Organic Mass Spectrometry, 1970, Vol. 3, pp. 1527 to 1533. Heyden & Son Limited. Printed in Northern Ireland

A CYCLIZATION REACTION IN THE ELECTRON-IMPACT INDUCED FRAGMENTATION OF SOME *N*-PROPARGYLIC OXOQUINAZOLINES AND ANILINES

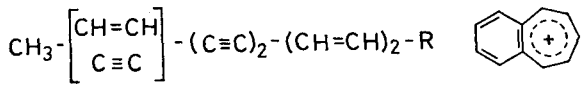
CONNY BOGENTOFT
Department of Organic Chemistry, Faculty of Pharmacy, Box 6804,
S-113 86 Stockholm, Sweden

(*Received* 22 *April* 1970; *accepted* 5 *May* 1970)

Abstract—Evidence for an acetylenic rearrangement, involving the ring-closure of ions containing the *N*-propargylaniline substructure to the corresponding quinoline ions, has been obtained in a study of the electron-impact induced fragmentation of 1,4-dihydro-4-oxo-2-phenyl-1-propargylquinazoline (I) and 1,2,3,4-tetrahydro-2-oxo-3-phenyl-1-propargylquinazoline (II). The *N*-propargylaniline moiety is formed from compounds I and II through the RDA process. *N*-Methyl-*N*-propargylaniline (III), which was examined as a model compound, was also found to undergo this rearrangement but *N*-methyl-*N*-propargyl-2,6-xylidine (IV), on the other hand, exhibits a quite different fragmentation pattern due to its blocking methyl groups, which prevent the rearrangement. Exact mass measurement and specific deuterium labelling were used to establish the fragmentation routes.

INTRODUCTION

CONTRADICTORY statements are found in the literature concerning the electron-impact induced rearrangement of acetylenic compounds.[1,2,3] According to Aplin and Safe,[1] compounds of type *a* undergo extensive rearrangement to give the $[C_{11}H_9]^+$ ion *b* as a major fragment. They also found that a related enynic C_7 alcohol afforded a $[C_7H_7]^+$ ion, commonly designated as the tropylium species. On the other hand, Bohlman and co-workers,[2] in their study on the spectra of several acetylenic compounds, assigned linear structures to both $[C_{11}H_9]^+$ and $[C_7H_7]^+$. In our investigation[4]

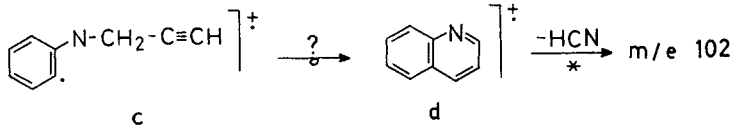


a b

of the mass spectrum of 1,2,3,4-tetrahydro-2,4-dioxo-1-propargyl-3-propylquinazoline, there were indications of an acetylenic rearrangement involving ring-closure of the *N*-propargylaniline moiety *c* to the quinoline ion *d*, which then loses HCN in the normal way (Scheme 1).

The rearrangement, which implies formation of a new carbon–carbon bond, could be formulated as an intramolecular aromatic substitution. Some related reactions have been listed in a recently published review.[5]

In order to test the proposed rearrangement and get further insight into its general validity, the mass spectra of compounds I and II, which easily generate the *N*-propargylaniline ion, have been examined in detail. The mass spectra of the models III and IV have also been recorded.



SCHEME 1.

DISCUSSION

1,4-*Dihydro-4-oxo-2-phenyl-1-propargylquinazoline* (I) *cf.* Fig. 1

The main fragmentation route of this type of compound has been shown[6] to occur *via* the RDA decomposition, in the present case leading to *m/e* 157 (*e*). Two distinct

