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A Novel One Pot Conversion of Primary Nitroalkanes to Hydroximoyl Chlorides

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Treatment of primary nitroalkanes with a base and the subsequent reaction with $TiCl_4$ gave the hydroximoyl chlorides in good yields. Copyright © 1996 Elsevier Science Ltd

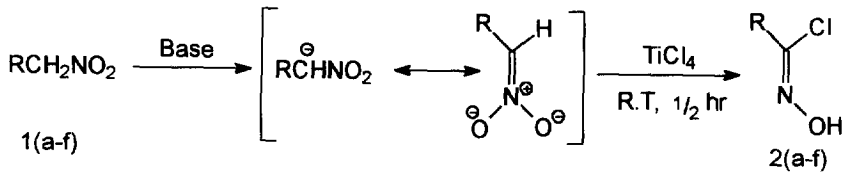
Nitro compounds are versatile building blocks and intermediates in organic synthesis,[1] since they easily undergo carbon-carbon bond formation and the nitro group can be converted into variety of functional groups such as carbonyl, oxime, hydroxylamine, amines, alkanes or nitroso compounds. In addition, primary nitroalkanes were also frequently used for the *in situ* generation of an important 1,3-dipole *viz.* nitrile oxide.[2]

Even though the dehydration of primary nitroalkanes (Mukaiyama's method[2]) is one of the commonly used methods of generating nitrile oxides, the other most convenient method is the dehydro halogenation of hydroximoyl chlorides.[3]

In recent years hydroximoyl chlorides have received much attention. This is primarily due to the fact that the generation of nitrile oxides can be controlled by the external addition of base, hence the most frequently encountered problem of dimerisation of the nitrile oxide can be avoided. It was also observed that the nitrile oxides generated[4] from hydroximoyl chlorides with the aid of Lewis acids or organometallic reagents, increases the electrophilicity of carbon atom of nitrile oxides. In addition recently, metal coordinated nitrile oxides obtained from hydroximoyl chlorides are useful in achieving regio and stereo control in the 1,3-dipolar cycloaddition reactions.[5]

Usually hydroximoyl chlorides are obtained by chlorination of aldoximes.[6] In connection with our ongoing research on the hydroximoyl chlorides,[7] herein we report a novel one pot conversion of primary nitroalkanes to hydroximoyl chlorides. This reaction involves an initial treatment of primary nitroalkanes with a base and the subsequent reaction with $TiCl_4$ to get the hydroximoyl chlorides in good yields (**Scheme-1**),(**Table-1**).

Scheme-1



Dedicated to my mentor Dr. G.H. Kulkarni on the occasion of his 65th birthday.

Table-1 Synthesis of hydroximoyl chlorides from primary nitroalkanes.

Compd No.	R	Solvent	Base	m.p. (°C)	Isolated Yield (%)
2a	Benzyl	CH_2Cl_2	NaOMe	89(87)	75
2b	*p*-Methyl benzyl	CH_2Cl_2	NaOMe	82(82)	71
2c	1-Naphthyl	CH_2Cl_2	NaOMe	113	78
2d	2-Naphthyl	CH_2Cl_2	NaOMe	127	65
2e	Ethyl	CH_2Cl_2	NaOMe	oil	68†
2f	Carbmethoxy	Benzene	NaH	59	70
2a	Benzyl	Benzene	NaH	89	75
2b	*p*-Methyl benzyl	Benzene	NaH	82	72
2a	Benzyl	Benzene	KH	89	63

The value in the parenthesis refers to the literature[7b] m.p.(°C). † Since this hydroximoyl chloride was found to be unstable, it was immediately converted into the corresponding 2-isoxazoline derivative *via.* nitrile oxide and the yield is based on the isolated yield of 2-isoxazoline derivative.

A typical procedure for the synthesis of phenylacetohydroximoyl chloride (**2a**) using NaOMe as a base is as follows. To a stirred solution of NaOMe (0.01 mole) in dry methanol (2 ml), was added dropwise phenylnitroethane (**1a**) (0.01 mole) in dry methanol at room temperature. The mixture was stirred for 20 minutes, the solvent was removed and the resulting sodium salt was dried in vacuo for 3 hrs. To this was added dry CH_2Cl_2 (10 ml) and the suspension was cooled to 0°C and a slight excess of $TiCl_4$ (0.012 mole 1M solution in CH_2Cl_2) was added dropwise under argon atmosphere. The resulting mixture was stirred at room temperature for 1/2 hr and usual work up gave phenylacetohydroximoyl chloride (**2a**) purified by column chromatography and identified by m.p, IR, ^1H NMR and ^{13}C NMR.

Though the conversion of primary nitroalkanes to nitrile oxides is known, the generation from hydroximoyl chlorides has advantages in regio and stereo control in cycloaddition reactions. In addition, several useful synthetic transformations of hydroxmioyl chlorides were also reported.[4, 8] Thus the method described herein offers a novel route for the synthetically important hydroximoyl chlorides from nitroalkanes.

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