Unusual Mass Spectrometric Fragmentation of *N,N'*-Diethyl-*N,N'*-diphenylurea

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The electron impact mass spectrum of *N,N'*-diethyl-*N,N'*-diphenylurea contains the ion m/z 164 which is of low abundance at normal energy of ionizing electrons but prominent at 15–20 eV. The mechanism of its formation has been revealed by means of labelled compounds. It is rationalized in terms of an unusual formation of styrene lost as a neutral molecule.

INTRODUCTION

The mass spectral fragmentation of alkyl-, aryl- and alkylarylureas has been reported several times.[1–5] Their mass spectra were quoted as 'an almost copybook example of simple fragmentation',[1] because the predominant part of the fragment ions corresponds to the cleavage α to the carbonyl group and to a simple transfer of hydrogen. This holds also for 75 eV spectra of Centralite I compounds, i.e. *N,N'*-diethyl-*N,N'*-diphenylurea (**1**) and its nitro derivatives. However, in addition a less prominent peak at m/z 164, ions *a* (erroneously assigned as m/z 165[2]), was observed in the spectra of all samples of **1**. This peak with the elemental composition $C_9H_{12}N_2O$ cannot even partly be ascribed to an impurity such as *N*-ethylphenylurea, because the purification by crystallization, chromatography and chemical means (treatment with nitrous acid and with *p*-toluenesulfonyl chloride) did not change its relative abundance. However, ion *a* which is normally of low abundance becomes the base peak of the spectrum when the energy of the ionizing electrons is decreased to about 13–15 eV. Its formation has no analogy to other derivatives of urea and is the subject of this study.

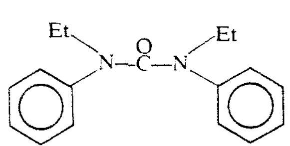
The formation of *a* corresponds to loss of a neutral particle(s) with the overall composition C_8H_8 and it requires the transfer of two hydrogens. The transfer can proceed in two or more steps, with the elimination of one or more neutral particles, but if there are any intermediates their abundance in the mass spectra is very low (Fig. 1 (a and b)). The single metastable transition reveals that the decay of the ionized molecules or their isomers is the only rate-determining reaction leading to ion *a*: m^*/z 100.3 (calc. 100.42); 1st field free region, $V/V_0 = 1.64$ (calc. 1.634).

A series of reactions leading to *a* may be suggested. Those which formally begin with the transfer of one hydrogen from the methyl group to the carbonyl oxygen or to the opposite nitrogen, and differ mutually in the origin of the second hydrogen were considered the most probable. To study the mass spectral fragmentation, the ureas labelled with deuterium on both phenyls (**1a**), in the methyl groups of both ethyls (**1b**), and unsymmetrically labelled in the methylene group on one nitrogen and in the phenyl on the other nitrogen (**1c**) were prepared.

RESULTS AND DISCUSSION

The spectra of the deuterium labelled ureas (**1a**–**1c**) are shown in Fig. 2(a–c). The abundances of ions relevant to the elucidation of the fragmentation mechanism leading to ions *a* are presented in Table 1. The fragmentation is unfavourably influenced by the rather large isotope effects (frequently observed in competitive reactions of low critical energy); nevertheless, the results are unambiguous.

With the urea labelled on both phenyls (**1a**) the ion *a* retains three deuterium atoms so that the three remaining deuterium atoms are neatly lost with the leaving phenyl group (mean labelling degrees: $\alpha_{M,d_n} =$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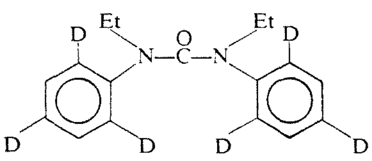
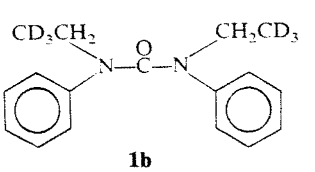

