The Oxidation of Trimethylsilylated Amides to Hydroxamic Acids

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A method for the oxidation of trimethylsilylated amides to the corresponding hydroxamic acids is described. The method utilises aprotic oxidants, based on Mo^{V} peroxides and has been demonstrated for the oxidation of a variety of secondary amides. The oxidation is particularly efficient for aromatic amides and has been applied to the synthesis of herbicides of the 2,4-dihydroxybenzoxazinone class.

A VARIETY of natural products containing hydroxamic acid functions have become known in recent years.[1] This group of compounds possesses a wide range of biological activities, including the important role of hydroxamic acids in certain iron-transporting systems, which has attracted increasing attention to such materials.[2] Biosynthetic studies have indicated that *in vivo* formation of hydroxamic acids can occur either by acylation of hydroxylamines or by the direct *N*-hydroxylation of amides.[3] Whereas *N*-acylation of hydroxylamines has long been used for the *in vitro* synthesis of hydroxamic acids, the direct oxidation of amides has only very recently come under scrutiny. Some previous work on this problem has been published and a method for the oxidation of imino-ethers to hydroxamic acids has been reported, although yields are generally low.[4]

Following the discovery that trimethylsilylation of secondary amides activates them towards oxidation to hydroxamic acids by the peroxo-molybdenum complex MoO_5·HMPA [5] the scope of this reaction has been investigated in more detail.

RESULTS AND DISCUSSION

The trimethylsilylation of amides is a well documented process [6] which generally gives good yields (Table 1).

Spectroscopic evidence, including that obtained from ^{13}C n.m.r. studies, indicates that simple amides and lactams are silylated exclusively on nitrogen, whereas cyclic unsaturated lactams, such as 2-pyridone, are *O*-silylated, and acetanilides give isomeric mixtures of O–Si and N–Si forms.[7] The derivatives are sensitive to water and protic solvents, being solvolysed to the parent amide.

In order to oxidise trimethylsilylated amides aprotic oxidants are required, and for this reason the application of molybdenum(v) oxides was investigated. Such oxidants have a further advantage. Since molybdenum is known to form stable complexes with hydroxamic acids, there existed the possibility that, after oxidation, the product hydroxamic acid would become complexed with the molybdenum ion, thus avoiding further, over-oxidation during the reaction.

Molybdenum pentaoxide complexes (1) are stable, covalent diperoxo-species.[8] A variety of donor ligands, L^1 and L^2, are known but with hexamethylphosphoric triamide (HMPA) occupying one site, insoluble complexes with either a vacant (2), or occupied, *e.g.* (3), second site are known.[9] The bis(dimethylformamide) complex (4) was also of use in our work. Most of the peroxo-complexes have limited solubility in organic solvents and, owing to an equilibrium between free and ligated species in solution, the complexes generally decompose above 40 °C. The dimethylformamide complex (4) was the preferred oxidant; although the HMPA complexes are more readily prepared, since they precipitate from aqueous media, the water-soluble dimethylformamide complexes are more stable on storage and there is no residual water ligand to interfere with the subsequent oxidation. Furthermore the released dimethylformamide ligands interfere less in the work-up procedures than hexamethylphosphoric amide. Oxidations with the various complexes differed little, other than longer reaction times required for the fully co-ordinated species (4). Since oxidations with these peroxo-complexes are thought to involve substrate–molybdenum complex formation,[10] competing strong

TABLE 1

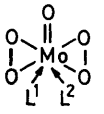
Trimethylsilylation of secondary amides

Amide	Silylating agent	Yield (%)	B.p.	Lit. b.p.
(5)	Me_3SiCl,NEt_3	56	114—117 °C at 100 mmHg	79—80 °C at 12 mmHg [a]
(8)	Me_3SiCl,NEt_3	70	51—52 °C at 2 mmHg	71—81 °C at 6 mmHg [b]
(10)	Me_3SiCl,NEt_3	50	114—115 °C at 60 mmHg	111—111.5 °C at 6 mmHg [c]
	Me_3SiCl,NaH	89		
(12)	Me_3SiCl,NEt_3	73	115—120 °C at 50 mmHg	*d*
(14)	Me_3SiCl,NEt_3	62	88—89 °C at 150 mmHg	*d*
(16)	Me_3SiCl,NEt_3	42	90—92 °C at 0.5 mmHg	*d*
(18)	Me_3SiCl,NEt_3	56	105—106 °C at 15 mmHg	105 °C at 13 mmHg [e]
	BSA [e]	95		
(20)	$(Me_3Si)_2NH$	75	98 °C at 2 mmHg	61—62 °C at 0.2 mmHg
(22)	$(Me_3Si)_2NH$	83	112—115 °C at 1.5 mmHg	75—76 °C at 0.2 mmHg [f]
(24)	Me_3SiCl,NaH	80	135—140 °C at 1 mmHg	88—90 °C at 0.2 mmHg [f]
(26)	Me_3SiCl,NEt_3	26	131—134 °C at 3 mmHg	106 °C at 0.15 mmHg [h]
(28)	$(Me_3Si)_2NH$	40	80—85 °C at 1.0 mmHg	*d*

