Rearrangement Reactions of Aziridinylbenzaldoximes

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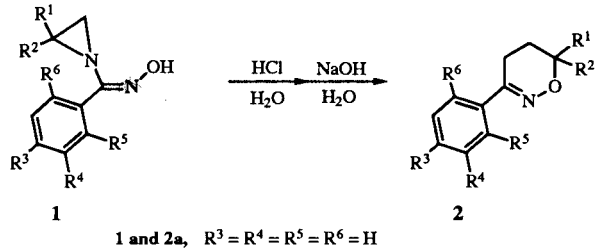
Received February 9, 1996

Reactions of 2,2-dimethylaziridine with benzohydroximoyl chlorides [ArC(Cl)=NOH] give aziridinylbenzaldoximes **1**. It has been found that the aziridine ring in these compounds undergoes ring opening in hydrogen chloride-dioxane solution to give (*Z*)-*N*-hydroxy-*N'*-(2-chloro-2-methylpropyl)benzenecarboximidamides [ArC(NHCH$_2$CR^{1}R^{2}Cl)=NOH, **4**]. Treatment of **1** with hydrochloric acid followed by neutralization with aqueous sodium hydroxide gave 6,6-dimethyl-3-aryl-1,2,4-oxadiazines **2**. Reaction of **4** with sodium hydride in dioxane gave 5-isopropyl-3-aryl-4,5-dihydro-1,2,4-oxadiazoles **5**. Reaction of the 4,5-dihydro-1,2,4-oxadiazoles **5** with *N*-chlorosuccinimide gave the heteroaromatic 1,2,4-oxadiazoles **6**. It is suggested that reactions of **4** with sodium hydride in dioxane solution involve the conjugate base of **4** which undergoes a 1,2-hydride shift that is concerted with loss of chloride ion. In aqueous sodium hydroxide solution it is suggested that the conjugate base of **4** undergoes ionization of the chlorine atom followed by nucleophilic attack by the oximate anion.

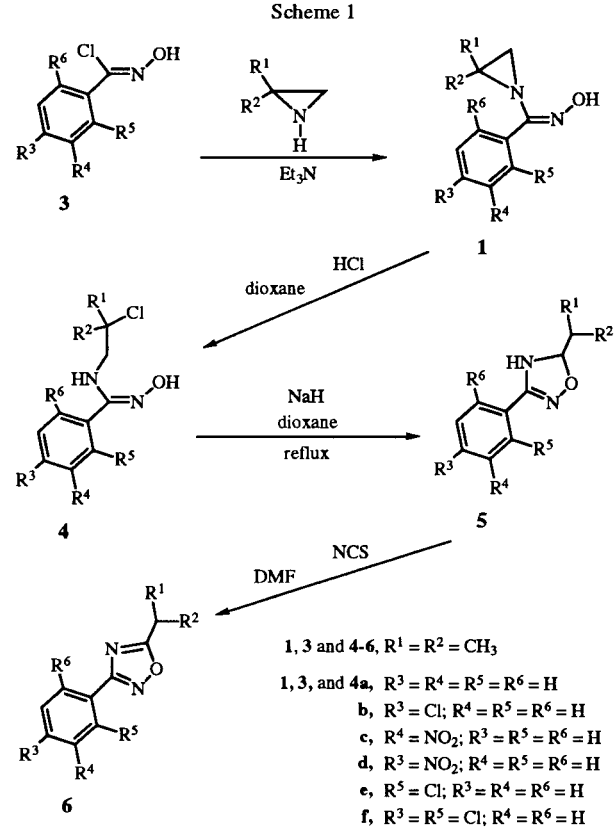
J. Heterocyclic Chem., **33**, 1583 (1996).

In 1966 Rajagopalan and Talaty [1] reported *via* a communication on a new method for the synthesis of 4,5-dihydro-6*H*-1,2,4-oxadiazines (**2**, R^1 = H; R^2 = H or CH$_3$). Aziridinylbenzaldoximes [2] were prepared by the reaction of aziridine or 2-methylaziridine with benzohydroximoyl chlorides **3** (Scheme I). Treatment of aziridinylbenzaldoximes **1** (R^1 = H; R^2 = H or CH$_3$) with aqueous hydrochloric acid followed by reaction with aqueous sodium hydroxide solution gave 4,5-dihydro-6*H*-1,2,4-oxadiazines **2** (R^1 = H; R^2 = H or CH$_3$). Rajagopalan and Talaty also reported that they were able to isolate an intermediate open-chain benzenecarboximidamide **4** (R^1 = R^2 = R^4 = R^5 = R^6 = H; R^3 = Cl in Scheme I) which resulted from ring opening of the aziridine ring of **1** with hydrochloric acid. Isomerization of **1** could not be accomplished in the presence of iodide ion.



1 and 2a, R^3 = R^4 = R^5 = R^6 = H
b, R^3 = Cl; R^4 = R^5 = R^6 = H
c, R^4 = NO$_2$; R^3 = R^5 = R^6 = H
d, R^3 = NO$_2$; R^4 = R^5 = R^6 = H
e, R^5 = Cl; R^3 = R^4 = R^6 = H
f, R^3 = R^5 = Cl; R^4 = R^6 = H
g, R^3 = CH^3; R^4 = R^5 = R^6 = H
h, R^5 = R^6 = Cl; R^3 = R^4 = H

Scheme 1



1, 3 and 4-6, R^1 = R^2 = CH$_3$
1, 3, and 4a, R^3 = R^4 = R^5 = R^6 = H
b, R^3 = Cl; R^4 = R^5 = R^6 = H
c, R^4 = NO$_2$; R^3 = R^5 = R^6 = H
d, R^3 = NO$_2$; R^4 = R^5 = R^6 = H
e, R^5 = Cl; R^3 = R^4 = R^6 = H
f, R^3 = R^5 = Cl; R^4 = R^6 = H
g, R^3 = CH$_3$; R^4 = R^5 = R^6 = H
h, R^5 = R^6 = Cl; R^3 = R^4 = H

5 and 6a, R^3 = R^4 = R^5 = R^6 = H
5b, R^3 = Cl; R^4 = R^5 = R^6 = H
5 and 6c, R^3 = CH$_3$; R^4 = R^5 = R^6 = H

In the only other report on this rearrangement that we are aware of, Sasaki and Yoshioka [3], isomerized 1-(5-nitro-2-furoyl)aziridinylketoxime to 3-(5-nitro-2-furyl)-4,5-dihydro-6*H*-1,2,4-oxadiazine by treating the ketoxime with concentrated hydrochloric acid in acetone followed by reaction with an aqueous sodium carbonate solution.

Our work was initially concerned with the development of methods for the synthesis of 4,5-dihydro-6*H*-1,2,4-oxadiazines **2**. Because 2,2-dimethylaziridine is relatively easy to prepare [4], we decided to use it for the synthesis of 1,2,4-oxadiazines using the method described by Rajagopalan and Talaty. When we carried out the conversion of the 2,2-dimethylaziridinylbenzaldoximes to 1,2,4-oxadiazines using this method the yields were very poor (less than 1%). Improved yields were achieved by a slight modification of the procedure as communicated by Rajagopalan and Talaty. They reported that the aziridinylbenzaldoxime was dissolved in a minimum amount of hot concentrated hydrochloric acid and evaporated to dryness. If instead, the solution was evaporated to approximately 15 ml of solution and then neutralized, the yields were increased to 20-40%. We have determined that the low yields were due to hydrolysis of **4** and/or **2** to benzoic acid.

In order to reduce the amount of hydrolysis it was decided to carry out the procedure in steps using anhydrous conditions for the ring opening reaction. The ring opening was accomplished by the reaction of 2,2-dimethylaziridinylbenzaldoximes **1a-g** with anhydrous hydrogen chloride dissolved in dioxane (Scheme I). An X-ray structural analysis of the 4-chloro derivative of the ring-opened compound **4b** established the location of the gem-dimethyl groups and the configuration of the compound (Figure 1 and Tables 1-7).

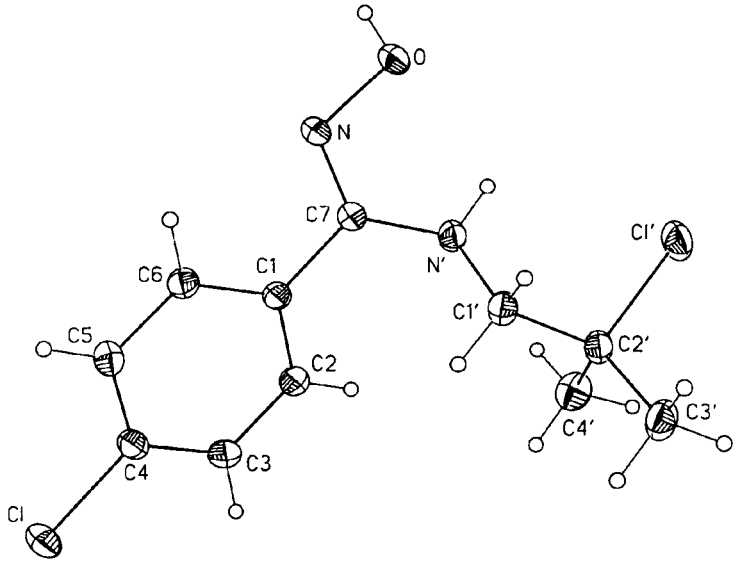


Figure1. ORTEP view of the molecular structure of **4b**. Thermal ellipsoids are scaled to the 30% probability level. Hydrogen atoms are drawn to an arbitrary scale.