1a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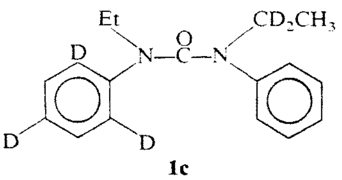
1c

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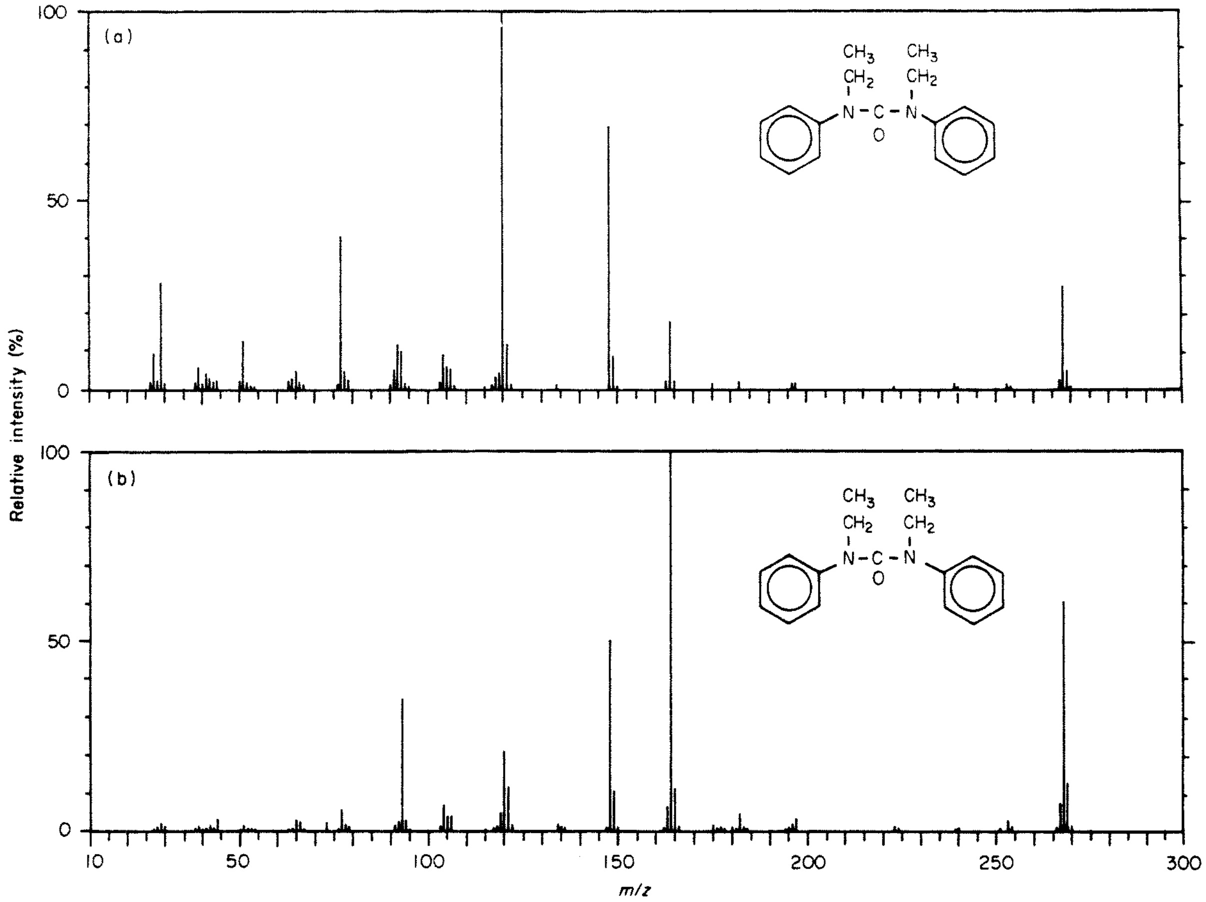


Figure 1. Mass spectra of *N,N'*-diphenyl-*N,N'*-diethylurea (**1**) determined at (a) 75 eV; (b) 15 eV.