[a] K. Rühlmann and B. Rupprich, *Annalen*, 1965, **686**, 226. [b] M. J. Hurwitz and P. L. Benneville, U.S.P. 2,876,209 (*Chem. Abs.*, 1959, **53**, 12321d). [c] L. Birkofer, H. Dickopp, and S. K. Maglis, *Chem. Ber.*, 1969, **102**, 3094. [d] New compound. [e] Bistrimethylsilylacetamide. [f] H. E. Baumgartner, A. Staklis, and E. M. Miller, *J. Org. Chem.*, 1965, **30**, 1203. [g] J. F. Klebe, H. Finkbeiner, and D. M. White, *J. Amer. Chem. Soc.*, 1966, **88**, 3390. [h] M. Fukui, K. Itoh, and Y. Ishii, *J.C.S. Perkin II*, 1972, 1043.

donor ligands or very polar solvents competitively inhibit the reaction and oxidations were best carried out in chloroform or, routinely, dichloromethane solutions.

After *N*-trimethylsilyl-2-piperidone was stirred with (2) in dichloromethane at room temperature for 2 d, evaporation afforded a yellow crystalline solid, analysing as $C_{10}H_{16}MoN_2O_6$. The i.r. spectrum of this compound showed intense peaks at 945 and 920 cm^{-1}, characteristic of a *cis*-MoO_2 group, and a peak at 1 590 cm^{-1} indicative of a complexed hydroxamate carbonyl function. Accordingly this complex was assigned structure (6). With aqueous ferric chloride solutions a cherry-red colour, characteristic of Fe(III)–hydroxamate complexes, slowly

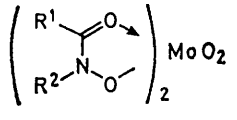


(1) L^1 = DMF, L^2 = vacant
(2) L^1 = HMPA, L^2 = vacant
(3) L^1 = HMPA, L^2 = H_2O
(4) L^1 = L^2 = DMF

developed; iron is known to displace molybdenum from its hydroxamic acid complexes.[11]

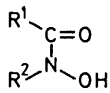
Similar complexes were isolated from the peroxomolybdenum oxidation of other trimethylsilylamides. The carbonyl stretching frequencies in the complexes were generally 20—30 cm^{-1} lower than in the free hydroxamic acids. The complexes are relatively stable although it was found that attempted treatment of the complexes with hydrogen sulphide, aimed at precipitation of the metal as its sulphide, also caused reduction of the hydroxamic acid to the parent amide. This reduction was general for several molybdenum hydroxamates (see Experimental section). Liberation of the uncomplexed hydroxamic acids was accomplished by extraction of the molybdenum ion with warm ethylenediaminetetraacetic acid (EDTA) at pH 9. Since many of the hydroxamic acids are water-soluble, their efficient recovery required continuous extraction with either chloroform or dichloromethane after adjustment of the pH of the solution to 7.5. In this manner 90—100% recoveries of the hydroxamic acids from their molybdenum complexes was achieved.

The scope of the oxidation reaction has been examined.



(6)

The oxidations of silylated secondary aliphatic amides (Table 2) gave, with the exception of ε-caprolactam (10) low yields (<16%) of the corresponding hydroxamic acids. In the series of lactams (5), (8), and (10) the range of yields, from 0 to 42%, may in part reflect the stability of the molybdenum hydroxamates. Whereas



	R^1		R^2	
(5)		$[CH_2]_4$		(7)
(8)		$[CH_2]_3$		(9)
(10)		$[CH_2]_5$		(11)
(12)	Pr^n		Bu^n	(13)
(14)	Me		Bu^n	(15)
(16)	Ph		Pr	(17)
(18)	Me		Ph	(19)
(20)	Me		*p*-ClC_6H_4	(21)
(22)	Me		*p*-$MeOC_6H_4$	(23)
(24)	Me		*p*-$NO_2C_6H_4$	(25)
(26)	Ph		Ph	(27)
(28)	2,4,6-$Me_3C_6H_2$		Me	(29)

the complex of *N*-hydroxy-2-piperidone (6; R^1, R^2 = $[CH_2]_4$) could be synthesised directly from the hydroxamic acid (7),[12] attempted formation of the complex from *N*-hydroxysuccinimide afforded, instead, succinic acid.

By contrast to the aliphatic amides, hydroxylation of a series of acetanilides consistently gave moderate yields (40—50%) of hydroxamic acids (Table 2) over a wide range of experimental conditions. Attempts to improve the yields, either by using an excess of oxidant or sub-

