

## N-Nitroso Derivatives of 1-Substituted-2-iminopyrrolidines

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In a recent paper Thoman and Hunsberger (2) described the synthesis, isolation, and characterization of *N*-nitrosoketimines. They showed that introduction of electron-withdrawing substituents into the system adjacent to the imine-carbon atom increased the stability of the nitroso derivatives, but that electron donating substituents had the opposite effect. Steric considerations, however, seemed to be of even greater importance: the more sterically crowded the molecule, the more stable it was (3).

In this note we wish to report the synthesis of *N*-nitroso derivatives of cyclic amidines, more specifically those of 1-(substituted phenyl)-2-iminopyrrolidines (I, III-XV) and 1-cyclohexyl-2-iminopyrrolidine (II):

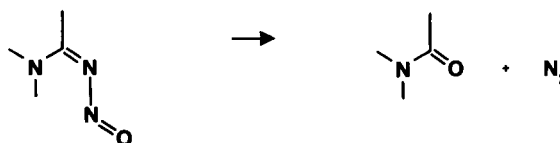


R = -phenyl	I
-cyclohexyl	II
-2-methylphenyl	III
-3-methylphenyl	IV
-4-methylphenyl	V
-2,6-dimethylphenyl	VI
-3,5-dimethylphenyl	VII
-2-chlorophenyl	VIII
-2,6-dichlorophenyl	IX
-2-bromophenyl	X
-3-bromophenyl	XI
-4-bromophenyl	XII
-2-nitrophenyl	XIII
-3-nitrophenyl	XIV
-4-nitrophenyl	XV

As expected the introduction of a nitrogen atom in conjugation with differently substituted phenyl groups had a marked effect on the stability of the *N*-nitrosoketimines, all of which were much more stable in the solid state than in solution. As solid most were stable for months at  $-4^\circ$ , but at room temperature only the cyclohexyl derivative survived for several hours.

For example, crystalline 1-cyclohexyl-2-nitrosoiminopyrrolidine was stored at  $-4^\circ$  for more than 12 months without noticeable decomposition, but a 0.1 molar carbon tetrachloride solution of this compound stored under identical conditions decomposed quantitatively within 5 hours into 1-cyclohexyl, 2-pyrrolidinone.

Differences in stability between the various products were determined by infrared spectroscopy by measuring the speed of conversion from nitrosimine into the corresponding pyrrolidinone:



To this end the decrease in NO absorbance and increase in CO absorbance of 0.08 molar nitrosimine solutions in chloroform were measured and plotted as a function of time. Also measured was the CO absorbance of 0.04 molar chloroform solutions of the corresponding pyrrolidinones. Because of the quantitative character of the conversion these data enabled us to determine a "half life" for each nitrosimine under the given instrumental conditions. Thus we obtained the following sequence in order of decreasing stability in solution: R = -cyclohexyl- > -2,6-dimethylphenyl > -2,6-dichlorophenyl- > -2-nitrophenyl  $\approx$  -2-methylphenyl > -2-chlorophenyl > -2-bromophenyl  $\approx$  -3-nitrophenyl > -phenyl  $\approx$  -3,5-dimethylphenyl > -3-methylphenyl  $\approx$  -4-methylphenyl > -4-bromophenyl > -3-bromophenyl  $\gg$  -4-nitrophenyl.

The 2-substituted and 2,6-disubstituted phenyl compounds are the more stable ones, whether the phenyl substituents are electronegative or electropositive, indicating the importance of steric factors. This agrees with the previously mentioned observations by other authors (2,3).

The parent ketimines were synthesized using modified versions of Kwok and Pranc's method (4). According to this method 1-substituted-2-iminopyrrolidines are synthesized by cyclization of 4-chlorobutyronitrile with primary amines. Modifications were necessary in the case of phenyl derivatives, where the speed of reaction was strongly influenced by the type and position of the phenyl substituent, as shown in Table I.

Most imines were isolated and purified as their hydrochloride salts because purification by distillation of several high boiling bases themselves resulted in decomposition.

The *N*-nitrosoketimines (Table II) were prepared by modification of the method used by Kuhn, *et al.*, for the preparation of *N*-nitroso, *N*-methylacetamide (5).

