The chemistry of
the nitro and nitroso
groups

Edited by

HENRY FEUER

Purdue University
Lafayette, Indiana

Part 2

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The Chemistry of Functional Groups
Preface to the Series

The series 'The Chemistry of Functional Groups' is planned to cover in each volume all aspects of the chemistry of one of the important functional groups in organic chemistry. The emphasis is laid on the functional group treated and on the effects which it exerts on the chemical and physical properties, primarily in the immediate vicinity of the group in question, and secondarily on the behavior of the whole molecule. For instance, the volume *The Chemistry of the Ether Linkage* deals with reactions in which the C–O–C group is involved, as well as with the effects of the C–O–C group on the reactions of alkyl or aryl groups connected to the ether oxygen. It is the purpose of the volume to give a complete coverage of all properties and reactions of ethers in as far as these depend on the presence of the ether group, but the primary subject matter is not the whole molecule, but the C–O–C functional group.

A further restriction in the treatment of the various functional groups in these volumes is that material included in easily and generally available secondary or tertiary sources, such as *Chemical Reviews, Quarterly Reviews, Organic Reactions*, various 'Advances' and 'Progress' series as well as textbooks (i.e. in books which are usually found in the chemical libraries of universities and research institutes (should not, as a rule, be repeated in detail, unless it is necessary for the balanced treatment of the subject. Therefore each of the authors is asked *not* to give an encyclopedic coverage of his subject, but to concentrate on the most important recent developments and mainly on material that has not been adequately covered by reviews or other secondary sources by the time of writing of the chapter, and to address himself to a reader who is assumed to be at a fairly advanced post-graduate level.

With these restrictions, it is realized that no plan can be devised for a volume that would give a *complete* coverage of the subject with *no* overlap between the chapters, while at the same time preserving the readability of the text. The Editor set himself the goal of attaining *reasonable* coverage with *moderate* overlap, with a minimum of

cross-references between the chapters of each volume. In this man-
ner, sufficient freedom is given to each author to produce readable
quasimonographic chapters.

The general plan of each volume includes the following main
sections:

(a) An introductory chapter dealing with the general and theo-
retical aspects of the group.

(b) One or more chapters dealing with the formation of the func-
tional group in question, either from groups present in the molecule,
or by introducing the new group directly or indirectly.

(c) Chapters describing the characterization and characteristics
of the functional groups, i.e. a chapter dealing with qualitative and
quantitative methods of determination including chemical and
physical methods, ultraviolet, infrared, nuclear magnetic resonance,
and mass spectra; a chapter dealing with activating and directive
effects exerted by the group and/or a chapter on the basicity, acidity
or complex-forming ability of the group (if applicable).

(d) Chapters on the reactions, transformations and rearrangements
which the functional group can undergo, either alone or in con-
junction with other reagents.

(c) Special topics which do not fit any of the above sections, such
as photochemistry, radiation chemistry, biochemical formations and
reactions. Depending on the nature of each functional group treated,
these special topics may include short monographs on related func-
tional groups on which no separate volume is planned (e.g. a chapter
on 'Thioketones' is included in the volume *The Chemistry of the Carbonyl
Group,* and a chapter on 'Ketenes' is included in the volume *The
Chemistry of Alkenes*). In other cases, certain compounds, though con-
taining only the functional group of the title, may have special
features so as to be best treated in a separate chapter as e.g. 'Poly-
ethers' in *The Chemistry of the Ether Linkage,* or 'Tetraaminoethylenes'
in *The Chemistry of the Amino Group.*

This plan entails that the breadth, depth, and thought-provoking
nature of each chapter will differ with the views and inclination of
the author and the presentation will necessarily be somewhat uneven.
Moreover, a serious problem is caused by authors who deliver their
manuscript late or not at all. In order to overcome this problem at
least to some extent, it was decided to publish certain volumes in
several parts, without giving consideration to the originally planned
logical order of the chapters. If after the appearance of the originally

planned parts of a volume, it is found that either owing to non-delivery of chapters, or to new developments in the subject, sufficient material has accumulated for publication of an additional part, this will be done as soon as possible.

