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NOVEL STUDIES ON 5-AMINO-2-METHYLNAPHTH(1.2)-IMIDAZOLE AND 5-AMINO-2-METHYL-3-OXONAPHTH-(1.2)IMIDAZOLE

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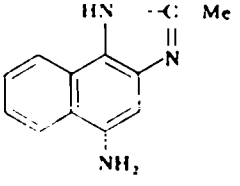
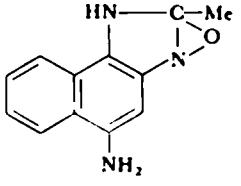
Abstract—A novel synthesis of 5-acetylamino-2-methylnaphth(1.2)imidazole (V) and 5-acetylamino-2-methyl-3-oxonaphth(1.2)imidazole (VII) is described. The validity of the structure proposed for Meldola's base (II) is discussed. Preparation of 5-acetylamino-2-methyl-3-oxonaphth(1.2)imidazole derivatives X and XI, 2-methyl-3-oxonaphth[(1.2)imidazole]-[(3.4)triazole] (XII), 2,5-dimethyl-3-oxonaphth[(1.2),(3.4)]bisimidazole (XIII) is also reported.

MELDOLA *et al.*[1] claimed that reduction of 1-acetylamino-2,4-dinitronaphthalene with tin and hydrochloric acid gave 5-amino-2-methylnaphth(1.2)imidazole (I). Markfeldt[2] reported the preparation of the same compound when the reduction was carried out with iron and hydrochloric acid. Later, Meldola[3] indicated that Markfeldt's base was different from his and erroneously attributed that difference to structural isomerism.



I



II

Fischer[4] confirmed this difference and showed that Meldola's base contained one O atom more and assigned structures I and II* to Markfeldt's and Meldola's compounds respectively.

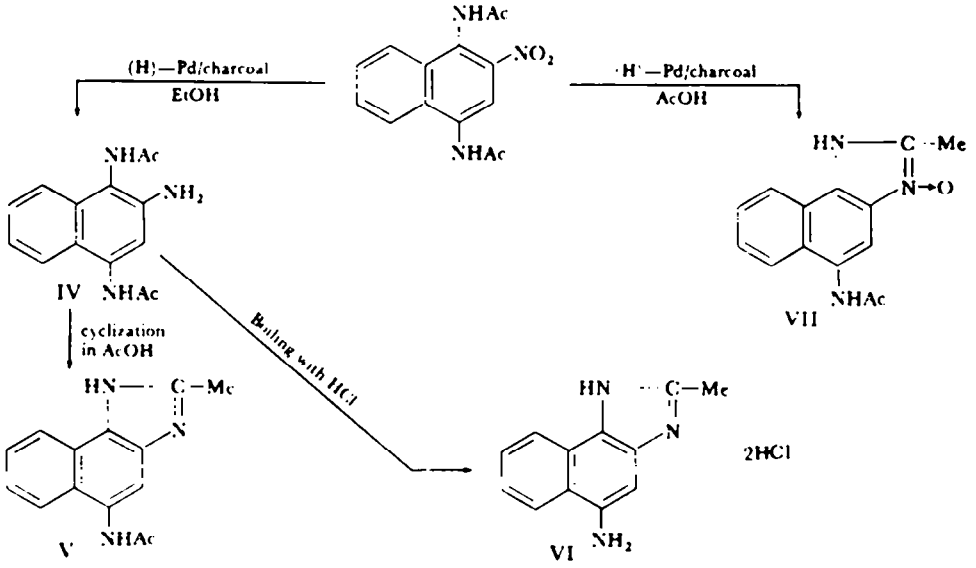
It is now found that 2-nitro-1,4-diacetylaminonaphthalene (III) is reduced by hydrogen on Pd–C to 2-amino-1,4-diacetylaminonaphthalene (IV). Boiling IV in glacial acetic acid effects cyclization to 5-acetylamino-2-methylnaphth(1,2)imidazole (V), whereas boiling with hydrochloric acid effects both cyclization and hydrolysis to VI.

Compound V and the amine prepared from VI proved to be identical with the monoacetyl derivative of Markfeldt's base and the base itself (I) respectively, thus confirming structure I for the latter compound.

