

**713.** *Amine Oxidation. Part VII.\* Cleavage of Tetra-N-substituted 1,2-Diamines by Manganese Dioxide.*

By E. F. CURRAGH, H. B. HENBEST, and A. THOMAS.

Diamines containing the grouping,  $R_2N \cdot CH_2 \cdot CH_2 \cdot NR_2$  are cleaved by manganese dioxide at the central C-C bond to give *N*-formyl compounds. Examples of such diamines include the bicyclo-compound,  $N(CH_2 \cdot CH_2)_3N$ , which is oxidised to 1,4-diformylpiperazine.

Experiments with monoamines are reported that help to define the scope of manganese dioxide-amine reactions. Further examples are given that show the dependence of the yields of products upon the oxidant : amine ratio used.

EARLIER work<sup>1</sup> showed that dialkylanilines are oxidised by active (hydrated) manganese dioxide<sup>2</sup> in at least three ways: (a) conversion of *N*-methyl into *N*-formyl groups, exemplified by the oxidation of dimethylaniline (IA) to *N*-methylformanilide; (b) oxidation of *N*-ethyl-amines to acetaldehyde (and secondary amines), exemplified by diethylaniline (IB); and (c) cleavage of substituted ethylenediamines to *N*-formyl compounds, exemplified by the oxidation of 1,4-diphenylpiperazine (IC) to *NN'*-diformyl-*NN'*-diphenylethylenediamine.

The last of these reactions is the most unusual being, as far as we know, the only method for cleaving substituted ethylene diamines to *N*-formyl compounds. More diamines have now been oxidised and the results, together with those from some related

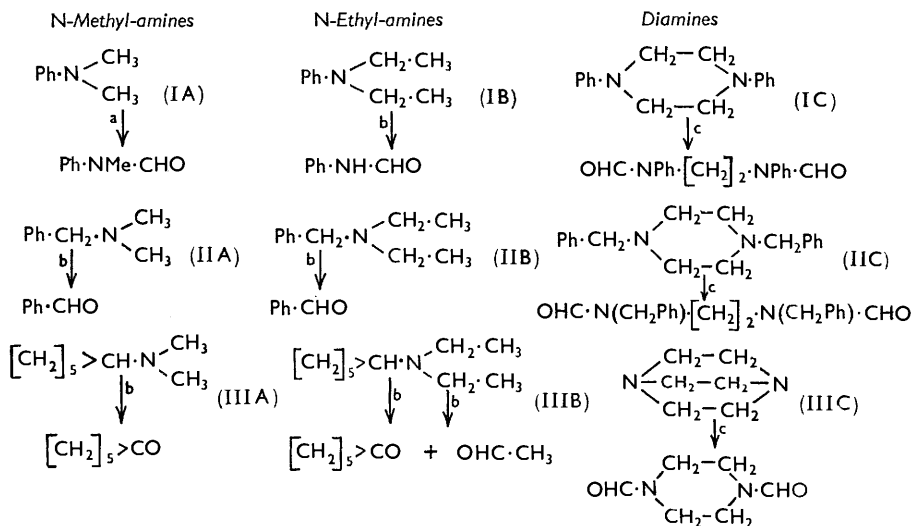
\* Part VI, preceding paper.

<sup>1</sup> Henbest and Thomas, *J.*, 1957, 3032.

<sup>2</sup> Comprehensive review by Evans, *Quart. Rev.*, 1959, 13, 61.

monoamines are summarised in the formulæ below, the arrows starting from the main point of attack in the amine and the lower-case letters specifying the type of general reaction (a, b, or c) involved.

The dialkylanilines (IA and B) are oxidised at carbon atoms adjacent to nitrogen. In the related dialkylbenzylamines (IIA and IIB) oxidation mainly occurs at the methylene



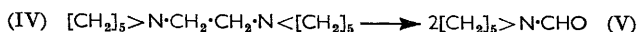
groups between the phenyl and the amine group, benzaldehyde being formed. When the same weight ratios manganese dioxide : amine were used, higher yields of benzaldehyde were obtained from diethylbenzylamine (IIB) than from dimethylbenzylamine (IIA). Oxidation of tribenzylamine proceeded less readily, presumably for steric reasons, benzaldehyde (23%) and unchanged amine (70%) being obtained with a 50 : 1 weight ratio oxidant : amine.

