

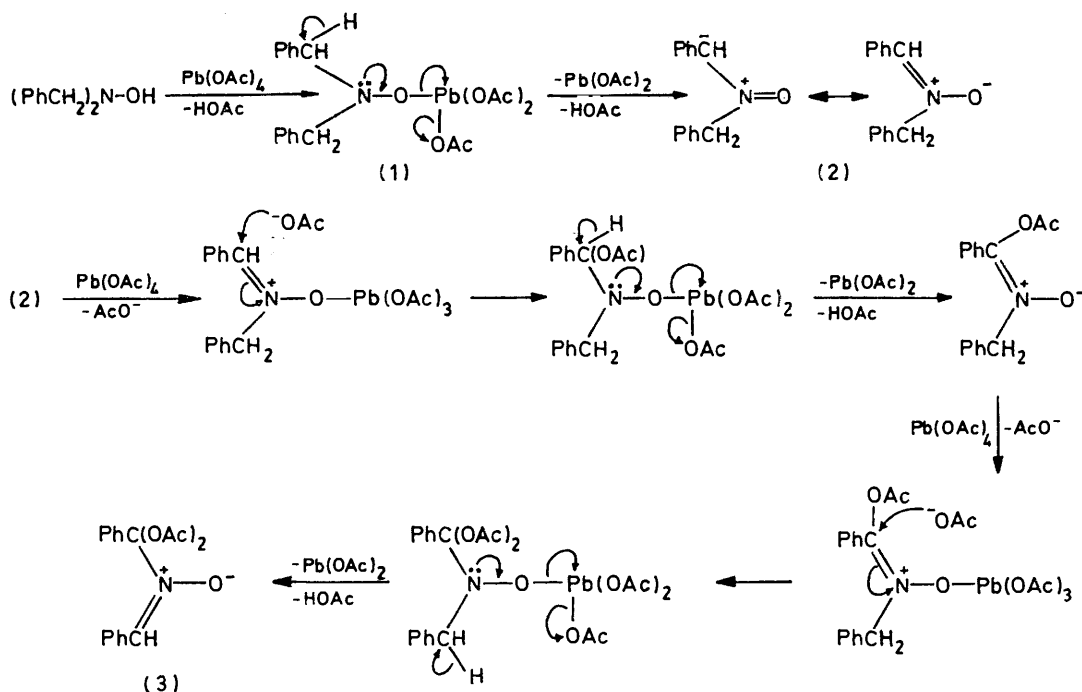
Reactions of Lead(IV). Part XXVI.¹ Oxidation of Some Derivatives of Hydroxylamine

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Lead tetra-acetate reacts in one or more of several ways with substituted hydroxylamines, depending on their structures. These are: formation of a 1,3-dipolar compound (*NN*-dibenzylhydroxylamine), oxidative rearrangement (e.g. *O*-benzylhydroxylamine), oxidative dimerisation (e.g. *N*-benzoyl-*O*-benzylhydroxylamine), and dehydrogenation (e.g. isoxazolidine).

WE report the results of a brief survey of the oxidation of some derivatives of hydroxylamine by lead tetra-acetate. They illustrate, for a small but representative selection of compounds, the variety of types of reaction which can be effected by the oxidant; thus, depending

satisfactorily accounted for as in Scheme 1; similar steps have been suggested as occurring in the oxidation of 4,5,5-trimethyl- Δ^1 -pyrroline 1-oxide by lead tetra-acetate, where an acetoxy-nitrone, although not isolated, is considered a likely precursor of the final product.⁴



SCHEME 1

on the structure of the compound, it may undergo formation of a 1,3-dipole, oxidative rearrangement, oxidative dimerisation, or dehydrogenation. In each case, reaction occurred readily at room temperature.