However, when the reduction of III using the above method was carried out in

* The correctness of this structure is discussed later.

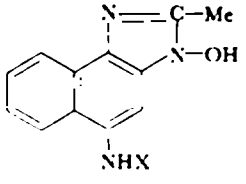
[1] R. Meldola and F. W. Streatfeild, *J. Chem. Soc.* **51**, 691 (1887).
[2] O. Markfeldt, *Ber. Dtsch. Chem. Ges.* **31**, 1174 (1898).
[3] R. Meldola and L. Eynon, *J. Chem. Soc.* **77**, 1159 (1900).
[4] O. Fischer, *J. Prakt. Chem.* **75**, 88 (1907).



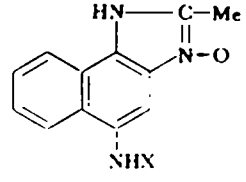
glacial acetic acid another product (VII) different from III is obtained. Compound VII was found to be identical with the monoacetyl derivative prepared by Meldola.[3] The important role played by the solvent should here be emphasized.

Fischer[4] assigned structure II to Meldola's base on the basis that: (a) it gave I on reduction with iron and hydrochloric acid, (b) on deamination it yielded a compound which could further be reduced to 2-methylnaphth(1.2)imidazole with iron and hydrochloric acid, (c) II is similar in properties (high m.p. and decomposition on distillation) to the oxoanhydrobenzimidazoles of Niementowski.[5] The author however did not forward any direct proof for the tricyclic ring in this structure.

In addition to structure II, Meldola's product may also be represented by structures VIIIa or IXa.*



VIII
a, X = H
b, X = Ac



IX
a, X = H
b, X = Ac

Concerning the monoacetyl derivative of Meldola's base it was found that structure VIIIb should be excluded because: (a) analysis of active hydrogen indicates absence of—OH group, (b) IR spectrum confirms this result (absence of the characteristic—OH band), (c) NMR spectrum shows no splitting of the singlet of the second Me group at 2·6 ppm, which should be the case if formula VIIIb (N-substituted-β-naphthylhydroxylamine) was correct as a result of the presence of an α-proton to the Me group.

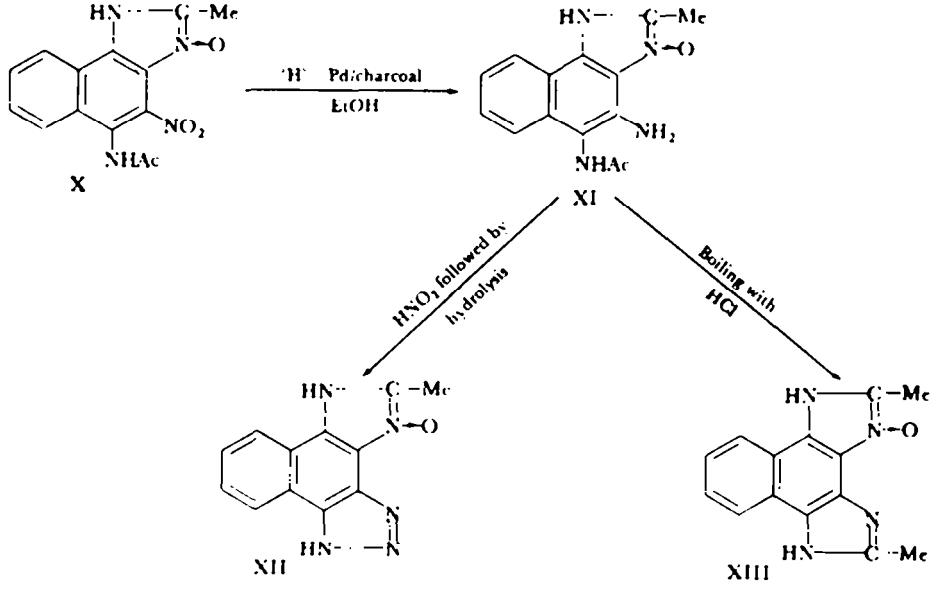
* Niementowski postulated analogous structures for his oxoanhydrobenzimidazole derivatives.

[5] St. Von Niementowski, *Ber. Dtsch. Chem. Ges.* **20**, 1874 (1887); *Ibid.* **25**, 86 (1892).

