Tetrahedron Letters, Vol.22, No.17, pp 1599 - 1600, 1981
Printed in Great Britain

0040-4039/81/171599-02$02.00/0

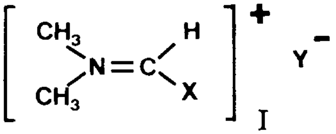
VILSMEIER REAGENT FOR A HIGH YIELD CONVERSION OF ALDOXIMES TO NITRILES

By Jean-Pierre DULCERE

Laboratoire Associé au C.N.R.S. n° 109 - Faculté des Sciences et Techniques de Saint-Jérôme
Rue Henri Poincaré - F - 13397 MARSEILLE CEDEX 13

SUMMARY : Chloromethylenedimethylammonium chloride was used to convert aldoximes 1b-g to nitriles 2b-g.

Vilsmeier reagents I have previously been used almost exclusively for formylation (1). More recently they were shown to be useful reagents in organic synthesis.



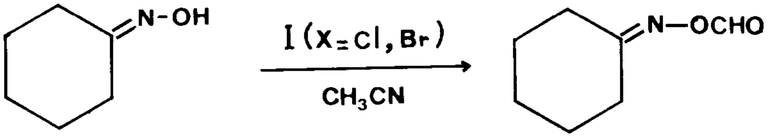
I

X = Halogen
Y = X, SO_2X, PO_2X_2, etc ...

Particularly, the ability of I to give rise to products of substitution with substrates bearing a labile hydrogen atom received interesting applications for alkyl halide (2) or ester (3) preparations from alcohols or acids.

We now report a general synthesis of nitriles from aldoximes under mild conditions, using chloromethylenedimethylammonium chloride (I, X = Cl (3)).

When a solution of cyclohexanone oxime 1a in CH_3CN was allowed to react at 0°C with an equivalent of I (X = Cl or Br) in CH_3CN, we observed after hydrolysis the formation of the O-formylated derivative 2a in a quantitative yield (4).

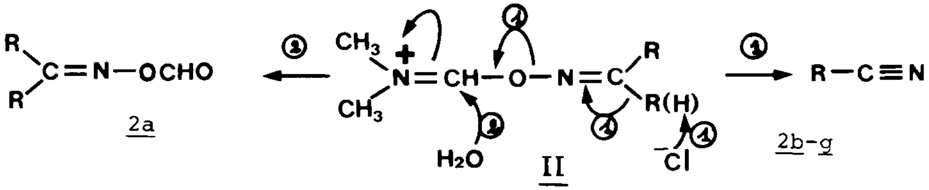


1a 2a

On the other side, when the reaction was performed on the aldoximes 1b-g at -10°C, the corresponding nitriles 2b-g were obtained in good to excellent yields.(TABLE I)

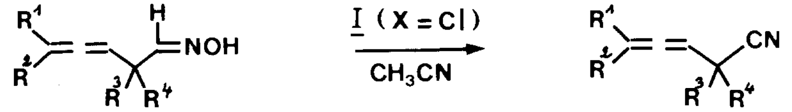
It is interesting to notice that the allenic nitriles 2b, 2c, 2d have previously been prepared from the same starting material (with PCl_5/Et_2O) in only ~50 % yield (7).

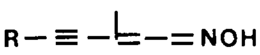
The O-formylated derivative 2a and the nitriles 2b-g formations both occur *via* the intermediate II.



2a II 2b-g

TABLE I *(All products gave satisfactory microanalyses and mass spectrums)*



			Yields (5)
1b	$R^1=R^2=R^3=R^4=CH_3$	2b	95 %
1c	$R^1=R^3=R^4=CH_3$; $R^2=C_2H_5$	2c	90 %
1d	$R^1-R^2= -(CH_2)-_5$; $R^3=R^4=CH_3$	2d	92 %
1e	(Z)-benzaldoxime	2e benzonitrile	95 %
			
1f	R=H	2f (6)	83 %
1g	$R=Si(CH_3)_3$	2g	85 %

Concerning the ketoxime 1a, the intermediate II is hydrolyzed and the formylated compound 2a isolated. A different pathway is involved in the case of the aldoximes 1b-g, resulting in an attack of the hydrogen by the chloro counterion to give rise to the nitriles (2b-g) formation ; a molecule of DMF is then recovered by this process.

From a preparative point of view, the greater reactivity of the Vilsmeier reagent when compared with the dichloromethylenedimethylammonium chloride (8,9) permits to perform this reaction on sensitive substrates at lower temperatures.

In conclusion, for the mild condition required and the high yields obtained, we assume that the readily available Vilsmeier reagent is particularly efficient to convert aldoximes to nitriles.

For these reasons, this method competes advantageously other ones recently published (10).

REFERENCES AND NOTES :

1 - G. HAZEBROUCQ, Ann. Pharm. Franç., 1966, 24, 793.
M.R. de MAHEAS, Bull. Soc. Chim. Fr., 1962, 1989.
2 - D.R. HEPBURN, H.R. HUDSON, Chem. and Ind., 1974, 664 and J.C.S. Perkin I, 1976, 754.
M.R. YOSHIHARA, T.EDA, K.SAKAKI, T. MAESHIMA, Synthesis, 1980, 746.
3 - P.A. STADLER, Helv. Chim. Acta, 1978, 61, 1675.
4 - Spectroscopic data of 2a : IR (cm^{-1}) : 1680-1720 ; NMR (δppm) 1,75 m (6H) ; 2,63 m (2H) ; 3,77 m (2H) ; 9,23 s (1H).
5 - Yields of pure isolated product (silica gel column).
6 - Spectroscopic data : (2f) IR : 3300 FF, 3080 F, 2240 FF, 2100 FF, 1600 FF ; NMR : 1,93 d (3H) J = 1Hz ; 3,63 s (1H) ; 5,47 m (1H).
(2g) IR : 2230 FF, 2160 F, 1600 FF ; NMR : 2,30 d (3H) ; 5,20 quad. (1H) J = 1Hz ; $Si(CH_3)_3$ (9H) reference.
7 - J. GRIMALDI, A. CORMONS, C.R. Acad. Sci. Paris, 288 série C, 1979, 557.
8 - H.G. VIEHE, Z. JANOUSEK, Angew. Chem. Internat. Edit., 12, 806, (1973).
9 - V.P. KUKHAR, V.I. PASTERNAK, Synthesis, 1974, 563.
10 - A. CAROTTI, F. CAMPAGNA, Synthesis, 1979, 703 and references therein.
G. SOSNOVSKY, J.A. KROGH, Synthesis, 1978, 703.
G. OLAH, Y.D. VANKAR, Synthesis, 1978, 702.

(Received in France 30 January 1981)