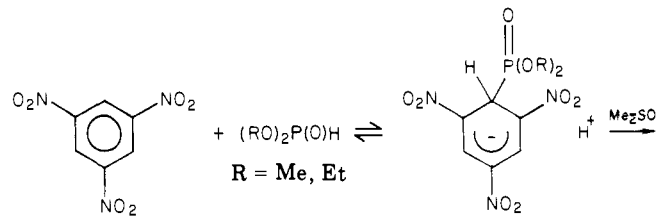
61

mechanism of the transformation. However, this transformation should include nucleophilic substitution of a hydrogen atom and be accompanied by AlkH release, and that seems unlikely. The picrylphosphonates **60** may further react with excess trialkyl phosphite to give the σ complexes **61**.[127]

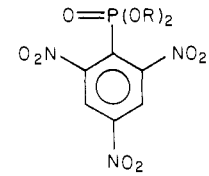
A very unstable σ complex, **62**, was observed in the reaction between picryl fluoride and $(MeO)_3P$;[129] the eventual products were picrylphosphonate, MeF, TNT, and dimethylfluorophosphate. The first and the second compounds result from a S_NAr type reaction involving Arbuzov's rearrangement, while the two other species are thought to be generated from the phosphorane **63**.[129] Picrylphosphonate is also formed from the reaction of picryl chloride with trialkyl phosphite.[129]

A kinetic study of the reaction of TNB with $(EtO)_3P$, $(EtO)_2PPh$, and $EtOPPh_2$ has shown that in this series the rates of both the forward and the back reactions increase, but the back reaction accelerates faster, so that the equilibrium constant decreases.[128] Consequently, substitution of a phenyl for the alkoxy group makes the σ complex **58** less stable. From this it becomes clear that in the case of Ph_3P the formation constant of the σ complex **58** is too small for the complex to be observed.[128]

There is recent evidence[130] for the reaction between TNB and P(V) compounds, e.g., dialkyl phosphites $(MeO)_2P(O)H$ and $(EtO)_2P(O)H$. Such reactions afford σ complexes **64** and are accelerated in the presence of bases promoting the ionization of dialkyl phosphites. Just like the σ complexes of trimethyl and triethyl phosphite, the σ complexes **64** in Me_2SO undergo conversion to the picrylphosphonates **60**.[130] As in the case of the transformation of **59** into **60**, the authors[130] do not consider the mechanism of the conversion **64** → **60**. However, direct transformation of **64** to **60** seems unlikely, because it should involve H_2 elimination. We presume that **64** is more likely to give **60** via oxidation by atmospheric oxygen.



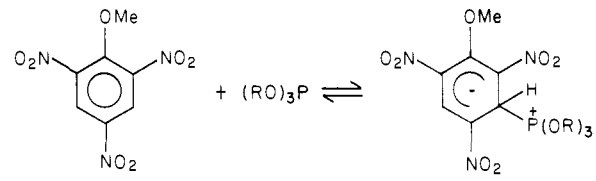
64



60

The σ complexes **64** were characterized by ^1H NMR and UV spectra. Significantly, the ambident $[(RO)_2PO]^-$ anions attack TNB to form a C–P rather than a C–O bond, since in ^1H NMR spectra of the σ complexes **64** the signal of the protons at the sp^3 carbon atom splits on the phosphorus atom with the constant 21 Hz characteristic of the CH–P fragment.[130]

Trialkyl phosphites $(RO)_3P$ (R = Me, Et, Pr) in Me_2SO also react with TNA.[131] The process leads only to 1,3 σ complexes **65** whose structure was established by ^1H NMR.

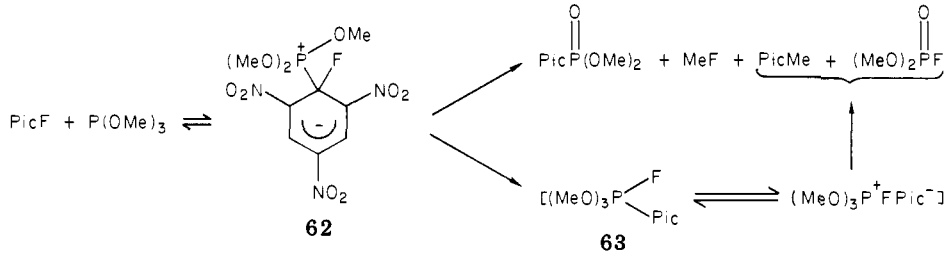


65

R = Me, Et, Pr

It should be noted that TNA is much less active in complex formation with phosphorus compounds than TNB. Indeed, after 48 h the yield of the σ complex **65** in the solution is as low as 10–15%. The presence of picric acid in the reaction mixture, evidently due to TNA interaction with Me_2SO,[132] is therefore not surprising.

As contrasted to TNB, in the absence of bases TNA forms no σ complexes with $(RO)_2P(O)H$. In the presence of Et_3N, however, the reaction takes 1–2 h at room temperature and leads to a 1,3 σ complex, **66** (X = OMe).[131]



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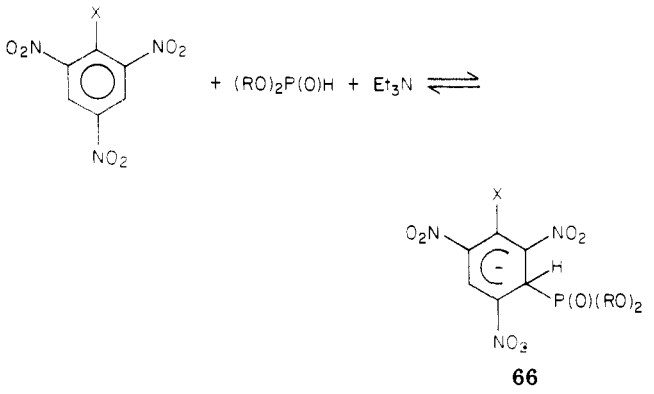
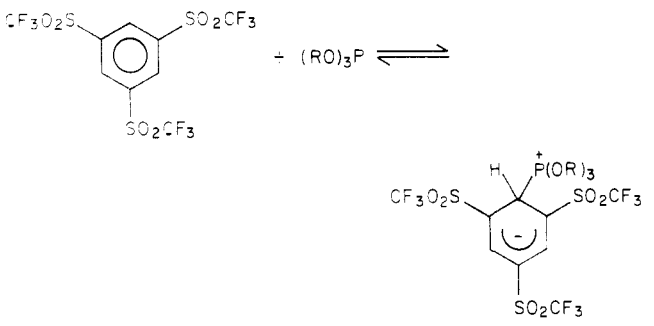


66

R = Me, Et; X = Me, OMe

TNT is even less active than TNA with respect to $(RO)_3P$ and $(RO)_2P(O)H$, and in the absence of base no reaction occurs. On addition of triethylamine, the interaction with $(MeO)_2P(O)H$ was observed, with the σ complex **66** (X = Me) as a product. Note that both TNT and TNA give rise only to 1,3 σ complexes, which was explained by steric reasons.[131]

Another substrate reacting with trimethyl and triethyl phosphite to form zwitterion σ complexes is TMSB.[133] The σ complexes **67**, which result from addition of trialkyl phosphites to TMSB in Me_2SO, were characterized by UV and ^{19}F and ^1H NMR spectra.



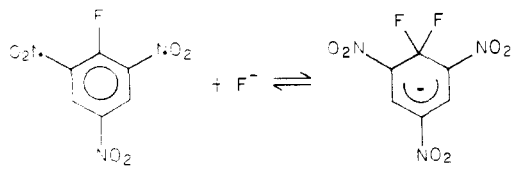
67

R = Me, Et

In the ^{19}F NMR spectrum of **67** (R = Et) the signal of the p-SO_2CF_3 group is situated, as is the case with the σ complex with Na_2SO_3, in lower field than the o-CF_3SO_2 group signal. The authors interpret this fact in terms of the electron-accepting effect of the CF_3SO_2 group, which is more pronounced in the para position. Not unexpectedly, the σ complexes **67** proved much more stable than the complexes **58** (K_{form} of **67** is greater by a factor of 10) and do not give rise to the corresponding phosphonates.[133]

E. Anionic σ Complexes with Halide Ions

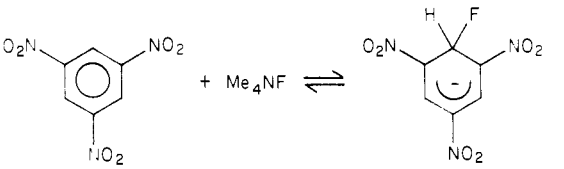
Of all the conceivable σ complexes between halide ions and polynitro aromatics, only two σ complexes with the fluoride anion have been described in the literature. The first one was obtained from picryl fluoride and KF



68

in acetonitrile in the presence of 18-crown-6-ether and characterized by ^{19}F and ^1H NMR spectra.[134] The σ complex **68** is rather stable at room temperature, though under the action of trace amounts of water rapidly yields potassium picrate.[134]

The second σ complex (**69**) was isolated in the reaction between TNB and Me_4NF in THF and described by ^1H NMR and UV spectra.[135] Incidentally, under



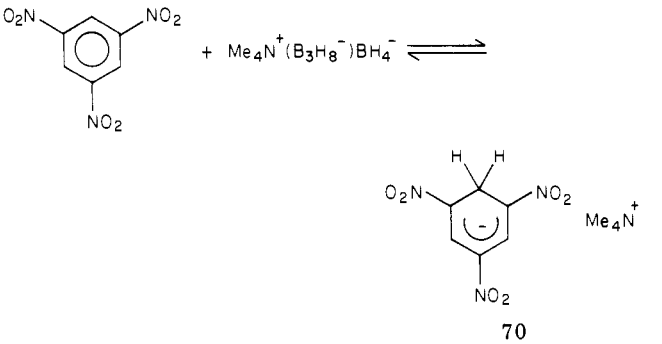
69

similar conditions no chloride σ complex is formed.[135]

The reaction between TNB and KF in benzene in the presence of 18-crown-6-ether was reported to involve coloring (an absorption band with λ_{max} = 450 nm),[136] presumably associated with the formation of TNB σ complex with the F^- anion. However, Terrier et al.[134] failed to reproduce these data.

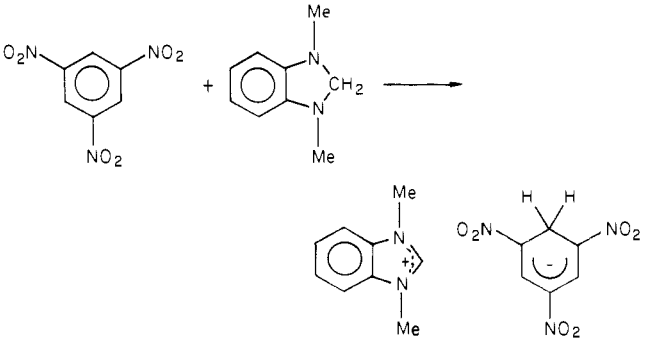
F. Anionic σ Complexes with Hydride Ion

The hydride complex **70** (**70** represents all the hydride complexes whatever the cation) was first isolated by Taylor in the reaction of TNB with tetramethylammonium borohydride in acetonitrile and characterized by ^1H NMR and electronic spectra.[137] Later it was



70

found that Me_4NBH_4 can be substituted by tetramethylammonium salts of other borohydrides, e.g., $B_3H_8^-$, $B_9H_{14}^-$, $B_{10}H_{13}^-$, $B_{10}H_{14}^{2-}$, $B_{10}H_{15}^{6-}$,[138] and by $NaBH_3(CN)$.[139] An elegant method for obtaining the σ complex **70** was suggested by Pozharsky et al.[140] It is based on the reaction between TNB and dihydro derivatives of nitrogen heterocycles (1,3-dimethylbenzimidazoline, 1,3-dimethylnaphtho[2,3-*d*]-imidazoline, 1-benzyl-1,4-dihydronicotinamide, 1,3-di-



70

methyl-2,3-dihydropyrimidine, etc.) that readily form stable cations by loss of a hydride ion. The interaction between TNB and a model coenzyme NADH, which also leads to the σ complex **70**, is worth special attention, since it can be of use to biochemists for investigating the mechanism of redox reactions and for analytical purposes[140] (see ref 139 and 141 on the use of **70** as a biochemical assay).

Another reported source of hydride ions in the reaction with TNB is tributylstannyl hydride in the presence of an equimolar amount of a salt, Me_4NX (X = F, Cl).[135] Without the ammonium salt, Bu_3SnH yields a complex mixture of reduction products. It is the nucleophilic assistance of halide ions which increases the basicity of tributylstannane in the complex **71** so much that it becomes a source of hydride ions.

The σ complex **70** was isolated in a high yield (75–85%).[135] As mentioned in section IIE, TNB with Me_4NF gives rise to the fluoride complex **69**, which when treated with Bu_3SnH, is converted into the hydride complex **70**. Considering, however, that the formation of the σ complex **69** is essentially reversible and relatively slow, it may be thought that the hydride complex is primarily formed by direct interaction of TNB with Bu_3SnH rather than via **69**. This is evidenced also by the fact that **70** is formed from TNB and Bu_3SnH in the presence of Me_4NCl which cannot give a corresponding chloride σ complex with TNB.[135] When one proceeds from Bu_3SnH to Bu_3GeH, the yield of **70** (as shown by UV spectra) decreases to <1%, the main reaction product being **69**.[135]

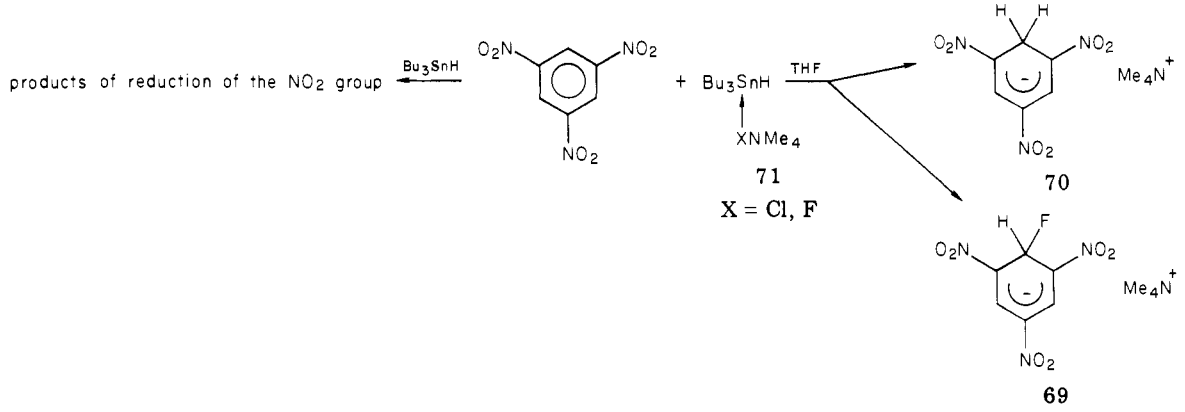
The σ complex **70** is stable in water, but in the presence of bovine serum albumen the rate of its decomposition in neutral or weakly alkaline medium increases by a factor of 10^4. The ultimate product isolated in a high yield is 3,3′,5,5′-tetranitroazoxybenzene.[141] Albumens from other animal sources are considerably less active as catalysts. The authors[141] suggest a mechanism for this interesting reaction.

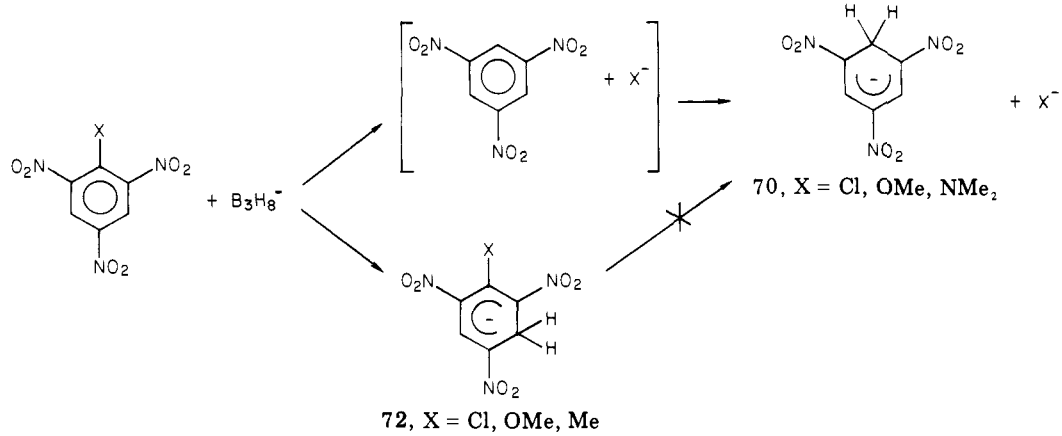
The formation of stable hydride 1,3 σ complexes **72** was observed by interaction between 1-X-2,4,6-trinitrobenzenes (X = Cl, OMe, NMe_2, Me) and $Me_4NB_3H_8$.[138] A process parallel to this reaction is nucleophilic substitution of the X group by the hydride ion and the formation of the hydride σ complex **70** from the resulting TNB.