NN-Dibenzylhydroxylamine.—Reaction with 1 mol. equiv. of the oxidant gave the nitrone (2). It is likely that it is formed, by way of ligand exchange, from the intermediate (1), and the reaction has an analogy in that of benzaldehyde phenylhydrazone with lead tetra-acetate where there is evidence for the mediation of the 1,3-dipole $\text{PhC}=\text{N}^+-\text{N}^-\text{Ph}$.² When 3 mol. equiv. of the oxidant were employed, the diacetylated nitrone (3) was obtained. This has previously been isolated from oxidation of the nitrone (2),³ and its formation can be

¹ Part XXV, R. O. C. Norman, R. Purchase, C. B. Thomas, and J. B. Aylward, preceding paper.

² W. A. F. Gladstone, J. B. Aylward, and R. O. C. Norman, *J. Chem. Soc. (C)*, 1969, 2587.

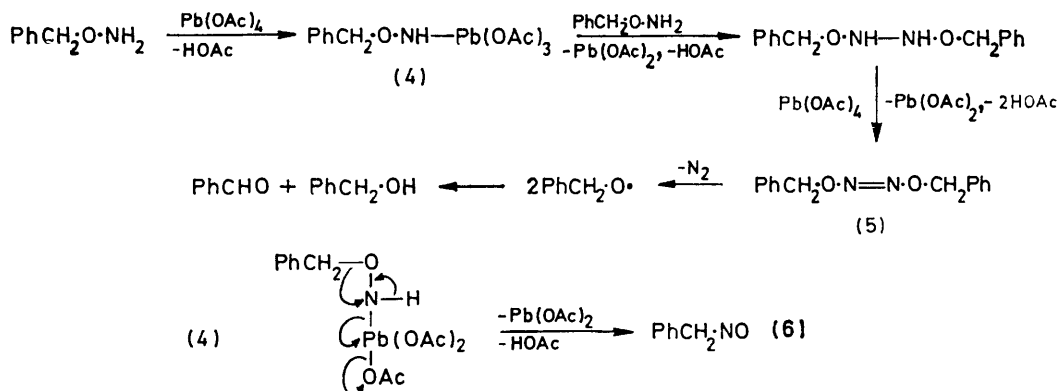
O-Benzylhydroxylamine.—The behaviour of *NN*-dibenzylhydroxylamine suggested that a possible intermediate from *O*-benzylhydroxylamine with lead tetra-acetate would be the 1,3-dipole, $\text{PhCH}=\text{O}^+-\text{N}^-\text{H}$. However, we found no evidence for this. Oxidation gave the dimer of α -nitrosotoluene (6) (20%) and an oil which contained benzyl alcohol (31%) and benzaldehyde (18%). Competing modes of reaction are indicated. One path is likely to be oxidative dimerisation to give dibenzyl hyponitrite (5) (cf. formation of the corresponding tetrazene from *NN*-dibenzylhydrazine¹); thus, some dialkyl hyponitrites have been obtained from *O*-alkylhydroxylamines with sodium hypobromite,⁵ while

³ L. A. Neiman, S. I. Kirillova, V. I. Maimind, and M. M. Shemyakin, *Zhur. obshchei Khim.*, 1965, **35**, 1932.

⁴ N. J. A. Gutteridge and F. J. McGillan, *J. Chem. Soc. (C)*, 1970, 641.

⁵ L. Seed, B. P. 795, 824/1958 (*Chem. Abs.*, 1959, **53**, 219).

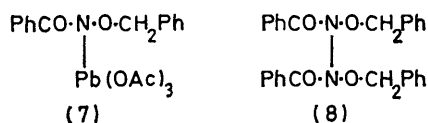
dibenzyl hyponitrite is known to fragment readily to benzyloxy-radicals and thence, by disproportionation, to yield benzyl alcohol and benzaldehyde⁶ and would do so under work-up conditions. The second path, which was reported independently⁷ after this work had been completed, involves a novel O-to-N rearrangement. One possible mechanism for this is shown in Scheme 2; an alternative is that the intermediate (4) undergoes α -elimination to give the *O*-nitrene, PhCH₂ON, which then rearranges. We cannot distinguish between these, but note the following. There is evidence that *O*-methylhydroxylamine gives the corresponding nitrene



