A New Method for Conversion of Aldoximes into Nitriles: Use of Chlorothionoformates

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Summary *p*-Chlorophenyl chlorothionoformate in the presence of pyridine dehydrates aldoximes under extremely mild conditions.

VERY few mild procedures have been established for dehydration of aldoximes,[1] but in those cases where the vigorous conditions normally prescribed[2] are acceptable, the sequence constitutes an important preparative route to nitriles. We have examined the response of several aldoximes towards *p*-chlorophenyl chlorothionoformate[3] and find that nitriles are produced at room temperature in a process that is both rapid and exceptionally mild.

The method involves addition of a solution of the oxime and pyridine (1 and 2 equiv., respectively) to a solution of the reagent (2 equiv.) followed by isolation of the nitrile, usually by chromatography.†

Results with the new process are shown in the Table, in which the yields refer to analytically pure‡ product obtained, with the exception of heptanonitrile which was prepared on a larger scale, from 1 mmole of aldoxime. In these experiments the reaction time was 1·5 h, but production of the nitrile is probably complete much sooner.

For comparative purposes (*E*)-*p*-chlorobenzaldoxime was treated with *p*-chlorophenyl chloroformate under the above conditions and, though the oxime was rapidly acylated, no nitrile was detectable (i.r. control) even after a 16 h reaction period. Mechanistically, the new process probably involves formation of an *O*-acyl derivative (1) and the facility with which it decomposes[4] may reflect a rapid (*E*) → (*Z*) isomerization and subsequent collapse, and/or the thermodynamic instability of the system (2) with respect to its isomer (3).§

In principle, the substantial driving force available[5] from

TABLE

Oxime	Yield of nitrile
(*E*)-Veratraldoxime[a,b]	61·0%
(*E*)-*p*-Nitrobenzaldoxime[c]	70·3
(*E*)-*p*-Chlorobenzaldoxime[b]	60·8
(*Z*)-*p*-Chlorobenzaldoxime[b]	42·4
Heptanaldoxime[b,d]	42·7

[a] Nomenclature of J. E. Blackwood, C. L. Gladys, K. L. Loening, A. E. Petrarca, and J. E. Rush, *J. Amer. Chem. Soc.*, 1968, **90**, 509. [b] Diethyl ether used as reaction solvent. [c] Dichloromethane used as reaction solvent. [d] Prepared according to the procedure of E. W. Bousquet, *Org. Synth.*, Coll. Vol. II, p. 313, and crystallised from petroleum, the material was a mixture of the (*Z*)- and (*E*)- isomers in the molar ratio of *ca.* 6 : 1. *Cf.* G. G. Kleinspehn, J. A. Jung, and S. A. Studniarz, *J. Org. Chem.*, 1967, **32**, 460.

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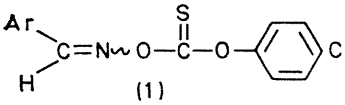
† Reaction mixtures were protected from moisture and oxygen as a matter of routine. It was convenient, though not essential, to remove residual *p*-chlorophenol by extraction into dilute aqueous potassium hydroxide.

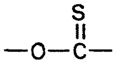
‡ Analytical values accurate to ± 0·3%. The compounds were identical with authentic specimens.

§ There is ample precedent for (*E*)-(*Z*) interconversion and derivatives of (*Z*)-aldoximes are well known to be much less stable with respect to nitrile production than their (*E*)-isomers.[2b]

the conversion of (2) into (3) could involve [for an (*E*)-derivative] a cyclic process (4). In so far as the essential features of such an array are comparable with (5) (a retro-ene reaction[6]), the thermal concerted process represented by (4) is one in which orbital symmetry is conserved. Similar possibilities, generalized in (6), may also apply to the pyrolysis of various imino-ethers[7] of structure (7) and to the observation, made many years ago but undeveloped in terms of its possibilities as a *mild* synthetic method, that certain combinations of aldoxime and aryl isothiocyanate afford nitriles.[8]

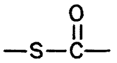


(1)



$-O-\overset{\overset{S}{\|}}{C}-$

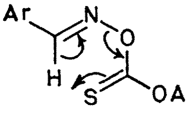
(2)



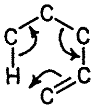
$-S-\overset{\overset{O}{\|}}{C}-$

(3)

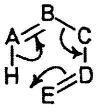
Work with methyl chlorothionoformate[9] indicates that our method is not limited to reagents of the aromatic series.



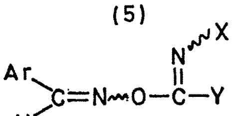
(4)



(5)



(6)



(7)

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[1] P. J. Foley, jun., *J. Org. Chem.*, 1969, **34**, 2805; T. J. Bentley, J. F. McGhie, and D. H. R. Barton, *Tetrahedron Letters*, 1965, 2497; *cf.* J. H. Pomeroy and C. A. Craig, *J. Amer. Chem. Soc.*, 1959, **81**, 6340.

[2] (a) D. T. Mowry, *Chem. Rev.*, 1948, **42**, 189; (b) H. Metzger in "Methoden der Organischen Chemie," Houben-Weyl, Stuttgart, 1968, 4th edn., vol. X, part **4**, p. 1.

[3] Readily available by the method of D. L. Garmaise, A. Uchiyama, and A. F. McKay, *J. Org. Chem.*, 1962, **27**, 4509.

[4] *Cf.* J. H. M. Hill and L. D. Schmookler, *J. Org. Chem.*, 1967, **32**, 4025.

[5] C. H. DePuy and R. W. King, *Chem. Rev.*, 1960, **60**, 431.

[6] For a review of the ene reaction see H. M. R. Hoffmann, *Angew. Chem. Internat. Edn.*, 1969, **8**, 556.

[7] H. Hettler and H. Neygenfind, *Tetrahedron Letters*, 1966, 6031; E. Grigat and R. Pütter, *Chem. Ber.*, 1966, **99**, 2361.

[8] An. Obregia and C. V. Gheorghiu, *J. prakt. Chem.*, 1930, **128**, 239; C. V. Gheorghiu, *ibid.*, 1931, **130**, 49.

[9] D. Martin and W. Mucke, *Chem. Ber.*, 1965, **98**, 2059.