SKELETAL REARRANGEMENTS INDUCED BY CHEMICAL IONIZATION—I

ANALOGY TO SOLVOLYSIS†

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Abstract—In contrast to the usual expectation in chemical ionization (CI) mass spectrometry, the CI spectra of a series of aryl 4-nitro-Δ'-cyclohexenes show very low intensity protonated molecular ions while a major share of the ion current is carried by rearrangement ions. The intervention of a rearrangement long known in the solvolysis of cyclohexenyl carbenium ions can account for the observed CI behaviour.

The analytical value of chemical ionization mass spectrometry[1] derives from the usual observation of simple spectra dominated by the intensity of the protonated molecular ion $(M+1)^+$. This expectation is dramatically breached in the CI spectra of a series of aryl substituted nitrocyclohexenes reported herein. Our observations are exemplified by the isobutane CI spectrum of 3,5,6-triphenyl-4-nitrocyclohexene which exhibits an $[M+1]^+$ ion carrying only 0.4% of the total ionization above m/z 90 $(\%\Sigma_{90})$ while the base peak in the spectrum which carries $30\%\Sigma_{90}$ is a rearrangement ion composed of two of the phenyl groups and a methine carbon $[(C_6H_5)_2CH]^+$.

Skeletal rearrangement processes which are common in electron ionization mass spectra[2] are of less frequent occurrence in chemical ionization mass spectra. In the literature there are only a limited number of skeletal rearrangements reported under CI conditions.[1,3] One reason for these differential observations is the driving force pushing the odd electron ions, formed on EI, to fragment so as to separate the radical from the charge. Thus prior rearrangement within the molecular cation radical will be revealed when it falls apart. This driving force is absent in the commonly encountered protonated and hence even electron ions encountered in CI sources. Although the $[M+1]^+$ ion may be extensively rearranged this will remain hidden in the absence of fragmentation.

Of great importance is the opportunity these revealed rearrangements give to elucidating the overlap between carbenium ion chemistry in solution and in mass spectrometers.[3] In the former situation the details of molecular reorganization

can be monitored via NMR spectrometry whereas in the mass spectrometer we are constrained to product analysis. In the case herein we shall see that the interesting extrusion of a single carbon bearing hydrogen and two aryl groups from the protonated triarylnitrocyclohexenes can be reasonably connected to the long known contraction of 6- to 5-membered ring carbenium ions.[4]

Moreover we have previously studied the EI behaviour of this class of aryl nitrocyclohexenes[5] and the present study acts to complete this picture for the behaviour of these materials in mass spectrometers subject to differential ionization mechanisms.

The compounds under discussion are exhibited in Scheme 1.

EXPERIMENTAL

Preparation of the compounds. The di- and trisubstituted nitro-cyclohexenes were prepared by well described procedures.[6,7] The *exo* and *endo* adducts formed were carefully separated on silica gel by chromatographic techniques. Structure and stereochemistry were assigned from spectral data. All the NMR spectra were recorded on a Varian T-60 instrument.

Scanning of the Samples.[8] CI spectra of all the compounds were recorded on Finnigan Mass Spectrometer 3200, using methane and isobutane as reactant gases, the pressure of which was maintained at 1 torr. The temp of ionization chamber was between 140° to 214°.

RESULTS AND DISCUSSION

Table I exhibits the percentage of total ionization above m/z 90 for the outstanding ions in the CI spectra of the compounds listed in Scheme 1. A heuristic scheme, which must await further evidence for confirmation, (from low temperature
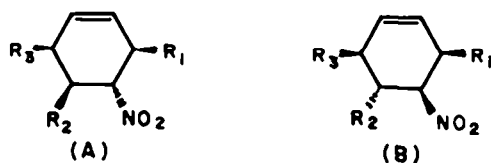
(1)	$R_1 = R_3 =$ phenyl; $R_2 =$ H	Isomer A
(2)	$R_1 = R_3 =$ phenyl; $R_2 =$ H	Isomer B
(3)	$R_1 = R_2 = R_3 =$ phenyl	Isomer A
(4)	$R_1 = R_2 = R_3 =$ phenyl	Isomer B
(5)	$R_1 = R_3 =$ phenyl; $R_2 = -C_6H_4-CH_3(P)$	Isomer A
(6)	$R_1 = R_3 =$ phenyl; $R_2 = -C_6H_4-CH_3(P)$	Isomer B
(7)	$R_1 = R_3 =$ phenyl; $R_2 = -C_6H_4-Cl(P)$	Isomer A
(8)	$R_1 = R_3 =$ phenyl; $R_2 = -C_6H_4-Cl(P)$	Isomer B
(9)	$R_1 = R_3 =$ phenyl; $R_2 = -C_6H_4-F(P)$	Isomer A
(10)	$R_1 = R_3 =$ phenyl; $R_2 = -C_6H_4-F(P)$	Isomer B
(11)	$R_1 = R_3 =$ phenyl; $R_2 = -C_6H_4-Br(P)$	Isomer A
(12)	$R_1 = R_3 =$ phenyl; $R_2 = -C_6H_4-Br(P)$	Isomer B
(13)	$R_1 = R_3 =$ phenyl; $R_2 = 2-$Furyl	Isomer A
(14)	$R_1 = R_3 =$ phenyl; $R_2 = 2-$Furyl	Isomer B
(15)	$R_1 = R_3 =$ phenyl; $R_2 = 2-$Thienyl	Isomer A
(16)	$R_1 = R_3 =$ phenyl; $R_2 = C_6H_4-CN(P)$	Isomer A