SCHEME 2

with lead tetra-acetate, since the appropriate aziridine was isolated from reaction in the presence of tetramethylethylene.⁸ We failed to trap the nitrene from *O*-benzylhydroxylamine in the presence of methyl acrylate (the same products were obtained as in the absence of the trap), so that possibly in our case, as a result of the superior migratory aptitude of benzyl as compared with methyl in nucleophilic rearrangements, the benzyl group migrates within the intermediate (4) as shown in Scheme 2 faster than the intermediate undergoes α -elimination, whereas the reverse is true for the corresponding intermediate from *O*-methylhydroxylamine. Finally, the dimer of α -nitroso-*p*-chlorotoluene was obtained from the oxidation of *O*-*p*-chlorobenzylhydroxylamine.

N-Benzoyl-*O*-benzylhydroxylamine.—Oxidation gave the dimer (8) (*cf.* ref. 9), possibly by reaction of a second molecule of the hydroxylamine with the lead-derivative (7) formed from the first (*cf.* reaction of *N*-benzoyl-*N*-benzylhydrazine to give the corresponding tetrazene¹).

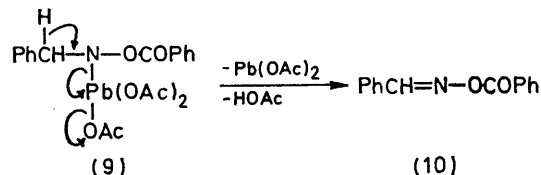


O-Benzoyl-*N*-benzylhydroxylamine.—Oxidation of the hydrochloride of this hydroxylamine gave *O*-benzoyl-

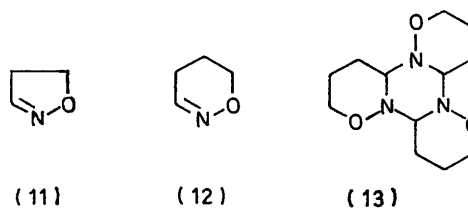
benzaldehyde oxime (10) and traces of benzaldehyde, benzyl acetate, benzoic acid, and benzonitrile. This dehydrogenation, which presumably occurs by way of the intermediate (9) as shown, prompted us to study the potential utility of the oxidant for dehydrogenating cyclic hydroxylamines.

Isloxazolidine and Tetrahydro-1,2-oxazine.—Both compounds underwent dehydrogenation readily, giving the hitherto unknown heterocyclic products (11) and (12), respectively. The tetrahydro-oxazine also gave (12) when treated with bromine in chloroform, which no doubt accounts for King's observation¹⁰ that the

tetrahydro-oxazine, and isloxazolidine, 'behave as highly unsaturated substances to bromine water.'



At room temperature the oxazine derivative (12) slowly became viscous and eventually solidified. The mass spectrum of the product showed a molecular ion at *m/e* 255, that is, three times the molecular weight of the



reactant, and the remainder of the spectrum was also satisfactorily accounted for in terms of the formation of a trimer of (12). Analogy with the structure of the product from the spontaneous trimerisation of 2,3,4,5-

⁸ S. J. Brois, *J. Amer. Chem. Soc.*, 1970, **92**, 1079.

⁹ J. H. Cooley, M. W. Mosher, and M. A. Khan *J. Amer. Chem. Soc.*, 1968, **90**, 1867.

¹⁰ H. King, *J. Chem. Soc.*, 1942, 432.

⁶ S. K. Ho and J. B. de Sousa, *J. Chem. Soc.*, 1961, 1788.

⁷ R. Partch, B. Stokes, D. Bergman, and M. Budnik, *Chem. Comm.*, 1971, 1504.

tetrahydropyridine¹¹ suggests that the trimer from the oxazine has the structure (13). The isoxazoline (11) did not polymerise at room temperature.

