Pakistan J. Sci. Ind. Res., Vol. 23, No. 5 October 1980

# PREPARATION AND MECHANISM OF FORMATION OF ARYL OXAZOLES AND IMIDAZOLES FROM NITROESTERS

Y.A.M. Marghlani, S.A.M. Metwally, A.M. Mahmoud and A.M. Osman

*Chemistry Department, Faculty of Education, King Abdul Aziz University, Mecca, Saudi Arabia*

(Received January 24, 1979; revised March 20, 1980)

Acidic reduction of *ortho*-nitroesters leads to either oxazoles or amidophenols according to the reducing conditions. The mechanism of this reduction was studied in detail. Imidazoles were prepared similarly by acidic reduction of *ortho*-nitroanilides.

Reduction of *ortho*-nitrosoesters gave only the corresponding aminophenols and carboxylic acids.

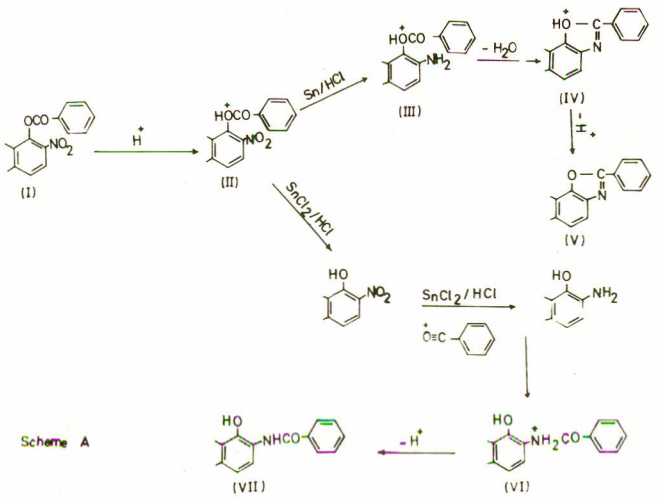
## INTRODUCTION

Reduction of *ortho*-nitroesters gives mainly heterocyclic compounds, however there is much discussion about this subject in the literature [1,2]. The present investigation is an attempt to clarify this problem and to prepare a variety of heterocyclic compounds.

Acidic reduction of a series of *o*-nitroesters, e.g. *o*-nitrophenyl benzoate, *o*-nitro-α-naphtyl benzoate and *o*-nitro-β-naphthyl benzoate led to different reaction products depending on the reduction conditions. Thus, reduction of the entitled nitroesters (I) with stannous chloride in an acidic medium gave the corresponding *o*-amidophenols (VII) as a main product, while reduction with tin and hydrochloric acid gave mainly aryl oxazoles (V). This behaviour reflects the sensitivity of these nitroesters towards reducing agents and by analysing the results of these reactions, it became apparent that the controlling factors are the comparative rates of reduction of the nitro group or the hydrolytic fission of the ester group.

Attempts were made to isolate the intermediate products which lead to either oxazoles or amidophenols. It was possible to isolate the intermediate aminoesters (III) when reduction was conducted with tin and hydrochloric acid for few minutes or by a short quantitative catalytic reduction using palladium charcoal catalyst. These aminoesters (III) are transformed to the corresponding oxazoles (V) just by heating over their melting points or by further heating in either tin – hydrochloric acid or stannous chloride–hydrochloric acid medium. This means that formation of the aminoester is essential as a precursor for the oxazole. On the other hand no intermediate could be obtained by the reduction of the nitroesters (I) with stannous chloride and hydrochloric acid, while full reduction leads to amidophenols (VIII).

From this study it may be postulated that, with tin




Scheme A

and hydrochloric acid, the rate of reduction of the nitro group is faster than hydrolysis of the ester group. Accordingly the reaction proceeds in the normal way and ends with the formation of the oxazole molecule (V). On the other hand, with stannous chloride and hydrochloric acid reduction of the nitro group is not fast and this offers a chance for the hydrolytic fission of the ester group to precede reduction of the nitro group and the reaction ends with the formation of amidophenols (VIII).

These reactions may be represented as indicated in scheme A.

In all cases the reaction is considered to be initiated with protonation of the *o*-nitroester to give the corresponding oxonium ion (II) [3]. This ion, in presence of a strong reducing agent and at pH 5 (Sn/HCl) undergoes reduction to the corresponding amine (III) which is readily dehydrated to give the oxazole (V).