Despite the oxidation of the amines (IIA and B) at their benzyl methylene groups, 1,4-dibenzylpiperazine (IIC) gave an *NN'*-diformyl compound (80%) by cleavage of the ring by reaction (c).

The substituted cyclohexylamines (IIIA and B) were the first fully saturated tertiary amines to be oxidised. Each gave cyclohexanone, the yields being 85% and 50% (oxidant : amine ratio 100 : 1) from the dimethyl and the diethyl compound respectively. The latter amine was also oxidised at an ethyl group, to give acetaldehyde (55%). [The yields of the products from the reactions occurring by conversion (b) are calculated on the basis that the oxidation of a tertiary amine gives one molecule each of carbonyl compound and secondary amine; no account can at present be taken of the likely further oxidation of the secondary amines to carbonyl compounds.] Cyclohexanone was also obtained by oxidation of cyclohexylamine; a larger oxidant : amine ratio (>250 : 1) was required to give the best yields (>50%) of ketone.

The oxidation of triethylenediamine (IIIC) was of interest as mechanisms involving the transference of hydride ion from the amine in an intermediate step are presumably prohibited. This amine was oxidised, ring cleavage giving 1,4-diformylpiperazine, but a larger oxidant : amine ratio was required than for an open-chain diamine (*e.g.*, IV). Various experimental conditions were tried but the best yield of diformylpiperazine was only 9% (16% after allowance for recovered starting material). More of the product is probably formed but much may be lost by reaction with, or by adsorption on, the excess of dioxide (oxidant : amine 70 : 1) necessary for the oxidation of an appreciable proportion

of this diamine. It seems that saturated *N*-formyl compounds are particularly difficult to recover from manganese dioxide; when a sample of 1-formylpiperidine (V) was treated with fresh dioxide for a short time, only 26% of it was recovered. Nevertheless, 1-formylpiperidine (V) was obtained in 50% yield from 1,2-dipiperidinoethane (IV) when only a



20 : 1 oxidant : amine ratio was used.

Dimethylaniline is oxidised by manganese dioxide to *N*-methylformanilide in 78% yield,<sup>1</sup> but oxidation of *N,N*,2,6-tetramethylaniline and *NN*-dimethyl-1-naphthylamine under the same conditions gave difficultly volatile resins, apart from unchanged starting materials and a trace of 1,4-naphthaquinone from the latter amine. The different behaviour of these amines may be connected with the lack of coplanarity of the dimethylamino-groups with the ring systems. For this reason, the tetramethylaniline does not react readily with diazonium salts.<sup>3</sup> The naphthylamine also behaves differently from dimethylaniline in its reaction with *t*-butoxy-radicals.<sup>4</sup>

Benzoquinuclidine was not appreciably oxidised by manganese dioxide at 20° or 61°. Thus reactions of the types (a) and (b) are strongly inhibited when the nitrogen is at the bridgehead of a tricyclic system containing 6-membered rings. The experiments with triethylenediamine (IIIC) indicate, however, that the geometrical requirements of the diamine-cleavage reaction (c) are less stringent.

#### EXPERIMENTAL

Manganese dioxide used was the material supplied by J. Woolley, Sons and Co. Ltd. Chloroform was first used as the reaction solvent, but methylene chloride was later adopted. The manganese dioxide was washed at the end of the reaction with fresh methylene chloride and then with methylene chloride-methanol (10 : 1). M. p.s were taken on a Kofler stage.

*NN*-Dimethylbenzylamine (IIA).—The amine (0.1 g.) in chloroform (50 c.c.) was shaken at 20° with manganese dioxide (5 g.) for 15 hr. The filtrate was extracted with dilute acid to remove unchanged amine [recovered subsequently as its picrate (0.167 g., 62%), m. p. and mixed m. p. 83—84°] and added to 2,4-dinitrophenylhydrazine reagent (10 c.c.). The solution was concentrated under reduced pressure to about 5 c.c., benzaldehyde 2,4-dinitrophenylhydrazone (45 mg., 21%), m. p. and mixed m. p. 236—237°, separating. Improved yields of benzaldehyde (as 2,4-dinitrophenylhydrazone) were obtained when larger amounts of dioxide were used:

Dioxide : amine wt. ratio .....	50	150	250	350	450	600
Benzaldehyde, yield (%) .....	21	41	48	50	45	39

Experiments with a 50 : 1 ratio were also carried out in stirred, boiling chloroform as solvent; the yields of benzaldehyde 2,4-dinitrophenylhydrazone were 24% and 31% for reaction times of 7 hr. and 12 hr. respectively.

