Oxidation of Pyridine Carboxylic Acid Hydrazides with Active and Ordinary Manganese Dioxide

RASHID IQBAL AND FARNAZ MALIK
Department of Chemistry, Quaid-e-Azam University, Islamabad, Pakistan.

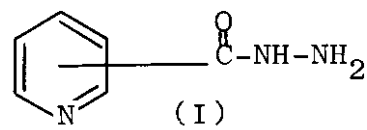
(Received Ist January, 1983)

Summary: Oxidation of the three isomeric pyridine carboxylic acid hydrazides with active mangnese dioxide in chloroform has been studied. The parallel reactions with ordinary manganese dioxide were also carried out. Pyridine-2-carboxylic acid hydrazide behaves differently than the other two isomers in these reactions.

Introduction

Active manganese dioxide has been effectively used for the oxidation of a variety of organic compounds including unsaturated alcohols[1], substituted analines [2], diamines[3], hydrazines [4] and hydrazones[5]. Kelly et.al. [6] reported the formation of carboxylic acids when hydrazides of peptides were oxidized with active manganese dioxide. Recently Haksar et.al.[7] reported that hydrazides of substituted salicylic acids on oxidation with active manganese dioxide in chloroform yield the corresponding aldehydes along with other products. It was also eatablished that the solvents play an important role in determining the oxidation products in such reactions. The results of Haksar et.al.[7] revealed two important points; first the corresponding aldehyde is formed only when the oxidation is carried out in chloroform as solvent and second the corresponding amide is only formed when ammonia is added to the reaction mixture.

In an attempt to prepare the three isomeric pyridine aldehydes, we have studied the oxidation reactions of the three isomeric pyridine carboxylic acid hydrazides (I) with active manganese dioxide in chloroform. In addition the parallel reactions with commercially available manganese dioxide were also studied.