The hydroxylamines we have studied are more reactive towards lead tetra-acetate than are their mono-functional relatives such as alcohols and amines; for example, benzylamine, dibenzylamine, and *N*-alkylbenzamides are stable towards the oxidant at room temperature.¹² The enhanced reactivity represents another example of the 'α-effect,'¹³ and has previously been noted as a feature of hydroxylamine oxidations in the case of the reaction of *NN*-dibenzylhydroxylamine with *t*-butyl hydroperoxide.¹⁴

EXPERIMENTAL

General experimental details including the oxidation procedure are as described in the preceding paper.¹ In addition, a g.l.c. column containing 10% Embaphase silicone oil on acid- and alkali-washed Embacel kieselguhr was employed to check purities.

NN-Dibenzylhydroxylamine, prepared by the method of Wragg and Stevens,¹⁵ had m.p. 124–125° (from ethanol) (lit.,¹⁵ 123°). *N*-Benzoyl-*O*-benzylhydroxylamine and *N*-benzoyl-*O*-*p*-chlorobenzylhydroxylamine, prepared from sodium benzohydroxamate¹⁶ and the appropriate aryl-methyl halide according to the general method of Brady and Peakin,¹⁷ had m.p. 105–107° (from benzene) (lit.,¹⁸ 102–103°) and 159–162° (lit.,¹⁹ 162°), respectively. *O*-Benzylhydroxylamine hydrochloride, prepared from the cleavage of *N*-benzoyl-*O*-benzylhydroxylamine with hydrogen chloride in ethanol,¹⁹ had m.p. ca. 240° (decomp.) (lit.,¹⁹ 230–232°). Basification yielded *O*-benzylhydroxylamine, b.p. 104° at 12 mmHg (lit.,²⁰ 118–119° at 30 mmHg), τ 2.7 (5H, s, ArH), 4.7br (2H, s, exchangeable, NH₂), 5.3 (2H, s, PhCH₂), pure by g.l.c. *O*-*p*-Chlorobenzylhydroxylamine, similarly prepared, had m.p. 40–42° (lit.,²¹ 38°), τ 2.7 (4H, m, ArH), 4.6br (2H, s, NH₂), and 5.4 (2H, s, CH₂). α-Nitrosotoluene dimer, prepared by the method of Emmons,²² had m.p. 122–125° (from carbon tetrachloride) (lit.,²² 116–118°). *O*-Benzoyl-*N*-benzylhydroxylamine hydrochloride, prepared from benzylamine and dibenzoyl peroxide in warm benzene, followed by treatment with hydrogen chloride,²³ had m.p. 142–144° (from ethanol) (lit.,²³ 141°). The free base decomposed on distillation *in vacuo* and on attempted g.l.c. analysis and its purity could not be checked. The hydrochloride salt was used in oxidation studies.

Tetrahydro-1,2-oxazine hydrochloride and isoxazolidine hydrochloride were prepared by the method of King.¹⁰ Basification afforded tetrahydro-1,2-oxazine, b.p. ca. 70° at 80 mmHg, τ 4.8 (1H, s, exchangeable, NH), 6.1 (2H, m, 6-H₂), 6.85 (2H, m, 3-H₂), and 8.3 (4H, m, 4- and 5-H₂), pure by g.l.c., and isoxazolidine, b.p. 70–80° at ca. 50

mmHg, τ 5.25br (1H, s, NH), 6.3 (2H, m, 5-H₂), 7.0 (2H, m, 3-H₂), 7.9 (2H, m, 4-H₂), pure by g.l.c., respectively.

