A Novel Synthesis of Imino Oximes *via* α-Nitrosation of Schiff Bases

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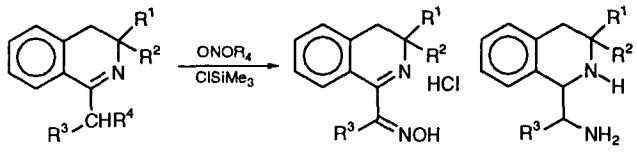
A new, efficient reagent–TMSCl/alkyl nitrite–is proposed for the conversion of imines into oximino derivatives, precursors of some important 1,2-diamines.

Table 1 Nitrosation of 3,4-dihydroisoquinolines with TMSCl/alkyl nitrite reagent

No.	Compound	Solvent	Oxime·HCl	Yield (%)	m.p./°C	Footnote
1	**1a**	$CHCl_3$	**2a**	89	271	*a*
2	**1a**	MeCN	**2a**	93		*a*
3	**1b**	$CHCl_3$	**2b**	62	220	*b*
4	**1c**	MeCN	**2c**	88	218	*c*
5	**1d**	EtOAc–Et_2O	**2d**	75		*d*
6	**1d**	MeCN	**2d**	98	235	*d*
7	**1e**	$CHCl_3$	**2e**	0		*e*

[a] *Z*-isomer. MS [isobutane],174 + 57. In-beam electron ionization [BEI], 174. [b] MS 202 + 57,BEI 202, *E*-isomer. [c] MS 250 + 57,BEI 250, *E*/*Z* mixture (TLC) [d] MS 188 + 57,BEI 188, *E*/*Z* mixture (TLC) [e] Starting material was recovered.

1,2-Diamines of type **3a** are traditionally synthesized by multistage procedures either by the introduction of a nitrogen-containing fragment into isoquinoline or by cyclisation of an appropriate non-cyclic precursor into the isoquinolinic system. In this communication we report a "short-cut" route to **3** *via* nitrosation of Schiff bases by a new reagent—butyl or *tert*-butyl nitrite (**4a** or **4b**)/trimethylsilylchloride (TMSCl) in chloroform or acetonitrile. Thus, imine **1a** in ethanol-free $CHCl_3$ is mixed with an equivalent of TMSCl and the mixture is warmed to 30 °C, after which an equivalent of **4a** or **4b** is added and the mixture is left at room temperature for 16–18 h. During that period an exothermic reaction occurs and a crystalline chloride precipitates. After filtration, washing with $CHCl_3$ and drying, imino oxime **2a** (89%) is obtained. Crystallization from EtOH gives pure **2a**, m.p. 270.5–271.5 °C. The free base is obtained by the action of aqueous ammonia, m.p. 156–158 °C, from EtOH. The above-mentioned sudden temperature jump in the reaction mixture is probably not connected with the long induction period of the reaction, but instead with solid-phase formation from the over-saturated solution of imino oxime chloride. When the mixture of reagents is kept boiling the same sudden crystallization is associated with significant reflux intensity at an indeterminate moment within *ca.* 1 h.



1a-e **2a-d** **3a-d**

a $R^1 = R^2 = R^3 = R^4 = H$
b $R^1 = R^2 = Me$, $R^3 = R^4 = H$
c $R^1 = R^2 = R^3 = H$, $R^4 = Ph$
d $R^1 = R^2 = R^3 = H$, $R^4 = Me$
e $R^1 = R^2 = H$, $R^3 = R^4 = Me$

RONO
4
a R = Bu^n
b R = Bu^t

As outlined in Table 1, this imine nitrosation procedure is quite general for the synthesis of a variety of oximes, beginning with 1-alkylisoquinolines with an α-CH_2 group. *Gem*-Me substituents completely block the reaction. Interestingly, the TMSCl/alkyl nitrite combination was the only satisfactory way to yield imino oximes of type **2**. TMSI- or $NaNO_2$-based reagents were unsatisfactory in respect of oxime yields. Also unsatisfactory were NOCl and $NOBF_4$. As to the mechanism of TMSCl alkyl nitrite oximination, this remains somewhat obscure. The process probably includes prior *N*-nitrosation with subsequent NO migration to carbon.[1]

Reference

1 R. E. Lyle, W. E. Kruger and V. E. Gunn, *J. Org. Chem.*, 1983, **48**, 3547.

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