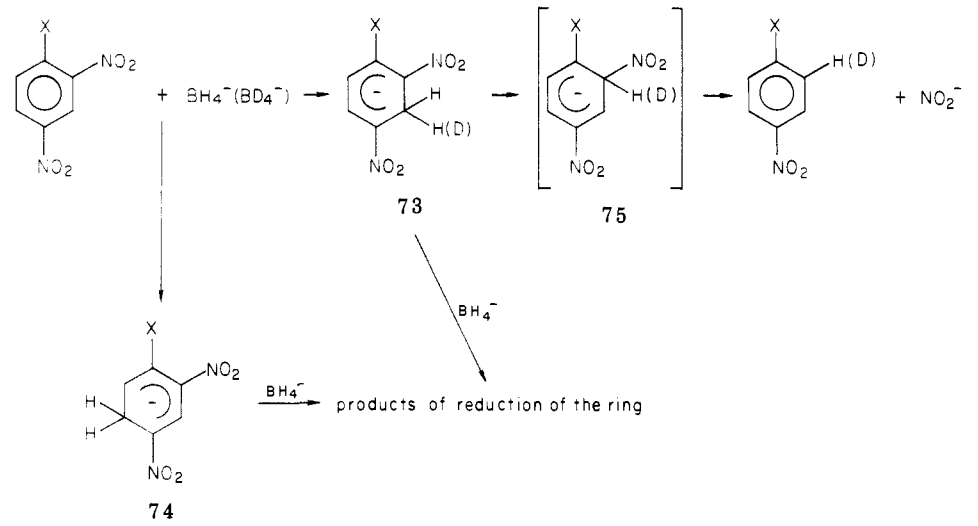
A study on the effect of substituents X on the nucleophilic substitution has shown that the principal role in this process is played by the electrophilic assistance of the boron atom.[138] Indeed, if the "pure" S_NAr mechanism had operated, the yield of the σ complex **70** in the series Cl, OMe, NMe_2 would have decreased, as the capacity for being split off decreases in this series. The actual picture is quite the opposite: the yield of **70** in this series is 25%, 35%, and 100%, and the strength of the B–X bond increases mainly in this manner.[138] It is important to note that this reaction is the first example of nucleophilic substitution under the action of the hydride ion.

Note that the resulting TNB may be reduced by sodium borohydride to the hydride σ complex as well as further, e.g., to 1,3,5-trinitrocyclohexane.[142,143] A similar pattern is observed in the reaction of 1-X-2,4-dinitrobenzenes with an excess of $NaBH_4$.[144,145]

Gold and his co-workers[145] have recently reported nucleophilic substitution of the nitro group under the action of sodium borohydride and found out the role played by hydride σ complexes as intermediates in this reaction. Depending on the nature of X, 1-X-2,4-dinitrobenzenes gave rise to the hydride 1,3 σ complex **73** (X = OMe, OEt, NH_2, $NHNH_2$, NMe_2, NHPh, NPh_2), the hydride 1,5 σ complex **74** (X = H, CN), or







73 75 74

both complexes at once (X = F, Cl, Br). It was shown that the final product of the reaction (at the 1:1 ratio between the reagents), 1-X-4-nitrobenzene, is formed exclusively from the substrates that were observed to yield 1,3 σ complexes. Therefore the authors suggested the following three-stage mechanism involving the formation of the 1,3 σ complex **73** and its subsequent conversion into **75**. The evidence for the migration of the hydride ion was obtained with the use of 3-deuterio-2,4-dinitroanisole. The final product contained deuterium in the 2-position. Unfortunately, the conversion of the σ complex **74** remained obscure. Though this mechanism appears largely similar to ipso substitution, the authors believe a more precise term is "vicinal attack".[145]

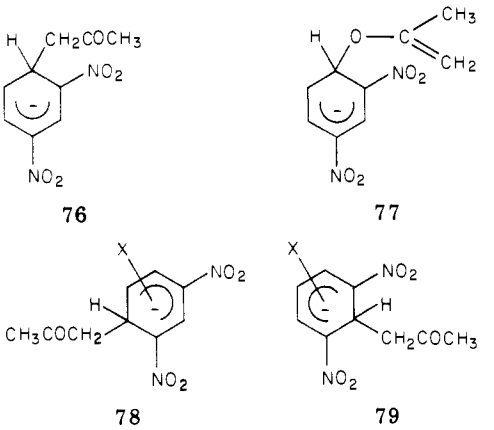
It was reported that deuterium exchange in the system 1,3,5-tricyanobenzene–$NaBD_4$ (or $LiAlD_4$) also occurs via the formation of a corresponding hydride σ complex.[146]

G. Anionic σ Complexes with Carbanions

The feasibility of a stable product of addition of carbanions to an aromatic substrate was first demonstrated by Janovsky, who discovered the reaction between *m*-DNB and alkaline aqueous acetone.[13,14] A similar process was later observed with many other ketones, aldehydes, and polynitro aromatics (see, for instance, ref 8), and the resulting σ complexes with a C–C bond were called Janovsky complexes. Their structure for a long time remained under dispute;[8] only as late as in 1949 Canbäck[147] observed that the absorption spectra of the Janovsky and the Meisenheimer complexes were similar and suggested that the Janovsky complex is a cyclohexadienate ion.

Generally speaking, the Janovsky reaction may lead to several σ complexes differing in the character of addition to *m*-DNB as well as to the ambident acetonate ion. Unambiguous ^1H NMR,[148] ^{13}C NMR,[25] and IR[149] evidence indicates, however, that acetone adds to *m*-DNB in the ketone form to give rise to **76** (the isomeric σ complex **77** has not yet been isolated).

No data have been reported on anionic σ complexes formed by addition of acetone (or some other oxo compound) in its enol form. At the same time the enolate of 1,1-diphenylacetone with p-$XC_6H_4NO_2$ (X = F, Cl) gives only a substitution product with a C–O bond,[157] which indicates that under certain conditions σ com-



76 77 78 79

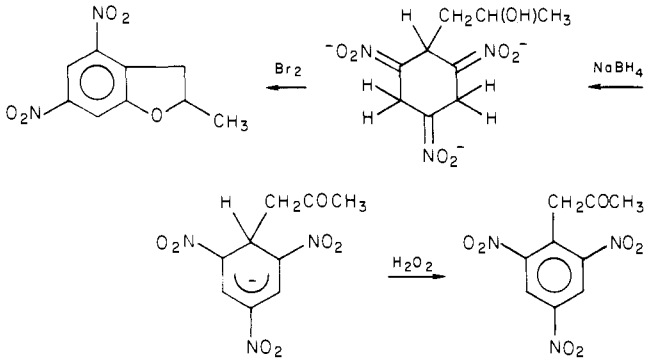
plexes with the enol form of acetone may in fact exist.

Several attempts to isolate the Janovsky complexes failed[150,151] before the addition products of acetone and acetophenone to 3,5-dinitrobenzenesulfonic acid[152] and 3,5-dinitrobenzoic acid[153] in alkaline medium were obtained and identified (1960). Three years later Gitis and Kaminsky developed a spectrophotometrically controlled method for the synthesis of Janovsky complexes and obtained σ complexes of acetonylpotassium with *m*-DNB[149] and a number of substituted *m*-DNB.[123] Kimura[154] used silica gel chromatography to separate the Janovsky complex from the Zimmermann complex[155,156] (see below).

Acetonylpotassium reacts with substituted 1-X-3,5- and 1-X-2,4-DNB to form isomeric σ complexes **78** and **79** in a ratio depending on the nature of X (in contrast to the methoxide ion, acetonate ion does not form a 1,1 σ complex with 1-X-2,4-DNB). For instance, 1-X-3,5-DNB (X = Me, OMe) yields only σ complexes of the type **78**[158] while in the case of X = COOEt,[123,158] CF_3,[49,123,158] CN,[49] COOMe and COO^-,[50] and $CONH_2$ and $CON(CH_2)_5$[159] a mixture of **78** and **79** is formed, **79** always being less stable and gradually forming **78** (k_{isom} = 1.4×10^{-4} s^{-1} for X = $CON(CH_2)_5$ in the acetone–methanol mixture); also measured were the isomerization constants for the corresponding complexes with cyclohexanone for X = $CON(CH_2)_5$, COONa, and CN.[160] Likewise, acetonylpotassium reacts with 1-X-2,4-DNB to yield a mixture of **78** and **79** in which **79** prevails for X = OMe and COOMe,[123,161] F, Cl, Br, and I,[162] and Me, Et, *i*-Pr, and *t*-Bu[161] and **78** for X = SEt, SCN.[123] This effect of sulfur-containing substituents on the ratio between the isomers was attributed[123] to

the high electron-accepting capacity of the sulfur atom with its unoccupied 3d orbitals.

TNB also gives rise to a Janovsky σ complex **80** isolated by Kimura[163] and Gitis.[149] Its structure was es-



80

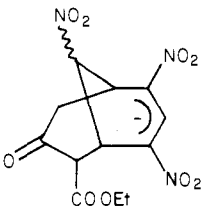
tablished by UV and IR spectroscopy as well as chemically, i.e., by analysis of products of its oxidation by hydrogen peroxide[163] and reduction by sodium borohydride.[164,165] The first reaction leads to 2,4,6-trinitrobenzyl methyl ketone, the second to 4,6-dinitro-2-methyl-2,3-dihydrobenzofuran. The structure of **80** was proven by ^1H NMR spectroscopy[166] and confirmed by X-ray diffraction analysis[167] as well as by ^{13}C NMR spectroscopy;[25] the fluorescence spectra of this complex were also investigated.[168]

In alkaline media substituted 1-X-2,4,6-trinitrobenzenes (X = OEt, OPh, Cl, NMe_2, Me, OMe, COOH, COOMe, SMe) react with acetone to afford products of kinetic control, i.e., a 1,3 σ complex[169-173] whose conversion to 1,1 σ complexes was not observed. This is in agreement with the greater strength of the C–C bond as compared to that of the carbon atom bonds with other nucleophiles (i.e., MeO^- ion) whose isomerization is extremely fast.[30,31a]

As mentioned above, *m*-DNB and TNB can react with ketones other than acetone. As early as the 1930s Zimmermann[155,156] worked out a technique for colorimetric determination of 17-keto steroids by means of a reaction with excess *m*-DNB in alcoholic KOH. More recently, σ complexes of *m*-DNB with ketones of a general formula CH_3COCH_2R (R = Me, Et, *n*-Pr, *i*-Bu, *n*-Bu) were described,[174] as well as TNB σ complexes with $MeCO(CH_2)_2COMe$,[166] MeCOPr-*i*,[166] Et_2CO,[166,175] $(PhCH_2)_2CO$,[175] cyclopentanone,[175] cyclohexanone,[175] and $(CO)_3MnC_5H_4CH_2COCH_3$.[176] Methyl ethyl ketone and acetylacetone yielded two isomeric σ complexes due to the possible deprotonation of the methyl as well as the methylene group in these compounds.[166]

In alkaline media aldehydes react with *m*-DNB and TNB to give σ complexes formed by addition of the alcoholate of the aldol of the corresponding aldehyde to the nitro aromatic substrate.[177] Only the use of triethylamine, a base incapable of giving rise to aldol condensation, made it possible to obtain a σ complex of propionaldehyde with TNB; its structure was established by spectral methods.[178]

Sodium acetoacetic ester and sodium malonic ester react with polynitro aromatics to give rise to colored adducts whose structure has long remained obscure.[18,179] By now it has been shown that the reaction between sodium malonic and cyanomalonic esters and TNB leads to σ complexes.[180] However, in the case of sodium acetoacetic ester the process does not stop at this stage; further conversion gives rise to a bicyclic σ complex, **81**, the final product of the reaction.[181] Only for TNA did



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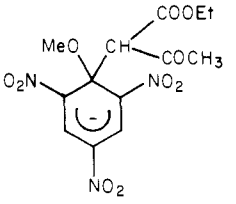


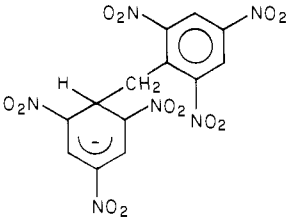
82

Strauss succeed in obtaining a regular product of addition of potassium acetoacetic ester,[119] identified spectroscopically as the 1,1 σ complex **82**. This finding was rather unusual, since 1,1 σ complexes with carbanions are not characteristic of TNA.[119]

Finally, σ complexes of TNB with DMF, dimethylacetamide, and Me_2SO are formed in the presence of solid KOH (σ complexes **88**, R = $CONMe_2$, CH_2CONMe_2, and CH_2SOMe, respectively).[183] The σ complex with Me_2SO also resulted from the reaction between TNB and dimsyl anion.[69] All these complexes were identified by UV, IR, and ^4H NMR spectroscopy, and in the case of Me_2SO mainly the formation of a C–C bond in the σ complex was confirmed.[183]

Along with carbonyl-containing species, other CH acids of sufficient acidity may also react with TNB and *m*-DNB. For example, σ complexes of TNB with conjugate bases of $MeNO_2$, $EtNO_2$, $EtCH_2NO_2$, and Me_2CHNO_2,[184] CHX_3 (X = Cl, Br, I),[185,186] $PhCH_2CN$,[179] and MeCN[187] were isolated and identified, as well as a σ complex of *m*-DNB with MeCN.[187] In pyridine solutions σ complexes result from the interaction of TNB with cyclopentadiene and with indene (but not fluorene) in the presence of Ag_2O.[188,203b] In the former reaction two isomeric σ complexes are formed by addition of a cyclopentadiene group at the 1 or 2 position; the indenyl complex is preceded by a σ complex of TNB with pyridine,[188] which is observed only in UV spectra and appears to be the only reported TNB σ complex with a tertiary amine.

Polynitro aromatics containing a *p*-methyl group may have it deprotonated under the influence of bases, thus giving rise to a carbanion capable of forming σ complexes with TNB.[189,190] TNB σ complexes with TNT (**83**),[189,190] 2,4-dinitrotoluene, 4,6-dinitro-*m*-xylene,[190] and



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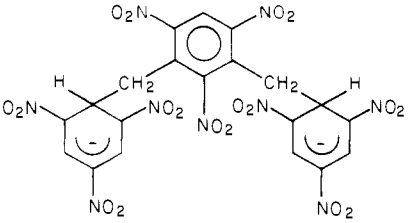
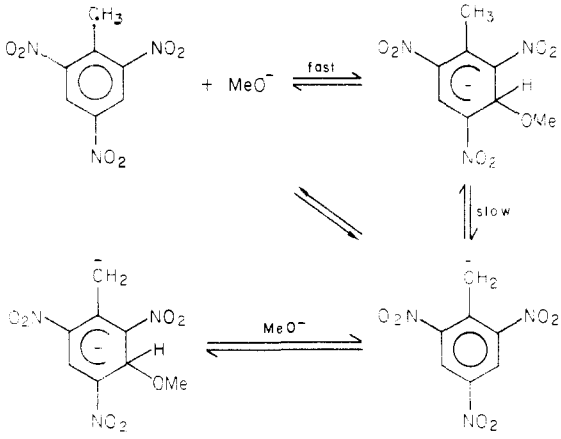


84

2,4,6-trinitro-*m*-xylene[189] were also reported. In excessive base the latter substrate may lose protons from both methyl groups and thus form an adduct with two TNB molecules (σ complex **84**).[189]

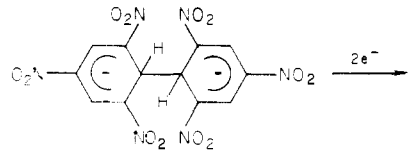
Reactions between TNT and alcoholate ions are worth special attention, since in these processes TNT may act as an electrophile as well as a nucleophile (after deprotonization of the methyl group[191,192]). The conditions for the manifestation of either property and the kinetics of conversion to the corresponding σ complex were studied by Bernasconi by means of a combination of the flow technique and the relaxation technique;[193] he found that when [TNT] ≫ [RO^-], TNT forms a σ complex with the 2,4,6-trinitrobenzyl anion and when [RO^-] ≫ [TNT], the dominant process is the addition of the methoxide ion to TNT and the formation of an anion radical. In both cases the σ complexes were observed only in the UV spectra and their structure was not determined (^{1}H NMR spectroscopy could not be used because of the presence of free radicals).[193] When [RO^-] > [TNT] formation of $(TNT)^-$ is the principal process. Fyfe et al.[40] have recently obtained complete evidence concerning the structure of intermediates in the TNT reaction with the methoxide ion (1:1) in Me_2SO–MeOH using the flow technique with the recording of ^{1}H NMR spectra. They have shown that the first (fast) stage gives rise to a methoxy TNT 1,3 σ complex which in stopped flow shows fast conversion to the 2,4,6-trinitrobenzyl anion, whose potassium salt was isolated from the reaction mixture. The action of excessive methoxide gives rise to the 1,3 σ complex **85**.