TABLE 2

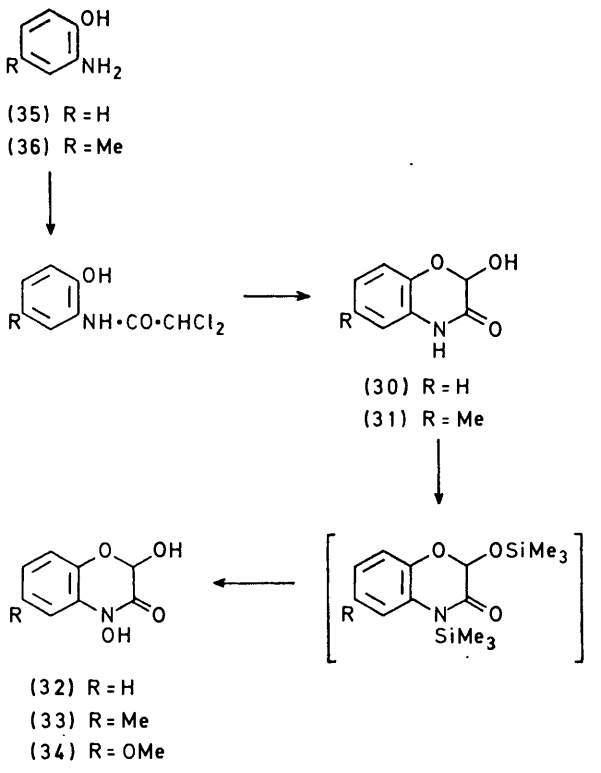
Oxidation of trimethylsilylated amides

Amide	Oxidant	Mol ratio of oxidant	Solvent	Reaction time	Yield (%) [a]
(5)	(2)	0.5	CH_2Cl_2	48 h	14
(8)	(2)	0.5	CH_2Cl_2	14 d	trace
	(4)	0.5	CH_2Cl_2	14 d	0
(10)	(1)	0.5	CH_2Cl_2	36 h	42 [b]
	(2)	0.5	CH_2Cl_2	3 d	23
(12)	(2)	0.5	CH_2Cl_2	6 d	14
(14)	(4)	0.5	CH_2Cl_2	48 h	16
(16)	(4)	0.5	CH_2Cl_2	15 h	34
(18)	(2)	0.5	CH_2Cl_2	45 h	45 [b]
(18)	(1)	0.55	CH_2Cl_2	6 h	47 [c]
(18)	(1)	5.0	CH_2Cl_2	4 h	25
(18)	(1)	0.1	CH_2Cl_2	4 h	30 [d]
(18)	(1)	0.5	C_6H_6	4 h	43
(18)	(1)	0.5	CH_3NO_2	24 h	11 [e]
(18)	MoO_5·HMPA·pyridine	1.0	CH_2Cl_2	6 h	43 [f]
(18)	(4)	1.0	CH_2Cl_2	15 h	42
(18)	MoO_5·pyr·H+	0.5	CH_2Cl_2	6 h	37 [g]
(20)	(4)	1.0	CH_2Cl_2	15 h	42
(22)	(4)	0.5	CH_2Cl_2	15 h	41
(24)	(4)	0.5	CH_2Cl_2	15 h	45
(24)	(4)	1.1	CH_2Cl_2	15 h	48
(26)	(2)	0.5	CH_2Cl_2	3 h	34
(28)	(4)	0.75	CH_2Cl_2	120 h	trace

[a] Hydroxamic acid yields based on starting trimethylsilylamide. [b] As Mo complex (6); release as free hydroxamic acid achieved in 90—100% yield. [c] Without isolation of the intermediate trimethylsilylacetanilide. [d] Yield based on oxidant. [e] 83% Parent amide recovered. [f] Pyridine *N*-oxide (10%) was also produced. [g] 53% Parent amide recovered.

strate, failed, owing to hydrolysis of the silylamide with a large quantity of oxidant or, in the latter case, partly because of the difficulties associated with separation of the hydroxamic acid from the excess of amide. The choice of the oxidant appears to have little effect on the yields, despite the fact that the monoligated complex (2) required shorter reaction times.

The above oxidation of anilides into the corresponding hydroxamic acid was adapted for oxidation of the benzoxazinones (30) and (31) into the derivatives (32) and (33) respectively. Such derivatives, *e.g.* (34), are



SCHEME

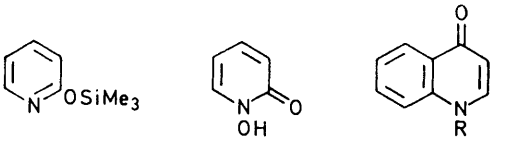
products which possess the property of inhibiting auxin binding in certain preparations. Virtanen has described a multistage synthesis of compounds (32) and (34) in overall yields of $<1\%$, which proceeds *via* acylation of aromatic hydroxylamine intermediates.[13] In our procedure (Scheme) the *o*-aminophenols (35) and (36) were acylated with dichloroacetyl chloride and solvolysed into the corresponding acetals (30) and (31). Silylation effected both protection of the acetal function and activation of the amide group. Oxidation with the molybdenum complex (4) directly, followed by release of the free hydroxamic acids, afforded compounds (32) and (33) in overall yields of 20%.

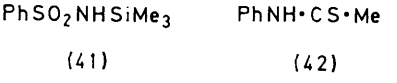
A brief examination of other substrates was also made. The oxidation of 2-(trimethylsilyloxy)pyridine (37) proceeded smoothly with 2 equiv. of the complex (4), to give a high (90%) yield of the corresponding hydroxamic acid (38). Similarly 4-quinolone (39), as its trimethylsilyl derivative, gave the corresponding hydroxamic acid (40) in 55% yield. In contrast silylated ureas, such as that from *NN*-diethyl-*N'*-phenylurea, did not produce the corresponding hydroxamic acid on oxidation. Carbamates also failed to give the desired oxidation products and the trimethylsilyl derivative of succinimide, as mentioned above, afforded succinic acid after work-up.