93.5%; $\alpha_{a,d_3} = 92.7\%$); thus, mechanisms suggesting the loss of a benzyne molecule are excluded.

With the urea labelled on both methyls (**1b**) just one deuterium is transferred from the methyl group before the elimination of the neutral part in the formation of *a* so that *a* generated from **1b** contains four deuterium atoms ($\alpha_{M,d_6} = 97.9\%$; $\alpha_{a,d_4} = 94.3\%$). Therefore the second hydrogen originates from the methylene group. This is confirmed by the behaviour of the unsymmetrically labelled urea **1c**. Here ion *a* is formed in two ways differing in the number of the deuterium atoms: in one way mostly unlabelled vinyl and phenyl are eliminated; the second way is characterized by the loss of approximately four deuterium atoms, three belonging to the phenyl group in analogy to **1a**, and one deuterium, as expected, to the loss from the methylene in the ethyl on the opposite nitrogen ($\alpha_{M,d_5} = 99.1\%$; $\alpha_{a,d_5} = 94.4\%$; $\alpha_{a,d} = 76.4\%$). (7.7% of ions *a* contain two deuterium atoms; these have not been taken into account.) The ratio of abundances of ions originating in both ways is nearly 3:1 in favour of the former, indicating a large isotope effect (see below).

The retention of deuterium atoms reveals a high degree of regiospecificity in hydrogen transfers. All observed data can be summarized by the mechanism shown in Scheme 1. The decomposition starts with the transfer of one hydrogen from a methyl group and the other one from the methylene of the same ethyl group. During these transfers a reorganization takes place in which the newly formed vinyl group gains a bonding interaction with the phenyl on the opposite nitrogen and joins with it to form a styrene molecule, which is lost as a neutral particle; the ionization energy of styrene[6] is by *c*. 0.2 eV higher than the ionization energy of *N*-phenyl-*N'*-ethylurea, 8.25 eV.[3] If the hydrogen accessibility of O, N and N' is comparable, then the tautomer with the lowest ionization energy is probably formed, so that the presence of ionized styrene, $[C_7H_8]^{+\cdot}$, would not be expected. In the assignment of this mechanism, it was supposed (1) that both hydrogens are transferred from the same ethyl group so that it changes to a vinyl group, and (2) that the vinyl and phenyl combine to form styrene. The first assumption seems to be substantiated by the simplicity of the mechanism (in the comparison with the complexity of the concept that methylene as a source of the second hydrogen belongs to the other ethyl). The second assumption deserves a comment. The formation of separate vinyl and phenyl radicals is excluded by energetic considerations, but the way in which the $C_{(\alpha)}$ of an ethyl group interacts with the phenyl group on the opposite part of the molecule is not yet clear. Analogous interactions in *N*-phenyl-*N'*-alkylureas have been discussed earlier.[7] In solutions of analogous thioureas, the barriers of internal rotation of the dimethylamino group reflect the equilibrium of two conformers: in one the methyl is situated above the plane of the opposite phenyl ring.[7] A similar conformation and a donation of lone pair electrons of the alkylated nitrogen to the ionized anilino system was suggested for the interpretation of ionization energies of *N*-phenyl-*N'*-alkylureas.[3] Possibly, the

