A Mild and Efficient Method for the Reduction of Oximes to Imines for Further *in situ* Reactions

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Tributylphosphine–diphenyl disulphide is an effective and mild reagent for reducing oximes to imines.

The reduction of ketoximes or their acetates to imines has been used to regenerate the parent ketones[1] and in the preparation of the synthetically versatile enamides.[2,3] We have found that tributylphosphine, in the presence of diphenyl disulphide, is a mild reagent for reducing ketoximes under essentially neutral conditions. This reagent has hitherto been used to convert alcohols into phenyl sulphides.[4]

We envisaged that the reactive species (**1**)[5] (Scheme 1) would react with the oxime to afford the intermediate (**2**) and benzenethiol. This intermediate could then be attacked by the benzenethiol generated to give diphenyl disulphide, tributylphosphine oxide, and the imine. We considered that the formation of the strong P–O bond and the breaking of the weak N–O bond would provide a sufficient driving force for this process.

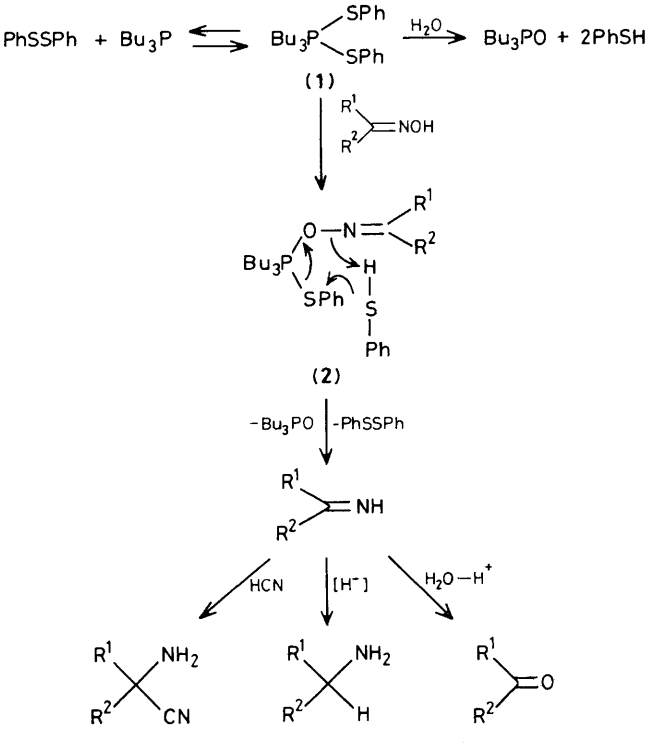
When tributylphosphine was added to a solution of the oxime (**3**) and diphenyl disulphide in tetrahydrofuran (THF), a smooth reaction occurred and the ketone (**4**) could be isolated in 85% yield after an aqueous work up. In a similar reaction, pregnenolone acetate (**6**) was obtained in 90% yield from the corresponding oxime (**5**).

In accordance with the formulated mechanism (Scheme 1), diphenyl disulphide appears to play a catalytic role and is recovered unchanged (>90%).

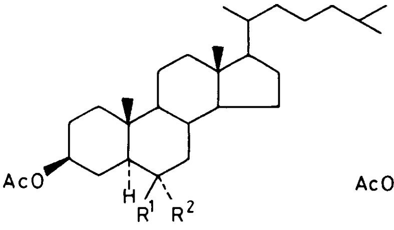
One notable advantage of this system over most other reagents is that it is self-drying and the reaction medium is therefore rigorously anhydrous. Under such conditions, the imine produced is protected against premature hydrolysis and may easily be intercepted to give a variety of useful products. For example, *in situ* acetylation affords the diacetylimide (**7**)[3] in 94% yield from oxime (**5**). The imine can also be reduced to the amine *in situ* with sodium cyanoborohydride and acetic acid. By such a modification of the reaction, the amide (**9**)[6] was prepared (after acetylation of the amine) in 93% yield from oxime (**8**). This constitutes a mild method for the overall reductive amination of even hindered ketones. Alternatively, the same intermediate imine can be trapped with hydrogen cyanide, generated *in situ* from sodium cyanide and acetic acid, to give the amino nitrile (**10**) (m.p. 149—152 °C; $[\alpha]_D$ −91°) in excellent yield. α-Amino nitriles are immediate precursors of α-amino acids (the Strecker synthesis).[7]

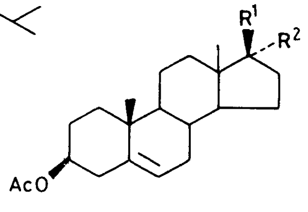
Other disulphides were on the whole less satisfactory. Reactions were either slow or led to appreciable amounts of Beckmann rearrangement products. For instance, the lactam (**11**) was produced in 90% yield from oxime (**8**) when 2,2′-dipyridyl disulphide was used. The tendency for Beckmann rearrangement was also solvent dependent, increasing in the order: pyridine, THF, CH_2Cl_2.

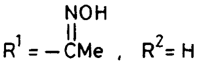
Furthermore, the same oxime (**8**) gave the novel phenyl imino sulphide (**12**) (m.p. 163—165 °C, $[\alpha]_D$ + 81°) in yields up to 60% when an excess of diphenyl disulphide was employed. The same compound could be isolated if the imine, prepared as above, was treated with phenylsulphenyl chloride.

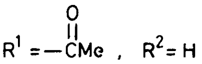


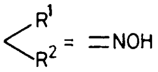
Scheme 1

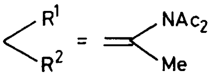


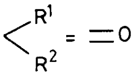


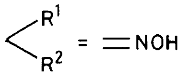
(**5**)

$R^1 = -\overset{\text{NOH}}{\overset{\|}{\text{C}}}\text{Me}$, $R^2 = H$

(**6**)

$R^1 = -\overset{\text{O}}{\overset{\|}{\text{C}}}\text{Me}$, $R^2 = H$

(**3**)


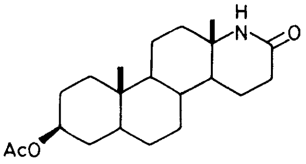
(**7**)


(**4**)


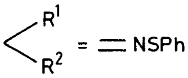
(**8**)


(**9**) R^1 = NHAc, R^2 = H

(**10**) R^1 = NH_2, R^2 = CN



(**11**)

(**12**)


As expected, aldoximes were simply dehydrated to the corresponding nitriles by the reagent.

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