Attempts were also made to persuade primary amides to react. In the event both the monosilylated derivatives of benzamide and acetamide produced only traces of hydroxamic acids. Bis(trimethylsilyl)acetamide showed irreproducible formation of acetohydroxamic acid, but yields were always very low.

Although benzenesulphonamide produced a mono-*N*-silylated derivative (41),[14] subsequent treatment did not cause any *N*-oxidation and the sulphonamide was recovered. Thioacetanilide (42) was also silylated but oxidation of the derivative afforded acetanilide, rather than the thiohydroxamate or *S*-oxide, which is the product of mild oxidation with hydrogen peroxide.

The behaviour of a few heterocyclic bases was examined. Whereas trimethylsilylated imidazole (43) with the complex (4) afforded a virtually quantitative recovery of imidazole on work-up, the benzimidazole derivative (44) produced the benzimidazole 1-oxide (45) in 10% yield, in addition to recovered starting material. Bis(trimethylsilyl)adenosine (46) gave small amounts of a new product (5% yield) which was assigned as the 1-oxide (47) by comparison of its properties with the known adenine 1-oxide.[15] The conversion of adenine into its 1-oxide is readily accomplished by standard peracid reagents. With pyridine a very slow oxidation to the *N*-oxide occurred with reagents such as (2) and (4); peroxomolybdenum complexes containing pyridine as a ligand can be prepared and are relatively stable.[8]

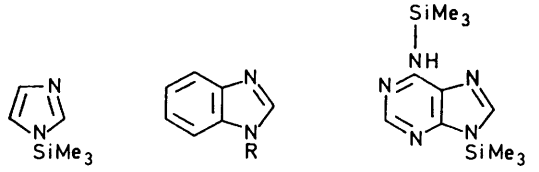




This behaviour of pyridine towards the reagents contrasts with the rapid formation of the *N*-oxide which is observed with organic peracids, and in the transition-metal-catalysed decomposition of peroxides.

Various alternatives to the trimethylsilyl group as an activating species and molybdenum pentaoxide as oxidant were briefly investigated. In contrast to the hydroxylation of carbanions by molybdenum pentaoxide,[16] the sodium, lithium, and iodomagnesium salts of acetanilide were unaffected. The imidate (48) was of particular interest but it, too, was not oxidised, the starting amide being recovered after work-up. Associ-

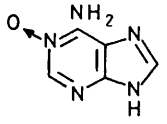
ation of the molybdenum oxidant with the silylated amides must, therefore, rely on the ability of the trimethylsilyl group to migrate to oxygen, the side-product from the oxidations being hexamethyldisiloxane. Amongst other acetanilide derivatives investigated the triphenylsilyl (49), trimethylstannyl (50), and tributylstannyl (51) derivatives were prepared. These all gave some hydroxamic acid product with the oxidant (2), but in yields of $<10\%$.



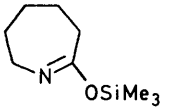
(43)

(44) R = $SiMe_3$
(45) R = OH

(46)



(47)



PhN(R)·CO·Me

(49) R = Ph_3Si
(50) R = Me_3Sn
(51) R = Bu_3Sn

Various alternatives to the peroxomolybdenum complexes were tried as oxidants of the silylated amides (especially acetanilide), including peracids, peroxides, and aromatic *N*-oxides, but none of these proved effective, the starting amide being recovered on work-up.[17]

EXPERIMENTAL

M.p.s were determined on a Kofler block. Infrared and ultraviolet spectra were recorded on a Perkin-Elmer 137 and a Pye–Unicam SP 8000 spectrophotometer, respectively. ^1H N.m.r. spectra were recorded on either a Varian T60 or JEOL MH-100 instrument and refer to solutions in deuteriochloroform unless stated otherwise; chemical shifts are given in p.p.m. (δ) from tetramethylsilane as internal standard. Mass spectra were either recorded on an A.E.I. MS 9 spectrometer or obtained from PCMU, Harwell.

Solvents were dried and freshly distilled before use. The silylation procedures were carried out under anhydrous conditions.[18]

Preparation of the Peroxomolybdenum Complexes.—(NN-*Dimethylformamido*)*oxodiperoxomolybdenum*(VI). Molybdic acid (20 g, 0.15 mol) was dissolved in 30% hydrogen peroxide (100 ml) at 35 °C. The yellow solution was cooled to 15 °C and dimethylformamide (10.95 g, 0.15 mol) added. The aqueous solution was partially evaporated under reduced pressure, maintaining the temperature below 35 °C. The resultant yellow crystals were collected by filtration, and washed thoroughly with ether and a small volume of methanol (2 × 25 ml). The hydrated complex was dried *in vacuo* over phosphorus pentaoxide to yield the *complex* (1) as a yellow powder (29.8 g, 75%), m.p. 102 °C (decomp.); $\nu_{max.}$ (Nujol) 1 665, 1 350, 975, 885, 875, and 720 cm^{-1}; δ 2.9 (3 H, s), 3.0 (3 H, s), and 7.9 (1 H, br s); $\lambda_{max.}$ (EtOH) 335 nm (log ε 3.9) (Found: active oxygen 25.4. $C_3H_7MoNO_6$ requires 25.7%).

