770. *Acylarylnitrosamines. Part VIII.*[1] *Reactions of Some* o-*Methoxy-nitrosoacetamido-compounds.*

By Yusuf Ahmad and D. H. Hey.

2-Methoxy-1- and 1-methoxy-2-nitrosoacetamidonaphthalene react with benzene in the normal manner to give 2-methoxy-1- and 1-methoxy-2-phenylnaphthalene respectively. In similar manner, 4-methoxy-3-nitrosoacetamidoquinoline gives 4-methoxy-3-phenylquinoline. Freshly prepared nitrosyl chloride is essential for the preparation of the nitroso-compounds. The presence of a methoxyl group in the *ortho*-position with reference to an acetamido-group does not prevent nitrosation, and such nitrosoacetamido-compounds display normal properties.

In a previous communication [1] it was reported that, contrary to the abnormal behaviour observed in a few quinoline compounds,[2] the 3-amino-group in pyridine, with a methoxyl group in the 2-, 4-, or 6-position with reference to it, behaves normally in reactions which result in its replacement by a phenyl group. It thus seemed likely that the abnormal behaviour reported for 3-amino-4-methoxy-quinoline (I; R = H) and -quinaldine (I; R = Me) was not associated with the difference in the structure of the isomeric *O*- and *N*-methyl derivatives (I) and (II). Nor could such behaviour be entirely attributed to the

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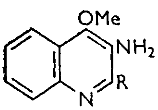
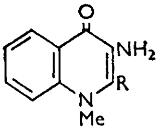
[1] Part VII, Ahmad and Hey, *J.*, 1954, 4516.

[2] Adams and Hey, *J.*, 1951, 1521.

proximity of the methoxyl group in the benzenoid structure (I), because it is known that *o*-anisidine reacts normally (as the diazonium salt) with pyridine to give a mixture of *o*-methoxyphenylpyridines [3] in 50% yield. On the other hand, it has been reported [4] that



(I)



(II)

derivatives of 5-amino-6-methoxyquinoline failed to react with pyridine to give pyridyl derivatives. Attention was therefore directed to similar reactions in the naphthalene series with derivatives containing an amino-group in an *ortho*-position with reference to a methoxyl group (*i.e.*, the carbocyclic analogues of the above quinoline compounds). Methoxynaphthylamines in which the amino- and the methoxyl group occur in separate rings have been successfully subjected to reactions which result in replacement of the amino-group by the phenyl group,[5] but similar reactions with naphthalene derivatives in which the methoxyl and amino-groups occur at adjacent positions in the same ring have not hitherto been investigated.

1-Acetamido-2-methoxynaphthalene underwent normal nitrosation and, when the *N*-nitroso-derivative was heated in benzene solution, it gave 2-methoxy-1-phenylnaphthalene in low yield. In similar manner nitrosation of 2-acetamido-1-methoxynaphthalene gave the nitroso-compound, which decomposed normally in benzene to give 1-methoxy-2-phenylnaphthalene; some 1-methoxynaphthalene was also isolated from this reaction. In the nitrosation of both acetamidomethoxynaphthalenes it was observed that only freshly prepared nitrosyl chloride in solution in acetic anhydride was capable of effecting the reaction. If an old solution was used the unchanged acetamido-compounds were recovered or unidentified products were formed.

These observations made it necessary to reinvestigate the nitrosation of 4-methoxy-3-acetamidoquinoline, and it was found that when freshly prepared nitrosyl chloride in acetic anhydride was used 4-methoxy-3-*N*-nitrosoacetamidoquinoline was obtained as viscous yellow oil. The nitroso-compound exhibited normal chemical properties, and it decomposed in warm benzene with evolution of nitrogen to give 4-methoxy-3-phenylquinoline in low yield.

In another investigation,[6] 8-acetamido-7-methoxyisoquinoline has also been converted into a normal nitroso-compound which decomposed in benzene to give 7-methoxy-8-phenylisoquinoline in the usual manner. It may thus be concluded that the presence of a methoxyl group in the *ortho*-position with reference to an amino-group, in both carbocyclic and heterocyclic compounds, does not prevent the nitrosation of the acetyl derivatives, and that such nitroso-compounds display their normal decomposition reactions.

EXPERIMENTAL

Light petroleum had b. p. 40—60°. The alumina used for chromatography was " Activated Alumina Type ' H ' " supplied by Peter Spence & Sons, Ltd.