85

The kinetics and thermodynamics for the formation of the 1,3 σ complex and $(TNT)^-$ were investigated.[182]

An interesting σ complex **86** was obtained by electrochemical reduction of TNB in acetone at controlled potential of the mercury cathode corresponding to the transfer of two electrons.[194] The complex was believed to rise from the addition of a TNB dianion to a TNB molecule; its structure was established by UV, IR, and ^{1}H NMR spectroscopy. Electrochemical reduction of **86** also involves transfer of two electrons and leads to a bicyclic σ complex, **87** (we should note that the structure of this complex has not been proved), which under the action of oxygen converts to the acetone σ complex **80**.[194,195] Likewise the σ complex **86** in acetone on the addition of base forms the σ complex **80**; at the same time the solution evolves oxygen, identified by polarography.[194]



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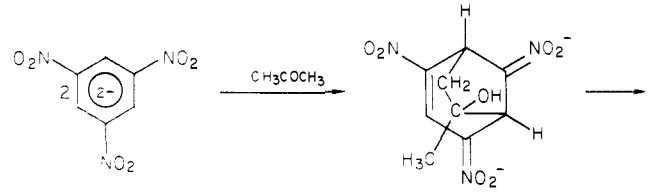

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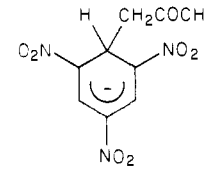

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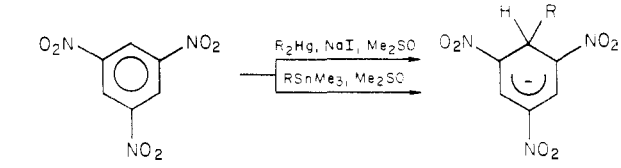
As is seen from the above data, the most common way of obtaining anionic σ complexes with a C–C bond is the reaction of an aromatic substrate in alkaline medium with an "acidic" species (pK_a < 25). In this manner σ complexes were synthesized from ketones, keto esters, diketones, aliphatic nitro compounds, and haloforms.[2-8]

Carbanions for this reaction may be also supplied by covalent organometallic species, e.g., mercury or tin compounds,[196-199] which, however, must contain strongly electrophilic groups (pK_a of the corresponding hydrocarbons RH < 28), which are ionizable under the conditions of nucleophilic catalysis (R_2Hg, RHgX, $RSnMe_3$).[196-199] This method appears milder and

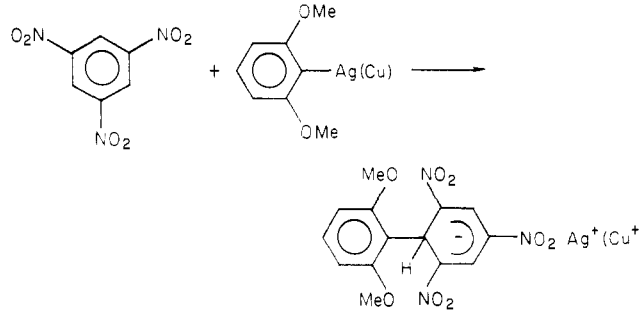


88

R = CH_3COCH_2,C_6F_5,PhCHCOOEt,CCl_3,$(CF_3)_2CH$, fluorenyl, indenyl, cyclopentadienyl

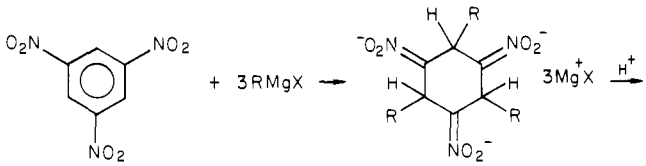
sometimes more convenient than the previous one, since the formation of σ complexes is not accompanied by the reactions between nitro aromatics and alkali.

It is possible to introduce a variety of radicals R [PhC≡C, hexenyl, 2-furyl, 2-thienyl, cymantrenyl ($(CO)_3MnC_5H_4$), phenyl, 2,6-dimethoxyphenyl, 2,4,6-trimethoxyphenyl, indenyl] including donor-substituted phenyls into TNB by means of more reactive organo-

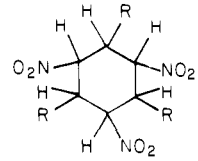


copper or silver compounds.[200-204] It should be noted that the complexes with Ag^+ are more stable than those with Cu^+.[202]

It might seem that the reaction with organolithium or magnesium compounds should be the most general method for the introduction of R into the molecule of an aromatic substrate. The reaction between the Grignard reagent and TNB[205,206] in ether and THF was first studied by Severin. The intermediates, presumed to have the structure **89**, were not identified, but on acidification of the reaction mixture by diluted acetic acid they yielded the corresponding 1,3,5-trialkyl-2,4,6-trinitrocyclohexanes. RMgX reacts in a similar



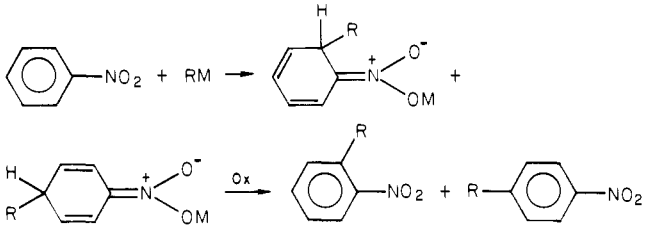
89



R = Me, Et, Pr, Bu

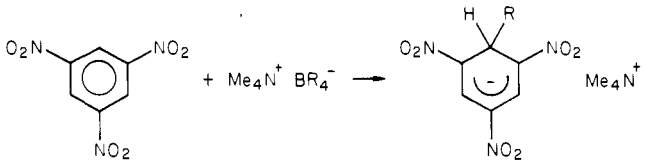
manner with *m*-DNB and 2,4-dinitrochlorobenzene.[207]

Usually, however, RMgX or RLi with nitro aromatics give a complex mixture of redox reaction products and adducts to the nitro group.[208-217] (It should be noted that mononitro aromatics may smoothly react with AlkMgX and AlkLi by way of 1,4 and 1,6 addition not complicated by the above-mentioned processes.[220-227]



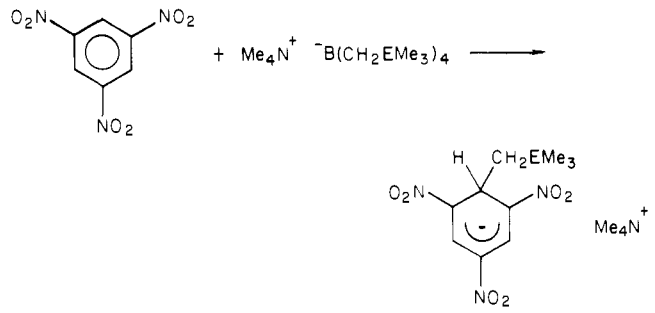
We do not discuss these interesting reactions in more detail since anionic σ complexes are only presumed.) Comparison of results obtained for different organometallic compounds suggests that this fact is due to the strong basicity of RLi and RMgX.

To introduce alkyl groups ($pK_a > 50$) into the TNB molecule Taylor[218] suggested a reaction with the corresponding tetraalkylborates so that the reactivity of the carbanions decrease due to the formation of ate complexes.



R = Me, *n*-Bu

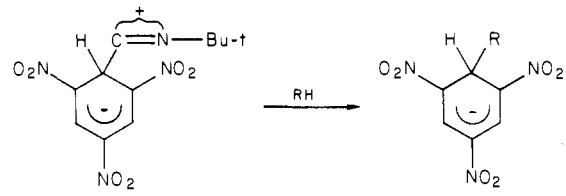
The same approach was used to obtain TNB σ complexes with Me_3ECH_2 groups, where E = Si, Ge, Sn.[219]



It should be noted that only the reaction with tetraalkylammonium salt of the borate is successful, while the lithium salt $(Me_3SiCH_2)_4BLi$ (as well as Me_3SiCH_2Li) yields a complex mixture of unidentified products.[219]

The anionic σ complex of the simplest carbanion, i.e., the cyanide ion, with TNB was obtained by the action of salts like Ph_4AsCN, Ph_4NCN,[84,228] or $Hg(CN)_2$ in the presence of NaI[197] on TNB. This complex proved unstable and was identified only from UV and ^1H NMR spectra.[197] Unstable 1,1 and 1,3 σ complexes (the latter are more stable) also result from the reaction between Ph_4AsCN and TNA.[229]

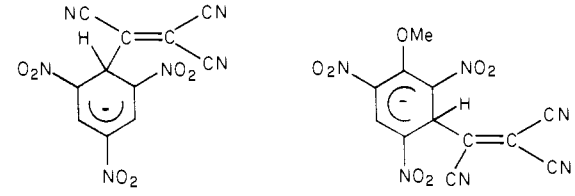
An interesting σ complex was obtained from TNB and *t*-BuNC in the presence of Cu_2O or Cu.[230] The structure ascribed to it on the grounds of UV and ^1H NMR data is **90**. The σ complex **90** is fairly labile and



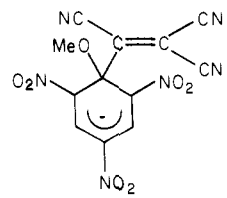
90 **88**

reacts with $CHCl_3$, indene, or cyclopentadiene to give rise to more stable σ complexes **88** (R is CCl_3, indenyl, or cyclopentadienyl).[230]

TNB or TNA show a peculiar reaction behavior with sodium methoxide in the presence of tetracyanoethylene (TCE).[231] The reaction leads to the σ complex **91** (for TNB) or the σ complexes **92**, **93** (for TNA) via methoxy σ complexes of TNB or TNA believed to be formed at the beginning of the reaction.[231] The σ



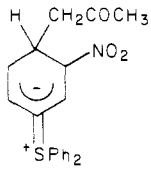
91 **92**



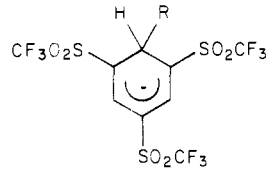
93

complex **93** is also formed in the TNA reaction with $Na^+(TCE)^{-\cdot}$. Several hypothetical mechanisms for these unusual reactions were advanced.[231]

A zwitterionic σ complex with a C–C bond (**94**) was observed in the reaction between alcoholic KOH and acetone solution of (*m*-nitrophenyl)diphenylsulfonium borofluoride.[232] Its structure was inferred from ^1H



94

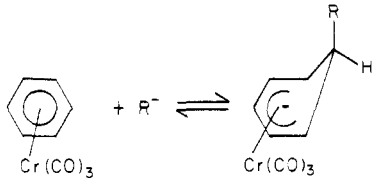


95

NMR evidence and confirmed by a synthesis from (*m*-nitrophenyl)diphenylsulfonium borofluoride and acetonylmercury chloride in the presence of Bu_4NI.[232]

TMSB anionic σ complexes of type **95**, where R = CH_3COCH_2, CN,[96] CH_2NO_2, CH_2CHO, $CH(COOEt)_2$,[233] were reported recently. As expected, they proved far more stable than their trinitrobenzene counterparts.

Of late, coordination with transition-metal carbonyls has become a popular means of activating aromatic substrates. Thus, anionic σ complexes **96** were obtained[234-236] from organolithium species and (benzene)tricarbonylchromium at −70 to −40 °C. The



96

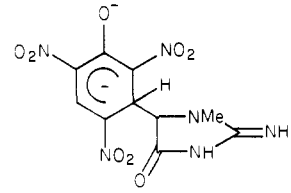
R = CMe_2CN, CH_2CN, $CH(SPh)_2$, 

structure of these σ complexes was determined by ^1H NMR and IR spectroscopy[235,236] and for R = 1,3-dithianyl by X-ray diffraction analysis.[236] Below 0 °C these compounds are stable for a long time; iodine or cerium–ammonium nitrate readily oxidizes them to a corresponding PhR in a high yield.[235,236]

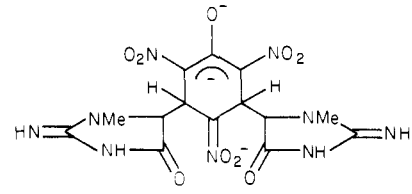
The intensive coloring which accompanies the formation of σ complexes with C–C bonds is used for determination of various types of natural products. (The Zimmermann reaction based methods for the determination of natural compounds will be discussed in section VC.) As a matter of history, these reactions were developed when no methods of determining the structure of the colored products existed. The relevant investigations, therefore, were largely of applied character and were carried out in somewhat another vein than the studies of classical anionic σ complexes. As a result, essentially similar reactions (of a compound containing an activated methylene group with a nitro aromatic substrate in alkaline medium) are known by different names depending on the type of the natural products and even the substrate. These reactions will be briefly discussed below.

In 1886 Jaffe[237] found that on addition of creatinine to alkaline sodium picrate the solution turns intensely red. In 1904 this reaction was employed by Folin[238] to develop a method which still remains an efficient means for the determination of creatinine (see, for instance, ref 239 and 252). First reports concerning the structure of the reaction products have appeared rather recently.[240-249] It was found that depending on the ratio between picric acid, alkali, and creatinine the solution may contain different σ complexes.[242,243]

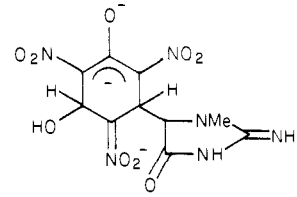
Thus creatinine reacts with excess picric acid to form creatinine picrate, which on addition of an alkali, gives rise to the σ complex **97**,[243,244] whose structure was established spectroscopically.[243-245] The complex is



97



98



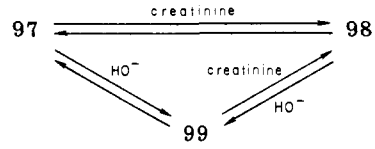
99

formed as a mixture of (theoretically) eight stereoisomers that does not lend itself to separation because of conversion into the picrate and the stereoisomers of **98**.[243] In excess alkali the isomers of **97** reversibly form **99**. (On acidification of the mixture of **97** and **99** the equilibrium is shifted toward the formation of **97**.[242]) On addition of excess creatinine both **97** and **99** give rise to three stereoisomers of the 1:2 σ complex **98**,[242,243] whose crystals were isolated by Kohashi et al. and identified on the basis of UV, IR, and ^1H NMR spectra.[242] In alkaline solutions any isomer of **98** forms an equilibrium mixture containing all three complexes. This fact is believed to indicate[242] that **98** possesses a cis pseudoequatorial structure.

Now, in the light of the foregoing facts the reaction between picric acid and creatinine apparently proceeds as follows:[243]

PiOH + creatinine ⇌ creatinine picrate

creatinine picrate → **97**

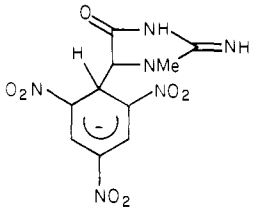


Butler[246] found that in a stoichiometric mixture of reagents the slow stage of formation of **97** is the interaction between the creatinine anion and the picrate ion rather than deprotonation of creatinine. In excess picrate, however, deprotonation becomes the rate-determining step.

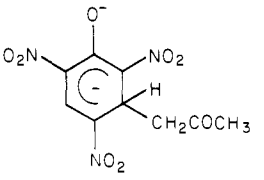
Using the Jaffe reaction for spectrophotometric de-

termination of creatinine it is of course desirable that the absorption intensity of a certain σ complex rather than the mixture be measured. Considering that in strongly alkaline media the σ complexes **98** and **99** and, possibly, the 1:2 σ complex of the picrate ion with OH ions are formed,[246] it was suggested[243] that the alkaline solution of creatinine be neutralized with excess picric acid in order to measure the absorption by **97** only. Similar recommendations on the use of a low concentration of alkali were, in fact, advanced earlier as well.[247,248] At any rate, however, the alkali concentration must be constant for both the sample and the reference.[249]

Deep coloring, which is evidently due to the formation of the σ complex **100**, results also from the action of creatinine on alkaline solution of TNB.[246] This reaction



100

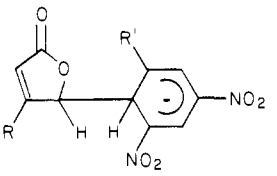


101

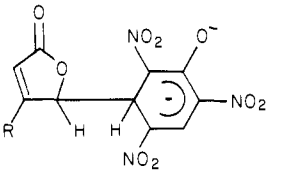
was shown to be 1000 times as fast as that with picric acid.[246] Unfortunately, TNB is poorly soluble in water and therefore cannot be used as a reagent for creatinine.[246]

Picric acid in alkaline media reacts also with other species containing an activated methylene group[250] including the simplest compound of this type, i.e., acetone.[246,251] This reaction leads to the σ complex **101** that was isolated as a solid.[251] This compound is about 1200 times less stable than **97**,[246] and kinetic studies have shown that the slow stage of its formation is the acetonate ion addition to the picrate ion.[246]

Three reactions named after their discoverers have been described in the literature for the determination of cardenolides. A color appears as cardenolide reacts with an alkaline solution of *m*-DNB (the Raymond reaction[253]), with 3,5-dinitrobenzoic acid (the Kedde reaction[254]), and with picric acid (the Baljet reaction[255]). These reactions were shown to lead to anionic σ complexes **102** or **103**, where R is digitoxin, and R′ is H or COO^-.[256] The color that results from the action of



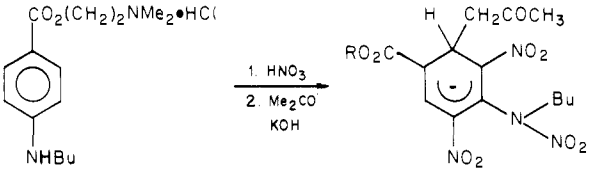
102



103

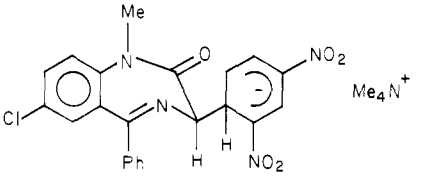
alkaline 2,4-dinitrophenyl phenyl sulfone (the Tattier reagent)[257-260] and 2,2′,4,4′-tetranitrobiphenyl[261] on various glycosides also appears to arise from the formation of corresponding σ complexes.