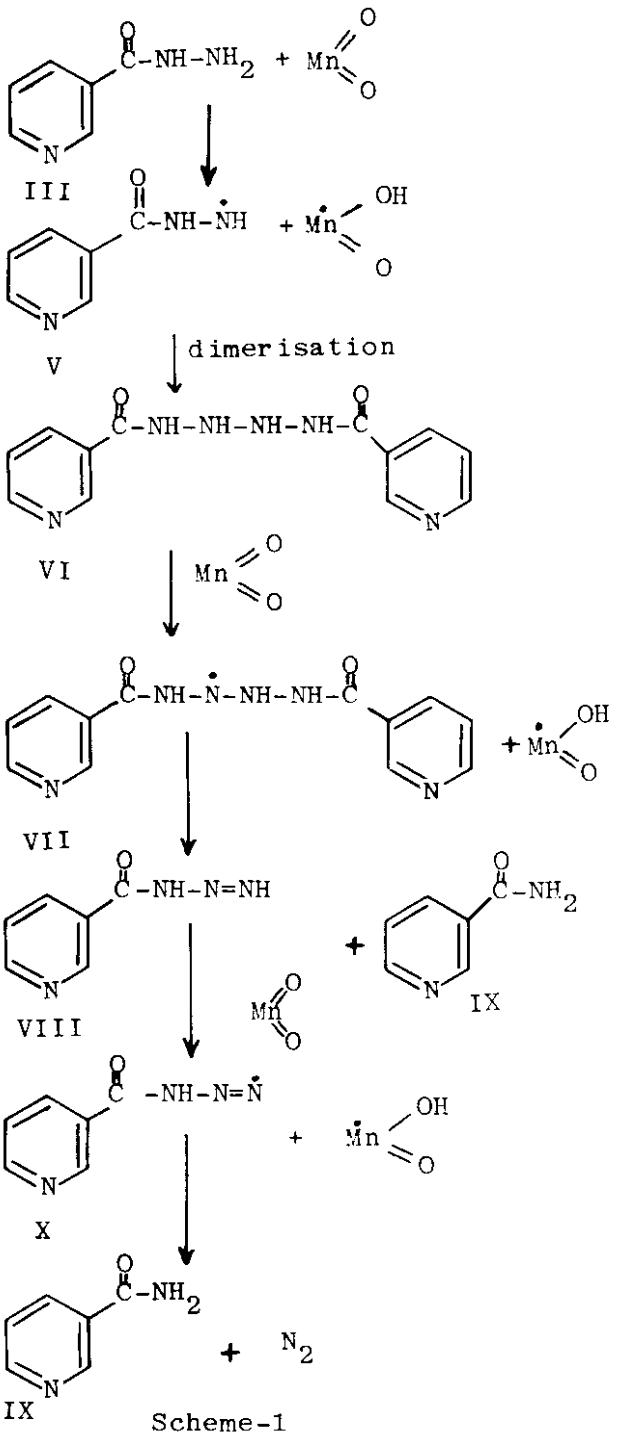


(I)

All the three isomeric pyridine carboxylic acid hydrazides when subjected to oxidation in chloroform at room temperature yielded the corresponding aldehydes in low yields. In case of pyridine-2-carboxylic acid hydrazide (II) a yellowish brown compound was also isolated which could not be identified. However, in case of pyridine-3-carboxylic acid hydrazide (III) and pyridine-4-carboxylic acid hydrazide (IV) the respective carboxylic acids and their amides were also obtained in yields better than those for the aldehydes. Under reflux for one hour, both (III) and (IV) yielded the corresponding carboxylic acid and the amide but no aldehyde. Under these conditions (II) yielded the same unidentified compound and no traces of carboxylic acid, the amide or the aldehyde.

At room temperature (20-21°) oxidation of three isomeric hydrazides with commercially available manganese dioxide, in chloroform, did not occur even on standing the reaction mixture for five hours. However, under reflux for one hour, (III) and (IV) yielded the respective amides only. Again (II), under these conditions, behaved diffe-

rently and the reaction did not occur. It is important to note that Haksar et. al.[7] observed the formation of amides only when ammonia was added to the reaction mixture. Thus (III) and (IV) have behaved differently than the hydrazides of substituted salicylic acids. The formation of corresponding amides as the oxidation products of (III) and (IV) may be expalined by a free radical mechanism as illustrated by Scheme 1 for the oxidation of (III). According to the scheme a free radical (V) produced as a result of hydrogen abstraction from (III) dimerizes to tetrazane (VI). Again a hydrogen atom is abstracted from (VI) to yield free radical (VII) which undergoes nitrogen-nitrogen bond cleavage to produce (VIII) and amide (IX). (VIII) once again undergoes hydrogen abstraction and yields the amide (IX) through free radical (X). This scheme of mechanism for the formation of amide (without addition of ammonia) fully accomodates the difference in the products of oxidation of (III) and (IV) when oxidized with active and commercially available manganese dioxide. Active manganese dioxide is regarded as a stronger and more reactive reagent than the ordinary manganese dioxide. Thus, when active manganese dioxide is used, radical (V) undergoes further reaction giving less opportunity to this radical to dimerize. Thus the formation of the amide (IX) is hindered and other products (i.e. the corresponding carboxylic acid and the aldehyde) are formed along with small amount of the amide. In case when ordinary manganese dioxide is used,probably, the chances of dimerization of (V) are increased due to the low reactivity of the reagent. This then leads to the formation of amide solely. As far as the formation of the aldehydes and the carboxylic acids is concerned, the mechanisms proposed by Haskar et.al.[7] for the formation of substituted salicylic acids and aldehydes, from the hydrazides of substituted salicylic acids, appear to be applicable in our case as well.



Experimental

Active manganese dioxide was prepared by Attenburrows method [8] from manganese sulphate monohydrate (BDH) and Potassium permangante (BDH) in alkaline medium. Pyridine-2-carboxylic

acid hydrazide (II) was prepared from pyridine-2-carbonylic acid (BDH) by the same method as described [9] for the synthesis of pyridine-4-carbonylic acid hydrazide from the corresponding carboxylic acid. Recrystallised from methanol, m.p. 99-100° (lit [13] m.p. 100-101°).