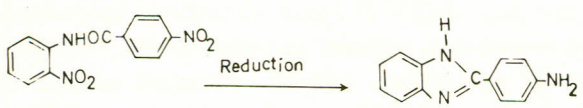
On the other hand, by using a considerably weaker reducing agent (stannous chloride/hydrochloric acid in ethanol), reduction of the nitro group is retarded and this offers a chance for the oxonium ion (II) to undergo a rate-

controlling heterolytic fission [3] producing a benzoylium ion and *o*-nitrophenol which is apt to be reduced to *o*-aminophenol. The benzoylium ion rapidly attacks the amino group which is more basic than the hydroxyl group towards acylation, to give an intermediate (VI) which loses a proton equivalent to that originally taken up to form the *o*-amido derivative (VII).

Further support for this mechanism is the fact that the presence of an electron attracting group (such as the nitro group) in the benzoate radical prevented acyl fission due to stabilisation of the oxonium ion and thus directed the reaction toward the formation of oxazole in almost quantitative yield and irrespective of the reducing agents.

Also it is to be taken into consideration that catalytic reduction of the nitroester produces only oxazoles through the stepwise reduction to the aminoester (III). Acyl fission is completely eliminated so the reaction proceeds only in one direction.

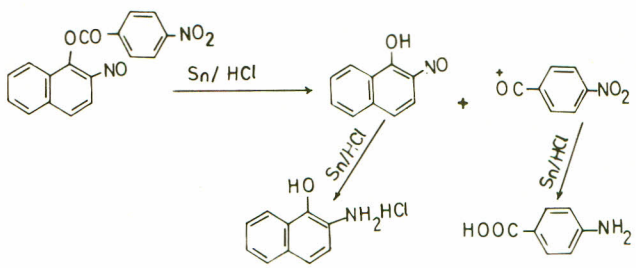
In an analogous manner, reduction of *N*-[*o*-nitrophenyl]-*p*-nitrobenzamide (VIII) gave 2-(*p*-aminophenyl) benzimidazole (IX).




(VIII) (IX)

In the light of the above findings, attempted reduction of *o*-nitrosoesters such as α-nitroso-β-naphthyl benzoate, β-nitroso-α-naphthyl benzoate, α-nitroso-β-naphthyl-*p*-nitrobenzoate, or α-nitroso-β-naphthyl-*p*-nitrobenzoate (X), gave only *o*-aminonaphthols and the corresponding acid derivatives.

As expected, the nitrosoester is difficult to reduce and




thus suffers initial acyl fission to produce a nitrosophenoxy radical which is then slowly reduced to aminophenol, while the acyl radical interacts spontaneously with water to give the corresponding carboxylic acid.

## EXPERIMENTAL

*Preparation of o-Nitroesters.* General Procedure: A mixture of the *o*-nitrophenol (1 mol) and the appropriate acid chloride (1 mol) was heated under reflux for 30 min in acetone and in the presence of anhydrous potassium carbonate. The mixture was filtered then concentrated and cooled, whereby the corresponding ester was deposited, filtered and crystallised from the proper solvent.

*o*-Nitrosoesters were prepared similarly by interaction of nitrosonaphthols with acid chlorides (Table 1).

*Reduction of o-Nitroesters:* (a) Reduction with Stannous Chloride/Hydrochloric Acid. The nitroester (1 mol) was dissolved in alcoholic hydrogen chloride and heated (2.5 hr) under reflux with stannous chloride (2 mol). The reaction mixture was cooled and the precipitated product was collected and dried, then crystallised from the proper solvent.