*NN*-Diethylbenzylamine (IIB).—This amine was oxidised as in the preceding experiment, in methylene chloride. The following yields of benzaldehyde 2,4-dinitrophenylhydrazone were obtained:

Dioxide : amine wt. ratio .....	50	100	250	350	400
Benzaldehyde, yield (%) .....	64	74	86	83	50

1,4-Dibenzylpiperazine (IIC).—The diamine (1 g.) in methylene chloride (150 c.c.) was shaken with dioxide (50 g.) at 20° for 18 hr. The product was a sticky solid that was dissolved in the minimum amount of benzene and filtered through deactivated alumina (10 g.). Crystallisation from methanol gave *NN'*-benzyl-*NN'*-di-formylethylenediamine (0.9 g., 80%), m. p. 99—100° (Found: C, 72.85; H, 6.85. C<sub>18</sub>H<sub>20</sub>N<sub>2</sub>O<sub>2</sub> requires C, 72.95; H, 6.8%). An authentic sample of this compound was prepared by heating *NN'*-dibenzylethylenediamine, 90% formic acid (2 g.),

<sup>3</sup> Friedlander, *Monatsh.*, 1898, **19**, 627.

<sup>4</sup> Henbest and Patton, preceding paper.

and acetic anhydride (0.2 g.) under reflux for 3 hr.; isolation with ether and crystallisation from methanol gave the diformyl compound (4.2 g., 82%), m. p. and mixed m. p. 99—100°. The infrared spectra of the two products were also identical (C=O peak at 1675 cm.<sup>-1</sup>).

NN-Dimethylcyclohexylamine (IIIA).—The redistilled amine (3 g.) in methylene chloride (500 c.c.) was shaken at 20° with manganese dioxide (300 g.) for 18 hr. The product, obtained by filtration and removal of solvent through a short fractionating column, was distilled to give cyclohexanone (1.92 g., 85%), b. p. 154—156°,  $n_D^{19}$  1.4519 (2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 160°). The yield of ketone fell to 67% when the dioxide : amine wt. ratio was reduced to 50 : 1.

NN-Diethylcyclohexylamine (IIIB).—The redistilled amine (3 g.) in benzene (300 c.c.) was stirred at 20° with the dioxide (150 g.) for 18 hr. At the same time, a stream of nitrogen was passed through the solution and thence into absorption bottles containing 2,4-dinitrophenylhydrazine reagent. Acetaldehyde was thereby collected as its 2,4-dinitrophenylhydrazone (2.31 g., 55%), m. p. and mixed m. p. 168°. The solution was filtered; the solvent was removed through a column and the residue distilled, to give cyclohexanone (0.9 g., 51%), b. p. 153—156° (2,4-dinitrophenylhydrazone, m. p. 160°).

Cyclohexylamine.—The amine (1 g.) was shaken with various amounts of manganese dioxide in methylene chloride (600 c.c.) for 18 hr. at 20°. Filtration and distillation gave cyclohexanone, b. p. 154—156°,  $n_D^{19}$  1.4505 (2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 160°):

Dioxide : amine wt. ratio .....	50	70	100	250	350
Cyclohexanone, yield (%) .....	26	27	43	51	53

Triethylenediamine (IIIC).—The amine (4 g.) in methylene chloride (400 c.c.) was shaken at 20° with manganese dioxide (280 g.) for 30 hr. After filtration, the dioxide was extracted (Soxhlet) with methanol for 12 hr. The solutions were combined and the solvents removed by careful distillation under reduced pressure through a short column. The residue (2.32 g.) was sublimed in a short-path still, to give unchanged amine (1.7 g., 40%). The residue was introduced in benzene on a column of alumina (30 g.). Elution with benzene-ether (1 : 1) gave 1,4-diformylpiperazine (0.451 g., 9%), m. p. 123° (from chloroform-dioxan) (Found: C, 50.4; H, 7.2. C<sub>6</sub>H<sub>10</sub>N<sub>2</sub>O<sub>2</sub> requires C, 50.7; H, 7.05%); carbonyl band at 1650 cm.<sup>-1</sup>.