Oxidation of NN-Dibenzylhydroxylamine.—(i) Lead tetra-acetate (5.0 g, ca. 0.01 mol) in dichloromethane (25 ml) was added to a solution of *NN*-dibenzylhydroxylamine (2.1 g, 0.01 mol) in dichloromethane (25 ml) during 35 min. Work-up gave *N*-benzylidenebenzylamine *N*-oxide (1.4 g, 66%), m.p. 83–84° [from cold benzene–light petroleum (b.p. 40–60°)] (lit.,²⁴ 81°) (Found: C, 79.2; H, 6.2; N, 6.8. Calc. for C₁₄H₁₃NO: C, 79.6; H, 6.2; N, 6.6%), ν_{max.} 1583 and 1589 cm⁻¹ (lit.,¹⁴ 1575 and 1590 cm⁻¹), τ 1.8 (m, *ortho*-protons), 2.7 (m, ArH), and 5.2 (s, ArCH₂).

(ii) Lead tetra-acetate (45 g) in dichloromethane (200 ml) was added to a solution of *NN*-dibenzylhydroxylamine (6.4 g) in dichloromethane (200 ml) under nitrogen during 2.5 h at 5°. The mixture was allowed to warm to room temperature during 1.25 h, then worked up to give *N*-benzylidene-α-diacetoxybenzylamine *N*-oxide (2.7 g, 27%), m.p. 98–100° (from ether) (lit.,³ 100–102°), ν_{max.} 1695, 1748, and 1790 cm⁻¹ (lit.,³ 1700, 1750, and 1794 cm⁻¹), τ 2.3 (m, *ortho*-protons), 2.6 (m, ArH) (–CH= presumably obscured), 7.85 (3H, s, OAc), and 8.05 (3H, s, OAc) (lit.,³ τ 2.2–2.8, 7.88, and 8.08); hydrolysis (warm 2M-HCl) gave benzaldehyde and benzoic acid.

Oxidation of O-Benzylhydroxylamine.—(i) Lead tetra-acetate (5.2 g) in dichloromethane (25 ml) was added to a solution of *O*-benzylhydroxylamine (1.2 g) in dichloromethane (25 ml) during 30 min. The mixture was stirred for a further 35 min and then worked up to give a semi-solid (1 g) which was mixed with cold carbon tetrachloride (ca. 15 ml). The insoluble material was recrystallised from carbon tetrachloride to give α-nitrosotoluene dimer (0.2 g), identical (m.p., mixed m.p., and i.r. spectrum) with authentic material,²² λ_{max.} 294 nm (log ε 3.93) [lit.,²² λ_{max.} 296 nm (log ε 3.93)], τ 2.7 (5H, s, PhCH₂), and 4.6 (2H, s, PhCH₂) (lit.,²⁵ 4.62), pure by t.l.c. The organic solution obtained after the removal of solid material was evaporated *in vacuo* to leave an oil which contained (g.l.c. analysis) benzyl alcohol and benzaldehyde *inter alia*.

(ii) *O*-Benzylhydroxylamine (2.5 g) in dichloromethane (150 ml) was added to a solution of lead tetra-acetate (22 g) in dichloromethane (75 ml) during 3 h. Work-up afforded α-nitrosotoluene dimer (0.45 g, 19%), m.p. and mixed m.p. 122°, and an oil which contained benzyl alcohol (31%) and benzaldehyde (18%). A duplicate experiment yielded α-nitrosotoluene dimer (0.5 g).

(iii) Repetition of experiment (i) but with the hydroxylamine in a mixture of dichloromethane (15 ml) and methyl acrylate (10 ml) gave benzyl alcohol, benzaldehyde, and α-nitrosotoluene in the same yields as in experiment (i) (some of the nitrosotoluene forming the isomeric oxime and being analysed as such by g.l.c.).

Oxidation of O-p-Chlorobenzylhydroxylamine.—Lead tetra-acetate (11 g) in dichloromethane (75 ml) was added to a solution of *O*-*p*-chlorobenzylhydroxylamine (3.1 g) in

¹⁹ P. Mamalis, J. Green, and D. McHale, *J. Chem. Soc.*, 1960, 229.

²⁰ R. Behrend and K. Leuchs, *Annalen*, 1890, 257, 206.