It is hoped that the series 'The Chemistry of Functional Groups' will include the titles listed below:

The Chemistry of the Alkenes (published)
The Chemistry of the Carbonyl Group (published)
The Chemistry of the Ether Linkage (published)
The Chemistry of the Amino Group (published)
The Chemistry of the Nitro and Nitroso Groups parts 1 and 2 (published)
The Chemistry of Carboxylic Acids and Esters (published)
The Chemistry of the Carbon–Nitrogen Double Bond (published)
The Chemistry of the Cyano Group (in press)
The Chemistry of the Carboxamido Group (in press)
The Chemistry of the Carbon–Halogen Bond
The Chemistry of the Hydroxyl Group (in preparation)
The Chemistry of the Carbon–Carbon Triple Bond
The Chemistry of the Azido Group (in preparation)
The Chemistry of Imidoates and Amidines
The Chemistry of the Thiol Group
The Chemistry of the Hydrazo, Azo, and Azoxy Groups
The Chemistry of Carbonyl Halides
The Chemistry of the SO, SO_2, $-SO_2H$, and $-SO_3H$ Groups
The Chemistry of the $-OCN$, $-NCO$, and $-SCN$ Groups
The Chemistry of the $-PO_3H_2$ and Related Groups

Advice or criticism regarding the plan and execution of this series will be welcomed by the Editor.

me in the solution of various major and minor matters and my thanks are due especially to Prof. Y. Liwschitz, Dr. Z. Rappoport, and Dr. J. Zabicky. Carrying out such a long-range project would be quite impossible without the non-professional but none the less essential participation and partnership of my wife.

The Hebrew University   SAUL PATAI
Jerusalem, ISRAEL

Foreword

The concept of this book arose from several discussions with Professor Saul Patai during my sabbatical leave at the Hebrew University of Jerusalem in the Spring of 1964. While disclosing his plans to edit a series of treatises concerned with the chemistry of functional groups, inclusion of the nitro and nitroso groups as the subject-matter for one of the volumes was brought forward. I accepted the editorship of such a treatise as part of the series because I considered it very worthwhile that up-to-date discussions on the theoretical, physical, and mechanistic aspects of these groups be unified in one publication by active workers in the field. For although several review articles, proceedings of various symposia, and isolated chapters in various books have concerned themselves with certain aspects of the chemistry of the nitro and nitroso groups—an active and exciting field of research—no self-contained book on the subject has been available.

As in the already-published books of this series, the subject-matter in this treatise has been considered from the viewpoint of the functional group. Instead of an encyclopedic coverage of all known reactions and compounds, the emphasis has been placed on basic principles, mechanisms, and recent advances in both theory and practice. It is hoped that by choosing this approach, a broad and concise picture of the importance of the nitro and nitroso groups has been attained.

The editing and publishing of a book which is made up of contributions from several authors are usually delayed by the fact that the deadline agreed upon is exceeded by some of the contributors. Such delay is unfortunate because it can sometimes result in obsolescence on some parts of a manuscript. To minimize such possibilities, which invariably occur when discussions in active fields of research are involved, and to keep the format of the book to a manageable size, it was decided to publish the treatise in two volumes.

It is with great pleasure that I acknowledge the cooperation of Professor Saul Patai, and the advice and suggestions in editorial matters of the Publishers.

I also express my gratitude to Dr. M. Auerbach, who did most of the painstaking work involved in preparing both the Author and Subject Index.

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CHAPTER I

Introduction of the nitro group into aromatic systems

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The preparation of aromatic nitro compounds is most often achieved with reagents capable of forming the nitronium ion, NO_2^+. The reagents capable of producing this ion are numerous, and the conditions employed are as varied as the aromatics being nitrated. Besides the common sulfuric acid–nitric acid combination for the production of NO_2^+, nitronium fluoroborate and other nitronium salts, nitrate esters, N_2O_4, N_2O_5, and metal nitrates plus sulfuric or Lewis acids are reagents which are believed to involve nitronium ion as the nitrating species.

·Nitric acid in acetic anhydride might at first appear to behave similarly. Yet, the resulting acetyl nitrate is somewhat anomalous

in its action. Moreover, the active nitrating agent from nitric acid
in acetic anhydride is uncertain, although it is probably protonated
acetyl nitrate and not nitronium ion.

The atypical procedures for the introduction of a nitro group into
aromatic systems consist of oxidation of nitroso and amino com-
pounds, replacement of diazonium ion, rearrangement of nitramines,
nucleophilic displacement by aryl anions on nitrate esters and other
suitable reagents such as N_2O_4 and tetranitromethane, and free-
radical processes involving $\cdot NO_2$. These procedures are employed
most often to overcome problems of orientation, but the sensitivity
of some aromatic systems to oxidation by the usual nitrating media
necessitate other methods of preparing the nitroarene.