The resulting amidophenol and amidonaphthols were characterised by m.p. and mixed m.p. determinations

Table 1

| Compound | Formula | M.p. (°C) | Yield (%) | Appearance and solvent of crystallisation | Found (%) C | Found (%) H | Found (%) N | Required (%) C | Required (%) H | Required (%) N |
|---|---|---|---|---|---|---|---|---|---|---|
| 1-Nitro-2-naphthyl benzoate | $C_{17}H_{11}O_4N$ | 142 | 82 | Yellow needles* | 69.81 | 3.92 | 4.78 | 69.62 | 3.75 | 4.77 |
| 2-Nitro-l-naphthyl benzoate | $C_{17}H_{11}O_4N$ | 115 | 91 | Yellow needles* | 69.73 | 3.88 | 4.92 | 69.62 | 3.75 | 4.77 |
| *o*-Nitrophenyl benzoate | $C_{13}H_9O_4N$ | 138 | 72 | Colourless needles* | 64.33 | 3.82 | 5.97 | 64.15 | 3.7 | 5.76 |
| 1-Nitro-2-naphthyl-*p*-nitrobenzoate | $C_{17}H_{10}O_6N_2$ | 207 | 82 | Colourless needles† | 60.72 | 3.11 | 8.41 | 60.35 | 2.95 | 8.28 |
| 2-Nitro-l-naphthyl-*p*-nitrobenzoate | $C_{17}H_{10}O_6N_2$ | 189 | 58 | Colourless needles† | 60.81 | 2.98 | 8.34 | 60.35 | 2.95 | 8.28 |
| *o*-Nitrophenyl-*p*-nitrobenzoate | $C_{13}H_8O_6N_2$ | 143 | 63 | Pale yellow needles† | 54.41 | 2.82 | 9.93 | 54.16 | 2.77 | 9.72 |
| 1-Nitrophenyl-2-naphthyl benozate | $C_{17}H_{11}O_3N$ | 114 | 80 | Yellow needles† | 73.85 | 4.21 | 2.21 | 73.64 | 3.97 | 5.05 |
| 2-Nitro-l-naphthyl benzoate | $C_{17}H_{11}O_3N$ | 162 | 82 | Yellow needles† | 73.93 | 4.22 | 5.16 | 73.64 | 3.97 | 5.05 |
| 1-Nitroso-2-naphthyl-*p*-nitrobenzoate | $C_{17}H_{10}O_5N$ | 196 | 73 | Yellow flakes† | 63.71 | 3.23 | 8.84 | 63.35 | 3.1 | 8.69 |
| 2-Nitroso-1-naphthyl-*p*-nitrobenzoate | $C_{17}H_{10}O_5N_2$ | 191 | 62 | Yellow needles | 63.61 | 3.36 | 8.76 | 63.53 | 3.1 | 8.69 |

*Ethanol †Acetone

Table 2

| Compound | Formula | M.p. (°C) | Yield (%) | Appearance and solvent of crystallisation | Found (%) C | Found (%) H | Found (%) N | Required (%) C | Required (%) H | Required (%) N |
|---|---|---|---|---|---|---|---|---|---|---|
| 2-Phenylbenzoxazole | $C_{13}H_9ON$ | 121 | 80 | Colourless needles* | 80.0 | 5.15 | 7.23 | 80.00 | 5.12 | 7.18 |
| 2-(*p*-Aminophenyl) benzoxazole | $C_{13}H_{10}ON_2$ | 174 | 82 | Colourless needles* | 74.33 | 4.85 | 13.52 | 74.28 | 4.76 | 13.33 |
| 2-Phenylnaphtho [1,2-d]-oxazole | $C_{17}H_{11}ON$ | 131 | 72 | Colourless needles (reddish tent) | 83.42 | 4.61 | 5.79 | 83.27 | 4.48 | 5.71 |
| 2-Phenylnaphtho-[2,1-d]-oxazole | $C_{17}H_{11}ON$ | 189 | 81 | Colourless needles† | 83.51 | 4.52 | 5.93 | 83.26 | 4.48 | 5.71 |
| 2-(*p*-Aminophenyl)-naphtho-[1,2-d]-oxazole | $C_{17}H_{12}ON_2$ | 236 | 80 | Colourless needles* | 78.55 | 4.62 | 10.83 | 78.48 | 4.61 | 10.76 |
| 2-(*p*-Aminophenyl)-naphtho-[2,1-d]-oxazole | $C_{17}H_{12}ON_2$ | 194 | 78 | Colourless needles* | 78.66 | 10.92 | 10.92 | 78.46 | 4.61 | 10.76 |

*Ethanol, †Methanol

with authentic samples as follows:

*o*-Amidophenol; colourless needles from ethanol, m.p. and mixed m.p. 136° [5]. (Calcd for: $C_{13}H_{11}O_2N$: C. 73.23, H 5.15; N 6.75. Found: C 73.4, H 5.26, N 6.66%).