Table 1

Crystallographic Data [a] for **4b**.

Formula	$C_{11}H_{14}N_2OCl_2$
Formula weight	261.15
a, Å	12.641(3)
b, Å	8.561(1)
c, Å	13.378(3)
V, Å^3	1279.5(5)
Z	4
F(000)	544
Crystal system	monoclinic
Space Group	$P2_1/c$
T, °C	-80
Radiation	Graphite monochromatized, MoKα (λ = 0.71069Å)
2θ range (°)	4-60
Scan speed (°/min) (1.2° ω scan)	4-8
ρ_{calc}, g/cc	1.36
Reflections measured	7786
Unique reflections	3740
R_{int}	0.0246
μ, cm^{-1}	4.89
Transmission factor range	N/A
Crystal size, mm	0.48 x 0.48 x 0.60
Reflections used	2551
Reflections rejected [b]	931
R(F), Rall(F) [c]	0.0375, 0.0586
R_w(F), R_w all(F)	0.0372, 0.0428
Goodness of fit	1.138
Parameters	662
Max |Δ/σ|	<0.2
Min, max peaks (e$^-$/Å^3)	-0.14, 0.17

[a] Data was collected on a Nicolet P3 diffractometer. Data was collected at reduced temperature using a Nicolet LT-2 low-temperature delivery system. Lattice parameters were obtained from the least-squares refinement of 32 reflections with 25.1< 2θ < 27.1° for $C_{21}H_{22}N_2O_4$. [b] Unobserved relections have F<4(σ(F)). [c] The function, $\Sigma w(|F_o| - |F_c|)^2$, was minimized and where $w = 1/(\sigma(F_o)^2 + (0.02F)^2)$.

The reaction of **4** with aqueous sodium hydroxide gave **2**. Unfortunately, the yields of the cyclization were no better than we obtained with the modified method of Rajagopalan and Talaty. In an attempt to increase the yield of these reactions, cyclization was then attempted with the open-chain benzenecarboximidamides **4a-c** by reacting them with sodium hydride in dioxane. Interestingly, the cyclizations under these conditions gave 3-aryl-4,5-dihydro-1,2,4-oxadiazoles **5a-c** as the only products in high yield (>79%). The structures of **5a-c** were determined from their ^{1}H-nmr and mass spectra. The isopropyl group appears as a doublet in the 90 MHz ^{1}H-nmr; at higher field (300 MHz) each doublet is split into another doublet (see **5b** in the Experimental). The nonequivalency of the isopropyl methyl groups, which gives rise to the two doublets at high field, is due to the presence of the chiral center at the carbon in position number **5** of the dihydro-1,2,4-oxadiazole ring. This nonequivalency is also apparent

Table 2

Fractional Coordinates and Equivalent Isotropic Thermal Parameters (Å^2) for the Non-Hydrogen Atoms of **4b**

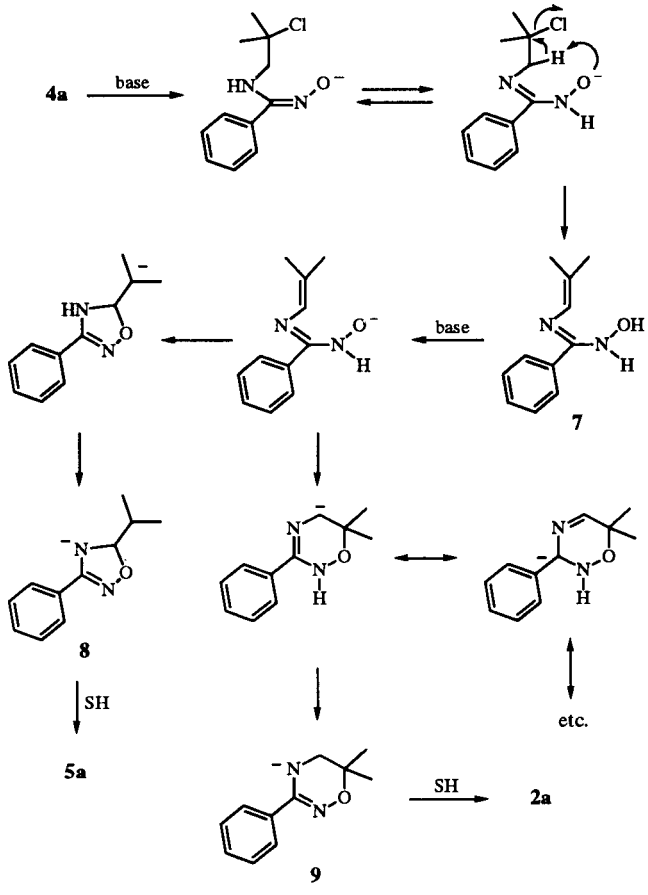
Atom	x	y	z	U
Cl	0.16429(4)	0.23860(5)	0.82694(4)	0.0453(2)
Cl'	0.94407(3)	0.21234(5)	0.91751(4)	0.0486(2)
N	0.52710(10)	0.0889(2)	0.60545(10)	0.0329(4)
N'	0.67707(10)	0.1708(2)	0.78212(10)	0.0341(5)
O	0.62740(10)	0.07306(14)	0.58433(10)	0.0408(4)
C1	0.46337(11)	0.17228(14)	0.73630(10)	0.0259(4)
C2	0.47840(13)	0.1286(2)	0.84292(11)	0.0324(5)
C3	0.38661(14)	0.1477(2)	0.87056(12)	0.0359(5)
C4	0.27941(13)	0.2121(2)	0.79180(12)	0.0311(5)
C5	0.26166(13)	0.2562(2)	0.68551(13)	0.0326(5)
C6	0.35423(13)	0.2357(2)	0.65854(12)	0.0308(5)
C7	0.56024(11)	0.1464(2)	0.70517(11)	0.0274(4)
C1'	0.71813(12)	0.3022(2)	0.86065(12)	0.0313(5)
C2'	0.83507(13)	0.2660(2)	0.96633(12)	0.0316(5)
C3'	0.8811(2)	0.4110(2)	1.0390(2)	0.0432(6)
C4'	0.8252(2)	0.1286(2)	1.0329(2)	0.0447(7)

For anisotropic atoms, the U value is Ueq, calculated as Ueq = 1/3 $\Sigma_i\Sigma_j$ U_{ij} a_i* a_j*. Aij where Aij is the dot product of the ith and jth direct space unit cell vectors.

in the 300 MHz ^{13}C-nmr spectra of **5b** and **c**. The mass spectrum is also consistent with this structure assignment with fragments corresponding to the loss of two hydrogen atoms (m/z = 180 for **5a**) and the loss of the isopropyl group (m/z = 147 for **5a**).

It was discovered in this work that a benzenecarboximidamide substituted with an electron-withdrawing group, **4c**, did not undergo this reaction. This compound gave a complex mixture of at least seven compounds, none of which was starting material, 1,2,4-oxadiazole, or 1,2,4-oxadiazine. This was determined from a tlc and ^{1}H-nmr spectrum of the mixture.

Mechanism I



Two of the 4,5-dihydro-1,2,4-oxadiazoles, **5a** and **c**, prepared by this method were reacted with *N*-chlorosuccinimide in DMF solution which converted them into the completely aromatic oxadiazoles **6a** and **c**.