Scheme 1.

NMR and solvolytic studies) would reasonably involve the initial protonation at the nitro group[9] so as to give loss of HNO_2. The loss of HNO_2 to lead to the carbenium ion might also be aided by the adjacent phenyl group[10] or by solvolytically precedented[11] participation of the homoallylic double bond. Thus the observation of a low intensity $(M + H)^+$ ion is reasonable and not of exceptional note. The loss of the phenyl or aryl groups plus one hydrogen and the protonated diene product of the retro-Diels-Alder reaction can reasonably be ascribed to alternative protonation by the ionized reagent gas on the phenyl or aryl groups or the ring double bond. Protonation at various sites in multifunctional molecules can be expected.[12] The key and striking observation in these molecules is the abundant (Table I) extrusion of the charged fragments $[CHR_2R_3]^+$, $[CHR_1R_2]^+$ and $[CHR_1R_3]^+$. It is difficult to understand how the substituted cyclohexene structure could yield such ions. It is certainly safe to conclude that an extensive rearrangement has occurred. As outlined below, a reasonable solution to this apparent conundrum may be found in the literature of cyclohexenyl carbenium ions.

Deno and Houser first reported on the basis of NMR data the opening of bicyclic alcohols to cyclohexenyl cations which then undergo ring contraction to cyclopentenyl ions.[13] Sorenson et al.[14] have reported that cyclopropyl allyl cations rearrange to cyclohexenyl cations which then rearrange further to cyclopentenyl cations. These workers have also shown that this carbocation system undergoes a series of degenerative rearrangements which scramble the ring positions[15]. Olah et al.[11,16] in their

studies of carbocations in super acid systems have observed that many substituted cyclohexenyl cations undergo ring contraction to form the substituted cyclopentenyl cations. Among these, generation of methyl cyclopentenyl cation from cyclohex-3-enol[11] in super acid provides a key analog for the present system. In related work when 2-phenyl cyclohexylamine and 2,3 dimethyl-6-phenyl-cyclohexylamine were treated with nitrous acid the corresponding ring contracted alcohols have been obtained in good yields.[17] Further research in this area has led to details of the scrambling mechanisms available in these ions.[18]

The research outlined above suggests the possibility of ring contraction in the $[M + H - HNO_2]^+$ ion produced in the CI of compounds 1–16 (Scheme 1). As part of the work reported in solution and discussed above the cyclohexenyl cation with positive charge at the β-position has been discussed. Scheme 2 outlines some of the possible directions this ion would take based on these NMR studies.[11,13-16,18]

The interconnections exhibited in Scheme 2 constitute an extremely complex kinetic system which has been studied in part by many workers and in which the individual rates and equilibria are strongly dependent on the substitution pattern of the cyclohexenyl cation precursor. These studies have for the most part been conducted in strong acid media at low temperatures, e.g. $< -50°$. Although temperature has a strong effect on these interconversions, the ring contraction is observed at the highest temperatures reported.[18] There is no reason to doubt that these rearrangements outlined