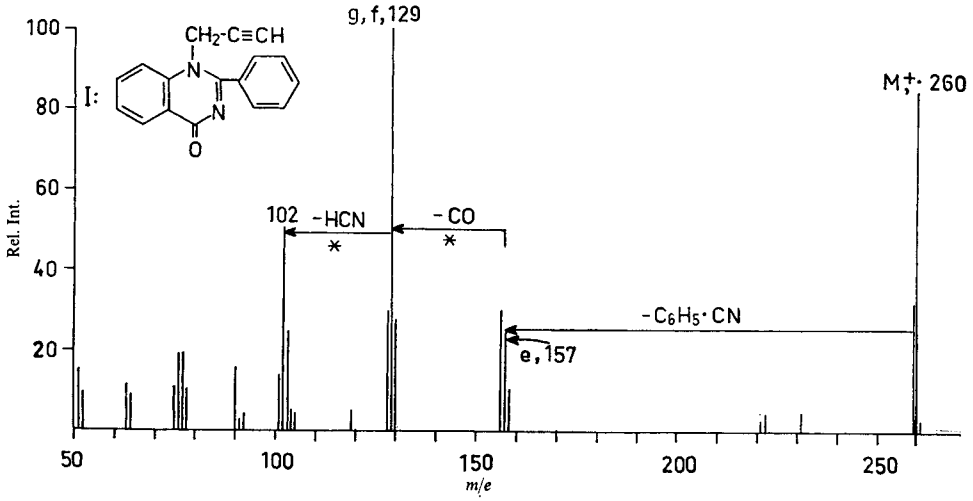
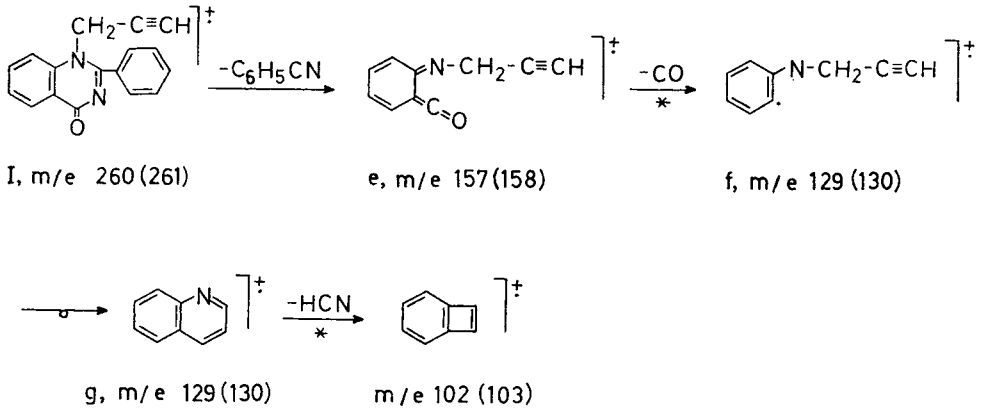


FIG. 1. Mass spectrum of 1,4-dihydro-4-oxo-2-phenyl-1-propargylquinazoline (I).

metastable ions, $157 \xrightarrow{*} 129$ and $129 \xrightarrow{*} 102$, indicate the further fragmentation pathway of species *e*. Deuterium labelling of the ethynic hydrogen of compound I proves this atom to be present in all the fragments obtained from I. (See Scheme 2, the figures within parenthesis referring to the corresponding peaks in the deuterated analogue of I.) High resolution measurement of *m/e* 102 reveals that the elemental composition of this ion is C_8H_8, which means that the 27 μ species lost from *m/e* 129 must be HCN. Consequently, the ion *f* must be involved in a rearrangement process with formation of a quinoline structure (*g*) before expulsion of an HCN molecule takes place, as outlined in Scheme 2.

1,2,3,4-*Tetrahydro-2-oxo-3-phenyl-1-propargylquinazoline* (II), *cf.* Fig. 2

The ion *m/e* 143 (*h*) (*cf.* Scheme 3) formed by an RDA reaction loses a hydrogen radical and then a 27 μ fragment, confirmed by the occurrence of appropriate metastable ions. The formed ion *m/e* 115 (*j*) corresponds to C_9H_8 as found by exact mass measurement. This process is analogous with that occurring in the fragmentation of compound I and means that the *m/e* 142 ion is represented by the quinoline structure *i*



SCHEME 2.