Table 3

Anisotropic Thermal Parameters for the Non-Hydrogen Atoms of **4b**

Atom	U11	U22	U33	U12	U13	U23
Cl	0.0377(2)	0.0583(3)	0.0511(3)	-0.0004(2)	0.0300(2)	-0.0069(2)
Cl'	0.0284(2)	0.0564(3)	0.0629(3)	-0.0009(2)	0.0230(2)	-0.0148(2)
N	0.0281(6)	0.0440(7)	0.0316(6)	-0.0034(5)	0.0182(5)	-0.0054(5)
N'	0.0241(5)	0.0405(7)	0.0359(6)	-0.0010(5)	0.0125(5)	-0.0122(5)
O	0.0316(5)	0.0591(7)	0.0390(6)	-0.0071(5)	0.0225(5)	-0.0142(5)
C1	0.0256(6)	0.0264(6)	0.0263(6)	-0.0022(5)	0.0126(5)	-0.0031(4)
C2	0.0298(7)	0.0401(7)	0.0260(6)	0.0038(5)	0.0119(5)	0.0024(5)
C3	0.0376(7)	0.0471(8)	0.0266(6)	0.0008(6)	0.0180(6)	0.0012(6)
C4	0.0299(7)	0.0325(6)	0.0358(7)	-0.0036(5)	0.0195(6)	-0.0067(5)
C5	0.0274(7)	0.0334(7)	0.0359(7)	0.0021(5)	0.0138(6)	0.0033(5)
C6	0.0295(7)	0.0357(7)	0.0268(6)	0.0005(5)	0.0129(5)	0.0047(5)
C7	0.0258(6)	0.0293(6)	0.0279(6)	-0.0008(5)	0.0133(5)	-0.0006(5)
C1'	0.0259(6)	0.0286(6)	0.0358(7)	-0.0004(5)	0.0114(5)	-0.0047(5)
C2'	0.0243(6)	0.0319(6)	0.0369(7)	-0.0012(5)	0.0129(6)	-0.0049(5)
C3'	0.0319(8)	0.0413(8)	0.0486(9)	-0.0061(6)	0.0122(7)	-0.0146(7)
C4'	0.0448(9)	0.0410(8)	0.0419(8)	-0.0007(7)	0.0149(7)	0.0054(7)

The Uij are the mean-square amplitudes of vibration in Å^2 from the general temperature factor expression:
exp[-2π^2(h^2a^{*2}U11 + k^2b^{*2}U22 + l^2c^{*2}U33 + 2hka*b*U12 + 2hla*c*U13 + 2klb*c*U23)]

Table 4

Fractional Coordinates and Isotropic Thermal Parameters (Å^2) for the Hydrogen Atoms of **4b**

Atom	x	y	z	U
H10	0.599(2)	0.022(3)	0.526(2)	0.064(7)
H'N	0.726(2)	0.146(3)	0.757(2)	0.057(6)
H2	0.550(2)	0.091(2)	0.895(2)	0.043(5)
H3	0.395(2)	0.117(2)	0.945(2)	0.051(5)
H5	0.191(2)	0.298(2)	0.632(2)	0.046(5)
H6	0.346(2)	0.261(2)	0.587(2)	0.055(6)
H1'A	0.733(2)	0.394(2)	0.8243(15)	0.040(5)
H1'B	0.660(2)	0.326(2)	0.8845(15)	0.037(4)
H3'A	0.891(2)	0.496(2)	0.996(2)	0.052(5)
H3'B	0.959(2)	0.391(3)	1.107(2)	0.070(7)
H3'C	0.823(2)	0.438(3)	1.064(2)	0.058(6)
H4'A	0.905(2)	0.103(3)	1.096(2)	0.063(6)
H4'B	0.794(2)	0.037(2)	0.986(2)	0.049(5)
H4'C	0.771(2)	0.153(2)	1.059(2)	0.050(5)

Table 5

Bond Lengths (Å) and Angles (°) for the Non-hydrogen Atoms of **4b**

1	2	3	1-2	1-2-3
C4	Cl		1.741(2)	
C2'	Cl'		1.838(2)	
O	N	C7	1.429(2)	110.5(11)
C7	N		1.294(2)	
C7	N'	C1'	1.364(2)	123.79(13)
C1'	N'		1.459(2)	
C2	C1	C6	1.399(2)	118.7(2)
C6	C1	C7	1.392(2)	120.55(14)
C7	C1	C2	1.483(2)	120.69(11)
C3	C2	C1	1.383(3)	120.69(12)
C4	C3	C2	1.383(2)	119.3(2)
C5	C4	Cl	1.384(2)	119.19(11)
C5	C4	C3		121.4(2)
Cl	C4	C3		119.40(14)
C6	C5	C4	1.388(3)	118.7(13)
C1	C6	C5		121.11(15)
N	C7	N'		123.4(2)
N	C7	C1		115.77(11)
N'	C7	C1		120.65(13)
C2'	C1'	N'	1.525(2)	112.02(11)
C3'	C2'	C4'	1.515(2)	111.81(15)
C3'	C2'	Cl'		107.80(13)
C3'	C2'	C1'		110.07(12)
C4'	C2'	Cl'	1.515(3)	107.24(12)
C4'	C2'	C1'		113.10(13)
Cl'	C2'	C1'		106.50(12)

Table 6

Bond Lengths (Å) and Angles (°) for the Hydrogen Atoms of **4b**

1	2	3	1-2	1-2-3
H'N	N'	C7	0.85(3)	112.9(12)
H'N	N'	C1'		113.2(13)
H1O	O	N	0.82(2)	102.(2)
H2	C2	C3	0.90(2)	120.(2)
H2	C2	C1		120.(2)
H3	C3	C4	0.98(2)	118.8(13)
H3	C3	C2		122.0(13)
H5	C5	C6	0.92(2)	119.(2)

Table 6 (Continued)

1	2	3	1-2	1-2-3
H5	C5	C4		122.(2)
H6	C6	C1	0.94(3)	117.1(15)
H6	C6	C5		121.8(15)
H1'A	C1'	H1'B	0.99(2)	110.(2)
H1'A	C1'	C2'		107.2(9)
H1'A	C1'	N'		110.3(11)
H1	C1'	C2'	0.95(2)	107.3(9)
H1'B	C1'	N'		109.8(10)
H3'A	C3'	H3'B	0.97(2)	109.(2)
H3'A	C3'	H3'C		110.(2)
H3'A	C3'	C2'		110.7(12)
H3'B	C3'	H3'C	0.99(2)	108.(2)
H3'B	C3'	C2'		111.5(14)
H3'C	C3'	C2'	0.96(3)	106.9(12)
H4'A	C4'	H4'B	0.99(2)	108.(2)
H4'A	C4'	H4'C		112.(2)
H4'A	C4'	C2'		110.(2)
H4'B	C4'	H4'C	0.96(2)	106.(2)
H4'B	C4'	C2'		111.5(13)
H4'C	C4'	C2'	0.92(3)	108.7(13)

Table 7

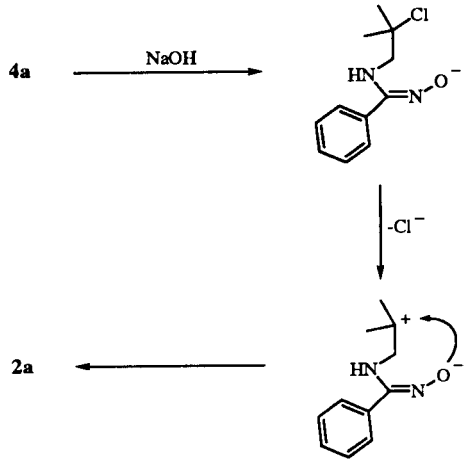
Torsion Angles (°) for the Non-hydrogen Atoms of **4b**

1	2	3	4	1-2-3-4
O	N	C7	N'	-6.7(2)
O	N	C7	C1	178.55(12)
C7	N'	C1'	C2'	154.9(2)
C1'	N'	C7	N	144.4(2)
C1'	N'	C7	C1	41.1(2)
C2	C1	C6	C5	0.2(3)
C6	C1	C2	C3	0.1(3)
C6	C1	C7	N	42.4(2)
C6	C1	C7	N'	142.73(13)
C7	C1	C2	C3	-177.75(14)
C7	C1	C6	C5	178.09(13)
C1	C2	C3	C4	-0.6(3)
C2	C3	C4	Cl	-179.2(2)
C2	C3	C4	C5	0.7(3)
Cl	C4	C5	C6	179.5(3)
C3	C4	C5	C6	-0.4(3)
C4	C5	C6	C1	-0.1(3)
N	C7	C1	C2	135.40(13)
N'	C7	C1	C2	-39.5(2)
N'	C1'	C2'	C1'	57.2(2)
N'	C1'	C2'	C3'	173.8(2)
N'	C1'	C2'	C4'	-60.4(2)

We suggest two possible pathways for the ring closure of **4** with sodium hydride in dioxane (Mechanisms I and III) In the first step of Mechanism I, sodium hydride removes a proton from the weakly acidic oxime hydroxyl group. The oximate anion brings about an intramolecular E2-type elimination to form the conjugated eneimine **7**. After deprotonation of **7**, the hydroxylamine anion undergoes addition to the alkene portion of the eneimine. Protonation of **8** in the reaction work-up leads to the 1,2,4-oxadiazole (**5a**). In Mechanism III, the oximate

anion undergoes tautomerism to **10**. A 1,2-hydride shift that is concerted with the elimination of chloride ion leads to a highly conjugated zwitterion **11**. Especially noteworthy is the fact that one of the resonance structures for **11** is a nitrone-like structure **11B**. Cyclization of **11** followed by tautomerism gives the 1,2,4-oxadiazole **5**. In this mechanism we suggest that the driving force for the rearrangement is neutralization of charge in an ionic species that is dissolved in a non-polar solvent (dioxane).