Bis(NN-*dimethylformamido*)*oxodiperoxomolybdenum*(VI). The above procedure, but with 2 mol of dimethylformamide, afforded the complex (4) (65%), m.p. 100—102 °C; $\nu_{max.}$ (Nujol) 1 660, 1 640, 1 350, 945, 875, 860, 680, and 655 cm^{-1} (lit.,[8] $\nu_{max.}$ 1 650, 945, 855, 680, and 655 cm^{-1}) (Found: active oxygen 19.67. Calc. for $C_6H_{14}MoN_2O_7$, 19.87%).

(*Hexamethylphosphoramido*)*oxodiperoxomolybdenum*(VI). This was prepared by the method of Mimoun *et al.*[8] Initially the hydrated complex (3) was produced (62%). Drying the complex (3) *in vacuo* over phosphorus pentaoxide for 5 d gave the title complex (2), m.p. 101—102 °C (decomp.) (Found: active oxygen 17.8; C, 20.5; H, 5.0; N, 11.8. Calc. for $C_6H_{18}MoN_3O_6P$: active oxygen, 18.0; C, 20.3; H, 5.1; N, 11.8%). This material was unstable and gradually lost its active oxygen during one month at room temperature. A slower but still noticeable loss of activity occurred at 0 °C.

The pyridine complex of (2) was prepared by the method of Vedejs [9] and the dipyridinium-μ-oxo-bis[oxodiperoxomolybdate(VI)] complex was prepared by the method of Mimoun *et al.*[8] (see Table 2 for their use).

General Silylation Procedures.—(A) Chlorotrimethylsilane (1.1 equiv.) was added dropwise to a solution of the amide (1 equiv.) and dry triethylamine (1 equiv.) in dry benzene and the mixture heated under reflux for 1—8 h. Triethylamine hydrochloride was filtered off under dry nitrogen, washed with benzene and the filtrate evaporated under reduced pressure. The residual oil was vacuum-distilled.

(B) Sodium hydride (50% dispersion in oil; 1 equiv.) was added during 15 min to a solution of the amide (1 equiv.) in dry THF. After hydrogen evolution had ceased (30—60 min), chlorotrimethylsilane (1.2 equiv.) was added and the mixture stirred at room temperature for 1 h. Removal of the sodium chloride, either by filtration under nitrogen or by centrifugation and decantation, and evaporation of the solvent afforded the crude silylamide which was distilled under reduced pressure.

(C) The amide was heated in an excess of hexamethyldisilazane, containing a drop of trimethylsilyl chloride, under reflux for periods up to 24 h. Evaporation of the excess of reagent left the silylated amide which was purified by vacuum-distillation.

The silylated amides were characterised by comparison of their physical properties with literature values. New compounds were analysed by ^1H n.m.r. spectroscopy followed by hydrolysis back to the parent amide. Because of the instability of many of the silylated products, microanalytical methods were avoided.

General Method for Preparation of Molybdenum Hydroxamate Complexes.—The trimethylsilylamide (1 equiv.) and the molybdenum pentaoxide complex (1—2 equiv.) in dry dichloromethane were stirred at room temperature until the oxidant had disappeared, producing a deep red solution. Evaporation and crystallisation of the residue, generally from methanol, gave the molybdenum bis(hydroxamate).

An alternative procedure was to start with the amide, without isolation of the intermediate silylamide. This procedure was generally adopted when hexamethyldisilazane was used as the silylating reagent. The residue, after evaporation of excess of reagent, was immediately dissolved in dichloromethane and oxidised.

General Method for the Liberation of Hydroxamic Acids from the Molybdenum Complexes.—The molybdenum com-

plex was dissolved in 1M-Na_4(EDTA) (pH 9.5). After 30 min the solution was adjusted to pH 7.5, and continuously extracted with dichloromethane (1—3 d). Evaporation of the solvent gave the hydroxamic acid.

Bis(N-*phenylacetohydroxamato*)*dioxomolybdenum*(VI). This was isolated as pale yellow crystals, m.p. 188 °C (decomp.); $\nu_{max.}$ (Nujol) 1 570, 940, and 900 cm^{-1}; δ 2.25 (3 H, s) and 7.5 (5 H, br s); $\lambda_{max.}$ (EtOH) 251 (log ε 4.26) (Found: C, 44.9; H, 4.0; N, 6.5. $C_{16}H_{16}MoN_2O_6$ requires C, 44.9; H, 3.8; N, 6.5%).

Bis(N-*phenylbenzohydroxamato*)*dioxomolybdenum*(VI). This was isolated as orange crystals, m.p. 169—170 °C (decomp.) (lit.,[12] m.p. 188 °C); $\nu_{max.}$ (Nujol) 1 540, 950, and 920 cm^{-1}.

Bis(N-*oxy*-2-*piperidonato*)*dioxomolybdenum*(VI). This was isolated as yellow crystals, m.p. 214 °C (decomp.); $\nu_{max.}$ (Nujol) 1 590, 945, and 920 cm^{-1} (Found: C, 33.8; H, 4.5; N, 7.75. $C_{10}H_{16}MoN_2O_6$ requires C, 33.7; H, 4.5; N, 7.9%).