I. ELECTROPHILIC NITRATION

Preparative electrophilic nitration can be done in a variety of media,
but those most often employed are mixed acid (nitric plus sulfuric),
aqueous nitric acid, nitric acid in acetic acid, and nitric acid in
acetic anhydride. However, in theoretical and mechanistic studies,
the number of electrophilic nitrating agents and the variety of
solvents employed are numerous. Nitronium tetrafluoroborate (and
similar salts of P, As, and Sb) and dinitrogen pentoxide are excellent
nitrating agents whose preparative value would be greater if they
were more readily available.

A. Theory

As most commonly effected, nitration of aromatics is a typical
electrophilic substitution by the nitronium ion, NO_2^+ (equation 1).

$$(1)$$

$$(1)$$
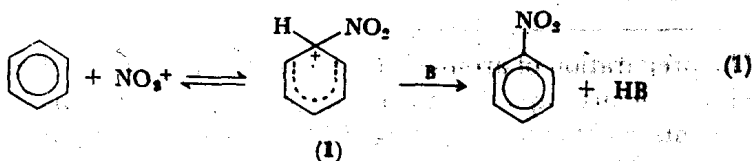
The formation of the σ-complex (1) is an ionic bimolecular process
sensitive to the individual reactivity of a particular aromatic and
to solvation effects. The exact products produced are governed by
the typical rules of orientation in electrophilic substitution, and
strong solvation of the nitronium ion retards the rate of nitration.
The velocity of the formation of the σ-complex is very rapid; where
the nitronium ion is involved in complex equilibrium with the

nitration medium, this formation is too fast to be rate determining. Because the loss of the proton from the σ-complex is also too fast to be even partly rate determining, a primary deuterium isotope effect is not observed in nitration. An exception has been found by Myhre[1] in the nitration of sym-nitrotri-t-butylbenzene wherein steric strain causes sufficient reversibility to the formation of the σ-complex to make the isotope effect detectable.

The major body of evidence in favor of nitration via the nitronium ion was first amassed by C. K. Ingold and coworkers in 1950 and has been summarized in numerous places[2-5]. Ingold himself was fully aware that dinitrogen pentoxide in carbon tetrachloride and acyl nitrates behave anomalously, and he maintained an open mind toward the possibility that species other than the nitronium ion might be responsible for nitration. Some writers[5-7], however, have tried to retain a simple picture with nitration always occurring via the nitronium ion. Such a simple concept seems unrealistic. Not only must one consider the nitrating agent to vary with the nitrating medium, but the transition to the σ-complex must be considered in greater detail.

The σ-complex or Wheland intermediate[8] is representable as a minimum in an energy–reaction coordinate profile and can be isolated under proper conditions; a σ-complex has been isolated from the reaction of trifluoromethylbenzene, nitryl fluoride, and boron trifluoride at −50° [9]. Even prior to its formation is the possibility of a less stable intermediate—a π-complex[10-11] —a multicentered, less directed interaction[12] of the nitronium ion with the electrons of the aromatics. Olah[13] has given evidence that formation of π-complexes may be rate determining in nitration by nitronium fluoroborate in sulfolane.

But more correctly, rates are controlled by activation energies which are determined by energy maxima, transition states, and not by intermediates, which are energy minima. Although the presence of an intermediate is useful in elucidating a reaction mechanism, an intermediate only restricts and hints at the dynamic process that leads to it[14]. In nitration this process is electrophilic yet it must also be partly nucleophilic because the electrophile receives its electron-pair from a donor, a nucleophile. More importantly, an electrophile sufficiently electrophilic to disrupt the resonance stabilization energy of benzene is going to be associated with some electron-rich species which must be displaced during formation of the σ-complex. Thus, in aromatic bromination there is a clear distinction between bromination by protonated hypobromous acid

and by molecular bromine wherein displacement of the bromide ion by the electrons of the aromatic is a significant portion of the transition state[15] (equation 2). From another viewpoint, electro-

$$(2)$$
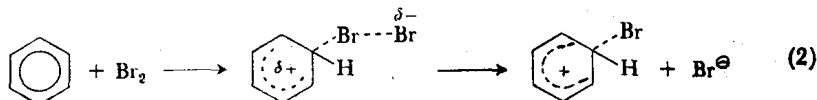
philes, depending on the medium, can be in various ground states. The two extremes are: (1) the electrophile is coordinated to a base by a directed covalent bond and is essentially a molecular entity and (2) the electrophile is a 'free' cation surrounded by several basic species through non-directed electrostatic interaction in a manner analogous to a cation in a crystal or an alkali metal cation in solution in water. Intermediate between these extremes are ion-pairs and a whole continuum of weak to strong, non-directed to directed, interactions of an electrophile with electron-donating substances.