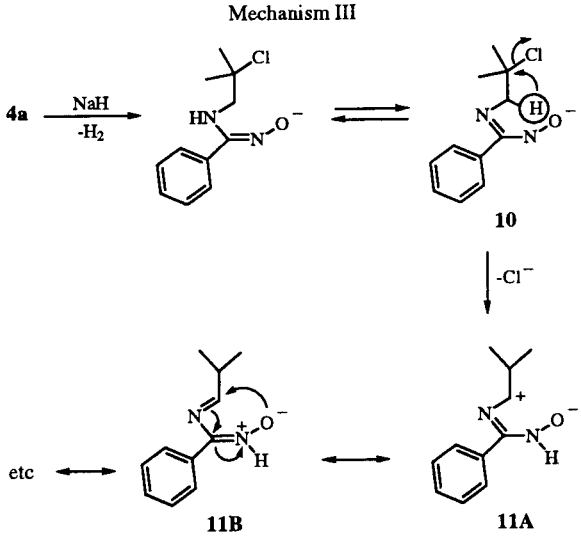
Mechanism II



We also suggest two possible pathways (Mechanisms I and II) for the formation of the 1,2,4-oxadiazines **2** from **4** in aqueous sodium hydroxide solution. In Mechanism I we suggest that the intramolecular addition of the hydroxylamine anion in the eneimine proceeds with a different regioselectivity in a polar solvent (water) to give the 1,2,4-oxadiazine **2**. An alternate pathway for the formation of **2** is shown in Mechanism II, In this mechanism the ionization of chloride ion takes place from the oximate anion. The resulting carbocation is trapped by the oximate anion to form a 1,2,4-oxadiazine. Since water is a good solvent for solvating ions, the 1,2-hydride shift does not take place because the driving force for neutralization of the positive charge is not required.

In our view Mechanism II and III are the most reasonable pathways for the formation of **2** and **5**. Work is in progress to delineate the mechanisms for these reactions.

Mechanism III



EXPERIMENTAL

General Procedures.

All reactions were carried out with reagent grade chemicals. The dioxane (Burdick and Jackson, distilled in glass) used for the preparation of the 3-aryl-4,5-dihydro-1,2,4-oxadiazoles **5** had to be freshly distilled from sodium metal in order for the reaction to proceed. The benzaldoximes and hydroximinoyl chlorides were prepared using the procedures described by Liu, Shelton and Howe [5]. The 2,2-dimethylaziridine was prepared by using the procedure described by Kost and Raban [4]. The ^{1}H-nmr spectra of each compound was determined for solutions in deuterated solvents with tetramethylsilane as an internal standard and using a Varian EM-390, a Varian Gemini 200 or a Varian Gemini 300 nmr spectrometer. The ^{13}C-nmr spectra were obtained either with a Varian Gemini 200 or a Varian Gemini 300 nmr spectrometer. Low resolution mass spectra were obtained with a Varian Saturn 3 ion-trap gc-mass spectrometer, and uv-visible spectra were measured in 95% ethanol with either a Cary 15 or a Cary 219 spectrophotometer. Infrared spectra were obtained using a Midac FT Infrared Spectrophotometer. Melting points were taken with an Electrothermal melting point apparatus using capillary tubes. Analyses of new compounds were carried out at Atlantic Microlab, Inc., Norcross, GA. and Midwest Microlab, Indianapolis, IN.

X-ray Experimental for (*Z*)-*N*-Hydroxy-*N'*-(2-chloro-2-methylpropyl)-4-chlorobenzenecarboximidamide (**4b**).

Crystals grew as colorless prisms by slow evaporation from diethyl ether-hexanes. The data crystal was cut from a much larger crystal and had approximate dimensions; 0.48 x 0.48 x 0.60 mm. The data were collected at -80° on a Nicolet P3 autodiffractometer using a graphite monochromator with MoKα radiation (λ = 0.71073Å) and equipped with a Nicolet LT2 low-temperature device. Details of crystal data, data collection and structure refinement are listed in Table 1. Four reflections (-5,-1,8; 1,1,-8; 1,5,2; 1,-4,4) were remeasured every 96 reflections to monitor instrument and crystal stability. A smoothed curve of the intensities of these check reflections was used to scale the data. The scaling factor ranged from 0.900 to 1.09. The data were corrected for Lp effects and absorption. The absorption correction was based on measured crystal faces. The transmission factors ranged from 0.8558-0.9003. Two equivalent sets of data, totaling 7786 reflections, were collected resulting in a R_{int} = 0.0246 for 3740 unique reflections. Data reduction and decay correction were performed using the SHELXTL-*Plus* software package [6]. The structure was solved by direct methods and refined on F by full-matrix least-squares with anisotropic thermal parameters for the non-H atoms. The hydrogen atoms were found in a ΔF map

and refined with isotropic temperature parameters The function, $\Sigma w(|F_o| - |F_c|)^2$, was minimized, where $w = 1/(\sigma(F_o))^2$ and $\sigma(F_o) = \{.5kI^{-1/2}\ [(\sigma(I))^2 + (0.0245*I)^2]^{1/2}\}$. The intensity, I, is given by $(I_{peak} - I_{background})x$(scan rate); where 0.0245 is a factor to downweight intense reflections and to account for instrument instability and k is the correction due to Lp effects and decay. The data were also corrected for secondary extinction effects. The correction is of the form: $F_{corr} = F_{calc}(1 + X*F_{calc}2/\sin 2\theta)^{1/4}$ where the extinction correction factor $X = 4.4(8) \times 10^{-6}$. Sigma (I) was estimated from counting statistics; $\sigma(I) = [(I_{peak} + I_{background})^{1/2} x$ (scan rate)]. A total of 202 parameters were refined to a final R = 0.0455 using 3740 reflections, with a wR = 0.0592 and a goodness of fit = 1.666. The R using all the data was 0.0455, with a wR = 0.0509. The maximum $|\Delta/\sigma| < 0.1$ in the final refinement cycle and the minimum and maximum peaks in the final difference electron density map were -0.20, 0.28 $e^-/Å^3$, respectively. Neutral atom scattering factors for the non-H atoms were taken from Cromer and Mann [7], with the anomalous-dispersion corrections taken from the work of Cromer and Liberman [8]. The scattering factors for the H atoms were obtained from Stewart, Davidson and Simpson [9]. Values used to calculate the linear absorption coefficient are from the International Tables for X-ray Crystallography (1974) [10]. All figures were generated using SHELXTL-*Plus*. [6]. The positional and thermal parameters, bond lengths, angles and torsion angles, figures and structure factor tables are listed in Tables 1-7. Other computer programs used in this work are listed elsewhere [11].

Benzohydroximoyl Chloride (**3a**).

Benzaldoxime (15.6 g, 0.129 mole) was dissolved in *N,N*-dimethylformamide (84 ml) at 25-30° and solid *N*-chlorosuccinimide (13.4 g, 0.100 mole) was added in 2.67 g (0.0200 mole) portions with stirring in a 600-ml beaker. The first addition of the *N*-chlorosuccinimide resulted in a slight decrease in temperature followed by a slight increase in temperature within the first ten minutes which confirmed the initiation of the reaction. The reaction was then kept below 35° by the rate of the addition of the *N*-chlorosuccinimide and intermittent cooling (dry ice-acetone bath). Completion of the reaction was noted by the cessation of the exotherm to room temperature. The solution was poured into ice water (400 ml) and extracted with ether (2 x 200 ml). The combined extracts were then washed with ice-cold water (2 x 200 ml). The organic layer was dried over anhydrous magnesium sulfate and the ether was removed using a rotary evaporator at aspirator pressure to give 14.5 g (0.0931 mole, 73%) of benzohydroximoyl chloride as a golden semi-solid. The crude benzohydroximoyl chloride was used for the next step without further purification (reported [12] mp 42-48°).

General Procedure for the Reaction of 2,2-Dimethylaziridine with Benzohydroximoyl Chlorides **1a-h**.

2,2-Dimethylaziridinyl-4-chlorobenzaldoxime (**1b**).

4-Chlorobenzohydroximinoyl chloride [5] (9.77 g, 0.0514 mole) dissolved in anhydrous diethyl ether (50 ml) was added through an addition funnel to an ice-cooled solution of 2,2-dimethylaziridine (4.27 g, 0.0600 mole), triethylamine (5.20 g, 0.0514 mole) and anhydrous ether (25 ml) in a 500-ml three-neck round-bottomed flask. The resulting solution was stirred for one hour. The solution was then extracted with water (50 ml) and the aqueous layer extracted with ether (2 x 50 ml). The organic layers were combined and dried over anhydrous magnesium sulfate. The ether was evaporated in a rotary evaporator to give opaque crystals (7.46 g, 0.0332 mole, 65%). Recrystallization from ether-hexanes gave 2,2-dimethylaziridinyl-4-chlorobenzaldoxime, mp 107.5-109°; ^{1}H nmr (90 MHz, deuteriochloroform): δ 7.57 (d, J = 9 Hz, 2H, aromatic H), 7.29 (d, J = 9 Hz, aromatic H), 2.22 (s, 2H, CH_2), 1.25 [s, 6H, $(CH_3)_2$] ppm; ^{13}C nmr (75 MHz, deuteriochloroform): δ 155.8 (*C*=N), 135.0 (*C*-C=N), 132.9 (aromatic C-Cl), 130.8 (aromatic CH), 128.4 (aromatic CH), 127.8 (aromatic), 41.8 [*C*$(CH_3)_2$], 40.8 (CH_2), 23.0 [$(CH_3)_2$] ppm; ir (Nujol): 3110, 1660 cm^{-1}.