²¹ B. Zeeh and H. Metzger, 'Methoden der Organischen Chemie: Nitrogen Compounds,' vol. 10, part 1, ed. E. Müller, Verlag, Stuttgart, 1971, p. 1192.

²² W. D. Emmons, *J. Amer. Chem. Soc.*, 1957, 79, 6522.

²³ G. Zinner, *Arch. Pharm.*, 1963, 296, 57.

²⁴ L. W. Jones and M. C. Sneed, *J. Amer. Chem. Soc.*, 1917, 39, 674.

²⁵ J. P. Freeman, *J. Org. Chem.*, 1963, 28, 2508.

¹¹ O. Červinka, in 'Enamines: Synthesis, Structure and Reactivity,' ed. A. G. Cook, Dekker, New York, 1969, p. 296.

¹² J. B. Aylward, *Quart. Rev.*, 1971, 25, 407.

¹³ J. O. Edwards and R. G. Pearson, *J. Amer. Chem. Soc.*, 1962, 84, 16.

¹⁴ H. E. De La Mare and G. M. Coppinger, *J. Org. Chem.*, 1963, 28, 1068.

¹⁵ A. H. Wragg and T. S. Stevens, *J. Chem. Soc.*, 1959, 461.

¹⁶ O. L. Brady and L. Klein, *J. Chem. Soc.*, 1927, 874.

¹⁷ O. L. Brady and F. H. Peakin, *J. Chem. Soc.*, 1930, 226.

¹⁸ E. Beckmann, *Ber.*, 1893, 26, 2633.

dichloromethane (25 ml) during 1.5 h. Work-up afforded a semi-solid which, on mixing with cold carbon tetrachloride, gave α -nitroso-*p*-chlorotoluene dimer (0.17 g), m.p. 124–125° (from carbon tetrachloride) (Found: C, 54.1; H, 3.9; N, 9.0. $C_{14}H_{12}Cl_2N_2O_2$ requires C, 54.0; H, 3.9; N, 9.0%), τ 2.6 (4H, m, ArH) and 4.6 (2H, s, CH_2), m/e 157, 155 (p - $ClC_6H_4CH_2NO^+$), 127, and 125 ($M/2 - 30$). The carbon tetrachloride solution obtained after the removal of solid material was evaporated *in vacuo* and the residue was mixed with light petroleum (b.p. 40–60°). The resulting solid decomposed on attempted recrystallisations from hot solvent and was not identified.

Oxidation of N-Benzoyl-O-benzylhydroxylamine.—Lead tetra-acetate (10.4 g) in dichloromethane (100 ml) was added to a solution of *N*-benzoyl-*O*-benzylhydroxylamine (4.6 g) in dichloromethane (225 ml) during 2.25 h. The mixture was worked up (solvent removed by evaporation *in vacuo* below 40°) to give NN'-dibenzoyl-NN'-bisbenzyloxyhydrazine (3.4 g), m.p. 63–64° (decomp.) [from ether-light petroleum (b.p. 40–60°)] (Found: C, 74.1; H, 5.5; N, 6.35. $C_{28}H_{24}N_2O_4$ requires C, 74.3; H, 5.3; N, 6.2%), ν_{max} 1280s and 1700s cm^{-1} , τ ca. 2.6 (20H, m, ArH), 4.9 (4H, s, $PhCH_2$); mass spectrum identical with that of benzyl benzoate, which was presumably formed by pyrolysis in the spectrometer.