Bis(N-*oxycaprolactamato*)*dioxomolybdenum*(VI). This was isolated as yellow crystals, m.p. 192—193 °C (decomp.); $\nu_{max.}$ (Nujol) 1 570, 930, and 900 cm^{-1}.

N-*Hydroxy*-2-*piperidone* (7). This was prepared by the general method, and had m.p. 50—51 °C (lit.,[19] m.p. 55—57 °C).

N-*Hydroxy*-ε-*caprolactam*. M.p. 77—78 °C (lit.,[19] m.p. 80—81 °C); $\nu_{max.}$ (Nujol) 3 100—2 700, 1 640 cm^{-1}; δ 1.8 (6 H, m), 2.4 (2 H, m), 3.3 (2 H, t), 6.6 (1 H, br s).

N-*Hydroxy*-N-*butylbutyramide* (13). This was obtained as an oil which gave a cherry-red colour with $FeCl_3$; $\nu_{max.}$ (film) 3 200 and 1 620 cm^{-1}.

N-(1,1-*Dimethylethyl*)-N-*hydroxyacetamide* (15). This was obtained as a colourless oil, b.p. 90 °C at 0.35 mmHg (lit.,[20] b.p. 93 °C at 0.5 mmHg); $\nu_{max.}$ 3 160 and 1 620 cm^{-1}; δ(CCl_4) 1.40 (9 H, s), 2.05 (3 H, s), and 7.0 (1 H, br s) (Calc. for $C_6H_{13}NO_2$: *M*, 131.094 6. Found. M^+, 131.094 6).

N-*Hydroxy*-N-*propylbenzamide* (17). Isolated as a crystalline solid, m.p. 66—69 °C; $\nu_{max.}$ ($CHCl_3$) 3 450 and 1 640 cm^{-1}; δ 1.0 (3 H, t), 1.7 (2 H, m), 3.5 (2 H, t), 7.0 (1 H, br s), and 7.4—8.0 (5 H, m) (Found: C, 67.3; H, 7.6; N, 8.0. $C_{10}H_{13}NO_2$ requires C, 67.0; H, 7.3; N, 7.8%).

N-*Hydroxyacetanilide* (19). Isolated as colourless needles, m.p. 65—66 °C (lit.,[21] m.p. 67—67.5 °C).

N-*Hydroxy*-4-*chloroacetanilide* (21). Isolated as colourless crystals, m.p. 111—112 °C (lit.,[21] m.p. 113 °C).

N-*Hydroxy*-4-*methoxyacetanilide* (23). Isolated as colourless needles, m.p. 98—101 °C; $\nu_{max.}$ (Nujol) 3 220 and 1 645 cm^{-1}; δ 2.2 (3 H, s), 3.8 (3 H, s), 7.1 (5 H, m), 8.0 (1 H, br s) (Found: C, 59.5; H, 6.1; N, 7.5. $C_9H_{11}NO_3$ requires C, 59.7; H, 6.1; N, 7.7%).

N-*Hydroxy*-4-*nitroacetanilide* (25). Isolated as colourless needles, m.p. 175—176 °C; $\nu_{max.}$ (Nujol) 3 200 and 1 640 cm^{-1}; δ(CD_3OD) 2.38 (3 H, s), 7.90 (2 H, d, *J* 10 Hz), and 8.10 (2 H, d, *J* 10 Hz) (Found: C, 48.8; H, 4.2; N, 13.95. $C_8H_8N_2O_4$ requires C, 48.95; H, 4.1; N, 14.3%).

N-*Hydroxybenzanilide* (27). Isolated as colourless needles, m.p. 119—120 °C (lit.,[22] m.p. 121 °C).

2-*Hydroxy*-2,4-*dihydro*-1,4-*benzoxazin*-3-*one* (30).—This was prepared by the method of Virtanen.[13] Dichloroacetyl chloride (5.0 g, 34 mmol) was added dropwise to a suspension of 2-aminophenol (7.4 g, 68 mmol) in dry ether (100 ml). The reaction mixture was stirred for 1 h at room temperature, filtered, and the dichloroamide isolated by crystallisation from the mother-liquor (7.1 g; 95%), m.p. 135—136 °C. A portion (2.2 g) was heated to boiling in aqueous sodium hydrogencarbonate solution (1.68 g in 80 ml) for 30 min, then cooled, and acidified with dilute HCl. The product was extracted with ether to give the benzoxazinone (1.50 g, 91%), m.p. 202—203 °C (lit.,[13] m.p. 201—203 °C).