Anal. Calcd. for $C_{11}H_{13}ClN_2O$: C, 58.80; H, 5.83; Cl, 15.78; N, 12.47. Found: C, 58.77; H, 5.86; Cl, 15.73; N, 12.46.

2,2-Dimethylaziridinylbenzaldoxime (**1a**).

This compound was obtained as clear crystals (64%) from ether-hexanes, mp 105-107.5°; ^{1}H nmr (90 MHz, deuteriochloroform): δ 7.48-7.78 (m, 2H, aromatic H), 7.23-7.78 (m, 3H, aromatic H), 2.22 (s, 2H, CH_2), 1.27 [s, 6H, $(CH_3)_2$] ppm; ^{13}C nmr (50 MHz, deuteriochloroform): δ 156.5 (C=N), 134.4 (aromatic *C*-C=N), 128.9 (aromatic CH), 128.1 (aromatic CH), 126.5 (aromatic CH), 41.6 [*C*$(CH_3)_2$], 40.7 (CH_2), 23.0 [$(CH_3)_2$] ppm; uv: λ_{max}, (log ε) 223 (4.05), 256 (3.76) nm; ir (Nujol): 3138, 1642 cm^{-1}.

Anal. Calcd. for $C_{11}H_{14}N_2O$: C, 69.45; H, 7.42; N, 14.72. Found: C, 69.50; H, 7.43; N, 14.69.

2,2-Dimethylaziridinyl-3-nitrobenzaldoxime (**1c**).

This compound was obtained as yellow crystals (72%) from ether-hexanes, mp 127.5-129°; ^{1}H nmr (90 MHz, deuteriochloroform): δ 8.52 (s, 1H, aromatic H), 8.52 (d, J = 7 Hz, aromatic H), 8.02 (d, J = 7 Hz, 1H, aromatic H), 7.59 (t, J = 7 Hz, 1H, aromatic H), 2.31 (s, 2H, CH_2), 1.25 [s, 6H, $(CH_3)_2$] ppm; ir (Nujol): 3300, 1670 cm^{-1}.

Anal. Calcd. for $C_{11}H_{13}N_3O_3$: C, 56.16; H, 5.57; N, 17.86. Found: C, 56.25; H, 5.60; N, 17.79.

2,2-Dimethylaziridinyl-4-nitrobenzaldoxime (**1d**).

This compound was obtained as light yellow crystals from ether-hexanes (52%), mp 144-145°; ^{1}H nmr (90 MHz, deuteriochloroform): δ 8.27 (d, J = 9 Hz, 2H, aromatic H), 7.82 (d, J = 9 Hz, 2H, aromatic H), 2.30 (s, 2H, CH_2), 1.25 [s, 6H, $(CH_3)_2$] ppm; ^{13}C nmr (75 MHz, deuteriochloroform): δ 155.3 (C=N), 148.1 (aromatic C-NO_2), 140.6 (*C*-C=N), 127.2 (aromatic CH), 123.6 (aromatic CH), 42.2 [*C*$(CH_3)_2$], 41.0 (CH_2), 23.1 [$(CH_3)_2$] ppm; uv: λ_{max} (log ε) 233 (3.94), 266 (3.93), 322 (3.74) nm; ir (Nujol): 3277, 1628, 1601 cm^{-1}.

Anal. Calcd. for $C_{11}H_{13}N_3O_3$: C, 56.16; H, 5.57; N, 17.86. Found: C, 56.24; H, 5.57; N, 17.96.

2,2-Dimethylaziridinyl-2-chlorobenzaldoxime (**1e**).

This compound was obtained as colorless crystals (90%) from chloroform-hexanes to give 2,2-dimethylaziridinyl-2-chlorobenzaldoxime, mp 139-140°; ^{1}H nmr (90 MHz, deuteriochloroform): δ 7.25-7.58 (m, 4H, aromatic H), 1.98 (s, 2H, CH_2), 1.32 [s, 6H, $(CH_3)_2$] ppm; ^{13}C nmr (75 MHz, deuteriochloroform): δ 156.1 (C=N), 133.7 (*C*-C=N), 132.8 (aromatic C-Cl), 131.0 (aromatic CH), 130.2 (aromatic CH), 129.0 (aromatic CH), 43.6 [*C*$(CH_3)_2$], 40.2 (CH_2), 23.1 [$(CH_3)_2$] ppm; uv: λ_{max} (log ε) 250 sh (3.51) nm; ir (Nujol): 3245, 1638, 1589 cm^{-1}.

Anal. Calcd. for $C_{11}H_{13}ClN_2O$: C, 58.80; H, 5.83; Cl, 15.78; N, 12.47. Found: C, 58.45; H, 5.71; Cl, 15.69; N, 12.24.

2,2-Dimethylaziridinyl-2,4-dichlorobenzaldoxime (**1f**).

This compound was obtained as white crystals from chloroform-hexanes (57%), mp 161-162°; ^{1}H nmr (90 MHz, deuteriochloroform): δ 7.18-7.58 (m, 3H, aromatic H), 2.00 (s, 2H, CH_2), 1.32 [s, 6H, $(CH_3)_2$] ppm; ^{13}C nmr (50 MHz, deuteriochloroform): δ 152.1 (C=N), 133.3 (aromatic *C*-C=N), 131.9 (aromatic C-Cl), 131.7 (aromatic C-Cl), 130.6 (aromatic CH), 128.5 (aromatic CH), 125.8 (aromatic CH), 41.6 [*C*$(CH_3)_2$], 39.2 (CH_2), 21.8 [$(CH_3)_2$] ppm; ir (Nujol): 3235, 1642, 1589 cm^{-1}.

Anal. Calcd. for $C_{11}H_{12}Cl_2N_2O$: C, 50.99; H, 4.67; N, 10.81; Cl, 27.36. Found: C, 50.89; H, 4.52; N, 10.76; Cl, 27.14.

2,2-Dimethylaziridinyl-4-methylbenzaldoxime (**1g**).

This compound was obtained as opaque crystals (57%) from ether-hexanes, mp 110-111°; gc-ms: m/z (relative intensity) 204 (29), 187 (10), 161 (19), 133 (100), 118 (57), 91 (83), 70 (57); ^{1}H nmr (300 MHz, deuteriochloroform): δ 7.50 (d, J = 8 Hz, 2H, aromatic H), 7.15 (d, J = 8 Hz, 2H, aromatic H), 2.34 (s, 3H, $ArCH_3$), 2.20 (s, 2H, CH_2), 1.24 [s, 6H, $(CH_3)_2$] ppm; ^{13}C nmr (75 MHz, deuteriochloroform): δ 156.6 (C=N), 138.9 (*C*-C=N), 131.6 [aromatic *C*(CH_3)], 128.9 (aromatic CH), 126.4 (aromatic CH), 41.6 [*C*$(CH_3)_2$], 40.8 (CH_2), 23.0 [$(CH_3)_2$], 21.2 ($ArCH_3$) ppm; uv: λ_{max} (log ε) 225 (4.05), 248 sh (3.90) nm; ir (Nujol): 3262, 1632, 1516 cm^{-1}.

Anal. Calcd. for $C_{12}H_{16}N_2O$: C, 70.56; H, 7.90; N, 13.71. Found: C, 70.62; H, 7.90; N, 13.73

2,2-Dimethylaziridinyl-2,6-dichlorobenzaldoxime (**1h**).

This compound was obtained as opaque crystals from ethanol-hexanes, mp 184-185°; ^{1}H nmr (90 MHz, d_6-dimethyl sulfoxide): δ 7.35 (s, 3H, aromatic H), 1.78 (s, 2H, CH_2), 1.42 [s, 6H, $(CH_3)_2$] ppm; ^{13}C nmr (50 MHz, deuteriochloroform): δ 150.3 (C=N), 134.5 (aromatic C-Cl), 132.4 (aromatic *C*-C=N), 130.0 (aromatic CH), 128.0 (aromatic CH), 43.0 [*C*$(CH_3)_2$], 37.1 (CH_2), 23.0 [$(CH_3)_2$] ppm; uv: λ_{max} (log ε) 260 (3.19) nm; ir (Nujol): 3244, 1640, 1584 cm^{-1}.

Anal. Calcd. for $C_{11}H_{12}Cl_2N_2O$: C, 50.99; H, 4.67; Cl, 27.36; N, 10.81. Found: C, 51.07; H, 4.68; Cl, 27.33; N, 10.78.

General Procedure for the Reaction of 2,2-Dimethylaziridinylbenzaldoximes **4a-h** with Hydrogen Chloride in Dioxane.

(*Z*)-*N*-Hydroxy-*N*'-(2-chloro-2-methylpropyl)benzenecarboximidamide (**4a**).