Oxidation of O-Benzoyl-N-benzylhydroxylamine Hydrochloride.—Lead tetra-acetate (5.2 g) in dichloromethane (40 ml) was added to a slurry of *O*-benzoyl-*N*-benzylhydroxylamine hydrochloride (2.6 g) and dichloromethane (40 ml) during 45 min. The mixture was stirred for 1 h and then worked up to give a semi-solid which was mixed with light petroleum (b.p. 40–60°). The petroleum-insoluble product was stirred with cold 2M-sodium hydroxide and the alkali-insoluble material (0.28 g) was recrystallised from methanol-water (1 : 1) to give *O*-benzoylbenzaldehyde oxime, m.p. 101–103° (lit.,²⁶ 101–102°) (Found: C, 74.8; H, 4.9; N, 6.2. Calc. for $C_{14}H_{11}NO_2$: C, 74.7; H, 4.9; N, 6.2%), ν_{max} 1680sh and 1733 cm^{-1} , τ 1.5 (1H, s, $CH=N$), 2.1 (m, *ortho*-protons), and 2.3 (m, ArH), pure by t.l.c. The light petroleum solution obtained after removal of solid material was evaporated *in vacuo* to leave an oil which contained (g.l.c. and mass spectrometry) traces of benzyl

acetate, benzaldehyde, and benzonitrile. An alkali wash of the oil yielded (on acidification) benzoic acid (40 mg), m.p. and mixed m.p. 122°.

Oxidation of Tetrahydro-1,2-oxazine.—(i) Lead tetra-acetate (10.5 g) in dichloromethane (50 ml) was added to a solution of tetrahydro-1,2-oxazine (1.7 g) in dichloromethane (50 ml) during 45 min. Work-up gave an oil which was distilled in a Kugelrohr distillation apparatus, maintained at 100° and 12 mmHg, to yield 5,6-dihydro-4H-1,2-oxazine (1.3 g, 76%) (Found: C, 56.35; H, 8.4; N, 16.2. C_4H_7NO requires C, 56.5; H, 8.3; N, 16.5%), ν_{max} 1620 and 3000 cm^{-1} , τ 2.7 (1H, m, olefinic 3-H), 6.0 (2H, m, 6-H₂), and 7.7–8.2 (4H, m, 4- and 5-H₂), m/e 85 (M^+ , 100%), 70 ($M - 15$), 57, 55, and 54, pure by g.l.c. The product slowly resinified at room temperature.

(ii) Bromine (2.5 g) in chloroform (25 ml) was added to a solution of tetrahydro-1,2-oxazine (1.7 g) in chloroform (20 ml) during 1 h at 20°. The solution was stirred for a further 15 min and then washed with sodium disulphite solution and water, dried ($MgSO_4$), and evaporated to leave an oil, identical (i.r. spectrum and g.l.c. characteristics) with the product obtained from the preceding lead tetra-acetate oxidation. The oil obtained from the oxidation with bromine solidified at room temperature to give *perhydrotri*-[1,2]oxazino[2,3-a:2',3'-c:2'',3''-e]-*s*-triazine (13) (Found: C, 55.8; H, 8.3; N, 16.1. $C_{13}H_{21}N_3O_3$ requires C, 56.5; H, 8.3; N, 16.5%), m/e 255 (M^+), 170 ($M - 85$), 86 (100%), 85 ($M - 2 \times 85$), 70, 55, and 54, m^* 113.2 (255 \rightarrow 170) and 42.5 (170 \rightarrow 85); t.l.c. showed one component, R_F 0.6 (benzene-methanol, 95 : 5).

Oxidation of Isoxazolidine.—Lead tetra-acetate [100 g; washed on the pad with dry light petroleum (b.p. 60–80°)] was added in small portions to a solution of isoxazolidine (15 g) in dichloromethane (500 ml) during 1 h. The mixture was stirred for 2 h and then worked up to give Δ^2 -isoxazoline (4.6 g, 33%) as a water-soluble oil, b.p. 149–150° (Found: C, 51.1; H, 6.9; N, 19.6. C_3H_5NO requires C, 50.7; H, 7.1; N, 19.7%), ν_{max} 840 and 3000 cm^{-1} , τ 2.9 (1H, m, olefinic), 5.9 (2H, m, 5-H₂), and 7.1 (2H, m, 4-H₂), pure by g.l.c.

We thank the S.R.C. for a Studentship (to R. P.).

²⁶ O. L. Brady and G. P. McHugh, *J. Chem. Soc.*, 1925, 2414.

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