Kovar and Bitter[262] have recently developed a method for determination of tetracain, a widely used local anaesthetic, from the color that appears as the products of tetracain nitration by concentrated HNO_3 (the Vitali–Morin technique) react with acetone and alkali. The colored products were identified as σ complexes **104**.[262] Kovar and Biegert in 1976 obtained an interesting σ complex, **105**, by the reaction between diazepam and *m*-DNB in the presence of Me_4NOH.[263]



104

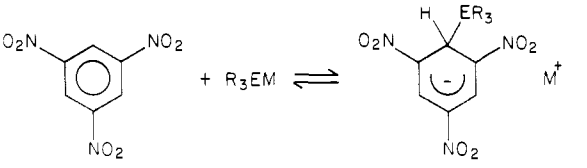
R = H; $(CH_2)_2NMe_2 \cdot HNO_3$; $(CH_2)_2NMeNO_2$



105

H. Anionic σ Complexes with Organometallic Anions R_3E^- (E = Si, Ge, Sn)

TNB reacts with anions containing elements of the 4B group R_3EM (R_3E = Me_3Si, Et_3Ge, Me_3Sn, Ph_3Sn; M = Li, K, Cs) to give anionic σ complexes with a C–E bond.[72,264] Such complexes were obtained by adding



106

E = Si, Ge, Sn; R = Me, Et, Ph; M = Li, K, Cs

the solution of R_3EM to TNB in THF in a vacuo (for K and Cs salts) or under argon (for Li salts) at −10 to −5 °C. The σ complexes **106** were isolated as brown amorphous powders showing low solubility in organic media and possessing characteristic electron and ^1H NMR spectra. The presence of paramagnetic impurities in these samples (from 10^{-2} to 10^{-1} mol % as indicated by ESR spectra) largely hinders their investigation by ^1H NMR spectroscopy.

The structure of **106** in the case of R_3E = Me_3Sn was confirmed by the observed quadrupole splitting in Mössbauer spectra, which points to the nonequivalence of the bonds on the tin atom.[72]

Solid σ complexes **106** may be stored for 7–10 days under vacuum or under argon. In air their decomposition is much faster, the lithium salts being more stable than the potassium salts. In vacuo these complexes are fairly stable even in diluted Me_2SO solutions ($\sim 10^{-5}$ M). In the presence of oxygen the decomposition of the dissolved complexes takes just 20–30 min, and dicyclohexyl-18-crown-6-ether makes the oxidation by oxygen virtually instantaneous.

One- and two-electron oxidants (tetracyanoquinodimethane, chloranil, iodine, $CuBr_2$, $Tl(OAc)_3$, *N*-bromosuccinimide (NBS), Ph_3CBF_4, Me_3SiCl) invariably break the C–E bond to convert σ complexes **106** into TNB. The reasons for this reaction pattern will be discussed in section VC.

III. Mechanisms for the Formation of Anionic σ Complexes

In principle, the formation of anionic σ complexes in reactions between nucleophiles and aromatic substrates may involve two alternative mechanisms, i.e., a heterolytic and a homolytic mechanism. The latter pathway, which conceivably includes a one-electron transfer stage followed by cage recombination of the radical pair, was discussed in the literature,[8,186] but no serious evidence supporting it has so far been reported. On the other hand, there are a number of facts favoring the heterolytic reaction pattern rather than the homolytic. For instance, Fyfe et al.[54] observed no CIDNP effect in the reaction between 1-cyano-3,5-dinitrobenzene with the methoxide ion studied by stopped-flow technique monitored by ^1H NMR spectra. These data, of course, do not completely rule out the one-electron transfer stage if we assume the lifetime of the radical pair in this reaction is very short.

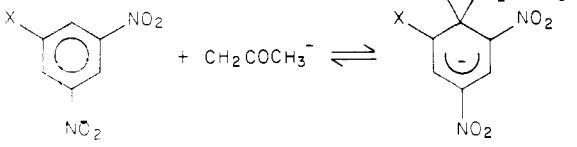
Another problem associated with the mechanism of formation of anionic σ complexes arises when a reaction proceeds in two stages. This situation is encountered when one deals with the interaction between aromatic substrates with primary or secondary amines and with CH acids in the presence of bases and when it is necessary to determine the rate-limiting stage of the process (this question for the reactions between TNB and amines was considered in section IIC).

More intricate mechanisms are plausible when the CH acid is a carbonyl-containing species. It is probably due to this fact that studies of the system "nitro aromatic compound–acetone–base", i.e., the earliest reaction leading to σ complexes, are still in progress.

In its simplest form the Janovsky reaction occurs as follows:

$$CH_3COCH_3 + B \rightleftharpoons CH_3COCH_2^- + BH^+$$

$$B = HO^-$$

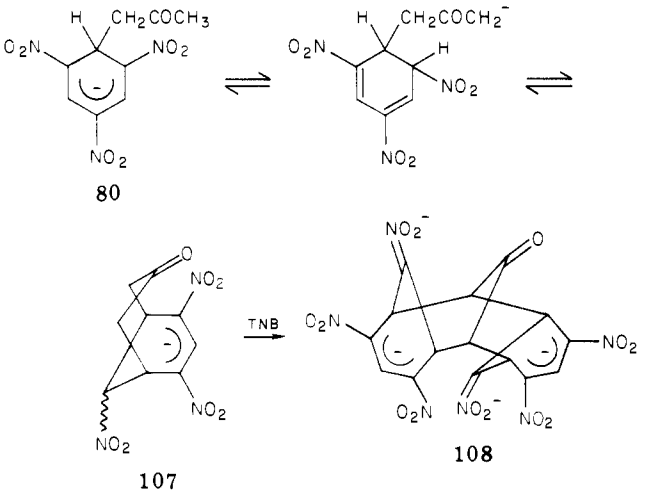


X = H

Its rate-determining stage is the formation of an anionic σ complex.[268,269]

Under certain conditions, however, the reaction between TNB and acetone in the presence of bases may proceed further. For example, Strauss[11,265] and Kohashi et al.[266,267] found that it eventually leads to a bicyclic σ complex **107**, especially with Et_2NH as the base (in excess of TNB the reaction leads to a tricyclic σ complex, **108**[267]). The cyclization rate of the σ complex **80** was several times lower than the rate of its formation.[180] Likewise, the final cyclization of TNB σ complexes with cyclohexanone and methyl acetoacetate is the slowest stage in the reaction.[180]

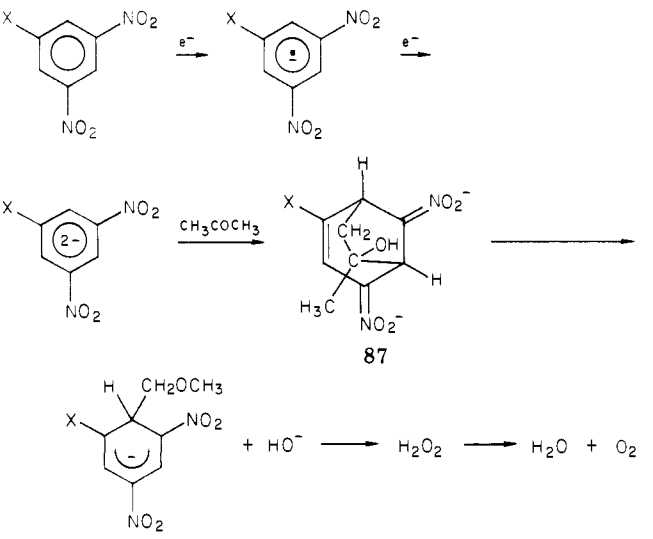
The reaction between TNB and acetone in the presence of KOH involved two parallel processes. The first process obeys the above cited mechanism for the Janovsky complex (B = OH, X = NO_2). The second reaction leads to formation of diacetone alcohol, which



slowly decomposes into the acetonate ion and thus acts as a source of this species when the conversion is high.[270] It is not unlikely that similar reactions take place in the interaction between TNB and acetone in the presence of MeONa, as long as chromatography reveals the presence of diacetone alcohol in the MeONa–acetone mixture.[171]

Several workers noted that the formation of a σ complex with CH acids is preceded by the emergence of a σ complex with the base.[99,171,186,188,268,269] Strangely enough, the role of these processes was not investigated. The anionic σ complex with the base is evidently the kinetically controlled reaction product, which gives rise to a more thermodynamically stable σ complex with a C–C bond according to a dissociative mechanism, which as proposed by Kimura et al.[171] took place in the reaction of TNA with acetone. A dissociative mechanism will be discussed at length in section VA. However, if instead of TNB a substrate that gives a stable σ complex with the base is used, the reaction may stop at the formation of this complex. Indeed, remarkably stable methoxy σ complexes of 1-methoxy-2,4-dinitronaphthalene[271] and TMSB[75] are not converted into acetone σ complexes in acetone solutions.

A special case of the formation of the Janovsky complex was discussed in ref 195 and 272–275. As shown in these papers dianions of TNB or *m*-DNB, obtained by reduction (electrochemically or by the dipotassium



X = H, NO_2

salt of the cyclooctatetraene dianion), form a complex with acetone that was identified as the rather unusual compound 87 (cf. with 107). Oxidation of this complex by O_2 or PbO_2 leads to the Janovsky complex.

The authors[195,272] argue that this mechanism (i.e., the interaction between the dianion resulting from reduction of a nitro aromatic compound by the base and the oxidized form of the base) is common for the formation of all the σ complexes.

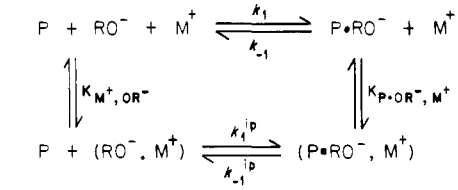
IV. Stability of Anionic σ Complexes

The stability of anionic σ complexes is the major problem of their chemistry. It bears a close relationship to the basic issue of nucleophilic aromatic substitution, i.e., with the role of anionic σ complexes as precursors of substitution products and with the determination of the limiting stage of the process according to Bunnett's S_NAr mechanism.[1] However, as has been mentioned above, the formation of 1,1 σ complexes is more often preceded by one or two isomeric (i.e., 1,3 or 1,5) σ complexes. Information on their stability, therefore, makes it possible to estimate their role in the reaction and the contribution of side reactions.

The factors investigated in connection with the stability of σ complexes include the nature of the aromatic substrate (type, number, and position of substituents) and the nucleophile, steric factors in both the substrate and the corresponding σ complex, the effect of the solvent, and temperature. Most aspects of this problem were discussed in reviews,[2,4,6,7] and some are considered in the present paper (see, for instance, section IIA).

The stability of a σ complex in solution is largely dependent on its interaction with the cation. The traditional definition of the complexes obtained as anionic σ complexes does imply, however, that in solution they exist as an equilibrium mixture of ions and ion pairs of various types. These equilibria have been extensively studied in the chemistry of carbanions.[276,277] However, no such investigations concerning anionic σ complexes have been carried out. At the same time there are a number of papers attempting to establish a correlation between the stability of σ complexes and their state in the solution.

In the late 1960s and early 1970s it was found that the rate constants of the forward (k_1) and the back (k_{-1}) reaction (and, therefore, the stoichiometric constant K_c[282-285]) of formation of methoxy σ complexes of nitro aromatic compounds depend on the concentration of the base[278,279] or the electrolyte.[280] These findings could not be adequately explained by the theory of salt effects. Thus, Crampton suggested[281,282] that this phenomenon was due to ionic association with the counterion in the σ complex. This idea was confirmed later,[282-286] and as no data on conductivity of σ complexes is available, the following facts were employed in this proof. It turned out that K_c for the methoxy 1,1 σ complex of 2-carbomethoxy-4,6-dinitroanisole (2-CO_2Me-4,6-DNA) shows virtually no increase for M = Li^+, a slight increase for M = Bu_4N^+, and a marked increase for M = K^+ with increasing concentration of MeOM.[282] The classic salt effect evidently cannot account for such phenomena. Then it was shown that addition of the electrolyte does not affect the activity of the substrate, which means the electrolytes affect either the state of MeOM or the state of the σ complex. As long as K_c for TNB methoxy σ complex did not increase with concentration of MeONa (over the same range of concentrations as in the case of the 2-CO_2Me-4,6-DNA methoxy σ complex),[106,283] it seems likely that the observed phenomenon is due to stabilization of the anion of σ complex by association with the cation.[282] Finally, conclusive evidence favoring the effect of association was obtained;[284] it was found that in the presence of equimolar (with respect to the base) amounts of 18-crown-6-ether the values k_1, k_{-1}, and K_c were practically independent of concentration of sodium methoxide over a wide enough range (0.0098–0.077 mol/L). In accordance with these facts, Crampton and Khan[282-285] and later Buncel et al.[287] advanced the following scheme for equilibria in solutions of σ complexes (the symbols used below are the same as in ref 282–285).



$K_1 = k_1/k_{-1}$ is the thermodynamical equilibria constant
$K^{ip} = k_1^{ip}/k_{-1}^{ip}$

This scheme suggests that the observed stoichiometric constant is expressed by

$$K_c = K_1(1 + [M^+]K_{P\cdot RO^-,M^+})/(1 + [M^+]K_{RO^-,M^+})$$

It is now evident that if the cation coordinates better with the σ complex than with the alcoholate ion, i.e., if $K_{P\cdot RO^-,M^+} > K_{RO^-,M^+}$, K_c will increase with concentration of M^+ and if, in contrast, $K_{RO^-,M^+} > K_{P\cdot RO^-,M^+}$, K_c will decrease with increasing concentration of M^+. It is also evident that the values of equilibrium constants K_1, K_{RO^-,M^+}, $K_{R\cdot PO^-,M^+}$, and K^{ip} will depend on the nature of the cation, the substrate, the alcoholate ion, the structure of the σ complex, and of course, the solvent. Each of these factors will be discussed below. Since the reactions of ROM were invariably studied in the corresponding alcohol ROH, the effect of the alcoholate ion and the solvent will be considered simultaneously.

(a) Effect of the Counterion. Data on the effect of counterions on $K_{P\cdot RO^-,M^+}$ are given in Table I (for the sake of comparison, the thermodynamic constants of formation of the corresponding σ complexes K_1 are also presented).[283] The table demonstrates that barium and calcium cations show the strongest association with the anions of σ complexes. The association of Na^+ is weaker, and that of tetrabutylammonium is extremely weak, with the association constant virtually independent of the substrate,[282] which is explained[282] in terms of the well-known effect of stabilization of large readily polarizable anions by tetraalkylammonium cations. As has been mentioned above, K_c for σ complexes of methoxide practically does not change with concentration of lithium methoxide.[282,283] The authors[282] attribute this fact to strong solvation of lithium cations and the resulting decrease in the capacity for the formation of ion pairs. For M = Na^+ and K^+ the differences in $K_{P\cdot RO^-,M^+}$ are not great, in agreement with the fact that the values of K_{RO^-,M^+} in alcohol are close

TABLE I. Association Constants of Methoxy Meisenheimer Complexes in MeOH with Cations[283]

substrate	K_1, L·mol^{-1}	$K_{P\text{-}OR^-,Na^+}$	$K_{P\text{-}MeO^-,Ba^{2+}}$	$K_{P\text{-}MeO^-,Ca^{2+}}$	$K_{P\text{-}MeO^-,Bu_4N^+}$
2-carbomethoxy-4,6-DNA	8.3	90	1.6×10^4	8×10^3	$\sim 10^a$
4-carbomethoxy-2,6-DNA	5.5	50	5×10^3		$\sim 10^a$
TNA	17.000	70	2×10^3	10^3	
2-chloro-4,6-DNA	3.4	25	1×10^3		$\sim 10^a$
TNB	17	<10	$<10^2$	$<10^2$	

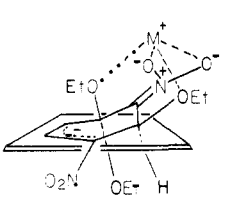
[a] Reference 282.