Pyridine-3-carboxylic acid hydrazide (III) was preapred from pyridine-3-carboxamide (E.Merck) by the same method as reported [10] for the preparation of pyridine-4-carboxylic acid hydrazide from the corresponding amide. Recrystallised from methanol, m.p. 160-161° (lit. [11d] m.p. 161-162°].

Pyridine-4-carboxylic acid hydrazide (IV) was obtained from (BDH) and was used without further purification.

Oxidation of Pyridine Carboxylic acid Hydrazides

(a) With active manganese dioxide at room temperature: In a 500-ml two necked round bottom flask was placed 10 g of Pyridine carboxylic acid hydrazide and 50.0 g of the active manganese dioxide. The flask was then equipped with a reflux condenser and a mechanical stirrer. Through the reflux condenser was added 250 ml of chloroform. The reaction mixture was then stirred for ten minutes. After this period of time, it was filtered to seperate out the inorganic residue. From this inorganic residue, the corresponding pyridine carboxylic acid was isolated in case of (III) and (IV). In the case of (II) an unidentified yellowish brown compound was isolated. From the filtrate, after removal of the solvent, two compounds were isolated in each case. In case of (III) and (IV) these were the corresponding aldehyde and the amide whereas in the case of (II) these were the corresponding aldehyde (isolated as its phenylhydrazone and 2,4-dinitrophenylhydrazone) and the same unidentified yellowish brown compound (as isolated from the inorganic phase). The results are given in Table 1.

(b) With active manganese dioxide under reflux: Same amounts of the hydrazides, active manganese dioxide and chloroform as mentioned in (a) above were refluxed for one hour. After this period of time the reaction mixture, while still hot, was filtered to seperate out the inorganic residue. In case of (III) and (IV) the corresponding acid and the corresponding amide were isolated, respectively, from the inorganic residue and the filtrate. In the case of (II), however, the same unidentified compound was isolated from both the phases. These results are also included in Table 1.

(c) With ordinary manganese dioxide at room temperature: Procedure (a) using commercialy available manganese dioxide (E.Merck) in place of active manganese dioxide with the same amounts of the reagents was adopted. In all the three cases no reaction occured at room temperature even in the extended time period of five hours.

(d) With ordinary manganese dioxide (E.Merck) in place of active manganese dioxide with the same amounts of the reagents was adopted. In case of (II) the reaction did not occur. In case of (III) and (IV) the corresponding amide was isolated from the filtrate in good yields. The results are also included in Table 1.

Characterization of the Products

(a) Pyridine aldehydes:

The characterization of the pyridine aldehydes as the reaction product was based on the following observations; +ve silver mirror test, +ve Fehling's solution test, carbonyl frequency in the IR spectrum (neat) at 1710 cm^{-1} and the aldehydic C-H frequencies at 2830 and 2700 cm^{-1}. In addition, the phenylhydrazones and 2,4-dinitrophenylhy-

Table-1: Oxidation of Pyridine Carboxylic Acid Hydrazides with Manganese Dioxide

Hydrazide	Manganese dioxide	Reaction temperature	Reaction time (min)	Products (% yield)
II	Ordinary	Room temperature*	300	No reaction
II	Ordinary	Under reflux	60	No reation
II	Active	Room temperature*	10	A** B(50)
II	Active	Under reflux	60	B(80)
III	Ordinary	Room temperature*	300	No reaction
III	Ordinary	Under reflux	60	C(80)
III	Active	Room temperature*	10	C(10),D(15),E(70)
III	Active	Under reflux	60	C(10),E(85)
IV	Ordinary	Room temperature*	300	No reaction
IV	Ordinary	Under reflux	60	F(85)
IV	Active	Room temperature*	10	F(10),G(10),H(70)
IV	Active	Under reflux	60	F(10),H(80).