Known Intermediates From Cyclohexenyl Cations[*]
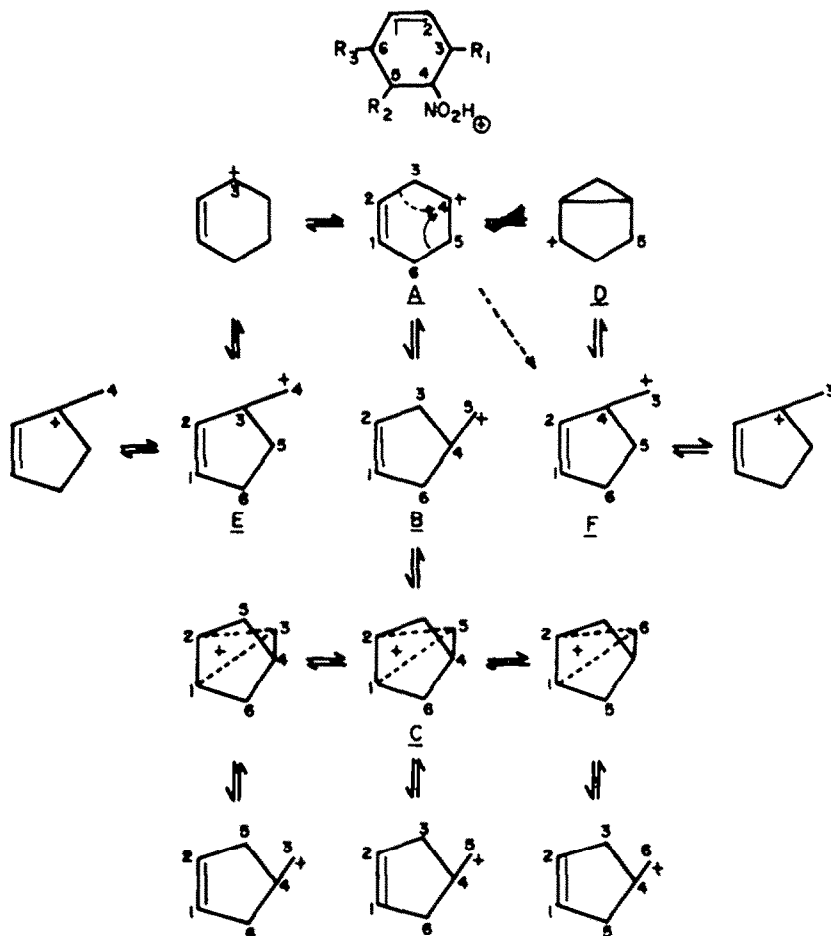
Scheme 2

[*] Only carbon skeleton shown. In addition the NMR research work shows the intervention of hydride transfers which would yield further rearrangements within each carbon skeleton.[11,13-16,18]

in Scheme 2 would be easily accessible to the cyclohexenyl cation generated by loss of HNO_2 from compounds 1–16 (Scheme 1) in the CI source of a mass spectrometer.

We are now offered an explanation for the expulsion rearrangement loss of $[CHRR]^+$ (Table I). Ring contraction from the initially produced cyclohexenyl cation could cast one carbon out of, although for the moment still attached to, the cycle. Before addressing the question as to how this now distinguished carbon may be ejected from the newly formed cyclopentenyl cation let us discuss the contraction step further. The initial precursor A (Scheme 2) can only push out either $C_5(B)$ or $C_3(F)$.

This might very well explain the observed fact (Table I) that the expelled group in all cases overwhelmingly contains R_2. Nevertheless either via intermediate C (Scheme 2) and/or by double bond participation to D (Scheme 2) C-3 and C-6 may occupy the expelled position. This longer route places R_1 and R_3 on the C to be ejected. The ion $[CHR_1R_3]^+$ is also encountered although with lower intensity. The CI results are not contradicted by expectations based on the known NMR intermediates (Scheme 2).

In the NMR studies discussed above, it was found that the ring contracted ion, e.g., E (Scheme 2) rapidly transfers hydride from C-3 to C-4 so as
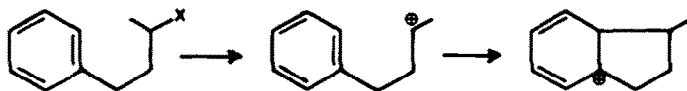
Scheme 3[*]

[*] See ref. 19 and references therein.