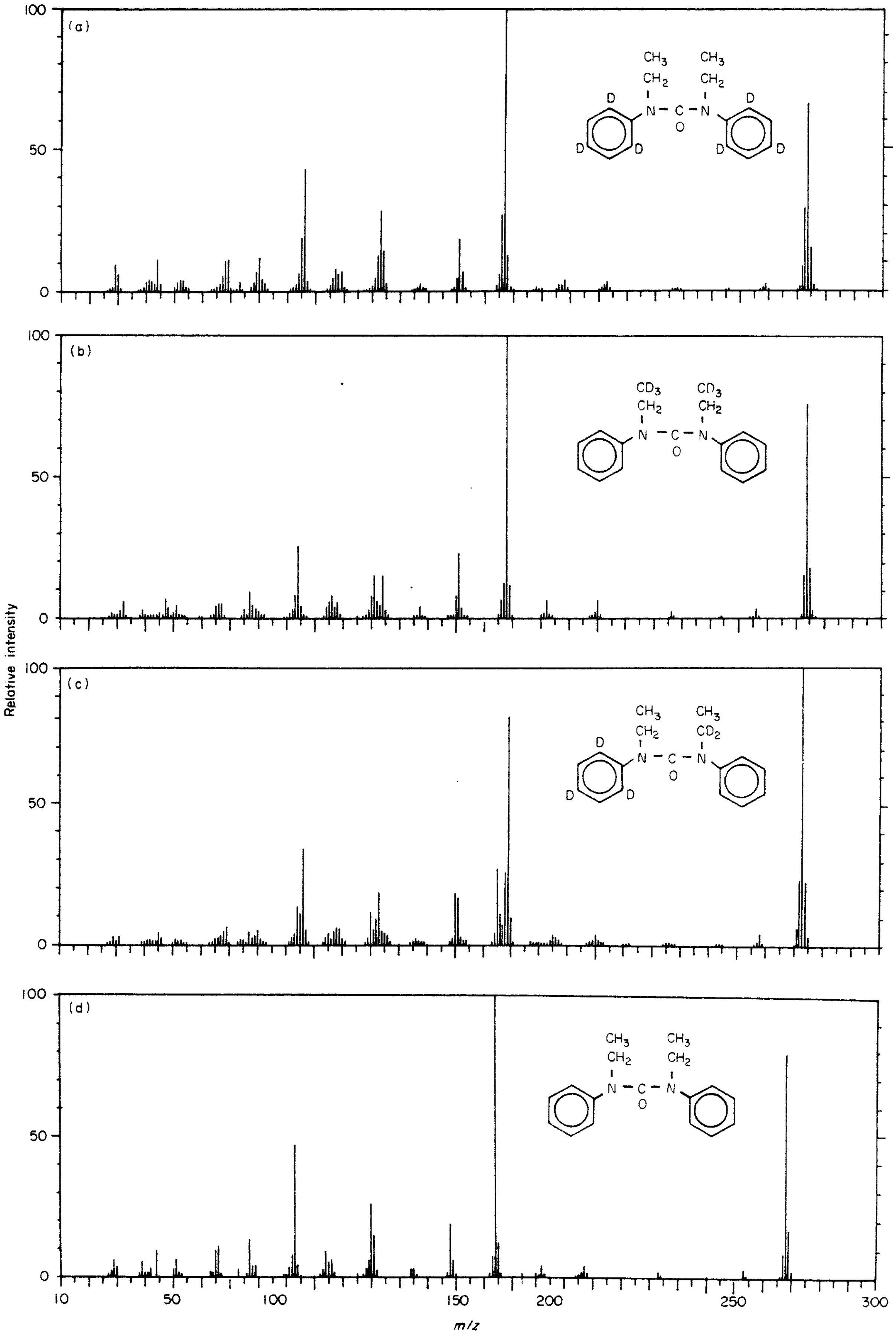
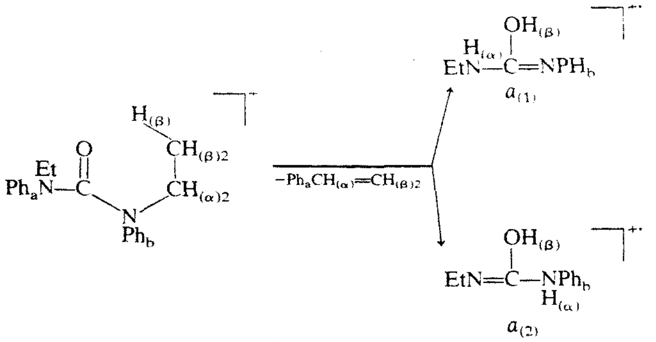


Figure 2. Mass spectra of labelled and unlabelled ureas: (a) **1a**; (b) **1b**; (c) **1c**; (d) **1**: 14 eV ionizing electron energy.