*o*-Amido-α-naphthol; colourless flakes from ethanol, m.p. and mixed m.p. 249° [5]. (Calcd for: $C_{17}H_{13}O_2N_2$: C 73.64, H 4.69, N 10.1. Found: C 73.82, H 4.81, N 10.22%).

*o*-Amido-β-naphthol; colourless needles from ethanol, m.p. and mixed m.p. 191° [6]. (Calcd for: $C_{17}H_{13}O_2N_2$: C 73.64, H 4.69, N 10.1. Found: C 73.71, H 4,73, N 10.31%).

(b) Reduction with Tin/Hydrochloric Acid: By repeating the previous experiments using tin and alcoholic hydrogen chloride, the corresponding aryloxazoles were obtained and identified by m.p. and mixed m.p. with authentic samples [7] (Table 2).

When *o*-nitrophenyl benzoate was heated with tin and alcoholic hydrogen chloride for 15 min only, then neutralised with dilute sodium bicarbonate; *o*-aminophenyl benzoate was deposited as colourless crystals, then recrystallised from ethanol into fine colourless needles, m.p. and mixed m.p. 71°[8] (Calcd. for: $C_{13}H_{11}O_2N$: C 75.23, H 5.15, N 6.57. Found: C 75.81, H 5.36, N 6.82%).

This product can be easily diazotised and shows an IR absorption band at 3322 $cm^{-1}$ characteristic of a primary amino group [9]. It was easily transformed to 2-phenylbenzoxazole by heating above its melting point.

*2-(p-Aminophenyl)-benzimidazole.N-*(*o*-nitrophenyl)-*p*-nitrobenzamide (2.87 g) was heated for 2 hr under reflux with stannous chloride (4.52 g) in alcoholic hydrogen chloride solution (200 ml). The reaction mixture was cooled and the crystalline product was filtered and dried. It was recrystallised from dil HCl into fine colourless needles which were treated with excess 4 *N* NaOH whereby the free base was precipitated as a yellowish white precipitate.

Colourless needles from 30% ethanol, m.p. and mixed m.p. 242° [10]. Yield; quantitative. Calcd. for: $C_{13}H_{11}N_3$: C 74.64, H 5.26, N 20.09. Found: C 74.83, H 5.32, N 20.41%).

*Reduction of o-Nitrosoestes*

The following is an illustrative example. α-Nitroso-β-naphthyl-*p*-nitrobenzoate (3.5 g) was heated for 3 hr under reflux with alc HCl (50 ml) and stannous chloride (5 g) or tin metal (7 g). The reaction mixture was cooled, whereby fine grey needles of 1-amino-2-naphthol hydrochloride were precipitated, collected and dried. It was recrystallised from dil hydrochloric acid into colourless needles, m.p. and mixed m.p. 220° [11], (violet melt) (dec. at 160°).

The product dissolved readily in water, its solution precipitated silver chloride when treated with silver nitrate and it acquired a violet tint when left in air. It was easily oxidised by hydrogen peroxide to 1,2-naphthoquinone.

Reduction of other nitrosoesters gave the corresponding *o*-aminophenol hydrochloride.

## REFERENCES


1. W. Bottcher, Ber., **16**, 1935 (1883).
2. A. Einhorn, Pfly, B., Ann., **311**, 34 (1900).
3. C.K. Ingolds, *Structure and Mechanism in Organic Chemistry* (Cornell, Ithaca, New York, 1953),p. 769.
4. E.L. Holljes and E.C. Wagner, J. Org. Chem., **9**, 31 (1944).
5. J. Meisenheimer, Ber., **57**, 296 (1924).
6. V.K. Auwers and M. Eckardt, Ann, **359**, 378 (1908).
7. V.V. Samayajulu, V.V. Subba, Current Science (India), **25**, 96 (1957).
8. M. Bergman, R. Ulpts and F. Camacho, Ber., **55**, 2805 (1922).
9. L.J. Bellamy, *The Infrared Spectra of Complex Molecules,* (Reprinted 1964). (Methuen, London, 1964), second edition.
10. B. Miklaszewski, S. Niementowski, Ber., **34**, 2953 (1901).
11. A.M. Osman and I. Bassioni J. Org. Chem., **27**, 558 (1962).