Reactivation of Acetylenic amine N-Oxide with Reactive Halides

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Study Reactions of acetylenic amine N-Oxide with reactive Halides

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Abstract: A new acetylenic amine derived from cyclic secondary amines such as piperidine were synthesized , these amine were oxidized with m-chloroper benzoic acid to the corresponding N-Oxides. The acetylenic amine and its oxide were investigated through the study of their physical and chemical properties ,spectral analysis (IR and UV) in addition to the micro analysis of the elements(C.H.N). Aqueous hydrochloric and hydrobromic acids ethanolic hydrogen chloride from the monomeric halides(II) of the amine oxide. dioxan solutions of hydrogen chloride, hydrogen bromide and hydrogen iodide or aqueous hydro iodic acid yield the dimiric hydrohalides(III).The monomeric hydrochloride and hydro bromide are converted to the dimiric hydro iodide (IV) by treated with sodium iodide. Reaction of the amine oxide which is readily split by picric acid. A mechanism for the formation of all complexes (II-V) as well as an explanation for the formation of all types of hydro halides were presented .

Keywords: Reactions ,acetylenic amine N-Oxide , reactive Halides

Introduction

Acetylenic amines are very important class of compounds for their pharmacological properties such as activity, low toxicity and easy to absorption from the body.

Moreover these compounds are electron rich and easy to bond with receptor protein(1) . some of their pharmaceutical uses as anticancer (2) and hypotensives agent(3).

In investigating the importance of acetylenic bond for pharmacological activity it was though possible that the electron rich acetylenic bond attaches itself to the positive binding site in the cholinergic receptor, in which case its presence is probably necessary for the effect(4).

N-Oxides are oxidations product of tertiary amines , they were found to exist as constituents of living matters. Recently, efforts have been devoid to study tertiary N-Oxide due to their natural occurrence in plant and animal tissues. They posed interesting problems as to the biochemistry and function of these compounds in biological systems(5). N-Oxides are more active than their corresponding tertiary amines. Hence several N-Oxides are important as pharmacological or toxicological agents(6).

Ultimately a vast number of tertiary amines drugs produces N-Oxides as metabolites or intermediates in drug metabolism(7). N-Oxides convert at the oxygen atom with a variety of electrophonic to give adducts which may be stable or react further according to the reagent and reagent and reaction conditions leads to the formation of complex compounds .

Materials and methods

A- Preparation of Tertiary amine N-Oxide:

General method for preparation acetylenic amine and their N-Oxide were prepared according to the literature (8). The full name and the physical properties of this compounds are listed in table (1). The ir bands position in cm-1 and uv/vis spectrum are shown in table (1).

B- Reaction of Acetylenic Amine N-Oxide with hydrogen Halids(9):

From a solution of (0.10 mole) of acetylenic amine N-Oxide (I) in 15 ml of concentrated hydrochloric acid , which was taken to dryness at diminished pressure over a steam bath , the mono hydrochloride (II) was obtained in 85% yield after recrystellization from acetone scheme (1).

Concentrated hydrobromic acid yielded the monomeric hydrobromide (II) by the same procedure. Concentrated hydroiodic acid yielded the dimeric hydroiode(III) by this procedure scheme (1). Treatment of an ethanolic solution of these hydrohalides with picric acid give the picrate of (I).

C- reaction of Acetylenic AmineN-Oxide with sodium Iodide:

To (0.03 mole) of sodium Acetylenic AmineN-Oxide (I) in (10) ml of acetone was added (4.5 gm) (0.03 mole) of sodium iodide in 25 ml of acetone. Yielding product (IV) .