2-*Methoxy*-1-N-*nitrosoacetamidonaphthalene*.—A 25% solution of nitrosyl chloride in acetic anhydride (15 c.c.) was added dropwise to a well-stirred mixture of 1-acetamido-2-methoxynaphthalene [7] (5·0 g.) in glacial acetic acid (20 c.c.) and acetic anhydride (15 c.c.) containing fused potassium acetate (15·0 g.) and phosphoric oxide (0·5 g.) at 0°. Stirring was continued for 20 min. after the addition, and the thin yellow paste was then poured on crushed ice and aqueous sodium hydroxide (40 g. in about 100 c.c.) with vigorous stirring. The nitroso-compound separated as an orange oil, which solidified (5·25 g. after being dried overnight at 0—2° *in vacuo*

[3] Haworth, Heilbron, and Hey, *J.*, 1940, 358.

[4] Coates, Cook, Heilbron, Hey, Lambert, and Lewis, *J.*, 1943, 401.

[5] Hey and Lawton, *J.*, 1940, 374, 384.

[6] Ahmad and Hey, unpublished work.

[7] Davis, *Chem. News*, 1896, **74**, 302.

over potassium hydroxide). A portion was purified by dissolution in cold dry ether (charcoal) and removal of ether *in vacuo* under moisture-proof conditions. 2-*Methoxy*-1-N-*nitrosoacetamidonaphthalene* was obtained as deep yellow powder, shrinking to a dark red melt with evolution of gas at 86—88° (Found: C, 63·6; H, 5·0. $C_{13}H_{12}O_3N_2$ requires C, 63·9; H, 4·9%). The nitroso-compound is fairly stable at room temperature.

2-*Methoxy*-1-*phenylnaphthalene*.—The above nitroso-compound (4·25 g.) was dissolved in dry " AnalaR " benzene (150 c.c.), filtered, and then heated under gentle reflux for 24 hr. under moisture-proof conditions. Nitrogen was evolved and the solution became dark red. After removal of solvent the dark red, tarry residue was dissolved in the minimum quantity of benzene and passed down a column of alumina, which was eluted first with light petroleum and then with light petroleum–benzene (1 : 1). Removal of solvent left a light yellow oil, which solidified to a very low-melting solid (0·5 g.), the *picrate* of which separated from benzene in deep red prisms, m. p. 151—152° (Found: C, 60·1; H, 3·7. $C_{17}H_{14}O,C_6H_3O_7N_3$ requires C, 59·6; H, 3·6%).

2-*Acetamido*-1-*methoxynaphthalene*.—Aceto-α-naphthalide was nitrated by Hodgson and Kilner's method,[8] and the resulting mixture of nitro-compounds was hydrolysed to 2- and 4-nitro-1-naphthol from which the former was removed by distillation with steam. The 2-nitro-1-naphthol was converted into 1-methoxy-2-nitronaphthalene by a method similar to that of Jones and Sleight,[9] by treating dry sodium 2-nitro-1-naphthoxide with methyl sulphate and toluene for 1 hr. at 110—120°. A solution of 1-methoxy-2-nitronaphthalene (7 g.) in methanol (170 c.c.) containing Raney nickel (7 g.) was shaken with hydrogen at room temperature and atmospheric pressure. The theoretical volume of hydrogen was rapidly taken up and the solution was filtered. Excess of solvent was removed and the cooled solution was poured into ice-cold water. The 1-methoxy-2-naphthylamine, which separated in quantitative yield (needles from dilute methanol; m. p. 48—49° [10]), was acetylated with acetic anhydride containing 3—4 drops of perchloric acid. The mixture was poured on ice, and the acetyl derivative was collected, washed with dilute sodium hydroxide and water, and dried (yield quantitative). 2-Acetamido-1-methoxynaphthalene crystallised from dilute methanol (charcoal) in pinkish-white plates, m. p. 131—132°.[10]

1-*Methoxy*-2-N-*nitrosoacetamidonaphthalene*.—Nitrosyl chloride in acetic anhydride (15% solution; 36 c.c.) was added dropwise to a stirred mixture of 2-acetamido-1-methoxynaphthalene (4 g.), fused potassium acetate (6 g.), glacial acetic acid (15 c.c.), acetic anhydride (10 c.c.), and phosphoric oxide (0·5 g.) at 0—5°. After 25 min. the mixture was poured on crushed ice containing sufficient aqueous sodium carbonate to make the mixture slightly alkaline. An orange-yellow oil separated, which solidified. It was filtered off quickly, washed with ice-cold water, and dried *in vacuo* over potassium hydroxide (yield almost quantitative). A small portion, purified by dissolution in cold dry ether (charcoal), gave 1-*methoxy*-2-N-*nitrosoacetamidonaphthalene* as a pale yellow amorphous powder, m. p. 73° (decomp.) (Found: C, 64·2; H, 5·1. $C_{13}H_{12}O_3N_2$ requires C, 63·9; H, 4·9%). The temperature during all these operations was kept below 5°.