TABLE II. The Effect of the Nature of the Alcoholate Ion and the Solvent on the Kinetic and Thermodynamic Constants of Sodium 1,1-Dialkoxy-6-dinitrocyclohexadienates[a]

X	CO_2R	NO_2	Cl	H
K_1, L·mol^{-1}				
R = Et	100[b]	3×10^5 [b]	53[b]	1.5×10^{-3} [b]
Pr	560[c]	2×10^5 [c]	280[c]	5×10^{-3} [c]
i-Pr	1500[d]		1100[d]	0.08[d]
k_1, L·mol^{-1}·s^{-1}				
R = Et	0.13[b]	17[b]	0.14[b]	0.01[b]
Pr	0.21[c]	28[c]	0.21[c]	0.016[c]
i-Pr	0.11[d]	≥ 50[d]	0.10[d]	0.01[d]
k_{-1}, s^{-1}				
R = Et	1.3×10^{-3} [b]	6×10^{-5} [b]	2.6×10^{-3} [b]	7.0[b]
Pr	3.8×10^{-4} [c]		7.5×10^{-4} [c]	3.1[c]
i-Pr	7.5×10^{-5} [d]		1×10^{-4} [d]	0.12[d]
K^{ip}, L·mol^{-1}				
R = Et	6.7×10^3 [b]		3×10^2 [b]	0.01[b]
Pr	8.4×10^3 [c]	2×10^5 [c]	4.5×10^2 [c]	0.011[c]
i-Pr	1×10^4 [d]		5×10^2 [d]	0.024[d]
k_1^{ip}, L·mol^{-1}·s^{-1}				
R = Et	4[b]	30[b]	0.5[b]	0.01[b]
Pr	6[c]	50[c]	0.75[c]	0.014[c]
i-Pr	10[d]	100[d]	1.8[d]	0.009[d]
k_{-1}^{ip}, s^{-1}				
R = Et	6×10^{-4} [b]		1.7×10^{-3} [b]	1.0[b]
Pr	7×10^{-4} [c]		1.7×10^{-4} [c]	1.3[c]
i-Pr	1×10^{-3} [d]		3.6×10^{-3} [d]	0.36[d]
$K_{P\text{-}RO^-,Na^+}$, L·mol^{-1}				
R = Me	1×10^2 [e]	7.0×10[e]	2.5×10[e]	7×10^2 [f]
Et	3.3×10^3 [b]		2.7×10^2 [b]	2.0×10^2 [b]
Pr	1.05×10^4 [c]	1×10^3 [c]	1.1×10^3 [c]	1.5×10^3 [c]
i-Pr	1.3×10^5 [d]		1×10^4 [d]	6×10^3 [d]

[a] Data for RONa in an alcohol ROH, K_{RO^-,Na^+} for R = Me, Et, Pr, and *i*-Pr = 4.9, 49, 672, and 1.9×10^4 L mol^{-1} respectively.[288-290] [b] Reference 285. [c] Reference 289. [d] Reference 290. [e] Reference 283. [f] Reference 286.

to each other.[288] These differences, however, do become substantial when a 1:2 σ complex is formed.[286] The reason, as suggested,[286] is that in **109** the ion-pair association constant is greater in the case of Na^+ than in the case of K^+.



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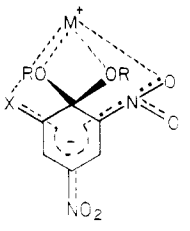

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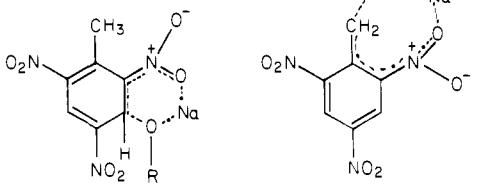
(b) Effect of the Substrate and the Structure of the σ Complex. Tables I and II show that association with a counterion affects the stability of σ complexes only if the latter are 1,1-dialkoxy σ complexes (no such effect was observed for TNB σ complexes with methoxide,[106,283] *n*-propyl alcoholate,[289] or isopropyl alcoholate[290] in the corresponding alcohols). For 1-alkoxy-6-X-2,4-dinitrobenzenes the association constants of the corresponding 1,1 σ complexes decrease in the series X = CO_2R > NO_2 > Cl > H; i.e., $K_{P\text{-}RO^-,M^+}$ depends on the substituent's capacity for coordination with the cation. These facts, along with the closeness of $K_{P\text{-}MeO,Na^+}$ and K_{assoc} of Na^+ with 12-crown-4- and cyclohexyl-18-crown-4-ethers[284] and X-ray diffraction patterns,[29] suggested[283,284] that the associate of the 1,1 σ complex has structure **110** (the cation is attached to the electronegative atoms of ortho substituents and the two alkoxy group oxygen atoms, the main role being played by the latter coordination). Hence it becomes clear why 1,3 σ complexes display virtually no association.[285,290] It is believed[290] that the marked association with the cation for 1,1 σ complexes is a major reason for their formation from 1,3 σ complexes.

(c) Effect of the Nature of the Alcoholate Ion and the Solvent. As the dielectric constant decreases in the series of solvents MeOH > EtOH > *n*-PrOH > *i*-PrOH, the ion-pair interaction between the cation and the alcoholate ion, as well as that with the anion of the σ complex increases. Thus, when one passes from one member of the series to another, the values of K_{RO^-,Na^+} and $K_{P\text{-}RO^-,Na^+}$ grow, on the average, by an order of magnitude, which means the contribution of ion pairs shows a pronounced increase. Addition of $NaClO_4$ shifts Crampton's equilibriums totally to the area of ion pairs and therefore makes it possible to determine k_1^{ip}, k_{-1}^{ip}, and K^{ip}.[290] In all the cases ion pairs (RO^-, Na^+) prove more reactive than the free ions; i.e., $k_1^{ip} > k_1$ (for methoxide ions such evidence is unavailable). However, the ion pairs of σ complexes do not always decompose

to parent particles slower than free ions; i.e., sometimes k_{-1}^{ip} is not less than k_{-1}. Accordingly, for a number of σ complexes (R = *i*-Pr, X = Cl, H) it was found that $K^{ip} < K_1$, which means that in these cases the alcoholate ion is better stabilized by association than the anionic σ complex.

The formation of σ complexes often involves side reactions such as deprotonation (for TNT and picramides) or dealkylation (for alkyl picrates). It was found that the occurrence of such reactions depends on the state of the nucleophile in the solution. For instance, it is thought that TNT can be deprotonated only under the effect of free isopropylate ions rather than ion pairs (*i*-PrO$^-$, Na$^+$), whereas the latter are responsible for the formation of the 1,3 σ complex.[287] The reason is that the 6-membered transition state **111** is more advantageous than the 8-membered state **112**.[287]



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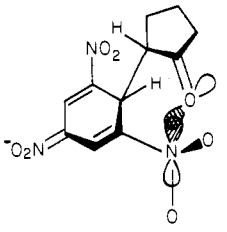

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Another likely reason for the observed phenomenon is that deprotonation occurs under the influence of a stronger base, and the free ion is a stronger base than the ion pair. On the contrary, the formation of a σ complex is dependent on the nucleophilicity of the reacting particle rather than its basicity.

Similar trends were observed in the reaction between sodium isopropyl alcoholate, DNA and 6-chloro-2,4-DNA; dealkylation which accompanied the formation of 1,1 σ complexes took place only via interaction with free alcoholate ions.[290] On addition of $NaClO_4$, which shifts the equilibrium *i*-PrO$^-$ + Na$^+$ ⇌ *i*-PrO$^-$, Na$^+$ to the formation of ion pairs, dealkylation becomes very slow, while the formation of σ complexes is accelerated so much that they become the sole products.[290]

Association with the cation is thought by Abe[291] to be responsible for the emergence of a second stage in the decomposition of the classical Meisenheimer complex in buffer solutions. This stage involves decomposition of the ion pair of the σ complex.

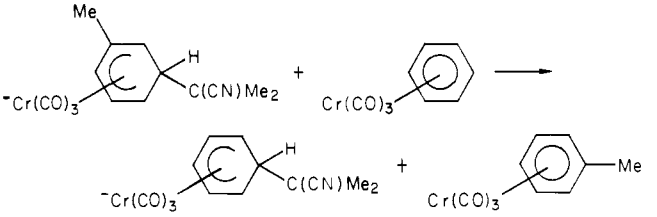
To conclude this section let us mention another case of a specific dipole interaction resulting in higher stability of the σ complex. It was observed by Strauss et al.,[292,293] who studied thermodynamic stability of carbanion complexes with TNB and reported unusually high stability of cyclopentanone σ complex. The authors[292] believe that this is due to the geometry of the molecule, which favors dipole–dipole interaction of the carbonyl with the nitro group (structure **113**).

V. Conversion of σ Complexes

The number of reaction types known to be typical of anionic σ complexes is fairly limited. They include transcomplexing and interaction with acids HX, alkylating agents, and oxidizing agents. Specifically, in these reactions σ complexes are in equilibrium with the initial reagents. Only in the light of this fact it is possible to understand certain numerous data on the reactions of σ complexes discussed in this section.

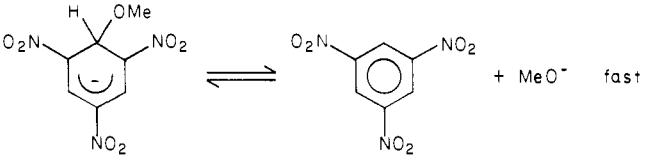
A. Transcomplexing Reactions

The term transcomplexing was suggested for the reactions in which a σ complex gives rise to another σ complex.[71,264] Such reactions stem from dissociation of σ complexes in solutions and from their different thermodynamic stability depending on the substrate and the nucleophile. In principle, there are three types of transcomplexing reactions. First, a σ complex with one nucleophile may give rise to a complex of the same substrate with another nucleophile under the effect of some agent. Second, σ complexes of a certain substrate may form σ complexes of another substrate with the same nucleophile. The third (simplest) type is isomerization of σ complexes (e.g., 1,3 → 1,1 σ complex transformation) considered above. Transcomplexing reactions of the second type are virtually unknown (data were reported on the formation of (benzene)tricarbonylchromium σ complex with $Me_2C(CN)Li$ according to[236]



however, the corresponding σ complex of (toluene)tricarbonylchromium was not identified), so we shall dwell upon the first type of reaction which has been observed many times.

Anionic σ complexes of TNB with hydroxy or methoxy groups on dissolution in acetone give rise to the acetone σ complex.[170,294] TNB complexes with DMF or Me_2SO react with water to give a hydroxy complex;[170] under the action of $CHCl_3$ or aniline, the methoxy complex of TNB is converted to a trihalomethyl[186] or anilide complex,[113,115] respectively, etc. However strange, the mechanism of these intriguing reactions has not been studied so far, with the exception of a particular case of transformation of the methoxy complex into the anilide complex. An early hypothesis claimed that the mechanism of this transformation is similar to that of S_N2 substitution at a saturated carbon atom.[295] In 1977, however, Buncel studied the kinetics of this reaction and advanced an alternative dissociation mechanism[113,115] with formation of a zwitterion σ complex as the slow stage.[113,115]



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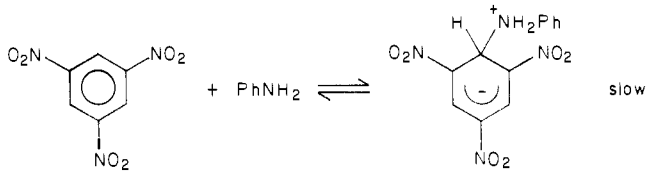

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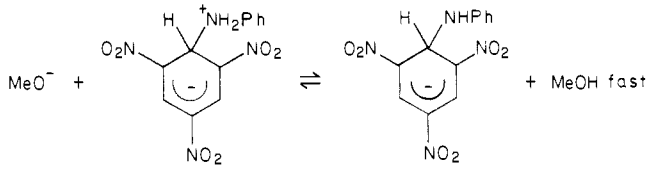

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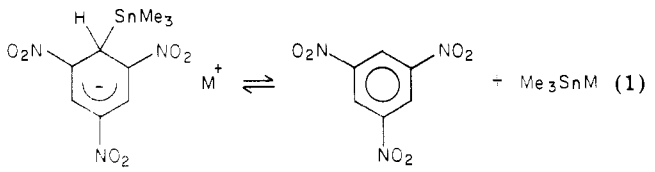
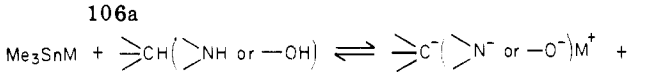
It must be noted that Buncel's mechanism appears to be confined to the particular case of a reaction with bases possessing a lone electron pair necessary for the nucleophilic attack on TNB.

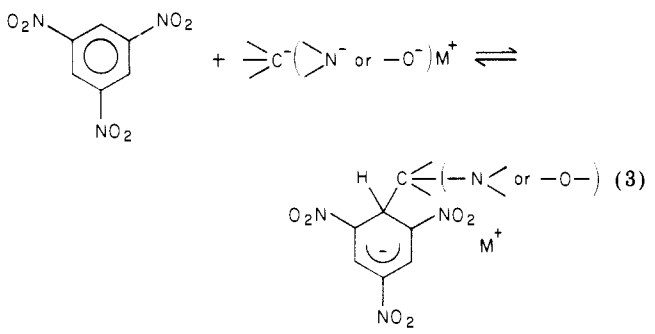
In a study of TNB anionic σ complexes with R_3E groups (type **106**) it was found[71,264] that these compounds (just TNB hydroxy and methoxy complexes) undergo slow dissolution in acetone to form a corresponding acetone σ complex. Addition of a small amount of water (2 % vol) to Me_2SO solutions of **106** results in hydroxy σ complexes. The following mechanism was advanced for these transcomplexing reactions:



106a



Me_3SnH (2)



The Me_3Sn^- anion formed by dissociation of **106a** metalates the CH acid (or NH and OH acid) to produce an anion which reacts with TNB to give rise to a new σ complex.

The possibility of transcomplexing, generally speaking, depends on the relationship between the equilibrium constants of reactions 1, 2, and 3; for the σ complex **106a** it is determined by reactions 2 and 3. The former is a reaction of transmetalation whose plausibility depends on the relationship between the pK_a of the acid and Me_3SnH. As long as the pK_a for Me_3SnH is equal to 23.5–23.8,[296] it is clear that metalation under the influence of Me_3Sn^- will take place only with acids whose $pK_a \leq 23$. Indeed, CH acids with $pK_a \sim 23$, e.g., $(C_6F_5)_2CH_2$ ($pK_a = 21.2$)[297] or C_6F_5H ($pK_a = 23$),[298] do not react with **106a** in Me_2SO, and C_6F_5H does not react even in a 3:1 mixture of C_6F_5H:Me_2SO.[71] Me_2SO ($pK_a = 33.3$) also does not react with **106a**. It appears that the pK_a of acetone ($pK_a = 20$) characterizes the upper limit of pK_a at which reaction 2 is still possible. In fact, it proceeds readily in the case of CH, NH, and OH acids with pK_a of 9–15 ($CHCl_3$, $C_6F_5CH_2COC_6F_5$, $CHBr_3$, succinimide).

With decreasing pK_a of the CH(NH, OH) acid the rate of reaction 2 will increase. On the other hand, the conjugated anion will become more stable and thus less reactive, so that its interaction with TNB (reaction 3) will slow down. Therefore, a lower limit of pK_a should exist, when transcomplexing will depend on whether the reaction between the anion and TNB is possible.[71] This limit is apparently situated in the 5–7 range: acetic acid ($pK_a = 4.76$) and trinitromethane ($pK_a = 0$) only decompose the σ complex without formation of a new species. The anions of these acids feature low reactivity; the acetate ion forms a σ complex with TNB very slowly and the yield is low, while potassium trinitromethanate does not react at all.[71,264]

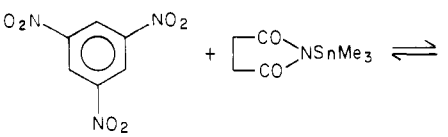
The above mechanism for the reaction between anionic σ complexes containing a C–E bond and various "acidic" compounds apparently holds for σ complexes with other types of bonds. For example, TNB σ complex with a Me_3SnO group (**29**) also may be converted into σ complexes with acetone, hydroxyl, or succinimide.