Structure II also is improbable due to steric effects (trials to construct a model using Stuart models of structure II were unsuccessful).

In the light of these results it is believed that IXa and IXb represent the correct structure for Meldola's base and its monoacetyl derivative respectively.

When VII is nitrated at 0–5° in a mixture of sulphuric and nitric acids a yellow mono nitro derivative (X) is obtained. Structure X is inferred from: (a) correct analytical figures, (b) reduction yields a mono amine (XI) which does not couple with diazonium salts excluding positions 5, 6, 7- and 8- of the original naphthalene ring, (c) IX undergoes cyclization to 2-methyl-3-oxonaphth[(1.2)imidazole]-[(3.4)-triazole] (XII) on treatment with nitrous acid followed by hydrolysis, (d) 2,5-dimethyl-3-oxo-naphth[(1.2), (3.4)]bisimidazole (XIII) is formed when XI is boiled with hydrochloric acid.



Compounds XII and XIII are the first examples in the literature of naphth[(1.2)-imidazole]-[(3.4)triazole] and naphth[(1.2), (3.4)]bisimidazole derivatives.

EXPERIMENTAL

2-Amino-1,4-diacetylaminonaphthalene (IV).* Compound III† (5 g) was dissolved in boilingE tOH (1·75 l.). Pd–C (1·4 g, 10%) was added to the hot soln which was hydrogenated at 70° for 30 min at normal press. The alcoholic soln was filtered while hot and the residue extracted with boiling EtOH. The mother liquor and the alcohol extracts were concentrated on a water bath. The white residue crystallized from EtOH as colourless needles, m.p. 261°, yield 91%. (Found: C, 65·30; H, 5·75; N, 16·08. $C_{14}H_{15}N_3O_3$ requires: C, 65·42; H, 5·88; N, 16·35%.) Compound IV is sparingly soluble in benzene, light petroleum and ether but dissolves in alcohol, chf, glacial AcOH and in 10% NaOHaq. With conc. H_2SO_4 it gives a dark red colour.

* H. H. Hodgson *J. Chem. Soc.* 1151 (1936) reported the preparation of the chlorostannate derivative of this compound by reducing 2-nitro-1,4-diacetylaminonaphthalene (III) with stannous chloride and HCl. The author was unsuccessful to obtain the free amino derivative. It is believed that Hodgson's compound cannot have this structure because reduction of acylated-*o*-nitronaphthyl-amines is known to lead to naphthimidazoles.

† Prepared according to Panizzon-Favre *Gazz. Chim. ital.* **54**, 838 (1924).

5-Acetylamino-2-methylnaphth(1.2)imidazole (V)[3]. A soln of IV (3·5 g) in glacial AcOH (50 ml) was heated under reflux for 1 hr. After concentration and cooling, a white substance separated. It was filtered off and washed several times with 10% NH_4OHaq to remove traces of AcOH. Crystallization from dil EtOH gave V (identified by m.p. and mixed m.p. with the acetyl derivative of Markfeldt's base), colourless needles, m.p. 285°, yield 92%. (Found: C, 70·63; H, 5·59; N, 17·87. $C_{14}H_{13}N_3O$ requires: C, 70·35; H, 5·48; N, 17·58%.) Compound V is sparingly soluble in benzene, chf and ether but dissolves in alcohol, glacial AcOH and in 10% NaOHaq. It gives no colour with conc. H_2SO_4.

5-Amino-2-methylnaphth(1.2)imidazole dihydrochloride (VI). Compound IV (5 g) was refluxed in AcOHaq (100 ml) and 20% HClaq (20 ml) for 2 hr. The mixture was concentrated and the separated pale coloured needles were crystallized from H_2O, yield 71%. (Found: C, 53·10; H, 4·60; N, 15·30; Cl, 26·50. $C_{13}H_{13}N_3Cl_2$ requires: C, 53·38; H, 4·85; N, 15·65; Cl, 26·26%.)