*20-21, ** Isolated as phenylhydrazone and 2,4-dinitrophenylhydrazone. A. pyridine-2-aldehyde; B.unidentified product; C.pyridine-3-carboxamide; D.pyridine-3-aldehyde E.pyridine-3-carboxylic acid: F.pyridine-4-carboxamide; G.pyridine-4-aldehyde; H.pyridine-4-carboxylic acid.

drazones of the three aldehydes were derived and their melting points were compared with literature values. This is illustrated by Table 2.

(b) Pyridine carboxamides:

These were identified on the basis that they evolved ammonia on heating with sodium hydroxide. IR spectrum (nujol) showed the characteristic peak at 1680 cm^{-1} in addition to doublet at 3200 and 3320 cm^{-1} region. Pyridine-3-carboxymide m.p. (obs) 128-130°,lit.[11c] m.p. 129-130°; pyridine-4-carboxamide m.p. (obs.) 155°, lit[11d] m.p. 156°.

c)Pyridine carboxylic acids:

Both the isolated carboxylic acids evolved carbon dioxide with aqueous sodium bicarbonate. IR spectrum (nujol) showed the characteristic carboxylic acid pattern i.e. a sharp peak at 1660 cm^{-1} and a broad peak at 3180-3210 cm^{-1} Pyridine-3-carboxylic acid m.p. (obs.) 235-236°, lit.[11b] m.p. 236°, pyridine-4-carboxylic acid m.p. (obs.) 312°,lit.[11d] m.p. 315°.

Table-2: Characterization of Pyridine Aldehydes

Aldehyde	B.P.(obs.)	B.P.(lit)	Phenyl hydrazone m.p.(obs.)	m.p.(lit)	2,4-Dinitrophenyl hydrazone m.p.(obs.)	m.p.(lit)
Pyridine-2-aldehyde	*	62°/13-14 mm[a]	181-182°	182[ob]	235-236°	237[ob]
Pyridine-3-aldehyde	62/5 mm	83°/77 mm[c]	158°	159[ob]	258-259°	259[ob]
Pyridine-4-aldehyde	77/12 mm	82°/16 mm[c]	176°	178[ob]	281°	283[ob]

(a) Ref.11a, (b) Ref.12, (c) Ref.11b, * Isolated only as phenylhydrazone and 2,4-dinitrophenylhydrazone

References

1. R.M.Evans *Quart.Rev.*, **13**, *61 (1959)*
2. H.B.Henbest and A.Thomas, *J.Chem.Soc.*, *3032 (1957)*
3. E.F.Pratt and T.P.McGovern., *J.Org.Chem.*, **29**, *1540 (1964)*.
4. I.Bhatnagar and M.V.George, *J.Org.Chem.*, **33**, *2407 (1968)*.
5. I.Bhatnagar and M.V.George, *J.Org.Chem.*, **32**, *2253 (1967)*.
6. R.B.Kelly, G.R.Unbreit and W.F. Liggett, *J.Org.Chem.* **29**, *1273 (1964)*.
7. C.N.Haksar, R.C.Malhotra and P. K. Ramachandran *Indian J.Chem.*, **17B**, *191 (1979)*.
8. J.Attenburrow, A.F.B.Cameron, J.H.Chapman, R.W.Evans, B.A. Hems, A.B.A.Jansen and T.Walker, *J.Chem.Soc.*, *1094 (1952)*.
9. S.P.Dutta and A.K. Acharyge, *Indian J.Appl.Chem.*, **29**, *99 (1966)*.
10. K.Shu., *Med.Prom.S.S.S.R.*, **11**, *19 (1957)*.
11. J.R.A. Pollock and R.Stevens (Editors) Dictionary of Organic Compounds, 4th Edition (1965), Eyre & Spottiswoode, London, a)p.2815, b)p. 2816, c)p.2420, d)p.2817.
12. E.H.Rood (Editor) Chemistry of Carbon Compounds, IVA, *Heterocyclic Compounds, Ist Edition (1957), Elsevier, New York, p. 553.*
13. H.H.Fox and T.T. Gibas, *J.Org.Chem.*, **17**, *1653 (1952)*.