2,2-Dimethylaziridinylbenzaldoxime (**1a**, 7.00 g, 0.0368 mole) was dissolved in a saturated solution of anhydrous hydrogen chloride in dioxane (150 ml) with heating and stirring in a 250-ml round-bottomed flask. The flask was equipped for reflux with a calcium chloride drying tube on top of the condenser. The solution was refluxed for 4 hours. The solution was cooled to room temperature and brought to *p*H 11 with the addition of 50% aqueous sodium hydroxide solution (75 g). The solution was extracted with chloroform (3 x 75 ml). The combined organic extracts were then washed with a saturated solution of sodium chloride solution (2 x 100 ml). The organic extract was dried over anhydrous magnesium sulfate, and the chloroform was removed using a rotary evaporator at aspirator pressure to give a white solid. The solid was recrystallized from diethyl ether-hexanes to give (*Z*)-*N*-hydroxy-*N*'-(2-chloro-2-methylpropyl)benzenecarboximidamide as white crystals (7.72 g, 0.0310 mole, 93%). Several additional recrystallizations from diethyl ether-hexanes gave the analytical sample, mp 137-138°; ^{1}H nmr (50 MHz, deuteriochloroform): δ 8.7-10.0 (broad s, 1H, OH), 7.24-7.62 (m, 5H, aromatic H), 5.82 (s, 1H, NH), 3.21 (s, 2H, CH_2), 1.45, 1.41 [two s, 6H, $(CH_3)_2$] ppm; ^{13}C nmr (50 MHz, deuteriochloroform): δ 156.0 (C=N), 131.1 (aromatic *C*-C=N), 129.5 (CH, aromatic), 128.6 (CH, aromatic), 128.3 (CH, aromatic), 70.4 [*C*$(CH_3)_2$], 55.6 (CH_2), 29.5 [$(CH_3)_2$] ppm; uv: λ_{max} (log ε) 259 (4.66) nm; ir (Nujol): 3399, 3212, 1644, 1576 cm^{-1}.

Anal. Calcd. for $C_{11}H_{15}N_2ClO$: C, 58.28; H, 6.67; N, 12.36; Cl, 15.64. Found: C, 58.12; H, 6.67; N, 12.31; Cl, 15.75.

(*Z*)-*N*-Hydroxy-*N*'-(2-chloro-2-methylpropyl)-4-chlorobenzenecarboximidamide (**4b**).

This compound was obtained as white crystals from ether-hexanes (90%), mp 114-115.5°; ^{1}H nmr (90 MHz, deuteriochloroform): δ 7.43 (s, 4H, aromatic H), 3.20 (s, 2H, CH_2), 1.45 [s, 6H, $(CH_3)_2$] ppm; ^{13}C nmr (50 MHz, deuteriochloroform): δ 155.4 (C=N), 135.8 (*C*-C=N), 130.0 (aromatic CH), 129.8 (aromatic C-Cl), 128.9 (aromatic CH), 70.4 [*C*$(CH_3)_2$] 55.8 (CH_2), 29.6 [$(CH_3)_2$] ppm; ir (Nujol): 3300, 3220, 1628 cm^{-1}.

Anal. Calcd. for $C_{11}H_{14}N_2Cl_2O$: C, 50.59; H, 5.40; N, 10.73; Cl, 27.15. Found: C, 50.60; H, 5.45; N, 10.73; Cl, 27.06.

(*Z*)-*N*-Hydroxy-*N*'-(2-chloro-2-methylpropyl)-3-nitrobenzenecarboximidamide (**4c**).

This compound was obatined as yellow crystals from chloroform-hexanes (98%), mp 104-105°; ^{1}H nmr (90 MHz, deuteriochloroform): δ 8.20-8.50 (m, 2H, aromatic), 7.50-7.98 (m, 2H, aromatic), 3.20 (d, 2H, CH_2), 1.47 [s, 6H, $(CH_3)_2$] ppm; ir (Nujol): 3420, 3250, 1645 cm^{-1}.

Anal. Calcd. for $C_{11}H_{14}N_3ClO_3$: C, 48.62; H, 5.19; N, 15.47; Cl, 13.05. Found: C, 48.67; H, 5.26; N, 15.38; Cl, 12.96.

(*Z*)-*N*-Hydroxy-*N*'-(2-chloro-2-methylpropyl)-4-nitrobenzenecarboximidamide (**4d**).

This compound was obatined as yellow crystals from chloroform-hexanes (96%), mp 144-145°; ^{1}H nmr (90 MHz, deuteriochloroform): δ 8.29 (d, J = 9 Hz, 2H, aromatic H), 7.68 (d, J = 9 Hz, 2H, aromatic H), 3.18 (d, J = 6 Hz, 2H, CH_2), 1.46 [s, 6H, $(CH_3)_2$] ppm; ^{13}C-nmr (50 MHz, deuteriochloroform): δ 154.8 (C=N), 148.6 (C-NO_2), 137.5 (*C*-C=N), 129.7 (CH, aromatic), 123.8 (CH, aromatic), 70.1 [*C*$(CH_3)_2$], 55.9 (CH_2), 29.6 [$(CH_3)_2$] ppm; uv: λ_{max} (log ε) 234 sh (3.90), 252 (3.97), 323 (3.48) nm; ir (Nujol): 3287, 3185, 1645, 1599 cm^{-1}.

Anal. Calcd. for $C_{11}H_{14}N_3ClO_3$: C, 48.62; H, 5.19; N, 15.47; Cl, 13.05. Found: C, 48.67; H, 5.26; N, 15.38; Cl, 12.96.

(*Z*)-*N*-Hydroxy-*N*'-(2-chloro-2-methylpropyl)-2-chlorobenzenecarboximidamide (**4e**).

This compound was obatined as opaque crystals from chloroform-hexanes, mp 150-151°; ^{1}H nmr (90 MHz, deuteriochloroform): δ 7.24-7.58 (m, 4H, aromatic H), 3.07 (s, 2H, CH_2), 1.42 [s, 6H, $(CH_3)_2$] ppm; ^{13}C nmr (50 MHz, deuteriochloroform): δ 156.2 (C=N), 139.3 (aromatic *C*-C=N), 130.2 (aromatic C-Cl) 129.9 (aromatic CH), 128.9 (aromatic CH), 128.5 (aromatic CH), 70.4 (CH_2), 55.2 [*C*$(CH_3)_2$], 28.5 [$(CH_3)_2$] ppm; ir (Nujol): 3397, 3256, 1653, 1597 cm^{-1}.

Anal. Calcd. for $C_{11}H_{14}N_2Cl_2O$: C, 50.59; H, 5.40; N, 10.73; Cl, 27.15. Found: C, 50.44; H, 5.43; N, 10.67; Cl, 27.24.

(*Z*)-*N*-Hydroxy-*N*'-(2-chloro-2-methylpropyl)-2,4-dichlorobenzenecarboximidamide (**4f**).

This compound was obtained as colorless crystals from ether-hexanes (31%), mp 151-152°; ^{1}H nmr (90 MHz, deuteriochloro-

form): δ 7.22-7.58 (m, 3H, aromatic H), 3.07 (s, 2H, CH_2), 1.45 [s, 6H, $(CH_3)_2$] ppm; ^{13}C nmr (75 MHz, deuteriochloroform): δ 152.3 (C=N), 136.4 (*C*-C=N), 134.9 (aromatic C-Cl), 132.7 (aromatic C-Cl), 129.7 (aromatic CH), 128.9 (aromatic CH), 127.3 (aromatic CH), 69.7 [$C(CH_3)_2$], 55.2 (CH_2), 29.7 [$(CH_3)_2$] ppm; uv: λ_{max} (log ε) 273 (3.21), 281 sh (3.78) nm; ir (Nujol): 3399, 3191, 1653, 1593 cm^{-1}.

Anal. Calcd. for $C_{11}H_{13}N_2Cl_3O$: C, 44.70; H, 4.43; N, 9.48; Cl, 35.98. Found: C, 44.42; H, 4.37; N, 9.29; Cl, 36.26.

(*Z*)-*N*-Hydroxy-*N'*-(2-chloro-2-methylpropyl)-4-methylbenzenecarboximidamide (**4g**).

This compound was obtained as colorless crystals form ether-hexanes (91%), mp 127-128°; ^1H nmr (90 MHz, deuteriochloroform): δ 7.40 (d, J = 8 Hz, 2H, aromatic H), 7.20 (d, J = 8 Hz, 2H, aromatic H), 3.23 (s, 2H, CH_2), 2.37 (s, 3H, $ArCH_3$),1.47 [s, 6H, $(CH_3)_2$] ppm; ^{13}C nmr (50 MHz, deuteriochloroform): δ 156.3 (C=N), 139.7 (*C*-C=N), 129.2 (CH, aromatic), 128.6 (CH, aromatic), 70.5 [$C(CH_3)_2$], 55.8 (CH_2), 29.6 [$(CH_3)_2$], 21.4 ($ArCH_3$); uv: λ_{max} (log ε) 211 sh (4.10), 225 (3.66) nm; ir (Nujol): 3395, 3239, 1640 cm^{-1}.