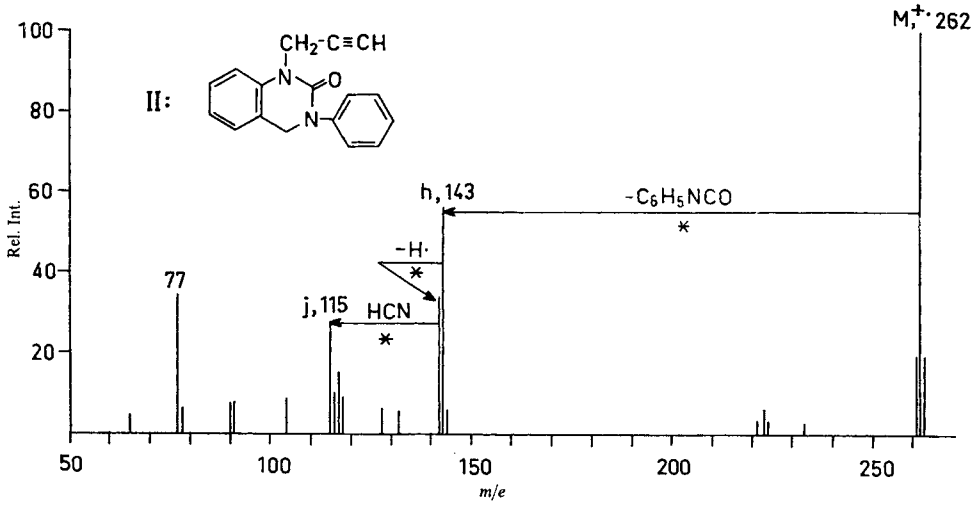
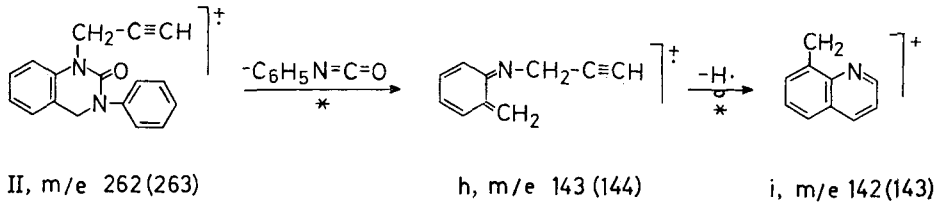


FIG. 2. Mass spectrum of 1,2,3,4-tetrahydro-2-oxo-3-phenyl-1-propargylquinazoline (II).

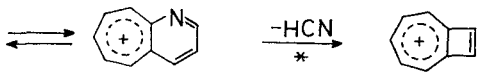
or the tropylium species *i'*, which then loses a molecule of HCN giving rise to *j*. It should be observed that the sequence outlined in Scheme 3 for compound II is almost identical with the fragmentation pattern found for 7-methylquinoline.[7] The figures within the parentheses refer to the corresponding peaks of the deuterated analogues 1,2,3,4-tetrahydro-2-oxo-3-phenyl-1-(3-d_1-propargyl)quinazoline and are in agreement with the break-down pattern depicted in Scheme 3.

N-Methyl-N-propargylaniline (III) *N-methyl-N-propargyl-2,6-xylidine* (IV)

In analogy with the results found for I and II, compound III should be able to rearrange to an *N*-methylquinolinium ion (*k*) by ejection of a hydrogen radical. It is apparent from Fig. 3 that the dominating feature in the spectrum of III is the intense $[M - 1]^+$ peak, indicating a very stable structure conveniently represented by structure *k*.



II, m/e 262(263) h, m/e 143(144) i, m/e 142(143)



i' j, m/e 115(116)

SCHEME 3.

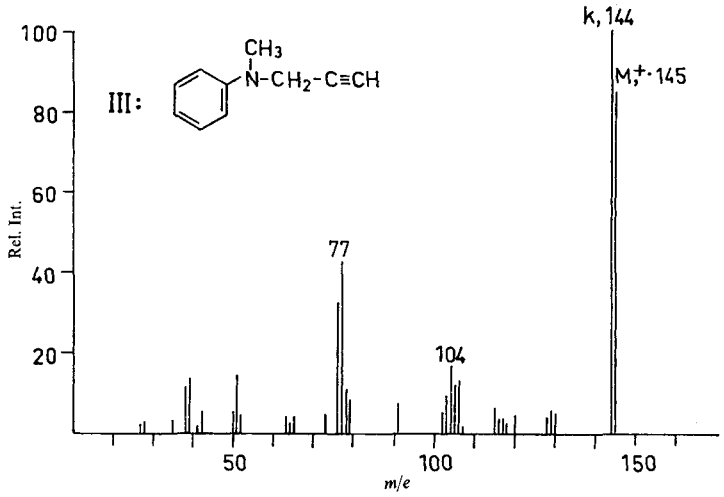
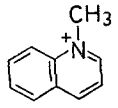


FIG. 3. Mass spectrum of *N*-methyl-*N*-propargylaniline (III).



k

To gain information on the origin of the hydrogen lost in the formation of the $[M]^{+\cdot}$ ion, the mass spectra of the deuterated analogues of III, *viz.* III:a and III:b were examined (*cf.* Fig. 5). The results support the proposed structure *k* and show that the hydrogens from the deuterated positions are not involved in the formation of the $[M - 1]^+$ ion. This indicates that the hydrogen lost stems from the ring.