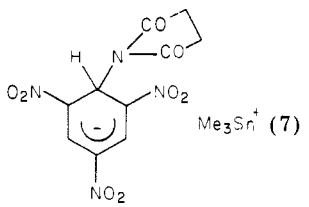
In solutions of **106a** or **29**, Me_3Sn^- or Me_3SnO^- anions can be trapped by such potential sources of a positive halogen as NBS and CBr_4.[71,264]

$$Me_3Sn^- (Me_3SnO^-)\ M^+ + RBr \rightarrow Me_3SnBr\ (Me_3SnOBr) + RM \quad (4)$$

$$TNB + R^- \rightleftharpoons [TNB{\cdot}R]^-\ M^+ \quad (5)$$

Addition of these species to **106a** or **29** in Me_2SO causes a rather fast formation of a succinimide or tribromomethyl complex. With excess NBS the succinimide complex gives rise to TNB. However, the mechanism of these reactions is perhaps more complex than indicated by (4); Me_3SnK with NBS in THF in vacuo affords a 60% yield of *N*-(trimethylstannyl)succinimide, which also can react with TNB to form a σ complex, **114**, whose yield is appreciably increased by addition of KBr.[71,264] These transformations may be represented as in eq 6–8. Their actual mechanism will evidently depend on the relationship between the reaction rates of (4) and (6). This means that in Me_2SO in the





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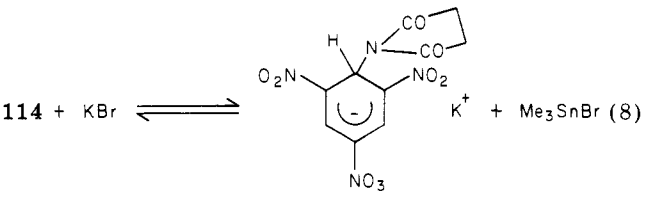

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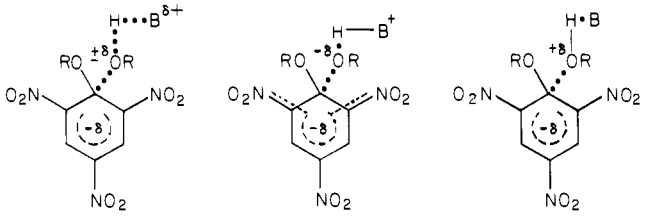
presence of TNB the σ complex **56** may, at least partly, be formed according to eq 4 and 5.

B. Reactions between σ Complexes and Electrophiles

The general mechanism of a reaction between an anionic σ complex and an electrophile E^+ may be presented, considering the sites susceptible to the attack (Scheme I) The pathway of this interaction will depend, firstly, on the stability of the σ complex in the solution and, secondly, on the reactivity of the electrophile. The more stable the complex (i.e., the lower its dissociation constant), the higher the probability that the reaction with the electrophile E^+ will follow the pathway "a" or "c" or, in other words, will involve the molecule of the complex itself. The same effect should, in principle, be exerted by an increase in the electrophilicity of E^+ (for the given σ complex) and the resulting decrease in selectivity of the attack. On the other hand, less stable complexes and less reactive electrophiles are apt to react according to the "b" pathway.

The reactions of σ complexes with the simplest electrophile, the proton, have been studied best of all. There is conclusive evidence that anionic σ complexes of nonsubstituted polynitrobenzenes with oxygen-, sulfur-, and nitrogen-containing nucleophiles revert to the parent nitro aromatic upon acidification.[6,7,19,91] Acidic decomposition of σ complexes of alcoholate ions with alkyl picrates leads to a mixture of the parent ether and a relevant product of substitution.[6,7,19,299,300] Several workers[36,38,300-302] arrived at a conclusion that this reaction for 1,1-dimethoxy complexes of different substrates involves specific acidic catalysis. However, Bernasconi[303-305] established the general acidic catalysis in this case. The reaction is thought[303,305] to be a concerted process involving a transition state **115** (i.e., following the "c" pathway of Scheme I typical of stable complexes). The alternative mechanism via dissocia-



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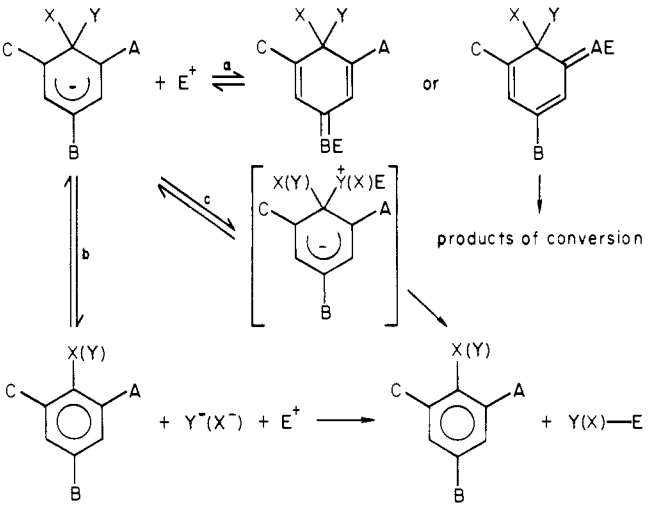
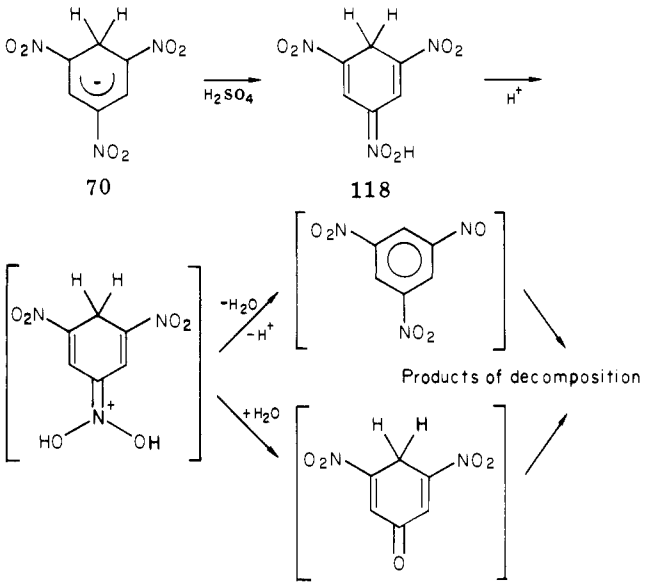
tion of the σ complex and transition states **116** and **117** is thought to be far less consistent with the observed kinetics of the reaction. Bernasconi[303] attributes the nonobservance of general acidic catalysis in earlier studies to the use of low concentrations of buffers and inefficient catalysts. The success of his own brilliant investigations was largely determined by the use of

SCHEME I



SCHEME II

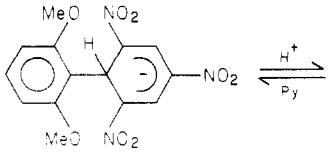


70 118

stopped-flow techniques with spectrophotometric monitoring and, particularly, its combination with the relaxation technique.

Acidification of anionic σ complexes of polynitrobenzenes with a strong carbon–nucleophile bond should apparently lead first to nitronic acid (pathway "a" of Scheme I). Indeed, the hydride σ complex **70** with acids does yield nitronic acid **118**, which is stable only in solution.[306] Its decomposition in acidic media begins with protonation followed either by dehydration to 1-nitroso-3,5-dinitrobenzene or hydration to 3,5-dinitrocyclohexanone. These products were not isolated; however, the reaction gave rise to 3,5-dinitroaniline, *N*-(3,5-dinitrophenyl)hydroxylamine, 3,3′,5,5′-tetranitroazoxybenzene, 3,3′,5,5′-tetranitrohydrazobenzene, 3,3′,5,5′-tetranitrodiphenylamine, and 3,5-dinitrophenole. This[306] confirms Scheme II.

Nitronic acid **120** was also isolated by Wennerström[201] on acidification of the carbon σ complex **119**. In ethanol this acid is completely dissociated, while in $CHCl_3$ the nondissociated form dominates. Under the influence of base the acid **120** forms a σ complex **119**, while the formation of **121** requires an oxidant. The same results were obtained for the σ complex from TNB and indene.[203b] On treatment with strong acid this complex



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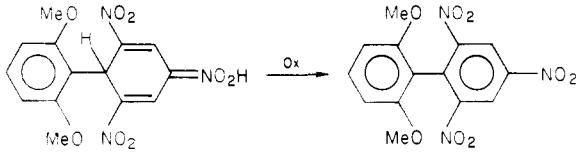


120 121

transformed into a nitronic acid—4-(1-indenyl)-3,5-dinitro-2,5-cyclohexadienenitronic acid.

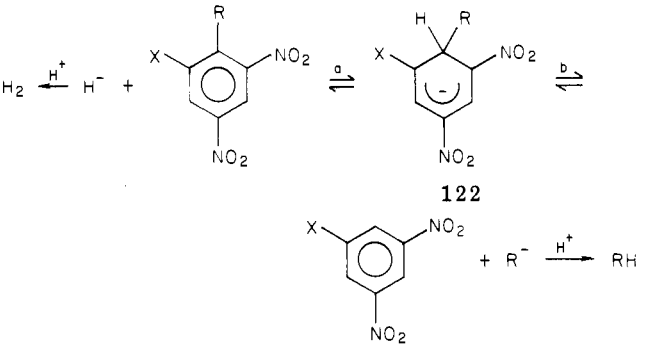
The acidity of the conjugate acid of the σ complex, a nitronic acid, was determined by Buncel and Eggimann[66c] for compound **27b** in aqueous sulfuric acid. The acidity of the nitronic acid has been evaluated with the aid of various acidity function techniques and the Bunnett–Olsen method and yielded pK_a values of −1.16 and −0.91, respectively.

Nitronic acids, however, were observed just in four papers. As a rule, acidification of stable σ complexes with a C–C bond leads either to the parent nitro aromatics[175,307,308] or to the corresponding products of substitution.[171,218,200] These facts may in principle be explained by the possible dissociation of **122** by loss of a carbanion (path b, Scheme III) or a hydride ion (path a) (both directions are included in path b of Scheme I). However, path a seems very unlikely. Therefore, the substitution products which were obtained by the acidification of **122** may be connected with the oxidation of σ complexes. Indeed, the emergence of 2,4-dinitrobenzyl methyl ketone in the products of acidic decomposition of the Janovsky complex was interpreted as associated with oxidation of the σ complex by *m*-dinitrobenzene according to Zimmermann's reaction (see below).[313] The formation of (2,4-dinitrophenyl)-acetophenone on acidification of *m*-DNB σ complex with acetophenone may be explained in the same manner.[309] In the case of TNB σ complexes and TNA 1,3 σ complexes such a reaction is impossible, and TNT, 1-butyl-2,4,6-trinitrobenzene,[218] and 3-acetonyl-2,4,6-trinitroanisole,[171] which are formed on acidification of the corresponding σ complexes, may appear only according to the a pathway. It is more possible, however, that acidic decomposition of σ complexes with CH acids leads to the relevant substituted products by virtue of oxidation by atmospheric oxygen. It is this reason that presumably accounts for the emergence of 2,4,6-trinitrotoluene on acidification of TNB σ complex with silver phenylacetylide.[202]

If the hydride ion in **122** (X = NO_2) was replaced by the MeO^- group, the direction a of Scheme III will become more advantageous thermodynamically. Indeed, on acidification of TNA 1,1 σ complex with potassium acetoacetate ester Strauss obtained a high yield of ethyl α-picrylacetoacetate.[119]

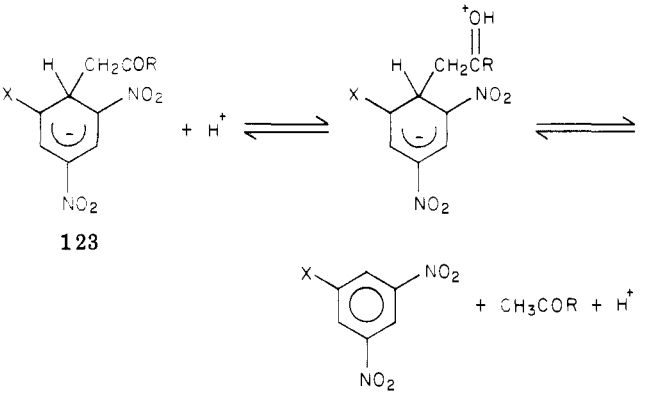
It was suggested that the acidic decomposition of TNB σ complexes with acetone and substituted acetophenones[310] could obey a mechanism similar to pathway c of Scheme I. The key stage of this mechanism is protonation of **123** at the carbonyl group, which may presumably occur simultaneously with the rupture of

SCHEME III



X = H, NO_2, CN, COOMe

the C–C bond.[310] The same mechanism was proposed for decomposition of the acetone σ complex of 1-(piperidinocarbonyl)-3,5-DNB.[159]

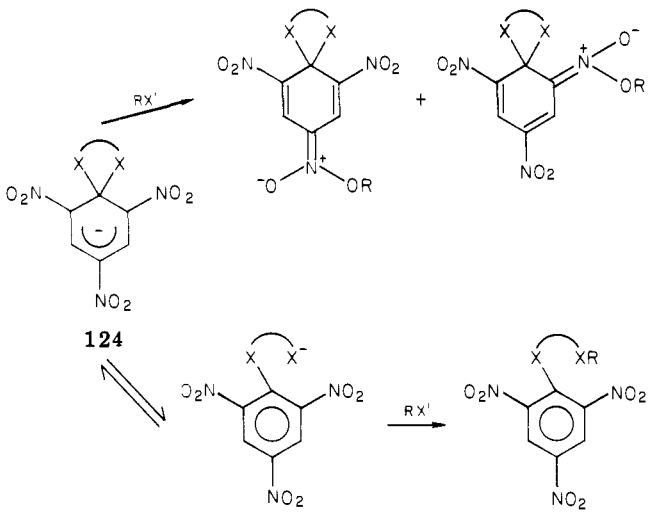


123

X = NO_2, R = Me, *p*-XC_6H_4
X = $CON(CH_2)_5$, R = Me

The Janovsky complex is less stable and its decomposition according to pathway b of scheme III takes place even in aprotic dipolar solvents;[311,312] it is accelerated by alcohol and water[311,312] and occurs almost instantly on addition of acids. Interesting facts were reported on the dependence of the Janovsky complex decomposition rate on the nature of alcohol,[311-313] its molar fraction,[311] and addition of D_2O.[313] However, the scheme suggested[311-313] does not provide a convincing explanation for these observations.

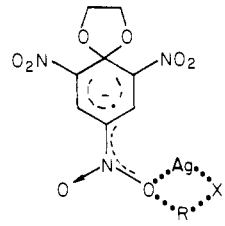
A recent study concerned reactions between Meisenheimer σ complexes and a variety of alkylating agents.[314-316] The results are in agreement with Scheme I. It was found, for example, that such agents as AlkX do not react with σ complexes. Stronger agents such as methyl fluorosulfate and triethyloxonium borofluoride, however, lead to the corresponding nitronate esters via an attack at the oxygen atoms pertaining to the *o*- and *p*-nitro groups. The yield in these reactions depends both on the stability of the σ complex and on the nature of the alkylating agent. For instance, methyl sulfate with the classical Meisenheimer complex forms TNA quantitatively; the action of $Et_3O^+BF_4^-$ leads, however, to 73% TNA, ethyl 4-*aci*-nitro-2,6-dinitro-1,1-dimethoxy-2,5-cyclohexadienate and a minor amount of an ortho isomer. More stable spirocyclic σ complexes may be alkylated by methyl fluorosulfate into a mixture of ortho and para nitrone esters with the latter predominating.[316] The formation of ortho isomers is completely suppressed in the presence of Et_3N. Another possible reaction path in which the open form



124

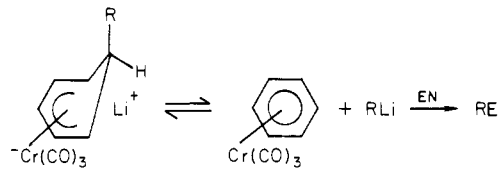
of the σ complex **124** takes part is the basic one if XX = SCH_2CH_2S (probably because of the high nucleophilicity of the mercaptide anion). As for alkylation of the silver salt of **124** (XX = OCH_2CH_2O) (such a salt could not be obtained for XX = SCH_2CH_2S), this occurs with other alkylating agents, e.g., alkyl halides.[315,316] The reaction leads to a mixture of o- and *p*-nitronates just as in the above process. At the same time the silver salt of the less stable classical Meisenheimer complex reacts with RX to yield only TNA.

