Pergamon

Tetrahedron Letters 43 (2002) 2037–2038

TETRAHEDRON
LETTERS

α-Nitrohydrazones: versatile intermediates for phosphonate derivatives formation from primary nitro compounds

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Received 27 August 2001; revised 25 January 2002; accepted 28 January 2002

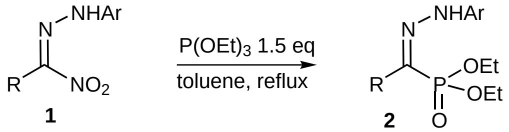
Abstract—Primary nitro compounds can be easily converted into hydrazonophosphonate derivatives through coupling with aryldiazonium salts followed by an Arbuzov-type reaction with phosphite. © 2002 Elsevier Science Ltd. All rights reserved.

Although the first additions of aryldiazonium salts to nitro compounds have been described at the end of the nineteenth century,[1] the resulting α-nitrohydrazones have found relatively few synthetic uses. Most of the described applications of these compounds stem from Huisgen's studies on the generation and [3+2] cycloaddition of nitrilimines derived from α-nitrohydrazones under basic conditions.[2–9] Our interest in both hydrazone chemistry and Umpolung reactions of nitro derivatives led us to examine the potential of various nucleophilic additions involving such nitrohydrazones. We now describe a new transformation allowing an easy access to functionalised phosphonates.

α-Aminophosphonic compounds are useful analogues of α-aminoacids which can be easily prepared by an Arbuzov-type reaction of phosphites on acid chlorides followed by oxime formation and reduction. We assumed that similar reaction of α-nitrohydrazones with triethyl phosphite would give phosphonohydrazones. As the reduction of hydrazonophosphonates has been already described,[10,11] the overall transformation would give an easy entry to aminophosphonic derivatives from primary nitro compounds.

Indeed when various α-nitrohydrazones **1** were heated with triethyl phosphite in toluene hydrazonophosphonates **2** were easily obtained in moderate yields (Scheme 1, Table 1).

The reaction appears to be compatible with a variety of functional groups. It is also interesting to note that the reaction conditions are smooth enough to permit the preparation of functionalised keto-phosphonate **2c**, **2d**, **2e** without any cyclisation to pyridazine. Indeed, starting hydrazone **1e** readily cyclises into pyridazine **3** by a mere treatment with potassium carbonate under phase-transfer catalysis (Scheme 2).



Scheme 1.

This new phosphonate formation probably involves an Arbuzov-type reaction with co-production of ethylnitrite; the low boiling point of the latter allows its easy removal from the reaction mixture as well as ensuring the absence of oxidation products.

In contrast to the Nef reaction, the potential of α-nitrohydrazones as an entry into carbonyl derivatives has been largely underestimated. Apart from their behaviour towards hydrolysis,[12] their use as electrophiles has only been reported in a study on the preparation of sulfur heterocycles.[13] In preliminary experiments, these authors present several simple nucleophilic additions (amine, thiol, cyanide) but no yields were given to ascertain the efficiency of the latter additions.[13]

In view of the importance of nitro compounds in C–C bond forming reactions (Michael, Henry reactions) and the ease with which nitronates react with diazonium salts, we believe that this approach offers a flexibility not available by other routes.

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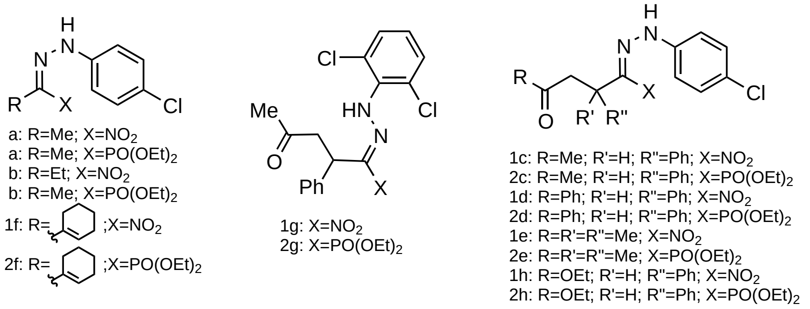
PII: S0040-4039(02)00208-3

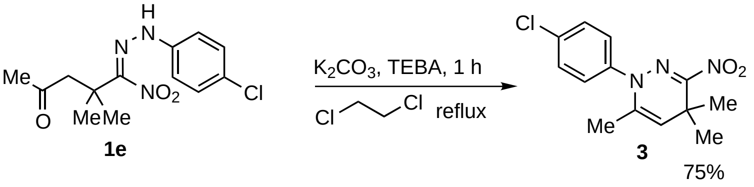
Table 1. Formation of phosphonate **2** from **1** in Scheme 1



Entry	Starting **1** (yield)[a]	Phosphonate **2**	Time (h)	Yield (%)[b]
1	**1a** (92)	**2a**	14	55
2	**1b** (80)	**2b**	7	66
3	**1c** (85)	**2c**	3	68
4	**1d** (60)	**2d**	9	50
5	**1e** (60)	**2e**	3	60
6	**1f** (45)	**2f**	1	57
7	**1g** (50)	**2g**	3	76
8	**1h** (70)	**2h**	4	71

[a] Prepared by addition of diazonium salt (1 equiv.) in water to a solution of sodium nitronate (prepared from nitro compound and sodium hydroxide) in water or methanol.

[b] Nitrohydrazones **1** (1 mmol) in toluene (5 ml) was refluxed with triethyl phosphite (1.5 mmol) until complete conversion and purified on silica gel.



Scheme 2.

Further studies aiming at exploring the scope of our process are currently under way.

Acknowledgements

We thank Professor S. Z. Zard for help and encouragement.

References

1. Padeken, H. G.; Schickh, O. v.; Segnitz, A. In *Methoden der Organischem Chemie(Houben-Weyl)*; Muller, E., Ed.; Thieme: Stuttgart, 1971; Band X/1, 142–152.
2. Claus, P. K. In *Methoden der Organischem Chemie(Houben–Weyl)*; Klamann, D.; Hagemann, H., Eds.; Thieme: Stuttgart, 1990; Band E14b/Teil 1, 36–37.
3. Huisgen, R. *Angew. Chem.* **1963**, 604–637.
4. Fliege, W.; Huisgen, R.; Clovis, J. S.; Knupfer, H. *Chem. Ber.* **1983**, *116*, 3039–3061.
5. Garanti, L.; Zecchi, G. *Synthesis* **1974**, 814–815.
6. Bizzozero, N.; Garanti, L.; Zecchi, G. *Synthesis* **1979**, 909–910.
7. Bruche, L.; Garanti, L.; Zecchi, G. *J. Heterocyclic Chem.* **1982**, *19*, 905–907.
8. Hassaneen, H. M.; Shawali, A. S. *Indian J. Chem. Sect. B* **1989**, *28*, 133–135.
9. Rösch, W.; Regitz, M. *Synthesis* **1987**, 689–693.
10. Kosolapoff, G. M. *J. Am. Chem. Soc.* **1948**, *70*, 1283.
11. Kudzin, Z. H.; Kotynski, A. *Synthesis* **1980**, *12*, 1028–1032.
12. Bamberger, E. *Chem. Ber.* **1898**, *31*, 2632.
13. Hassaneen, H. M.; Shawali, A. S.; Sherif, S. M. *J. Heterocyclic Chem.* **1980**, *17*, 1745–1749.