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A MILD REDUCTION OF ALIPHATIC NITRO COMPOUNDS TO IMINES FOR FURTHER *in situ* REACTIONS : A SIMPLE SYNTHESIS OF PYRROLES

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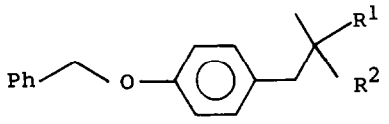
Tributylphosphine-diphenyldisulphide reduces nitroalkanes to imines which can be trapped intramolecularly to give pyrroles.

The reduction of aliphatic nitro compounds to imines may be achieved by various low valent metal salts[1-4] in media containing water and often acid. The imines are usually rapidly hydrolysed to carbonyl derivatives (Reductive Nef Reaction).

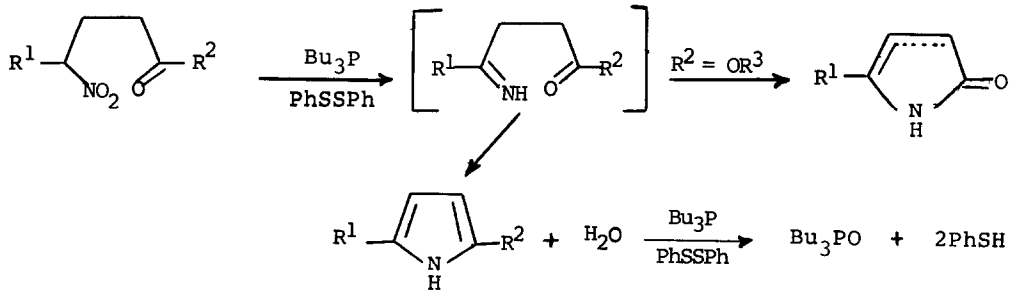
We have recently reported that tributylphosphine-diphenyldisulphide is an efficient reagent for the reduction of oximes to the corresponding imines in an anhydrous, neutral environment.[5] Furthermore, we have shown that the imines could be conveniently trapped leading to various useful functional groups. We now report that the same reagent is also capable of reducing nitroalkanes to imines.

When tributylphosphine is added to the nitro derivative (1) and diphenyl disulphide in tetrahydrofuran (THF) at room temperature, the corresponding ketone (2) is obtained, after hydrolysis with water, in 82% yield. As in the case of oximes, the intermediate imine can be trapped with hydrogen cyanide[5] generated *in situ* by incorporating solid sodium cyanide to the reaction mixture at the beginning and adding acetic acid once the reduction is over. The reagent reacts instantly and irreversibly with water. It, therefore, dries the sodium cyanide used and at the same time protects the imine against premature hydrolysis. Using this modification of the experimental conditions, the α-amino nitrile (3) is isolated in 70% yield. This constitutes a potentially one-pot transformation of a nitro group into a branched α-amino acid.[6]



(1) R^1 = H ; R^2 = NO_2
(2) R^1 = R^2 = O
(3) R^1 = $-NH_2$; R^2 = CN

Intramolecular trapping of the imine to give heterocycles illustrates the scope and versatility of this reaction. A suitably positionned carbonyl group in the molecule, gives cyclisation to a pyrrole (Scheme 1). Furthermore, the molecule of water produced is immediately removed by the reagent in an exothermic irreversible manner. This provides additionnal driving force for the process.

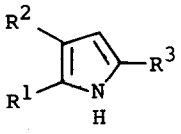


Scheme 1

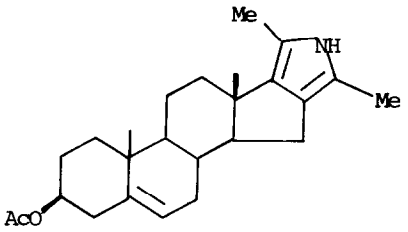
Indeed when nitro-ketone (**8**) is subjected to the usual reaction conditions using an excess of reagent, the pyrrole (**4**) is isolated in up to 90% yield. In a similar fashion, pyrroles (**5**), (**6**), and (**7**) (m.p. 205-211°C, $[\alpha]_D$ = -79°) were prepared from the corresponding nitroketones (**9**), (**10**) and (**11**) in 90%, 65% and 85% yield respectively. For the reduction of compound (**10**), replacing THF with dichloromethane proved advantageous.

Since 1,4 nitroketones are readily available by either Michael addition to α,β-unsaturated carbonyl derivatives[1,7,8] or addition of enolates to nitroolefins[1,9], a direct access to a wide variety of pyrroles is now at hand[10].