The authors who studied the reaction of the silver salt of **124** with alkyl halides suggested a four-centered transition state **125** and identified the reaction as that of the Ag^+–S_N2 type.[316]



125

Semmelhack et al.[235,236] studied the reaction of complexes **96** with various electrophiles (MeI, Ph_2CO,



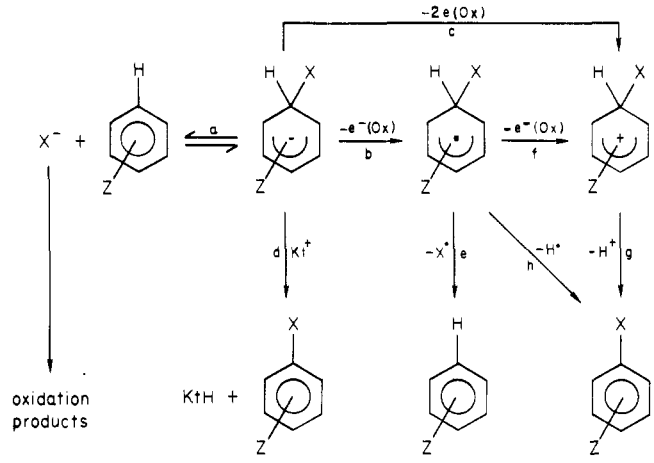
96

Ph_3CBF_4, *i*-Pr_3B). All these reactions resulted in (benzene)tricarbonylchromium and the corresponding R–E. The mechanism in this case apparently corresponds to path "b" of Scheme I.

C. Oxidation of Anionic σ Complexes

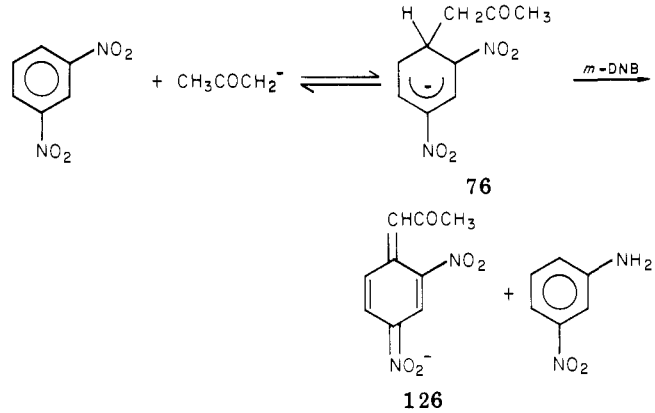
Anionic σ complexes with a hydrogen atom on the sp^3 carbon of the cyclohexadienate ring apparently cannot decompose spontaneously by loss of a hydride ion. Therefore, to obtain a substitution product from such a σ complex one has to oxidize the latter. This process may in principle be represented in Scheme IV. Scheme IV shows that oxidation of σ complexes may occur by

SCHEME IV



loss of one electron (path b), by loss of two electrons consecutively (paths b and f), or simultaneously (path c). Besides this, substitution may arise from the action of an acceptor of hydride ions Kt^+ (path d). Unfortunately, the mechanisms of oxidation of anionic σ complexes have not been studied, and usually it is impossible to make a choice between pathways b, c, d, and f. Pathway a allows for dissociation of the complex into its initial components, and the possible oxidation of the nucleophile X^- rather than the complex, respectively, so that the reaction leads to the parent aromatic substrate and the oxidation products of X^-. This mechanism is likely to operate in the oxidation of TNB σ complexes with R_3EM (E = Si, Ge, Sn).[72,264] On the other hand, this equilibrium may often be discarded when dealing with oxidation of thermodynamically stable complexes, say, with a C–C bond. Below we shall discuss the effect of various oxidants on such σ complexes.

Historically, the first example of oxidation of a σ complex is the Zimmermann reaction.[155,156] Several authors[309,317] suggested that the mechanism of this reaction involves oxidation of the initially formed Janovsky complex by excess *m*-DNB to **126**, the conjugate base of 2,4-dinitrobenzyl methyl ketone. This mech-



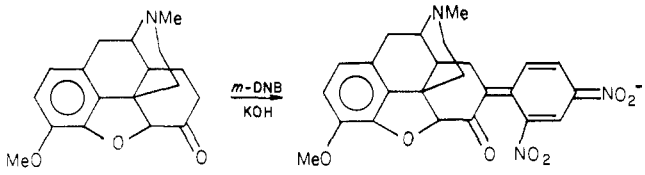
126

anism is supported by the presence of *m*-nitroaniline in the reaction products. The compound **126** was isolated and identified[163] and its structure established by ^{13}C NMR spectroscopy.[25]

The Zimmermann reaction was used as a basis for colorimetric determination of 17-keto steroids.[155,156,318-321] In a study dealing with 40 keto steroids and related compounds it was shown that the reactivity

of keto steroids depends on stereochemical surroundings of the oxo group,[319] suggesting that the Zimmermann reaction be used for the determination of the structure of keto steroids.

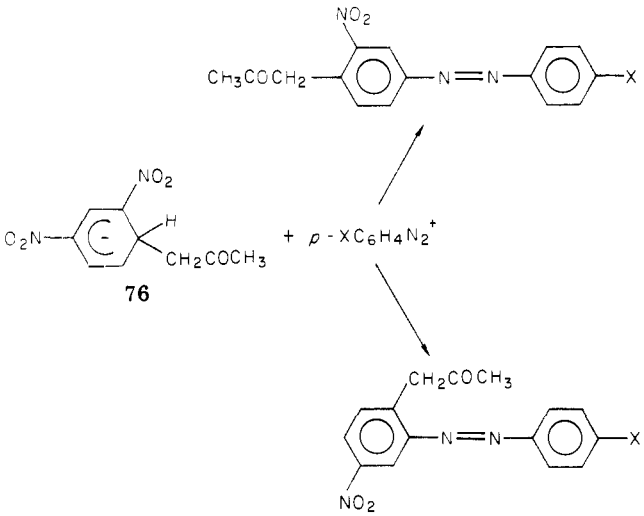
There is another color reaction based on the reaction of natural products with *m*-DNB in the presence of an alkali. It is called the Canbäck reaction[322] and is used in the analysis for dihydromorphinone, dihydrocodeinone, and hydroxydihydrocodeinone. The color was due to a Zimmermann complex which in the case of hydrocodone possesses structure **127**.[324]



127

Common inorganic oxidants, e.g., manganese(III) acetate,[325] can also convert the Janovsky complex into 2,4-dinitrobenzyl methyl ketone.

An unusual reaction was reported for the Janovsky complex with *p*-NO_2- (or *p*-Me_2N)$C_6H_4N_2^+$.[326] It involves oxidation of the σ complex followed by ipso substitution of the nitro group by the phenyldiazonium residue. The products were identified by IR, UV, and NMR spectroscopy.



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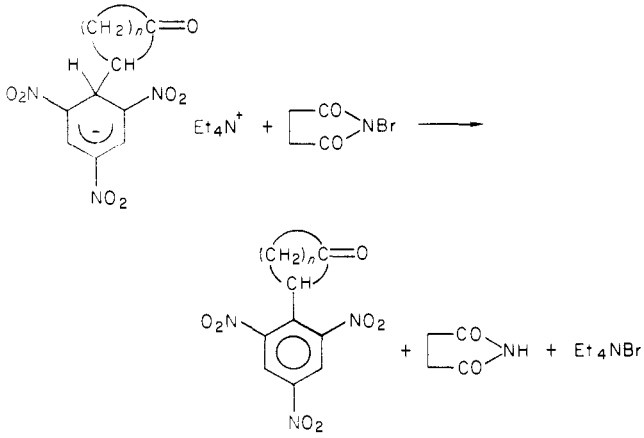
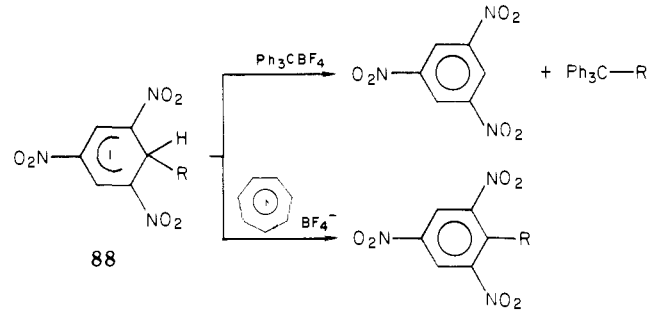
Quite a few one- and two-electron oxidants can oxidize TNB anionic σ complexes with carbanions so that the C–C bond is retained. For instance, in



Wennerström's pioneer investigations σ complexes obtained from TNB and organocopper (silver) compounds were oxidized by Cu_2O,[200] an adduct of pyridine and CrO_3,[201], *p*-benzoquinone,[203a,203b] and hydrogen peroxide in acidic medium.[203b] Smooth oxidation was also reported for σ complexes of TNB with 2-furyl- and 2-thienylcopper by *p*-benzoquinone.[203a] In the oxidation of TNB σ complexes with cyclic ketones, *N*-bromsuccinimide was successfully used as the acceptor of hydride ions;[327] the reaction led to a high yield of corresponding cyclic α-picryl-substituted ketones. The reaction is of general nature, and it may be employed for the synthesis of any α-picryl-substituted ketones.[327]

Another good acceptor of the hydride ion is tropylium borofluoride, reported as a means of oxidation of TNB σ complexes with cymantrenyl silver[204] and acetone-.[328,329] Note that trityl borofluoride reacts with TNB



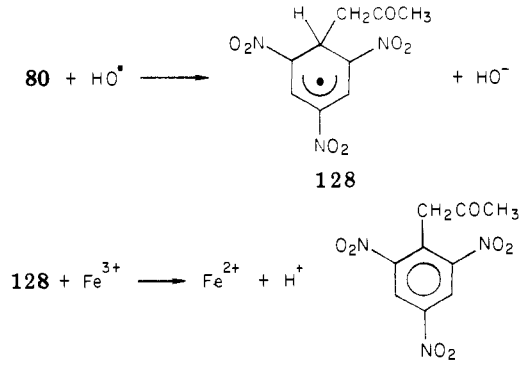
88

R = CH_2COCH_3, CH_2COPh, CH_2NO_2

σ complexes with acetone, benzophenone, and nitromethane in a different manner; the reactions lead to TNB and $Ph_3CCH_2COCH_3$, Ph_3CCH_2COPh, and $Ph_3CCH_2NO_2$, respectively.[328] In these reactions, as in the Ph_3CBF_4 reaction with **96**, trityl borofluoride apparently cannot oxidize the corresponding complexes. However, it may act as an electrophile with regard to the carbanions resulting from dissociation of the σ complexes, thus giving rise to Ph_3C–R.

The selection of oxidants capable of oxidizing TNB σ complexes with carbanions so that the C–C bond is intact has been considerably enlarged, and oxidation of the acetone complex **80** was investigated.[329] It was found that a variety of one- and two-electron oxidants ($AgNO_3$, $FeCl_3$, $Fe_2(SO_4)_3$, FeF_3 (but not $[Fe(CN)_6]^{3-}$), Fenton's reagent, $(NH_4)_2Ce(NO_3)_6$, H_2O_2, chloranil, $Pb(OAc)_4$, $HalO^-$ (Hal = Cl, Br, I), aqueous Cl_2, Br_2, I_2, tropylium borofluoride) convert **80** into 2,4,6-trinitrobenzyl methyl ketone in a high yield (60–80%). It was shown that the oxidation rate depends on the standard potential of the oxidant; a radical chain mechanism

$$Fe^{2+} + H_2O_2 \rightarrow Fe^{3+} + HO^{\cdot} + HO^-$$



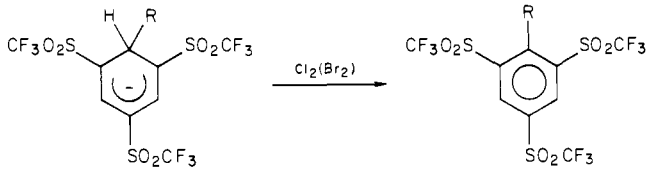
128

involving oxidation of the radical **128** by Fe^{3+} was suggested for oxidation of **80** by hydrogen peroxide.

The same authors report oxidation of tribromomethyl and trichloromethyl σ complexes of TNB by chlorine or bromine in Py or in *t*-BuOH to the corresponding 1-(trihalomethyl)-2,4,6-trinitrobenzenes in 68–77% yield.

σ Complexes of acetonate ion with *m*-DNB,[325] substituted *m*-DNB,[330] and TNB[325] were oxidized electrochemically into the corresponding benzyl methyl ketones. However, the mechanism advanced for this reaction[330] seems unlikely.

Oxidation of anionic σ complexes **95**, which possess remarkable thermodynamic stability (R = CH_2COCH_3, CN, CH_2NO_2, CH_2CHO, $CH(COOEt)_2$), by chlorine and bromine in water–organic media was studied.[233] The reaction, even for R = CN, leads to the corresponding 1-R-2,4,6-tris[(trifluoromethyl)sulfonyl]benzenes **129**; with R = CH_2CHO the carbonyl group is not involved.



95 **129**

σ complexes of (benzene)tricarbonylchromium with organolithium compounds were oxidized by iodine or cerium–ammonium nitrate to the corresponding Ph–R.[235,236] In some cases the process was performed in situ, without isolation and identification of σ complexes.[331]

The corresponding ArR were the products of oxidation of adducts formed by mononitro aromatics with the Grignard reagent[226] and with *n*-BuLi[224] by permanganate, bromine, and DDQ (see section IIG).

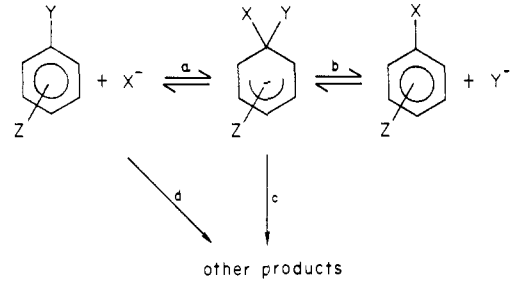
Oxidation of σ complexes so that the C–C bond is preserved is not only of theoretical interest but also of preparative significance, since it permits the introduction of new substitutents into aromatic molecules with electron-withdrawing groups. Unfortunately, the problem of oxidizing less stable σ complexes with bonds of other types is still largely unsolved.

VI. Spontaneous Transformation of σ Complexes

A general scheme for spontaneous transformation of σ complexes may be presented in Scheme V. If X^- is more nucleophilic than Y^-, the scheme read from the left-hand to the right-hand side apparently describes a process of nucleophilic aromatic substitution (pathway b reflects the decay of the intermediate σ complex). With X^- and Y^- possessing comparable nucleophilicity, the σ complex may decompose into the parent components via pathway b as well as pathway a. These transformations of σ complexes are closely related to the problems of nucleophilic aromatic substitution and are beyond the scope of our review.

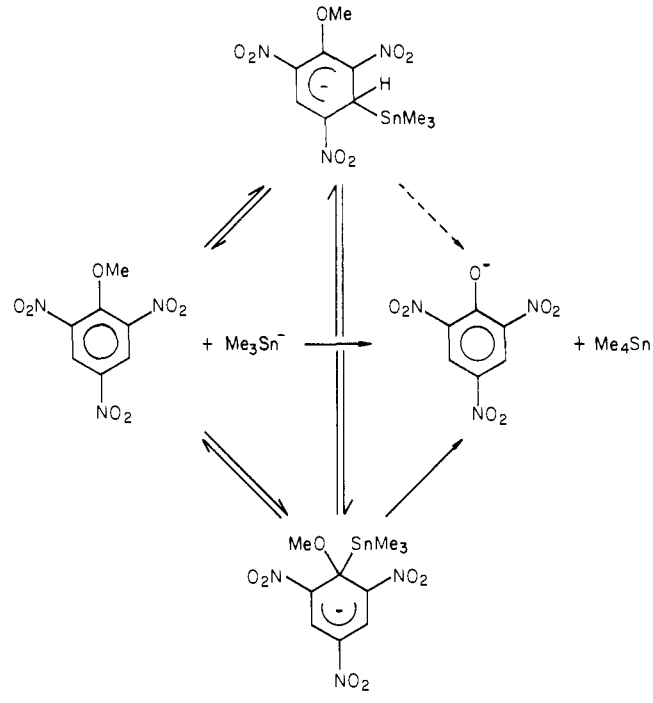
However, σ complexes may undergo a kind of transformation leading to products of high thermodynamic stability which differ from products of nucleophilic substitution.