Anal. Calcd. for $C_{12}H_{17}N_2ClO$: C, 59.87; H, 7.12; N, 11.64; Cl, 14.73. Found: C, 59.94; H, 7.17; N, 11.63; Cl, 14.79.

(*Z*)-*N*-Hydroxy-*N'*-(2-chloro-2-methylpropyl)-2,6-dichlorobenzenecarboximidamide (**4h**).

This compound was obtained as opaque crystals from ether-ethanol (93%), mp 165-166°; ^1H nmr (90 MHz, d_6-dimethyl sulfoxide): δ 7.47 (m, 3H, aromatic H), 3.00 (s, 2H, CH_2), 1.51 [s, 6H, $(CH_3)_2$] ppm; ^{13}C nmr (50 MHz, deuteriochloroform): δ 147.2 (C=N), 134.0 (aromatic C-Cl), 130.0 (aromatic C-H), 128.4 (aromatic *C*-C=N), 126.8 (aromatic CH), 69.2 [$C(CH_3)_2$], 53.0 (CH_2), 28.2 [$(CH_3)_2$] ppm; uv: λ_{max} (log ε) 267 sh (2.97), 273 (3.03), 281 (2.98) nm; ir (Nujol): 3304, 3242, 1659, 1584 cm^{-1}.

Anal. Calcd. for $C_{11}H_{13}N_2Cl_3O$: C, 44.70; H, 4.43; N, 9.48; Cl, 35.98. Found: C, 44.68; H, 4.24; N, 9.45; Cl, 35.88.

General Procedure for the Reaction of 2,2-Dimethylaziridinylbenzaldoximes **1a** and **b** and **d**-**h** with Concentrated Hydrochloric Acid Followed by Neutralization with Aqueous Sodium Hydroxide.

6,6-Dimethyl-3-phenyl-4,5-dihydro-6*H*-1,2,4-oxadiazine (**2a**).

2,2-Dimethylaziridinylbenzaldoxime (1.0 g, 0.0050 mole) was dissolved in concentrated hydrochloric acid (25 ml) in a 125-ml Erlenmeyer flask. The solution was evaporated to 15 ml of solution with heating and made basic to *p*H 11 with 50% aqueous sodium hydroxide solution (75 g). The solution was extracted with ether (2 x 100 ml) and the organic extract was dried over anhydrous magnesium sulfate. The ether was removed by rotary evaporation to give white crystals. The crude solid was recrystallized from ether-hexanes to give 6,6-dimethyl-3-phenyl-4,5-dihydro-6*H*-1,2,4-oxadiazine as white crystals (0.20 g, 0.0010 mole, 20%), mp 142-143°; ^1H nmr (90 MHz, deuteriochloroform): δ 7.15-7.40 (m, 3H, aromatic H), 7.40-7.90 (m, 2H, aromatic H), 5.70 (s, 1H, N H), 3.17 (d, J = 3 Hz, 2H, CH_2), 1.22 [s, 6H, $(CH_3)_2$] ppm; ^{13}C nmr (50 MHz, deuteriochloroform): δ 150.8 (C=N), 132.8 (*C*-C=N), 129.8 (aromatic *C*-CH_3), 128.3 (aromatic CH), 125.8 (aromatic CH), 69.0 [$C(CH_3)_2$], 49.2 (CH_2), 23.9 [$(CH_3)_2$] ppm; uv: λ_{max} (log ε) 223 (3.97), 265 (3.54) nm; ir (Nujol): 3194, 1607, 1568, 1532 cm^{-1}.

Anal. Calcd. for $C_{11}H_{14}N_2O$: C, 69.45; H, 7.42; N, 14.72. Found: C, 69.33; H, 7.39; N, 14.82.

6,6-Dimethyl-3-(4-chlorophenyl)-4,5-dihydro-6*H*-1,2,4-oxadiazine (**2b**).

This compound was obtained as white crystals from ether-hexanes (20%), mp 152-153°; gc-ms: m/z (relative intensity) 226 (M^+ + 2, 6.4), 224 (M^+, 21), 140 (14), 139 (35), 138 (45), 137 (100), 102 (42); ^1H nmr (90 MHz, deuteriochloroform): δ 7.46 (d, J = 8 Hz, 2H, aromatic H), 7.18 (d, J = 8 Hz, 2H, aromatic H), 6.07 (s, 1H, NH), 3.10 (d, J = 4.5 Hz, 2H, CH_2), 1.19 [s, 6H, $(CH_3)_2$] ppm; ^{13}C nmr (75 MHz, deuteriochloroform): δ 150.0 (C=N), 135.8 (aromatic *C*-C=N), 131.2 (aromatic C-Cl), 128.5 (aromatic CH), 127.1 (aromatic CH), 69.1 [$C(CH_3)_2$], 49.1 (CH_2), 23.9 [$(CH_3)_2$] ppm; uv: λ_{max} (log ε) 241 (3.58) ppm; ir (Nujol): 3341, 1609, 1564 cm^{-1}.

Anal. Calcd. for $C_{11}H_{13}N_2OCl$: C, 58.80; H, 5.83; Cl, 15.78; N, 12.47. Found: C, 58.79; H, 5.83; Cl, 15.71; N, 12.42.

6,6-Dimethyl-3-(4-nitrophenyl)-4,5-dihydro-6*H*-1,2,4-oxadiazine (**2d**).

This compound was obtained as yellow crystals from chloroform-hexanes (54%), mp 190-191°; ^1H nmr (90 MHz, deuteriochloroform): δ 8.26 (d, J = 9 Hz, 2H, aromatic H), 7.87 (d, J = 9 Hz, 2H, aromatic H), 5.01 (s, 1H, NH), 3.28 (d, J = 3 Hz, 2H, CH_2), 1.30 [s, 6H, $(CH_3)_2$] ppm; uv: λ_{max} (log ε) 255 sh (3.90), 265 (4.02), 335 (3.56) nm; ir (Nujol): 3329, 1601,1582 cm^{-1}.

Anal. Calcd for $C_{11}H_{13}N_3O_3$: C, 56.16; H, 5.57; N, 17.86. Found: C, 56.20; H, 5.60; N, 17.91.

6,6-Dimethyl-3-(2-chlorophenyl)-4,5-dihydro-6*H*-1,2,4-oxadiazine (**2e**).

This compound was obtained as opaque crystals from ether-chloroform (47%), mp 153-154°; ^1H nmr (90 MHz, deuteriochloroform): δ 7.24-7.65 (m, 4H, aromatic H), 4.98 (s, 1H, NH), 3.26 (d, J = 3 Hz, 2H, CH_2), 1.36 [s, 6H, $(CH_3)_2$] ppm; ^{13}C nmr (50 MHz, deuteriochloroform): δ 150.5 (C=N), 132.4 (*C*-C=N), 132.2 (C-Cl), 131.1 (aromatic CH), 130.6 (aromatic CH), 129.8 (aromatic CH), 126.8 (aromatic CH), 68.9 [$C(CH_3)_2$], 49.1 (CH_2), 24.0 [$(CH_3)_2$] ppm; uv: λ_{max} (log ε) 266 (3.17), 272 sh (3.10) nm; ir (Nujol): 3192, 1599, 1568 cm^{-1}.

Anal. Calcd. for $C_{11}H_{13}N_2OCl$: C, 58.80; H, 5.83; N, 12.47; Cl, 15.78. Found: C, 58.90; H, 5.85; N, 12.42; Cl, 15.73.

6,6-Dimethyl-3-(2,4-dichlorophenyl)-4,5-dihydro-6*H*-1,2,4-oxadiazine (**2f**).

This preparation initially gave a semi-crystalline viscous syrup. The crystals were separated from the viscous syrup by adding a small amount of ether and filtering the mixture. The solid was recrystallized from chloroform-hexanes to give opaque crystals (20%), mp 210-212°; ^1H nmr (300 MHz, deuteriochloroform): δ 7.45 (d, J = 8 Hz, 1H, aromatic H), 7.41 (d, J = 2 Hz, 1H, aromatic H), 7.28, 7.26 (dd, J = 2 Hz, 1H, aromatic H), 5.31 (s, 1H, NH), 3.26 (d, J = 3 Hz, 2H, CH_2), 1.36 [s, 6H, $(CH_3)_2$] ppm; ^{13}C nmr (75 MHz, deuteriochloroform): δ 149.6 (C=N), 136.2 (aromatic C=N), 133.3 (aromatic C-Cl), 132.2 (aromatic C-H), 130.8 (aromatic C-Cl), 129.9 (aromatic CH), 127.4 (aromatic CH), 69.3 [$C(CH_3)_2$], 49.2 (CH_2), 24.2 [$(CH_3)_2$] ppm; uv: λ_{max} (log ε) 265 (3.18), 272 (3.18) nm; ir (Nujol): 3187, 1595 cm^{-1}.

Anal. Calcd. for $C_{11}H_{12}N_2Cl_2O$: C, 50.99; H, 4.67; N, 10.81; Cl, 27.36. Found: C, 51.06; H, 4.67; N, 10.84; Cl, 27.42.