Table 1. Normalized intensities of ions *a* and of molecular ions[a]

m/z Compound	162	163	164	165	166	167	168	169	170	171	266	267	268	269	270	271	272	273	274	275	276
1	0.6	6.5	92.7	0.2							0.6	9.6	88.9	0.5	0.3						
1a			1.0	3.3	19.8	73.8	1.8	0.3								1.7	8.4	26.5	60.6	2.8	
1b				0.9	5.3	9.8	82.9	1.0								0.2	1.4	17.5	77.9	2.2	0.8
1c			2.9	18.8	4.5	3.9	17.1	52.3	0.5							4.2	17.2	73.8	2.8	2.0	

[a] Values, in percentages, were corrected for the neutral abundance of ^{13}C and ^{15}N.



Scheme 1

alignment of $C_{(\alpha)}$ with the opposite phenyl group is further facilitated by the transfer of hydrogen, e.g. by the McLafferty transfer from the methyl to the oxygen.

If only statistical factors were involved in the transfer of hydrogens, the abundances of ions *a* labelled with five deuterium atoms and those labelled with one deuterium atom should be equal. The observed ratio of abundances is nearly 3:1 in favour of a-d_5. This large isotope effect can be anticipated. It can be connected with the primary and secondary isotope effect of the methylene group labelled by two deuterium atoms and also by the secondary effect of the labelled phenyl-d_3 in recombination with the labelled vinyl group.

The distinction between the two tautomeric forms a_1 and a_2 (Scheme 1) is not possible with the usual mass spectral techniques. The unusual mechanism explains why the C_8H_8 loss could not be observed in the mass spectral fragmentation of some compounds of lower complexity, e.g. with *N*-ethylbenzanilide. The mechanism is probably limited to the structurally very similar class of compounds, and was observed for example with 4-nitro- and 4,4′-dinitro derivatives of **1**. No analogous ions $[M-C_8H_8]^{+\cdot}$ were found in the spectra of *N,N′*-diethyl-*N,N′*-diphenylthiourea; this may be related to the observation that a different electronic ground state is formed in molecular ions of thioureas.[3]

EXPERIMENTAL

A JEOL MS D 100 double focusing mass spectrometer was used, with the source temperature about 160 °C. The samples were introduced using a direct insertion probe. Determinations of elemental composition were made with PFK as the internal reference, resolving power 8000. The degrees of deuterium labelling were determined using ionizing electrons of low energy. Ions $[M-1]^+$ have a lower abundance with *N*-ethylaniline than with **1**; therefore a better reproducibility and accuracy was achieved with anilines, and values for the degree of labelling of ureas **1a–1c** were obtained by the multiplication of the labelling degrees of the appropriate anilines presupposing no isotope effect in the synthesis. The metastable transitions in the 1st field free region were recorded by scanning the acceleration voltage from 1.5 to 3.5 kV; all metastable ions were also detected on a sector type single focusing spectrometer MCh 1303.

Preparation of compounds

The ureas were prepared from the appropriately labelled *N*-ethylanilines via condensation with thiophosgene and oxidation of the corresponding thioureas.[8] For the preparation of **1c**, the requisite unsymmetrically deuterated thiourea was synthesized by condensation[9] of *N*-ethyl[2,4,6-d_3]aniline-*N*-thiocarbamoylchloride with *N*-([1,1-d_2]ethyl)aniline which was prepared from acetanilide on reduction with $LiAlD_4$. Analogously, reduction of [acetyl-d_3]acetanilide with $LiAlH_4$ gave *N*-([2,2,2-d_3]ethyl)-aniline. *N*-Ethyl[2,4,6-d_3]aniline was prepared from *N*-ethylaniline by direct exchange with D_2O.[10]

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