2,4-*Dihydroxy*-3,4-*dihydro*-1,4-*benzoxazin*-3(2H)*one* (32).—The lactam (30) (4.95 g, 30 mmol) was heated with bis(trimethylsilyl)acetamide (20 g, 100 mmol) under reflux for 1 h. Removal of the excess of reagent left a pale brown oil (9.3 g), which was dissolved in dichloromethane (20 ml) and stirred with the complex (4) (14.5 g, 45 mmol) for 8 h at room temperature. The solvent was removed and the residue dissolved in 1M-Na_4(EDTA) (100 ml). The basic solution was extracted with ether, to remove neutral products. After acidification, the aqueous layer was adjusted to pH 7.0 and continuously extracted with ether for 2 d. After evaporation, the crude product was purified by chromatography through polyamide powder (SC6; 50% v/v acetone–toluene as eluant) to afford the hydroxamic acid (32) as colourless needles (1.75 g, 33%), m.p. 153—154 °C (lit.,[13] 153 °C). The material sublimed at 50—55 °C at 0.005 mmHg; $\nu_{max.}$ (Nujol) 3 400, 3 360, 1 650, 1 040, 980, 830, and 750 cm^{-1}; $\lambda_{max.}$ (EtOH) 254 mm (log ε 3.6), 283 (3.5), 288 (3.5); *m/e* 181 (10%), 165 (10), 163 (7), 136 (41), 135 (100), 91 (26), 79 (57), 64 (21), 52 (38), and 18 (30) (Found: M^+, 181.037 5. Calc. for $C_8H_7NO_4$: *M*, 181.037 5).

2-*Hydroxy*-6-*methyl*-3,4-*dihydro*-1,4-*benzoxazin*-3(2H)-*one* (31).—In a similar manner to that above, 2-(αα-dichloroacetamido)-4-methylphenol was prepared from 2-amino-4-methylphenol. The *amide* had m.p. 136—137 °C; $\nu_{max.}$ (Nujol) 3 340, 3 180, 1 660, 1 595, 1 540, 1 200, 1 115, 805, and 625 cm^{-1}; *m/e* 237 (2%), 239 (9.5), 233 (15), 150 (100), 122 (37), 94 (22), 77 (14), and 2 (54) (Found: M^+, 233.001 3. $C_9H_9NO_2{}^{35}Cl_2$ requires *M*, 233.001 0).

Hydrolysis of the dichloroamide (2.34 g) with aqueous sodium hydrogen carbonate solution gave the *title compound* (1.70 g, 95%), m.p. 207—211 °C; $\nu_{max.}$ (Nujol) 3 220, 1 680, 1 610, 1 210, 1 070, 1 020, 865, and 805 cm^{-1}; *m/e* 179 (60%), 150 (100), 132 (60), 94 (35), 77 (32), and 39 (32) (Found: C, 60.3; H, 5.4; N, 7.8. $C_9H_9NO_3$ requires C, 60.3; H, 5.1; N, 7.8%).

2,4-*Dihydroxy*-6-*methyl*-3,4-*dihydro*-1,4-*benzoxazin*-3(2H)-*one* (33).—The benzoxazinone (31) (1.0 g, 5.6 mmol) was silylated with hexamethyldisilazane (5 ml) containing a trace of chlorotrimethylsilane at reflux for 12 h. After removal of the excess of reagent the residue was dissolved in dichloromethane (6 ml) and stirred with the complex (4) (1.80 g, 5.6 mmol) for 4 h at room temperature. The dichloromethane was evaporated off and the resulting oil was treated with 1M-Na_4(EDTA) solution. Ether extraction recovered unchanged benzoxazinone (31) (38%). Work-up of the acid fraction and purification through a polyamide column afforded the *title compound* (0.34 g; 31%), m.p. 160—161 °C; $\nu_{max.}$ (Nujol) 3 300, 3 200—2 500, 1 655, 1 610, 1 215, 1 050, 870, and 875 cm^{-1}; *m/e* 195 (10%), 179 (11), 173 (22), 149 (100), 104 (16), 93 (28), 78 (23), 47 (34), and 44 (52) (Found: C, 55.4; H, 4.7; N, 6.9. $C_9H_9NO_4$ requires C, 55.4; H, 4.65; N, 7.2%).

1-*Hydroxy*-2-*pyridone* (38).—2-(Trimethylsilyloxy)pyridine (167 mg, 1 mmol) was oxidised under the normal conditions with the complex (4) (360 mg, 1.1 mmol). After work-up, including purification by preparative t.l.c., the title compound was isolated (100 mg, 91%), m.p. 148—

169 °C (lit.,[23] m.p. 149 °C), identical in its properties and mixed m.p. to an authentic sample.

1-*Hydroxy*-4-*quinolone* (40).—4-Hydroxyquinoline (78 mg, 0.5 mmol) was silylated with hexamethyldisilazane in the usual manner before oxidation with the complex (4) (200 mg, 0.6 mmol). After work-up, including purification by preparative t.l.c. (SiO_2; 8% v/v MeOH–$CHCl_3$) the hydroxylated product was obtained (45 mg, 55%), m.p. 235—237 °C (lit.,[24] m.p. 238 °C) (Found: M^+, 161.047 9. Calc. for $C_9H_7NO_2$: M, 161.047 7).

Attempted Oxidation of Trimethylsilylsuccinimide.—Succinimide was silylated with chlorotrimethylsilane and triethylamine. The resulting oil (b.p. 68 °C at 1.5 mmHg) (lit.,[25] b.p. 72—73 °C at 2 mmHg) (682 mg, 4 mmol) was stirred with the complex (1) (498 mg, 2 mmol) in dichloromethane (10 ml) at room temperature for 15 h. Work-up, during which no positive hydroxamic acid test was obtained, afforded succinic acid (25%), m.p. 182—184 °C (lit.,[26] m.p. 184 °C).