At this time, three nitration systems have been sufficiently studied to warrant the conclusion that at least three distinctive electrophilic nitrating agents exist:

1. The complex fluoranion nitronium salts, particularly nitronium fluoroborate in sulfolane which acts as a solvated ion pair.
2. Nitric acid in acetic anhydride which reacts to produce acetyl nitrate which nitrates via its protonated form.
3. Nitric acid in concentrated sulfuric acid—mixed acid—which gives the solvated nitronium ion in a protic medium of high dielectric.

That these three systems contain distinctive nitrating entities is shown by their differences in both substrate selectivity and positional selectivity.

Competitive nitration with benzene shows that both nitronium fluoroborate and mixed acid have low substrate selectivity. The rate ratios are close to one (Table 1)[16]. Yet nitration in acetic anhydride gives much greater substrate selectivity, toluene being 27 times more reactive than benzene and biphenyl 16 times more reactive. The low substrate selectivity by nitronium fluoroborate is interpreted by Olah as evidence of the transition to the π-complex being rate determining. This interpretation is quite reasonable if one assumes that the nitrating entity is in a high ground state so that the rate-controlling transition state is closer to the starting materials. In acetic anhydride the actual nitrating agent is in a much lower
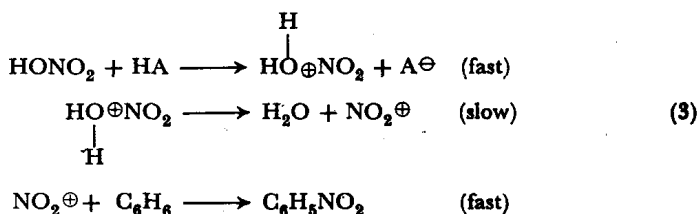
TABLE 1. Isomer distribution and relative rate for nitration with nitronium fluoroborate, mixed acid, and protonated acetyl nitrate[16].

		$NO_2BF_4(25°)/$ Sulfolane	$HNO_3/$ $H_2SO_4(25°)$	$HNO_3/Ac_2O(0°)$
o-Xylene	% 3 (o and m)	79.7[16a]	55[16c]	33[16d]
	% 4 (p and m)	20.3	45	67
	k_{Ar}/k_B	1.75[16b]	1.02[16c]	—
Biphenyl	% 2	75[16b]	37[16e] (35–40°)	68[16f](58[16g], 53°)
	% 4	23.8	63	32 (42, 53°)
	k_{Ar}/k_B	2.08[16b]	—	16[16f]
Toluene	% 2	65.4[16a]	56.4[16c]	61.4[16h]
	% 4	31.8	38.8	37.0
	k_{Ar}/k_B	1.67[16b]	1.24[16c]	27
Chlorobenzene	% 2	22.7[16a]	30[16i]	10[16j]
	% 4	76.6	70	90
	k_{Ar}/k_B	0.14[16a]	—	0.033[16k]
Acetanilide	% 2	—	19[16i]	68[16l](20°)
	% 4	—	79(20°)	30(20°)
Anisole	% 2	69[16m]	31[16n]	71[16o]
	% 4	31	67	28

energy state and the rate-controlling transition resembles the σ-complex. Figure 1 gives a pictorial representation of this concept.

Isomer distribution in the products is also quite different depending on the nitrating medium. This positional selectivity of various nitrating media is quite obvious in the nitration of o-xylene but only slightly evident in the nitration of toluene. The relatively invariant isomer distribution in the nitration of toluene is often quoted[17] as evidence for a single active nitrating entity, the nitronium ion. However, this insensitivity of toluene is general for all electrophilic substitutions and is characteristic of all monoalkylated benzenes. Knowles, Norman, and Radda[18] ascribed this insensitivity of toluene to the low polarizability of an alkyl group to the electron demands of an electrophilic reagent. Therefore, the fact that toluene always gives ca. 60 % o-nitrotoluene with varied nitrating agents is irrelevant.