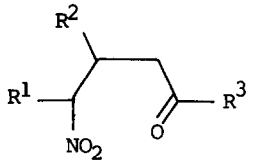
Alternatively, if an ester function is employed to intercept the imine a pyrrolin-2-one is obtained (Scheme 1). Thus, reduction of the nitro ester (**12**), prepared quantitatively by base catalysed addition of nitroethane to ethyl cinnamate, affords a 61% unoptimised yield of the 4-pyrrolin-2-one (**13**). Pyrrolin-2-ones are important as precursors of 2,2'-bipyrroles.[10a,11]



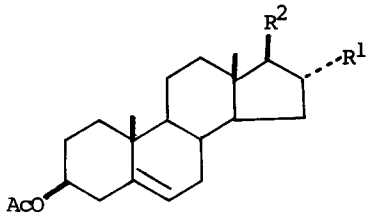
(**4**) R^1 = Me ; R^2 = R^3 = Ph
(**5**) R^1 = R^3 = Me ; R^2 = Ph
(**6**) R^1 = CO_2Et ; R^2 = R^3 = Ph

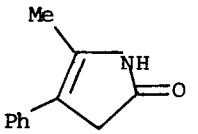


(7)



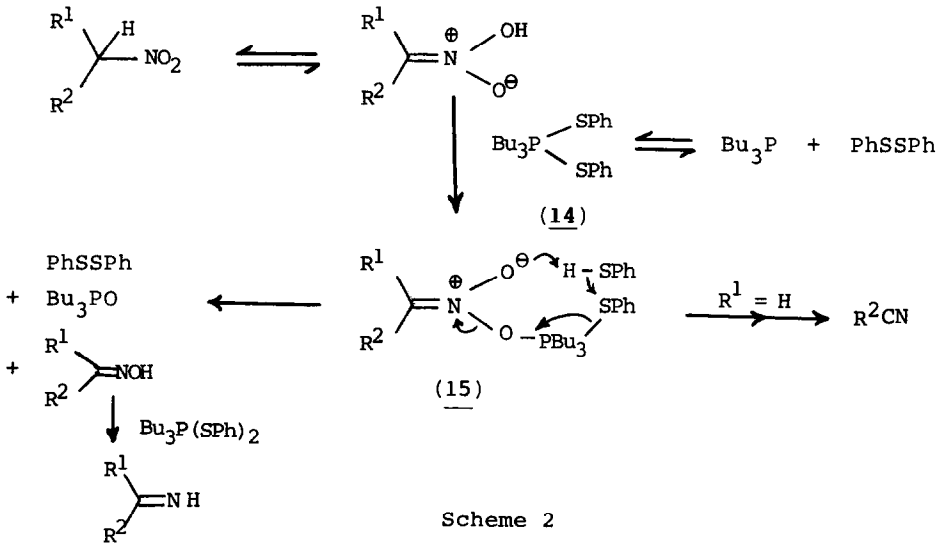
(8) R^1 = Me ; R^2 = R^3 = Ph
(9) R^1 = R^3 = Me ; R^2 = Ph
(10) R^1 = CO_2Et ; R^2 = R^3 = Ph
(12) R^1 = Me ; R^2 = Ph ; R^3 = OEt





(13)

(11) R^1 = $-CH(CH_3)NO_2$; R^2 = $-COCH_3$
(16) R^1 = H ; R^2 = $-CH_2NO_2$
(17) R^1 = H ; R^2 = CN



Scheme 2

From the standpoint of the mechanism, one analogous to the reduction of oximes[5] can be postulated (Scheme 2). The pentavalent phosphorous species (14) reacts with the nitronate to give the intermediate (15). This is then attacked by the thiophenol liberated to give the oxime, tributylphosphine oxide and diphenyldisulphide. Further similar reaction[5] of the oxime finally yields the imine. Although the role of the diphenyldisulphide is in principle catalytic and can be recovered unchanged, it is best to use it in equimolar quantities in order to keep a convenient rate of reaction. Only secondary nitro derivatives undergo the reduction. Primary nitroalkanes are smoothly dehydrated to the corresponding nitriles by the reagent. For example, the nitro steroid[12] (16) is transformed into the nitrile (17) in quantitative yield.[13]

REFERENCES

1. D. Seebach, E.W. Colvin, F. Lehr and T. Weller, Chimia, 33, 1 (1979) and references therein.
2. J.E. McMurry and J. Melton, J. Org. Chem., 38, 4367 (1973).
3. J. Hanson and T.D. Organ, J. Chem. Soc. (C), 1182 (1970).
4. R. Kirchhoff, Tetrahedron Letts, 2533 (1976).
5. D.H.R. Barton, W.B. Motherwell, E.S. Simon and S.Z. Zard, J. Chem. Soc., Chem. Commun., 337 (1984) and references therein.
6. R.J. Block, Chem. Rev., 38, 502 (1946).
7. "The Chemistry of the Nitro Group", H. Feuer, Ed., Interscience, New York, 1970.
8. E.D. Bergmann, G. Ginsburg and R. Pappo, Org. React., 10, 179 (1959).
9. D. Seebach, H.F. Leitz and V. Ehrig, Chem. Ber., 108, 1924 (1975); S. Ranganathan, D. Ranganathan and A.K. Melhorta, J. Am. Chem. Soc., 96, 5261 (1974).
10. See, inter alia : a) K.M. Smith, Quart. Rev., 25, 31 (1971); and references therein. b) G.W. Kenner, J. Rimmer, K.M. Smith and J.F. Unsworth, J. Chem. Soc., Perkin Trans I, 332 (1977); and references therein. c) P.D. Magnus and Y.-S. Or, J. Chem. Soc., Chem. Commun., 26 (1983). d) J.M. Patterson, Synthesis, 281 (1976).
11. G. Stork and R. Matthews, J. Chem. Soc., Chem. Commun., 445 (1970).
12. D.H.R. Barton, W.B. Motherwell and S.Z. Zard, Bull. Soc. Chim. Fr. (II), 61 (1983).
13. All new compounds gave satisfactory spectroscopic and microanalytical data.

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