D- Conversion of the Monomeric Hydrochloride and hydrobromide (II) to the Dimeric Hydroiodide (III):

To a solution of (0.02 mole) of the monohydrohalides (II) in (10 ml) of acetone was added (0.03 mole) of sodium iodide in (20 ml) of acetone. The solid product which separated immediately was filtered and washed with ethanol. This amounted to (1.08 gm) of sodium chloride and (1.91 gm) of sodium Bromide. From the filtrate was obtained (3.2 gm) (92%) of product which was shown to be identical to the dimeric hydroiodide(IV). Same analysis and infrared spectrum and no depression of its melting point in mixture.

Results and Discussion:

Scheme (1): Reactions Between N-Propargyl Pipredine N-Oxide and Reactive Halides

Reaction between (I) and the hydrogen halides or hydrohalic acids yields two types of products, the monomeric salts (II) and the dimeric compounds(III) in scheme(1). the particular interest is the fact that hydrogen iodide or hydroiodic acid forms only the dimeric hydroiodide (III) this is indicated by infrared spectra, which showed no free or associated hydroxyl groups. Instead, the broad band at 2970 cm-1, and the shape band at 1615 cm-1 . suggest an intermolecular chelate type of band between two amine oxide units. It is also significant that that the band at 2632 cm-1 and sharp band at 1605 cm-1. Thus ,it seems possible that the addition of a proton to the oxygen of a molecule of (LN→O) could yield a structure which under certain condition (discussed later) could lead to dimeraization to stability.

Further evidence for this intermolecular chelation was obtained from product (IV), which is formed from (LN→O) by treating with sodium iodide in acetone. In this compound the sodium ion replaces the proton in structure (III). This is indicated by the characteristic metallic chelate bands in its infrared spectrum at 2950, 1562, 1400 and 1387 cm-1. Again , the band at 1266 cm-1 , characteristic of the free nitrogen-oxygen linkage, is missing.

The dimeric hydroiodide is very stable; but the dimeric hydrobromide is less stable , and the dimeric hydrochloride is very unstable. The latter decomposes readily to the monomeric hydrochloride(II) on standing, on bending heated , or on crystallizing from polar solvent such as ethanol. The dimeric hydrochloride and hydrobromide will not form in aqueous solution. Dioxan solutions of these hydrogen halides give the best yields, on the other hand , both dioxin solutions of hydrogen iodide and aqueous hydro iodic acid give good yields of the stable dimeric hydroiodide.

The variation in stability of the intermolecular chelate bond in these dimeric hydrohalides suggests that there must be a significant difference in the electron density on the oxygen atoms of these compounds. This can be explained in terms of the electron donating power of the halide ion, which is either formed by the interaction of the hydrogen halide molecule with(I) in non-ionizing solvents or is already present in the aqueous hydroiodic acid reaction mixture. The ability to donate electrons decreases, of course, in the order, iodide ion, bromide ion, chloride ion. Thus, only the iodide ion seems capable of creating a sufficiently high electron density on the oxygen atom of the amine oxide to result in the formation of an intermolecular chelate bond that is stable in water or ethanol.

The reaction between (I) and methyl iodide in forming the nitrogen- methoxide type of linkage as shown in (V), yielded additional information concerning the nature of the nitrogen-oxygen bond. The ir spectrum of this ether shows a very strong band at 1215 cm-1 , which is in the range characteristic of aryl and unsaturated ethers and another band at 1050 cm-1 , typical of alkyle ethers is further evidence of the involvement of the oxygen in this linkage. However , the fact that treatment of (V) with an ethanolic solution of picric acid at room temperature yielded the picrate of (I) indicates that this linkage is much weaker than the usual ether linkage. The results of these experiments and the analysis of infrared spectra of the products that have been presented have been summarized in table (2).