Compound IV (*cf.* Fig. 4) exhibits a break-down pattern completely different from that of compound III. The $[M - 1]^+$ ion is of minor importance and the base

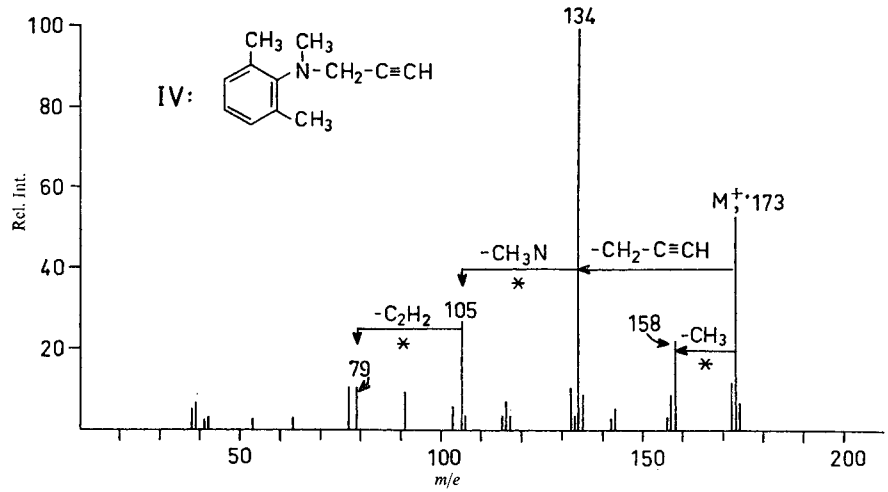


FIG. 4. Mass spectrum of *N*-methyl-*N*-propargylxylidine (IV).

peak *m/e* 134 is formed after N—C fission and loss of the propargylic chain. This type of cleavage is of much less significance for III. The corresponding peak in the spectrum of III, *m/e* 106, amounts to only 14% of the base peak.

CONCLUSIONS

In the present study of the mass spectra of the propargylic oxoquinazolines I and II, the results of deuterium labelling and high resolution measurements are accounted for by assuming an intramolecular aromatic cyclization, as outlined in Schemes 2 and 3.

Conclusive evidence for the mechanism proposed is given by the spectra of the models III and IV. These compounds display fragmentation modes completely different from each other due to the presence of methyl groups in both *ortho* positions of compound IV. In compound III, having free *ortho* positions, the cyclization is possible. The *ortho* methyl groups of IV, however, prevent the acetylenic chain from being attached to the benzene ring, resulting in a break-down pattern completely apart from that of the other compounds studied in the present work.

EXPERIMENTAL

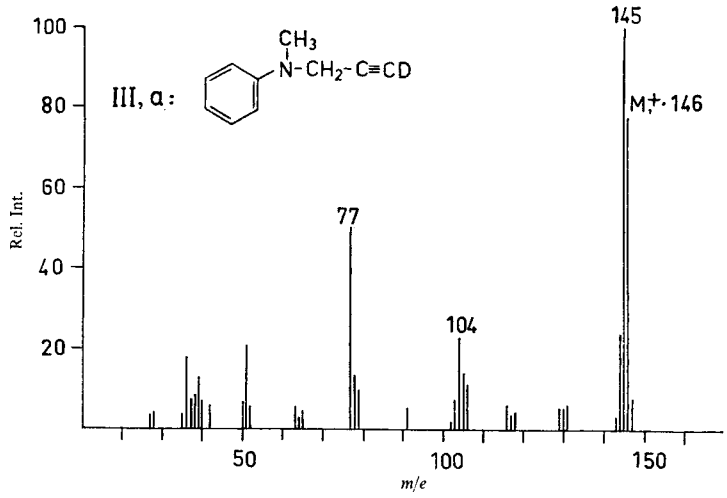
The mass spectra were recorded on an LKB 9000 mass spectrometer using a direct probe heated to a suitable temperature. The ionizing energy was maintained at 70 eV, the temperature of the ion source being kept at 270°C. Only peaks equal to or greater than 3% of the base peak are plotted in Figs. 1 to 5.