5-Acetylamino-2-methyl-3-oxonaphth(1.2)imidazole (VII).[3] Compound III (10 g) was dissolved in glacial AcOH (1·5 l.). Pd–C (1 g, 10%) was added to this soln and the mixture hydrogenated at normal temp and press. The reaction mixture was filtered and concentrated. The white ppt was washed with hot EtOH to remove traces of brownish impurity and crystallized from amyl alcohol. Compound VII (identified by mixing with a sample prepared by Meldola's method) crystallized as colourless plates, m.p. 292°, yield 96%. (Found: C, 65·98; H, 5·12; N, 16·53. $C_{14}H_{13}N_3O_2$ requires: C, 65·94; H, 5·14; N, 16·48%.) Compound VII is insoluble in chf, CCl_4, ether and alcohol but dissolves in glacial AcOH, amyl alcohol and in 10% NaOHaq. It gives no colour with conc. H_2SO_4.

5-Acetylamino-2-methyl-4-nitro-3-oxonaphth(1.2)imidazole (X). Compound VII (5 g) was treated with HNO_3 (10 ml, *d* 1·42) at 0°. Conc. H_2SO_4 (6 ml) was then added dropwise during 30 min so that the temp did not exceed 5°. Stirring was continued for another 60 min. The reaction mixture was poured into ice-cold water with vigorous stirring. The yellow ppt was filtered off, washed several times with cold H_2O and crystallized from EtOH as yellow crystals, m.p. 287° (dec.), yield 60%. (Found: C, 56·05; H, 4·16; N, 18·67. $C_{14}H_{12}N_4O_4$ requires: C, 56·05; H, 4·03; N, 18·68%.) Compound X is sparingly soluble in benzene, ether, chf and pet. ether but dissolves in glacial AcOH and alcohol. It gives a yellow colour with conc. H_2SO_4 and a reddish-orange soln with 10% NaOHaq.

5-Acetylamino-4-amino-2-methyl-3-oxonaphth(1.2)imidazole (XI). Compound X (3·5 g) was dissolved in EtOH (1·75 l.). Pd–C (0·8 g, 10%) was added and the mixture hydrogenated at normal temp and press. The reaction mixture was filtered and the filtrate was concentrated *in vacuo*. The white ppt crystallized from EtOH as colourless needles, m.p. 332° (unclear melt), yield 92%. (Found: C, 62·14; H, 5·57; N, 20·47. $C_{14}H_{14}N_4O_2$ requires: C, 62·27; H, 5·23; N, 20·75%.) Compound XI is sparingly soluble in benzene, ether, pet. ether and chf but dissolves in alcohol, glacial AcOH and in 10% NaOHaq. It gives no colour with conc. H_2SO_4.

2-Methyl-3-oxonaphth[(1.2)imidazole]-[(3.4)triazole] (XII). To a soln of XI (2 g) in EtOH (50 ml) was added conc. HCl (10 ml) and the mixture cooled to 0°. A soln of $NaNO_2$ (0·2 g) in H_2O was added dropwise to the above mixture with continuous stirring. When addition was complete, stirring was continued for further 3 hr. The temp of the reaction mixture was kept at 0–5°. After that another portion of conc. HCl (5 ml) was added and the mixture refluxed for 3 hr. After concentration and cooling, colourless needles separated. These were crystallized from alcohol, m.p. above 360°, yield 51%. (Found: C, 60·42; H, 4·14; N, 28·90. $C_{13}H_8N_6O$ requires: C, 60·30; H, 3·80; N, 29·31%.) Compound XII is sparingly soluble in benzene, pet. ether and chf but dissolves in alcohol, glacial AcOH and 10% NaOHaq. It gives no colour with conc. H_2SO_4.

2,5-Dimethyl-3-oxonaphth[(1.2),(3.4)]bisimidazole (XIII). A soln of XI (2 g) in 20% HCl (30 ml) was refluxed for 3 hr. The reaction mixture was concentrated and left to cool whereby colourless crystals separated. Crystallization from alcohol gave colourless needles, m.p. above 360° (shrinks at about 290°), yield 72%. (Found: C, 66·58; H, 4·93; N, 22·00. $C_{14}H_{12}N_4O$ requires: C, 66·72; H, 4·80; N, 22·23%.) Compound XIII is sparingly soluble in benzene, ether, chf and pet. ether but dissolves in glacial AcOH and in 10% NaOHaq. It gives no colour with conc. H_2SO_4.

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