A New Method for the Preparation of Hydroxamic Acids from Secondary Amides

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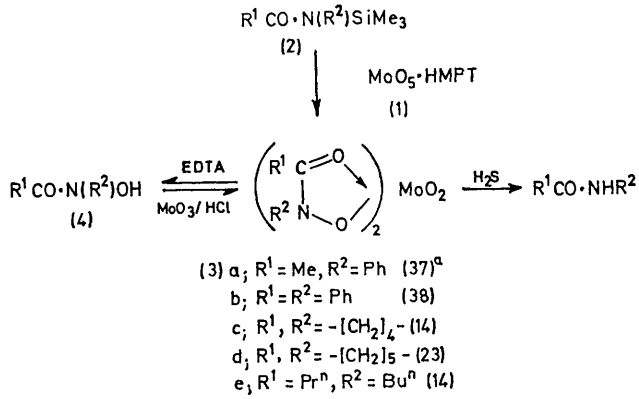
Summary *N*-Trimethylsilylamides are oxidized by diperoxo-oxohexamethylphosphoramidomolybdenum(VI) to give the corresponding hydroxamic acids, which are initially isolated as their Mo^{VI} complexes, but which can be liberated by treatment with ethylenediaminetetra-acetic acid (EDTA).

THE oxidation of amides to produce the corresponding hydroxamic acids is a well known biological process.[1] The corresponding *in vitro* process has attracted considerable interest but no general method has yet been described. One promising approach has been to convert secondary amides into their corresponding imino-ether derivatives before oxidation with a peroxy-acid.[2] We describe an alternative approach which involves oxidation of *N*-trimethylsilylated amides[3] with diperoxo-oxohexamethylphosphoramidomolybdenum(VI) (**1**).[4]

Typically, the *N*-trimethylsilylamide (**2a—e**) was stirred with the complex (**1**) in dichloromethane at room temperature. The reaction was monitored by appearance of a positive hydroxamic acid test with iron(III) chloride on aliquot portions. Reaction times varied from 3—5 h for the *N*-phenyl derivatives (**2a**) and (**2b**) to several days for the *N*-alkyl derivatives (**2c—e**). Evaporation of the reaction mixture followed by recrystallisation from alcohol afforded the corresponding dioxomolybdenum complexes† (**3**) in moderate yields (see Scheme). The complexes (**3**)



SCHEME

ª % Yield of isolated (**3**) from (**2**).
HMPT = hexamethylphosphoramide.

† New compounds gave satisfactory microanalyses and/or mass spectral fragmentation patterns.

are all pale yellow crystalline solids which exhibit a C=O stretching frequency at 1540—1590 cm^{-1} and two strong bands at *ca.* 950 and 920 cm^{-1} characteristic of the *cis*-O=Mo=O group.[5] With iron(III) chloride the complexes gave a slowly developing red colour typical of the free hydroxamic acid, thus reflecting the greater association constant for the iron(III) species rather than for the molybdenum.[6]

The free hydroxamic acids (**4**) could be liberated from the complexes (**3**) by treatment of the latter with hot aqueous 0·1N-EDTA solutions at pH 8, and continuous extraction of the aqueous solutions with dichloromethane.

The *in situ* oxidation of the amides into the corresponding free hydroxamic acids was also possible without isolation of the intermediates. Thus, treatment of acetanilide with an excess of hexamethyldisilazane in the presence of a trace of conc. sulphuric acid, followed by immediate oxidation of the crude trimethylsilyl derivative with the complex (**1**) and treatment of the products with EDTA, followed by solvent extraction, afforded the hydroxamic acid (**4a**) in 45% yield.

The hydroxamate complexes (**3**) could also be prepared by reaction of the hydroxamic acid in water or ethanol with a solution of molybdenum trioxide in conc. hydrochloric acid. The complex (**4b**) has previously been prepared by reaction of the hydroxamic acid with $(NH_4)_2MoOCl_5$ in ethanol.[7]

Treatment of the complexes (**3a** and **b**) in dichloromethane with hydrogen sulphide resulted in their rapid reduction (< 3 min) to give the corresponding amides in high yield. The corresponding reduction of the piperidone (**3c**) was slower; in one run a 25% yield of 2-piperidone formed after 3 h.

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