High resolution spectra were obtained using an Atlas SM 1 spectrometer. The results were within 3 ppm of the calculated values. All the compounds examined were chromatographically pure when checked by TLC.

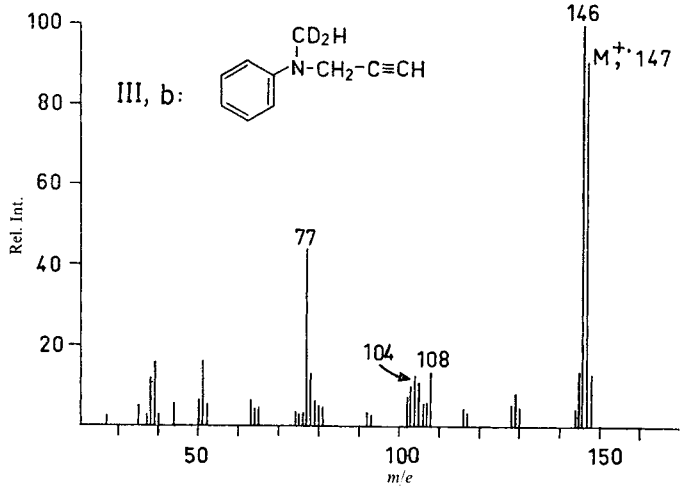
Deuterium labelling of compounds I and III was performed by recrystallization from deuterium oxide. The exchange was followed by examination of the IR spectra (Perkin–Elmer 337; KBr).

The preparation of compounds I and III have been described earlier.[8,9]

1,2,3,4-*Tetrahydro-2-oxo-3-phenyl-1-propargylquinazoline* (II). To a solution of 0·5 g of 1,2,3,4,-tetrahydro-2-oxo-3-phenylquinazoline[10] and 0·17 g of a sodium hydride preparation (50% in oil) in 30 ml of DMF was added 0·5 g of propargyl bromide. The mixture was heated to 50°C for 1 hr and then poured into 150 ml of water. The product was filtered off and recrystallized from light petroleum. Yield 59%. m.p. 101 to 102°C. Found: C, 78·3; H, 4·75; N, 10·59. $C_{17}H_{12}N_2O$ requires C, 78·4; H, 4·65; N, 10·76.



5(a)



5(b)

FIG. 5. Mass spectra of *N*-methyl-*N*-(3-d_1-propargyl)aniline (III : a) and N-d_2-methyl-*N*-propargylaniline (III : b).

N-Methyl-N-propargyl-2,6-xylidine (IV). A mixture of 5 g of *N*-methyl-2,6-xylidine, 2·6 ml of propargyl bromide and 11·8 g of sodium acetate in 100 ml of 60% aqueous methanol was refluxed for 4 hrs. The solution was extracted with 2 × 100 ml of ether and the solvent evaporated. The crude product was chromatographed on a silica gel column using chloroform/light petroleum 9 + 1. Yield 30%. m.p. (HCl) 155 to 157°C. Found: C, 68·3; H, 7·54; N, 6·83. $C_{12}H_{15}N$·HCl requires C, 68·3; H, 7·58; N, 6·65.

N-d_2-Methyl-N-propargylaniline (III:*b*). *N*-Formylaniline (1·0 g) was dissolved in 20 ml of ether and reduced with $LiAlD_4$ (0·4 g) at room temperature for 20 hrs. The mixture was hydrolyzed and the ether solution purified by passing over Al_2O_3. The *N*-(d_2-methyl)aniline obtained (0·6 g) was propargylated for 2 hrs and purified as described above for compound IV. Yield 20%. m.p. (HCl) 139 to 141°C. Lit.[9] m.p. (undeuterated): 142°C.

Acknowledgement—I am indebted to Dr Bengt Danielsson for his kind interest in this work and for valuable discussions. Acknowledgement is also made to Dr Ragnar Ryhage for running the spectra.

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