TABLE I  
1-(Substituted Phenyl)-2-iminopyrrolidines

Imine with R =	Yield	M.p. or B.p. (mm)		$\nu$ C = N in $\text{cm}^{-1}$	
		Imine	HCl Salt	Imine	HCl Salt
I (c)	44%	128-130° (2.0) (d)	221° (d,e)	1625	1680
II (a)	70%	80-83° (1.0) (f)	263° (f)	1620	1680
III (a)	75%	(g)	267°	1630	1670
IV (a)	95%	(g)	214°	1630	1670
V (a)	75%	67.7°	256°	1630	1670
VI (a)	76%	(g)	255°	1630	1670
VII (a)	44%	65.5°	246°	1630	1675
VIII (c)	57%	(g)	241°	1635	1675
IX (b)	25%	104.8°	240°	1635	1685
X (c)	55%	(g)	250°	1635	1670
XI (c)	70%	50.6°	243°	1625	1670
XII (c)	56%	93°	280°	1630	1680
XIII (b)	20%	82.6°	278°	1640	1685
XIV (c)	48%	109.7°	285°	1640	1685
XV (c)	55%	119.4°	240°	1640	1675

(a) Exothermic reaction after initial heating, similar to the reactions described in ref. 4. (b) Continued reflux required, much tarry side product. (c) Strongly exothermic reaction, chain-reacting into a decomposition reaction, unless slowed down by intermittent cooling. (d) Reference 4, 120-123° (0.8); 219-221°. (e) All hydrochloride salts melt with decomposition. (f) Reference 4, 71° (0.5); 260-263°. (g) High boiling bases decomposed upon distillation.

#### EXPERIMENTAL

Ir spectra of the ketimines were obtained in potassium bromide disks using a Perkin Elmer 521 instrument. The scanning of ir spectra of nitrosoketimines and monitoring of their decomposition was done from chloroform solutions, using the same instrument on time cycle.

Melting points were determined on a Mettler FP1 instrument (1°/min.), except for the imine hydrochloride salts, for which a Mel-Temperature apparatus was used.

Quantitative C, H, N, and Cl analyses were performed by Crobaugh Laboratories in Cleveland, Ohio. The values found for the imines were in satisfactory agreement with the calculated values. The same held true for the nitroso products, except for the 3,5-dimethylphenyl-, 2,6-dichlorophenyl-, 4-nitrophenyl-, and 2-nitrophenyl derivatives. Identification of the latter four was

based on their similarity with the other nitrosoketimines (reaction behavior, ir spectra, decomposition pattern, etc.).

#### 1-(Substituted phenyl)-2-nitrosoiminopyrrolidines.

A solution of imine in carbon tetrachloride (0.022 mole/200 ml.) was treated with NOCl (0.03 mole) in 25 ml. carbon tetrachloride at -20° in the presence of triethylamine (0.033 mole). All imines reacted instantaneously. After the addition of NOCl was completed the mixture was stirred for another ½ hour at -20°. Subsequently 300 ml. precooled petroleum ether was added and after additional stirring for 2 minutes the mixture was poured into 300 ml. of ice water. Filtration *via* a precooled filter and washing with ice water produced the *N*-nitrosoketimines which were recrystallized at low temperature from chloroform-petroleum ether giving brightly colored crystalline products.

TABLE II  
1-(Substituted Phenyl)-2-nitrosoiminopyrrolidines

Nitrosoketimine with R =	Color	Yield	m.p.	$\nu$ C = N in $\text{cm}^{-1}$	$\nu$ N = O in $\text{cm}^{-1}$
I	red/orange	7.5%	68° (a)	1570	1428
II	yellow/orange	6%	95°	1582	1420
III	light	47%	79°	1572	1427
IV	orange	56%	61°	1570	1420
V	yellow/orange	47%	70°	1563	1430
VI	orange	21%	75°	1579	1428
VII	red/orange	13%	52°	1568	1418
VIII	orange	61%	75°	1579	1433
XI	light purple	53%	77°	1563 1579 (b)	1437
X	light brown	5%	71°	1578 1592 (b)	1439
XI	orange	36%	61°	1579	1420
XII	light orange	42%	62°	1570 1581 (b)	1420
XIII	brown/orange	29%	55°	1580	1438
XIV	light purple	54%	74°	1580	1429
XV	red/brown	(c)			

(a) All nitroso compounds decomposed violently at their melting point. (b) Doublet. (c) We were unable to isolate this compound. The nitrosation reaction appeared identical to those of the other compounds, but during working-up procedures the red color changed to yellow brown, giving mainly the pyrrolidinone decomposition product, m.p. 122.5° (6).

## REFERENCES

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