Authentic 1,4-diformylpiperazine was made by heating piperazine (1 g.) with 98% formic acid (1.5 g.) containing a few drops of acetic anhydride for 3 hr. The product was isolated with chloroform and crystallised from dioxan to give the diformyl compound (1.3 g., 90%), m. p. and mixed m. p. 123°.

1,2-Dipiperidinoethane (IV).—The amine (5 g.) in methylene chloride (250 c.c.) was shaken at 20° with dioxide (100 g.) for 18 hr. After filtration, the dioxide was extracted (Soxhlet) with methanol for 12 hr. Removal of solvent from the combined solutions followed by distillation of the residue gave 1-formylpiperidine (3.0 g., 50%), b. p. 105°/10 mm.,  $n_D^{20}$  1.4840.

Recovery of 1-Formylpiperidine.—The amide (1 g.) in light petroleum (b. p. 40—60°) (100 c.c.) was shaken with dioxide (50 g.) for 15 min. The dioxide was washed with the following solvents in succession from which the stated amounts of starting material were then recovered: light petroleum (3 × 250 c.c. + initial 100 c.c.) gave 32 mg. of amide; methanol (3 × 250 c.c.) gave 0.153 g. of amide; methanol-water (1 : 1) (3 × 250 c.c.) gave 81 mg. of amide; total recovery of amide was 26%.

Tribenzylamine.—The amine (2 g.) in chloroform (250 c.c.) was stirred at 20° with dioxide (100 g.) for 40 hr. The dioxide was removed and the filtrate evaporated to a semi-solid product that on trituration with cold methanol gave unchanged amine (1.4 g., 70%), m. p. and mixed m. p. 90—91°. The methanol filtrate yielded benzaldehyde 2,4-dinitrophenylhydrazone (0.45 g., 23%), m. p. 236—237°.

N,N,2,6-Tetramethylaniline.—The amine (1.58 g.) in chloroform (300 c.c.) was stirred with dioxide (79 g.) at 20° for 19 hr. The filtrate and chloroform washings from the dioxide were extracted with dilute hydrochloric acid [basification gave unchanged amine (1 g., 63%)]. Removal of the chloroform under reduced pressure gave a red oil that did not distil under reduced pressure; nor could a solid picrate be obtained from it.

NN-Dimethyl- $\alpha$ -naphthylamine.—The amine (3 g.) in chloroform (300 c.c.) was stirred with dioxide (150 g.) at 20° for 18 hr. After filtration, the chloroform solution was extracted with dilute hydrochloric acid, and then dried and evaporated to give a viscous, deep red oil (1.4 g.). On attempted distillation at 0.5 mm. (130—240°), only a small amount (0.1 g., 4%)

of 1,4-naphthaquinone distilled. Crystallisation from methanol gave the pure quinone, m. p. and mixed m. p. 124—125° (Found: C, 75·8; H, 4·05. Calc. for  $C_{10}H_6O_2$ : C, 75·95; H, 3·8%). Basification of the acidic extract gave unchanged amine (1·1 g., 37%), b. p. 140—141°/13 mm.,  $n_D^{15}$  1·6240 (picrate, m. p. and mixed m. p. 142—144°).

*Benzoquinuclidine*.—Attempted oxidation of this amine (0·7 g.) in chloroform (120 c.c.) with dioxide (35 g.) for 17 hr. gave unchanged starting material (>90%) (m. p. and mixed m. p. 66—68°) from experiments at 20° and in refluxing solvent.

One of the authors (A. T.) thanks the Ministry of Education for a maintenance grant.

KING'S COLLEGE, LONDON, W.C.2.  
THE QUEEN'S UNIVERSITY OF BELFAST.

[Received, February 16th, 1960.]

---