Kinetic evidence for the nitronium ion as the active nitrating agent comes from the nitration of alkylbenzenes with nitric acid in either acetic acid or nitromethane. In an excess of nitric acid the rate is zero order, catalyzed by strong mineral acid and retarded by added nitrate ion without altering the zero order of the reaction. This finding was interpreted[19] as showing that the slow step in the reaction was formation of the nitronium ion (equation 3).

$$HONO_2 + HA \longrightarrow H\overset{H}{\underset{}{O}}\oplus NO_2 + A^\ominus \quad \text{(fast)}$$

$$HO\oplus NO_2 \longrightarrow H_2O + NO_2{}^\oplus \quad \text{(slow)} \qquad (3)$$
$$\underset{H}{|}$$

$$NO_2{}^\oplus + C_6H_6 \longrightarrow C_6H_5NO_2 \quad \text{(fast)}$$

Identical kinetic behavior would be observed also if the nitra-cidium ion, $H_2O\oplus NO_2$, reacted with acetic acid to produce protonated acetyl nitrate (equation 4).

$$H_2ONO_2{}^\oplus + CH_3-C\overset{O}{\underset{OH}{\big\langle}} \longrightarrow CH_3-C\overset{O-NO_2}{\underset{O-H \atop \oplus}{\big\langle}} + H_2O \quad \text{(slow)} \qquad (4)$$
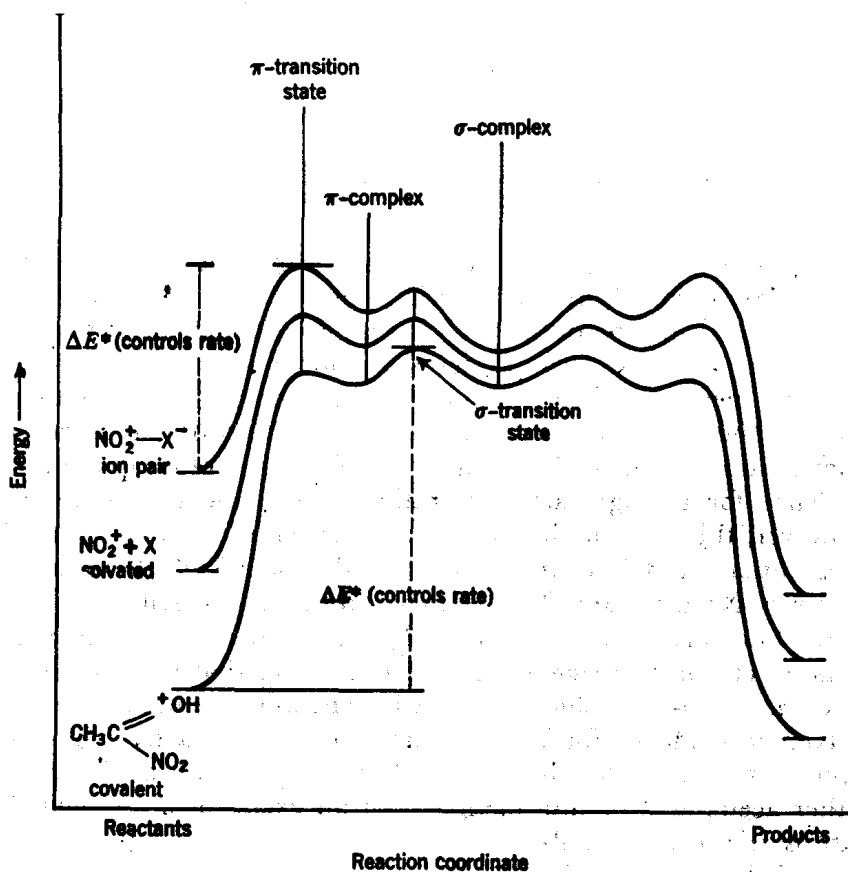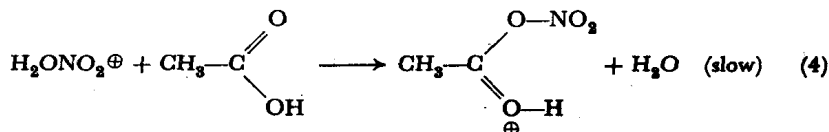

FIGURE 1. Effect of changing nitrating species on the rate-controlling transition state.