1-*Methoxy*-2-*phenylnaphthalene*.—A solution of 1-methoxy-2-*N*-nitrosoacetamidonaphthalene (4 g.) in dry " AnalaR " benzene (100 c.c.) was heated under gentle reflux for 24 hr. Nitrogen was evolved and the yellow solution became dark red. After removal of some of the solvent the solution was passed down a column of alumina, which was eluted with light petroleum. Removal of solvent gave a colourless oil, which solidified. Crystallisation from dry ether gave 1-*methoxy*-2-*phenylnaphthalene* (0·3 g.) in needles, m. p. 56—57° (Found: C, 86·8; H, 6·15. $C_{17}H_{14}O$ requires C, 87·1; H, 6·0%). Further elution of the column with benzene gave 1-methoxynaphthalene as a pale yellow oil (0·25 g.), which did not solidify. It gave an orange-red *picrate*, m. p. 127·5—128·5° (Found: C, 52·7; H, 3·55. $C_{11}H_{10}O,C_6H_3O_7N_3$ requires C, 52·7; H, 3·4%). The m. p. was not depressed on admixture with an authentic specimen prepared from 1-methoxynaphthalene.

3-*Acetamido*-4-*methoxyquinoline*.—3-Amino-4-methoxyquinoline was obtained as described by Adams and Hey,[2] the only modification made in the procedure being the use of 5% palladium–carbon instead of platinum for the reduction of the nitro-group. For acetylation of the amine in the cold with acetic anhydride perchloric acid was added in place of sulphuric acid

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[8] Hodgson and Kilner, *J.*, 1924, 808.

[9] Jones and Sleight, *J.*, 1954, 1780.

[10] Noelting, Grandmougin, and Freimann, *Ber.*, 1909, **42**, 1384.

as catalyst. The acetyl derivative crystallised from acetone (charcoal) in light yellow needles, m. p. 74°. When this was heated for 24 hr. under reflux with benzene (in which it was only sparingly soluble in cold) and the hot solution was allowed to cool slowly, 3-acetamido-4-methoxyquinoline separated quantitatively as colourless, long prismatic needles and the m. p. rose to 76°. No trace of the high-melting quinolone was isolated. The m. p. rose to 111—112° when the crystals were dried over potassium hydroxide *in vacuo* for a few days. Adams and Hey [2] quote m. p. 74° for the hemihydrate and m. p. 105° for the anhydrous compound.

4-*Methoxy*-3-N-*nitrosoacetamidoquinoline*.—A freshly prepared solution (25%; 8 c.c.) of nitrosyl chloride in acetic anhydride was added dropwise to a stirred mixture of 3-acetamido-4-methoxyquinoline (2·5 g.) fused potassium acetate (7·5 g.), glacial acetic acid (10 c.c.), acetic anhydride (7·5 c.c.), and phosphoric oxide (0·25 g.) at 0°. Stirring was continued for 15 min. and the thin yellow paste was poured on crushed ice and aqueous sodium hydroxide (20 g. in 50 c.c.). A thick yellow oil separated which failed to solidify. The oil was removed and the aqueous layer was extracted with " AnalaR " benzene. The oil, except for a small portion, was added to the benzene extract, and the yellow benzene solution was dried ($NaSO_4$) overnight below 10°. Purification of a small portion by dissolution in cold dry ether (charcoal) gave a pale yellow viscous oil, which was dried *in vacuo* over potassium hydroxide at 0° for 24 hr. (Found: C, 56·6; H, 5·0. $C_{12}H_{11}O_3N_3,\frac{1}{2}H_2O$ requires C, 56·7; H, 4·7%). The nitroso-compound, on being warmed above 60° or on storage at room temperature for a few days, darkened and underwent decomposition with evolution of gas.

4-*Methoxy*-3-*phenylquinoline*.—The dried benzene solution of the above nitroso-compound was heated under reflux for 24 hr. Nitrogen was evolved and the solution became dark red. Benzene was removed under reduced pressure and the dark red residue was digested with dry ether. The ether extract was filtered and evaporated. The residue in the minimum quantity of benzene was passed down a column of alumina, which was eluted with light petroleum–benzene (1 : 1). On removal of solvents a colourless oil was obtained, which solidified (0·25 g.). Its picrate separated from benzene in bright yellow needles m. p. 156—158°, alone or on admixture with the picrate of 4-methoxy-3-phenylquinoline.[2] A marked depression was recorded on admixture with the picrate of 1-methyl-3-phenyl-4-quinolone.[2]

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