Oxidation of (Trimethylsilyl)thioacetanilide (42).—Thioacetanilide (640 mg, 4.2 mmol) in dry ether (12 ml) was treated with butyl-lithium (1.7M, 2.5 ml, 4.2 mmol) under nitrogen and the resulting red solution was treated with chlorotrimethylsilane to give, after work-up, the silylthioamide (450 mg, 47%), b.p. 80—85 °C at 4 mmHg. A portion (250 mg, 1.1 mmol) was stirred with the complex (4) (365 mg, 1.1 mmol) in dichloromethane (1 ml) for 30 min. Evaporation of the solvent and crystallisation of the residue from methanol gave acetanilide (129 mg, 85%), m.p. 115—116 °C (lit.,[26] m.p. 115—116 °C).

Attempted Oxidation of Benzenesulphonamide.—The trimethylsilyl derivative (41) was prepared according to the literature method.[14] A sample (374 mg, 1.6 mmol) was stirred with the complex (1) (200 mg, 0.8 mmol) in dichloromethane (5 ml) for 48 h at room temperature. On work-up only the product of hydrolysis, benzenesulphonamide, was formed.

Preparation of Benzimidazole 1-*Oxide* (45).—Trimethylsilylbenzimidazole (500 mg, 2.6 mmol) was treated with the complex (4) (460 mg, 1.4 mmol) in dichloromethane (4 ml) at room temperature for 15 h. Separation of the crude reaction products by preparative t.l.c. (SiO_2, 2% v/v MeOH–$CHCl_3$) afforded benzimidazole (85%) and benzimidazole 1-oxide (35 mg, 10%), m.p. 211—214 °C (lit.,[27] m.p. 213—215 °C) (Found: M^+, 134.047 4. Calc. for $C_7H_6N_2O$: M^+, 134.048 0).

Attempted Oxidation of Adenine.—Adenine was silylated with hexamethyldisilazane in the normal manner to give the bis(trimethylsilyl)adenine (46) as a colourless oil.[28] Oxidation of a portion of this (from 108 mg adenine, 0.9 mmol) with the complex (4) (480 mg, 0.9 mmol) under the usual conditions was followed by chromatography (SiO_2, 15% v/v MeOH–$CHCl_3$) to yield recovered adenine and a more polar component corresponding to adenine 1-oxide (7 mg, 5%), m.p. 300 °C (slow decomp.) [lit.,[15] m.p. 297—307 °C (decomp.)]; $\lambda_{max.}$ (EtOH) 235 nm (log ε 4.15) (lit.,[15] $\lambda_{max.}$ 231 and 263 nm at pH 7) (Found: M^+, 151.049 1. Calc. for $C_5H_5N_5O$: M, 151.049 4).

Preparation and Reactions of Acetanilide Derivatives.—(a) (*Triphenylsilyl*)*acetanilide*. The sodium salt of acetanilide reacted with chlorotriphenylsilane in dry THF to give the triphenylsilyl derivative. Oxidation with complex (4) (1 : 1 mol ratio) in the normal manner, and isolation, afforded the hydroxamic acid (19) in 8% yield.

(b) (*Trimethylstannyl*)*acetanilide*. The sodium salt of acetanilide was treated with chlorotrimethylstannane in THF solution for 2 h. After filtering off the precipitated sodium chloride, evaporation afforded the stannyl derivative as an odoriferous oil. Direct oxidation with the complex (2) (1 : 1 mol ratio) in dichloromethane at room temperature for 2 h and work-up in the usual manner gave the hydroxamic acid (19) in 8% yield.

(c) (*Tributylstannyl*)*acetanilide*. The reaction was carried out in the same manner as for the trimethylstannyl derivative. A 5% yield of the hydroxamic acid (19) was obtained.

(d) *Metal derivatives*. Direct oxidation, with complexes (1) and (4), of the sodium salt of acetanilide (prepared with NaH), the lithium salt (prepared with butyl-lithium), or the iodomagnesium salt (prepared with 1 equiv. of methylmagnesium iodide) failed to produce any of the required hydroxamic acid (19).

Reduction of Bis(N-*phenylacetohydroxamato*)*dioxomolybdenum*(VI).—H_2S was passed into a solution of the molybdenum complex (0.428 5 g; 0.001M) in dichloromethane (10 ml). A brown precipitate formed rapidly, and after 3 min the mixture was filtered through Celite and the solution evaporated to give acetanilide (0.278 g; 100%), identical to an authentic sample. A ferric chloride test on the product was negative.

Reduction of Bis(N-*phenylbenzohydroxamato*)*dioxomolybdenum*(VI).—By the same procedure as above, benzanilide was obtained in 100% yield.

Reduction of Bis(N-*oxy*-2-*piperidonato*)*dioxomolybdenum*-(VI).—H_2S was passed into a solution of the molybdenum complex (0.178 2 g; 0.00 5M) in dichloromethane (10 ml) for 3 h and the mixture filtered through Celite. After extraction of the filtrate with 2N HCl (3 × 10 ml) evaporation of the dried dichloromethane solution afforded the recovered molybdenum complex (0.063 g; 33%). The acidic extracts were combined, basified with NaOH solution, and continuously extracted overnight to give 2-piperidone (0.025 g; 25%).

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