SCHEME V



A. Transformation of TNA σ Complexes

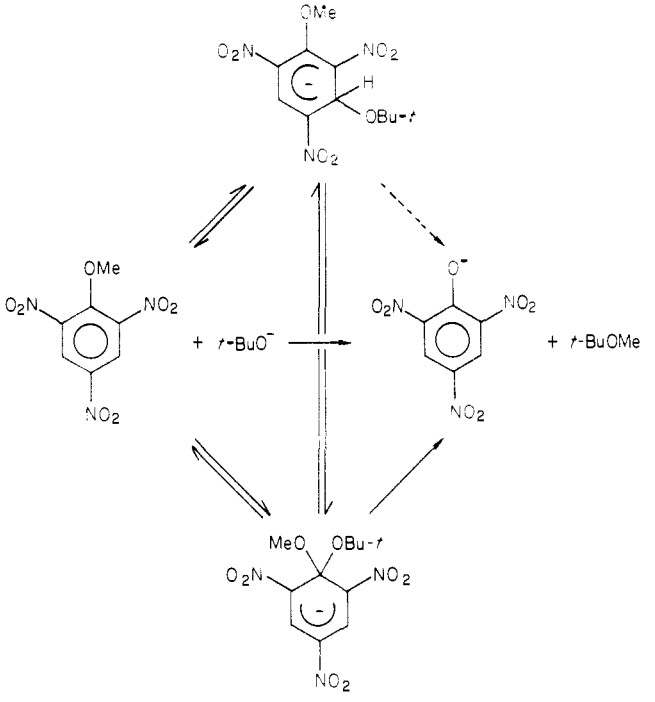
It has been mentioned more than once in this review that the formation of σ complexes with TNA is often accompanied by the generation of picrate ions (see e.g., ref 68, 91, 169); this was usually attributed to hydrolysis of the complex by traces of water according to an unknown mechanism. In recent studies, however, it was shown that the picrate can be formed under conditions where no water is present. Indeed, the reaction of Me_3SnM (M = Li, K) with a THF solution of TNA in vacuo results in the corresponding picrate (PiOM) and Me_4Sn.[332,333] In HMFTA, where the anionic σ complexes are known to be far more stable, ^1H NMR spectroscopy revealed the formation of a 1,3 σ complex, which was transformed into a 1,1 σ complex. The latter



slowly decomposed into a picrate and Me_4Sn.[333] Me_3SiLi in HMFTA reacts with TNA in a similar manner. TNA was found to display these unusual alkylating properties with regard to other nucleophiles as well.[332,333] For example, on addition of KI to anhydrous Me_2SO-d_6 solution of TNA a rapid reaction (2–3 min) results in a quantitative yield of PiOK and MeI. The reaction proceeds with the same smoothness in the case of Bu_4NI in acetone and KI in THF in the presence of 18-crown-6-ether. KF (Me_4NF), KBr, and KSCN also undergo fast and efficient methylation by trinitroanisole. With KNO_3, $NaHCO_3$, NaOAc, Na_2S, and KCl the reaction requires a week (on the average)

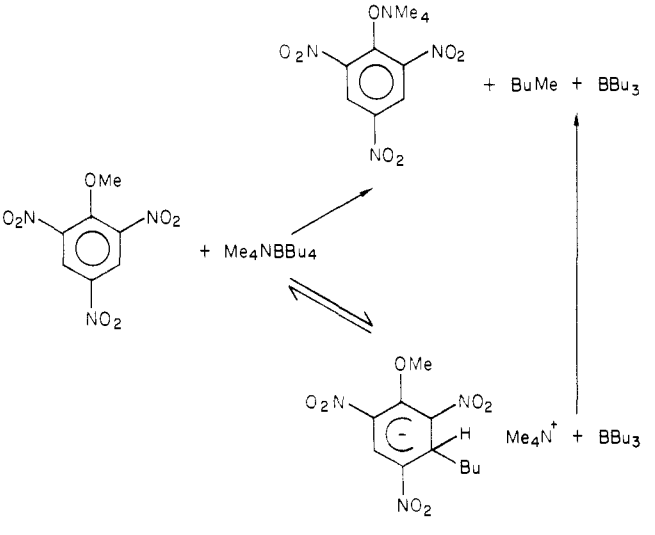
and is affected to a great extent by TNA interaction with Me_2SO. No intermediate σ complexes were observed in all the reactions listed.[333]

Very unstable σ complexes were observed by means of absorption spectroscopy in the reactions of TNA with $NaNO_2$, lithium succinimide (SLi), and $PhSO_2Na$, which lead to PiONa, MeONO, SMe, and $PhSO_2Me$, respectively. At least some of the picrate in these reactions is undoubtedly formed by decomposition of the σ complex.[333] Picrate and *t*-BuOMe result from decomposition of the unstable 1,3 and 1,1 σ complexes of TNA with *t*-BuOK. This mechanism may well operate



in decomposition of the classical Meisenheimer complex, since on long standing in Me_2SO this species gives rise to picrate. However, as long as the σ complex is stable and its decomposition is slow, it is not impossible that the picrate is due to the reaction of Me_2SO with the TNA resulting from dissociation of the σ complex.[132]

Interesting data were obtained for the reaction of TNA with carbanions,[333] the position of attack depending on the reactivity of the carbanion. For instance, *n*-BuLi and PhMgI in THF react with TNA to form picrate in a high yield. With a less reactive



carbanion, however, i.e., with Me_4NBBu_4 instead of *n*-BuLi, alkylation is accompanied by the formation of a 1,3 σ complex. These reactions must be parallel, since the 1,3 σ complex is stable enough and its decomposition to the picrate takes a whole week.

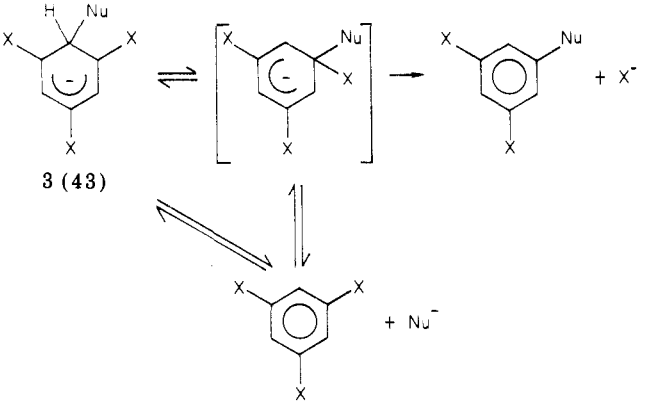
A labile 1,3 σ complex results from the interaction between TNA and KCN or $Hg(CN)_2$ in the presence of KI (in the latter case methylation of KI is involved). In 2–3 h the complex decomposes into picrate.[333]

The stable and unreactive tricyanomethyl anion does not react with TNA at all.[333]

In all these reactions, therefore, TNA acts as a methylating agent, with anionic σ complexes often being formed as precursors of picrates which result from their decomposition. The mechanism of this decomposition is not clear so far. It is not clear whether the methylation products and picrate are due to an S_Ni mechanism, i.e., by the transformation of the complex itself (path c of Scheme V), or more likely, the mechanism involves methylation of the nucleophile by TNA.

B. Transformation of TNB σ Complexes

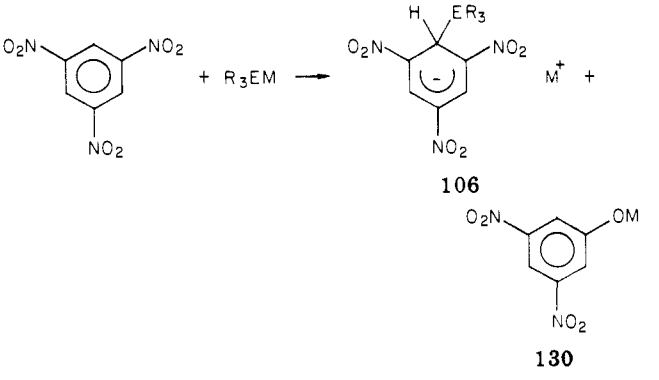
The simplest way of decomposition for complexes with a "poor" leaving group (e.g., the hydride ion in polynitrobenzenes) that does not lead to the parent reagents is the nucleophilic substitution of the neighboring electron-accepting group, or, in other words, a sort of ipso substitution. This process was observed by decomposition of the TNB methoxy complex **3**[106] or the TMSB thiophenolate (thiobutanolate) complex **43**[96] and



X = NO_2, Nu = MeO^-; X = SO_2CF_3, Nu = PhS^-, BuS^-

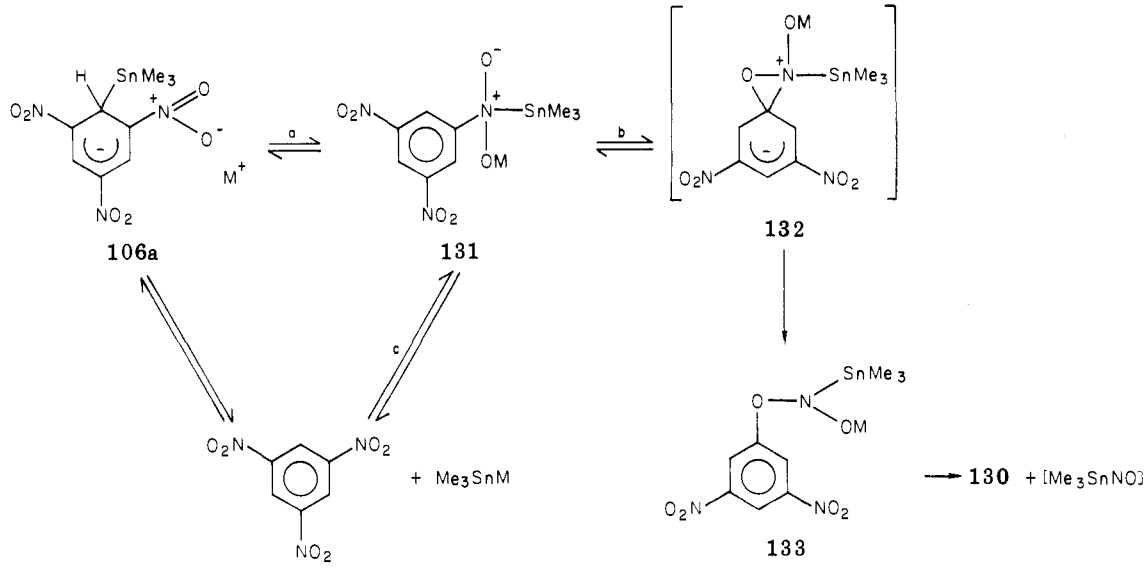
was found to lead to 3,5-DNA and 1-(phenylthio)(butylthio)-3,5-bis[(trifluoromethyl)sulfonyl]benzene, respectively.

A new decomposition pattern was discovered for σ

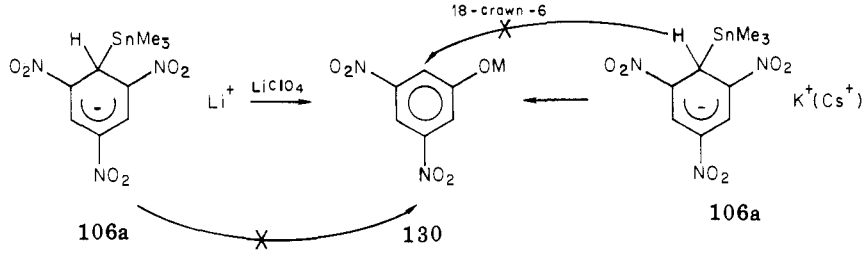


E = Ge, Sn; M = K, Cs

SCHEME VI



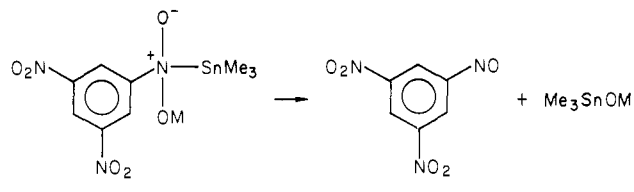
SCHEME VII



complexes of TNB with R_3E groups:[334] the reaction of TNB with potassium and cesium salts of R_3EM (in contrast to lithium salts) was found to lead, along with the corresponding σ complexes, to a byproduct that was the same for all these salts. This species was isolated and identified as potassium (cesium) 3,5-dinitrophenolate.[334] The amount of **130** in the reaction mixture depended on the duration of the reaction: it was a smaller amount the sooner the products were isolated. On dissolution of the σ complex obtained, e.g., **106a**, in M_2SO its concentration gradually decreased while at the same time the concentration of **130** increased.

The mechanism suggested for this conversion involved addition of Me_3Sn^- to the nitro group (intra- or intermolecularly) followed by migration of the aryl group to the oxygen atom (probably via an intermediary complex **132**) and then by further fragmentation into the reaction products. It is hard to say whether the zwitterionic spiro complex **132** is a transition state of the reaction or an unstable intermediate (Scheme VI).

A different kind of rearrangement of **131** would occur by fragmentation of Me_3SnOM from the complex and lead to another product, namely 1-nitroso-3,5-dinitrobenzene and the corresponding trimethylstannolate. The reaction presumably does not proceed in this direction because the resulting Me_3SnOM would have



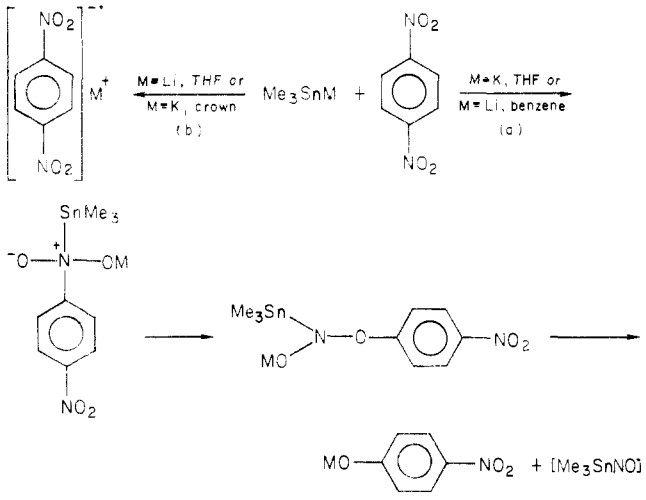
131

reacted with TNB (always available after reactions with Me_3SnM) to yield another σ complex. The latter species was obtained by a reaction between TNB and Me_3SnOLi. Its spectral characteristics, however, differ from those for **106a**.[334]

The most surprising feature of this reaction is its marked dependence on the counterion, i.e., the above-mentioned fact that it does proceed for K and Cs and does not proceed for Li salts. It seems likely that the reason for this effect is the different state of Me_3SnM (or σ complexes) salts in solution if the reaction is intermolecular (or intramolecular); in either case the lithium salts are more dissociated. Indeed, trimethylstannyl derivatives of alkali metals in solution are known to form an equilibrium mixture of contact and solvent-separated ion pairs and, possibly, free ions. In strongly solvating media like Me_2SO, HMFTA, or tetraglyme this equilibrium is shifted toward solvent-separated ion pairs and free ions.[335-338] It is only natural to expect that the greatest shift would be observed in the case of lithium derivatives.[336-338]

The fact that no **106** → **130** conversion takes place in the case of lithium salts indicates that this conversion essentially involves coordination of the alkali metal atom with the oxygen atom of the nitro group. Indeed, in reactions of TNB with Me_3SnK in THF in the presence of an equimolecular amount of 18-crown-6-ether the phenolate **130** is not formed, and the reaction leads only to the σ complex **106a**[334] (Scheme VII). This means that when coordination of the metal with the nitro group oxygen is difficult or impossible, no rearrangement occurs. If so, the rearrangement of **106a** (M = Li) into the phenolate **130** should be promoted by addition of an inorganic lithium salt. This expectation

SCHEME VIII

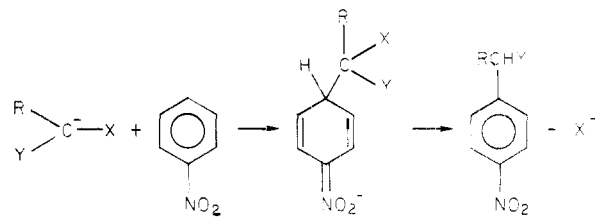


was confirmed.[334]

An alternative hypothesis claims that coordination of M^+ with the oxygen shifts equilibria a (or c) and b (Scheme VI) to the right-hand side and thus makes the irreversible conversion **131** (or **132**) → **133** possible.

Later it was shown that Me_3SnM reacts with the nitro group of other nitro aromatics according to the same pattern.[339] For instance, Me_3SnK smoothly reacts with *p*-dinitrobenzene (*p*-DNB) in THF to form potassium *p*-nitrophenolate in a high yield (70%) (path a, Scheme VIII). Under the same conditions Me_3SnLi reduces *p*-DNB to an anion radical (path b, Scheme VIII). By changing the reaction conditions (or, more precisely, the state of the reacting salt Me_3SnM in the solution), it was possible to make the former reaction proceed along the b path and the latter along the a path: Me_3SnK with *p*-DNB in THF in the presence of 18-crown-6-ether gave *p*-DNB anion radical (30–40%), while Me_3SnLi with *p*-DNB in benzene resulted in lithium *p*-nitrophenolate (40%).[339]

An unusual reaction (a suggested name is vicarious substitution) that formally leads to the substitution products of the hydride ion in an aromatic ring was reported by Makosza et al.[340,341] The mechanism ad-



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X = Cl, Y = SO_2Ph, SO_2NR_2; X = PhS, MeS, Me_2NCS_2; Y = CN; R = H, Ph

vanced for this reaction involves the formation of a σ complex **134**, which gives rise to the reaction product by substitution of the X group by the hydride ion.[340,341]

VII. References

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