Mechanistic Hypothesis
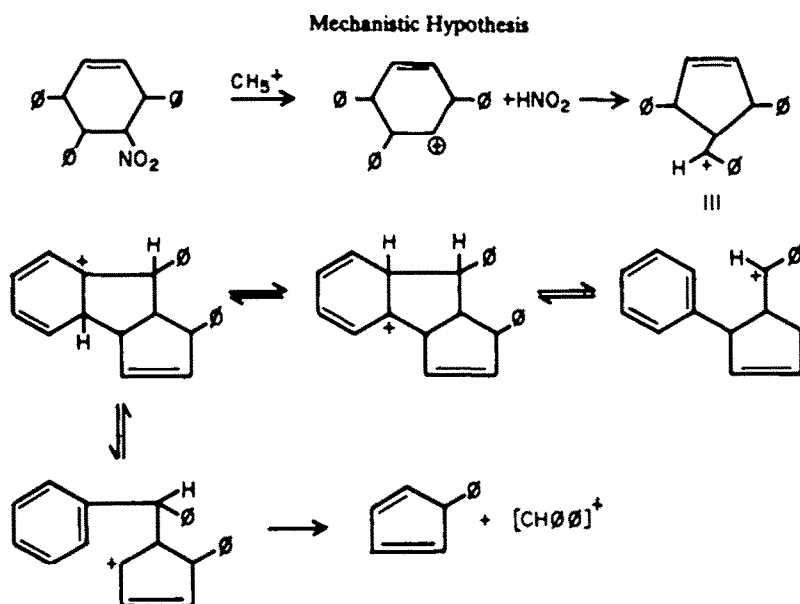
Scheme 4

to place the charge within the ring. A large body of evidence on intramolecular Friedel-Crafts alkylations and acylations[19] shows that the process depicted in Scheme 3 is rapid. Carbocations located so as to close the 5-membered ring are favourable. This is precisely the situation in the molecules discussed here (Scheme 1; Table I) and moreover such an intervention hypothesis could reasonably lead to the CI observed diarylmethinyl cation (Table I). This hypothesis leads to an overall mechanism which is outlined for compound 3 (Scheme 1) in Scheme 4.

The proposal in Scheme 4 is supported by: analogy to known solution carbocation chemistry; the expulsion of diarylmethinyl cations predominantly containing R_2 aryl groups of widely varying structure; a strong stereochemical dependence. The latter two observations would be difficult to understand if more random and extensive rearrangements were occurring prior to fragmentation.

The present study indicates that the substituted cyclohexenyl cation undergoes the same type of rearrangements under solvolytic conditions and in the CI source.

Table I[a] Partial spectrum expressed as percent of total ionization above m/z 90 for compounds 1-16

Cmp. No.	Reagent Gas[b]	$[M+H]^+$	$[(M+H)-(HNO_2)]^+$	$[(M+H)-(HNO_2)-(R_3H)]^+$ and/or $(R_1H)]^+$	$(R_2H)]^+$	Retro-Diels Alder[c] Diene ion	Protonated Diene	$[CHR_1R_2]^+$ and/or $[CHR_2R_3]^+$	$[CHR_1R_3]^+$
1	I	1.3	52	2.0	—			—	5.4
2	I	12	37	1.4	—			—	3.4
3	I	<.5	21	13[d]	—	1.2	.39	30	—
4	I	<.5	21	27[d]	—	3.5	2.4	17	—
5	I	<.5	29	2.7	6.2	2.3	.76	25	1.9
6	I	<.5	30	1.2	26	3.9	2.7	10.5	.78
7	I	<.5	18	3.2	14	2.0	.75	19	4.8
8	I	<.5	15	1.4	27	4.2	4.2	8.4	1.8
9	M	<.1	15	4.2	5.4	3.5	1.6	15	4.5
10	M	<.1	21	3.0	8.0	4.7	3.0	14	3.0
11	M	<.1	14	1.9	4.4	4.4	1.9	12	3.0
12	M	<.1	10	2.1	4.6	13	4.6	6.7	1.5
13	I	3.0	8.9	.6	2.2	4.5	1.2	11.4	1.2
14	I	7.5	15	<.5	9.6	4.4	4.4	9.2	<.5
15	M	1.3	13	<.5	8.5	8.5	3.1	21	1.8
16	M	5.3	7.3	1.7	1.0	2.0	.66	5.3	1.3

[a] Refer to Scheme 1, for the structures corresponding to the CMP.NO. here and the aryl groups designated by R_1, R_2 and R_3.
[b] I is isobutane and M is methane
[c] Comprising 1,4 substituted (R_1 and R_3) butadiene
[d] In these compounds $R_1 = R_2 = R_3 = $ phenyl(R). Hence it is denoted as $[(M+H)-(HNO_2)-(RH)]^+$.

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[8] In addition, the EI spectra were recorded for all materials in Scheme 1. The results support our earlier published observations.[5] We have in the course of this, recorded the normal metastable ions at 70 eV and determined the MIKE spectra for the $[M—NO]^+$ and $[M—HNO_2]^+$ ions from compound **3** in Scheme 1. These data and discussion may be found in: G. Sudhakar Reddy, Ph.D. Thesis, in preparation, National Chemical Laboratory, Poona, India (1979). This work will form the basis of a future publication.

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