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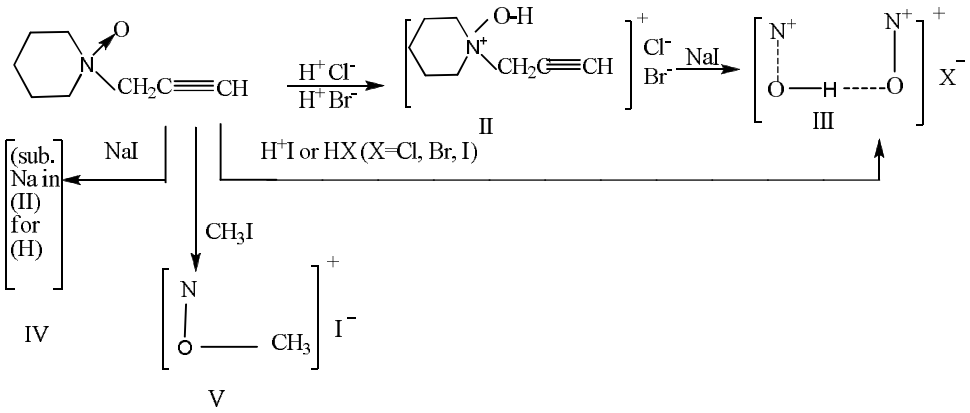


Scheme 1.

Table(1): physical properties of the ligand

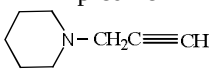
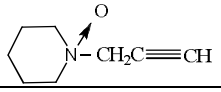
No.	Name and structure of compound	Yield %	colour	M.P °C picrate	Elemental analysis % found (% cal.)			Ir spectra cm^{-1}	Uv-Vis. nm
					C	H	N		
L	N-Propargyl Pipredine 	**90**	**Pale yellow**	**119-122**	**47.72 (47.69)**	**4.5 (4.45)**	**15.9 (15.87)**	**υ(ΞCH)3310,υ (CΞCH)2110, υ (CH)2960**	**314,386 In DMSO**
$L_{N\rightarrow O}$	N-Propargyl Pipredine N-Oxide 	**80**	**Pale yellow**	**137-138**	**45.65 (45.61)**	**4.43 (4039)**	**15.21 (15.17)**	**υ(ΞCH)3300,υ (CΞCH)2100,(CH)2960**	**289,382 In DMSO**

Table (2): The characteristic ir bands of the compounds

x	No.	υ(O-H) free cm-1	υ(N-O) cm-1	υ (O-H---O) cm-1
L	**Ia**	**-**	**965**	**-**
Br	**IIa**	**3600**	**920**	**-**
Cl	**IIb**	**3620**	**925**	**-**
I	**IIIa**	**-**	**935**	**3400**
Br	**IIIb**	**-**	**930**	**3400**
Cl	**IIIc**	**-**	**920**	**3400**
I	**IV**	**-**	**915**	**-**
I	**V**	**-**	**920**	**-**

دراسة تفاعلات الأمينات الاستلينية مع بعض الهاليدات الفعالة N- اوكسايد

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الخلاصة:

تضمن البحث تحضير الأمينات الاستلينية المشتقة من الامينات الثانوية الحلقية كالبيردين والتي تم أكسدتها بواسطة m-chloro per benzoic acid إلى الأوكسيد المقابل. تم تشخيص الأمينات الاستلينية واكاسبدها المحضرة بالطرق الفيزياوية والطيفية (الأشعة تحت الحمراء والأشعة فوق البنفسجية – المرئية) إضافة إلى التحليل الدقيق للعناصر (C.H.N). تم تحضير المحلول المائي والكحولي لحامض الهيدروكلوريك والهايدروبروميك من المونومر (II) للامين اوكسايد. محلول الديوكسان لكلوريد الهايدروجين وبروميد الهايدروجين ويوديد الهايدروجين والذي نتج عنه الدايمر الهاليد المائي (III). المونمرات للهايدروكلورايد والهايدرو بروماید تم تحويلها إلى دايمر الهايدرو ايوداید (IV) بمعاملتها مع يوديد الصوديوم . تم عزل اكاسيد الأمينات بشكل مشتق لحامض البكريك. ميكانيكية تكوين كل المعقدات (II-V) تم توضيحها بتكوين كل الأنواع من الهاليدات المائية .