6,6-Dimethyl-3-(4-methylphenyl)-4,5-dihydro-6*H*-1,2,4-oxadiazine (**2g**).

This compound was obtained as white crystals from ether-hexanes (73%), mp 144-145°; gc-ms: m/e 204 (65), 118 (70), 117 (100), 91 (34); ^{1}H nmr (300 MHz, deuteriochloroform): δ 7.45 (d, J = 8 Hz, 2H, aromatic H), 7.07 (d, J = 8 Hz, 2H, aromatic H), 5.38 (s, 1H, NH), 3.14 (d, 2H, CH_2), 2.29 (s, 3H, CH_3), 1.20 [s, J = 6 Hz, 6H, $(CH_3)_2$] ppm; ^{13}C nmr (75 MHz, deuteriochloroform): δ 150.8 (C=N), 139.7 (aromatic *C*-C=N), 129.9 (aromatic *C*-CH_3), 128.9 (aromatic CH), 125.7 (aromatic CH), 68.8 [*C*$(CH_3)_2$], 49.1 (CH_2), 23.8 [$(CH_3)_2$], 21.1 ($ArCH_3$) ppm; uv: λ_{max} (log ε) 227 (4.05), 273 (3.66) nm; ir (Nujol): 3310, 1599, 1561 cm^{-1}.

Anal. Calcd. for $C_{12}H_{16}N_2O$: C, 70.56; H, 7.90; N, 13.71. Found: C, 70.57; H, 7.92; N, 13.77.

6,6-Dimethyl-3-(2,6-dichlorophenyl)-4,5-dihydro-6*H*-1,2,4-oxadiazine (**2h**).

This compound was obtained as opaque crystals from ether-chloroform (45%), mp 195-196°; ^{1}H nmr (90 MHz, deuteriochloroform): δ 7.28 (s, 3H, aromatic H), 5.94 (d, J = 3 Hz, 1H, NH), 3.13 (d, J = 3 Hz, 2H, CH_2), 1.70 [s, 6H, $(CH_3)_2$] ppm; ^{13}C nmr (50 MHz, deuteriochloroform): δ 147.8 (C=N), 135.0 (aromatic C-Cl), 130.8 (aromatic *C*-C=N), 130.2 (aromatic CH), 127.4 (aromatic CH), 68.8 [*C*$(CH_3)_2$], 47.2 (CH_2), 24.0 [$(CH_3)_2$] ppm; uv: λ_{max} (log ε) 265 (2.93), 273 (2.98), 283 (2.92) nm; ir (Nujol): 3204, 1620, 1562 cm^{-1}.

Anal. Calcd. for $C_{11}H_{12}N_2OCl_2$: C, 50.99; H, 4.67; N, 10.81; Cl, 27.36. Found: C, 51.06; H, 4.63; N, 10.79; Cl, 27.34.

General Procedure for the Reaction of (*Z*)-*N*-Hydroxy-*N*'-(2-chloro-2-methylpropyl)benzenecarboximidamides **4a**, **4b**, and **4g** with Sodium Hydride in Dioxane.

5-Isopropyl-3-phenyl-4,5-dihydro-1,2,4-oxadiazole (**5a**).

(*Z*)-*N*-Hydroxy-*N*'-(2-chloro-2-methylpropyl)benzenecarboximidamide (5.66 g, 0.0250 mole) was dissolved in dioxane (60 ml) in a 100-ml three-neck round-bottomed flask fitted with a condenser, a calcium chloride drying tube and a solid addition funnel in a dry box. Sodium hydride (0.600 g, 0.0250 mole) was added through the solid addition funnel with stirring. The mixture was stirred and refluxed for 1.5 hours. Water (5 ml) was added and the mixture was extracted with ether (3 x 75 ml). The combined organic extracts were washed with saturated sodium chloride solution (2 x 100 ml). The organic extract was dried over anhydrous magnesium sulfate, and the ether was removed by rotary evaporation to give a white solid. The crude solid was recrystallized from ether-hexanes to give 5-isopropyl-3-phenyl-4,5-dihydro-1,2,4-oxadiazole as clear crystals (3.75 g, 0.0200 mole, 79%). Several additional recrystallizations from ether-hexanes gave the analytical sample, mp 97-98°; gc-ms: m/z (relative intensity) 190 (8), 188 (20), 147 (28), 119 (100), 104 (11), 91 (15), 77 (48); ^{1}H nmr (50 MHz, deuteriochloroform): δ 7.50-7.75 (m, 2H, aromatic H), 7.15-7.50 (m, 3H, aromatic H), 5.39 (m, 1H, NCHO), 2.88 [m, 1H, C*H*$(CH_3)_2$], 0.94 [d, J = 7 Hz, 6H, $(CH_3)_2$] ppm; ^{13}C nmr (50 MHz, deuteriochloroform): δ 156.1 (C=N), 130.5 (aromatic CH), 128.4 (aromatic CH), 126.3 (aromatic CH), 125.5 (aromatic *C*-C=N), 97.2 (N*C*HO), 33.6 [*C*H$(CH_3)_2$], 16.2, 16.1 [CH(*C*$H_3)_2$] ppm; uv: λ_{max} (log ε) 293 (3.50) nm; ir (Nujol): 3192, 1601, 1570, 1510 cm^{-1}.

Anal. Calcd. for $C_{11}H_{14}N_2O$: C, 69.45; H, 7.42; N, 14.72. Found: C, 69.37; H, 7.43; N, 14.77.

5-Isopropyl-3-(4-chlorophenyl)-4,5-dihydro-1,2,4-oxadiazole (**5b**).

This compound was obtained as clear crystals (66%) from ether-hexanes, mp 125-126°; gc-ms: m/z (relative intensity) 226 (5), 224 (14), 222 (35), 180 (7), 155 (33), 153 (100), 137 (15), 125 (23), 102 (10), 90 (31); ^{1}H nmr (90 MHz, deuteriochloroform): δ 7.59 (d, J = 8.5 Hz, 2H, aromatic H), 7.31 (d, J = 8.5 Hz, 2H, aromatic H), 5.40 (t, J = 5 Hz, 1H, N-CH), 5.07 (s, J = 6 Hz, 1H, NH), 1.53-2.13 [m, 1H, CH$(CH_3)_2$], 1.01 [d, J = 6 Hz, 6H, $(CH_3)_2$] ppm; ^{13}C nmr (75 MHz, deuteriochloroform): δ 155.1 (C=N), 136.7 (aromatic *C*-C=N), 128.7 (aromatic CH), 127.7 (aromatic CH), 124.1 (aromatic C-Cl), 97.5 (NCHO), 33.6 [*C*H$(CH_3)_2$], 16.4, 16.3 [CH(*C*$H_3)_2$] ppm; uv: λ_{max} (log ε) 235 (4.18), 295 (3.48), 300 (3.54) nm; ir (Nujol): 3231, 1597, 1559 cm^{-1}.

Anal. Calcd. for $C_{11}H_{13}N_2OCl$: C, 58.80; H, 5.83; N, 12.47; Cl, 15.78. Found: C, 58.74; H, 5.84; N, 12.40; Cl, 15.85.

5-Isopropyl-3-(4-methylphenyl)-4,5-dihydro-1,2,4-oxadiazole (**5c**).

This compound was obtained as clear crystals (95%) from ether-hexanes, mp 110-111°; gc-ms: m/z (relative intensity) 204 (5), 202 (40), 161 (19), 133 (100), 91 (30); ^{1}H nmr (75 MHz, deuteriochloroform): δ 7.53 (d, J = 8 Hz, 2H, aromatic H), 7.16 (d, J = 8 Hz, 2H, aromatic H), 5.39 (t, J = 4.5 Hz, 1H, NCHO), 4.80 (s, 1H, NH), 2.34 ($ArCH_3$), 1.90 [m, 1H, C*H*$(CH_3)_2$], 0.98 (d, J = 3 Hz, 3H, CHC*H*$_3$), 0.95 (d, J = 3 Hz, 3H, CHC*H*$_3$) ppm; ^{13}C nmr (75 MHz, deuteriochloroform): δ 155.9 (C=N), 140.9 (*C*-C=N), 129.3 (aromatic CH), 126.3 (aromatic CH), 122.7 (aromatic *C*-CH_3), 97.1 (N*C*HO), 33.6 [*C*H$(CH_3)_2$], 21.4 ($ArCH_3$), 16.4, 16.3 [CH(*C*$H_3)_2$] ppm; uv: λ_{max} (log ε) 290 (3.96) nm; ir (Nujol): 3200, 1601, 1564 cm^{-1}.

Anal. Calcd. for $C_{12}H_{16}N_2O$: C, 70.56; H, 7.90; N, 13.71. Found: C, 70.60; H, 7.90; N, 13.76.

General Procedure for the Reaction of 5-Isopropyl-3-phenyl-4,5-dihydro-1,2,4-oxadiazoles **5a** and **5c** with *N*-Chlorosuccinimide.

5-Isopropyl-3-phenyl-1,2,4-oxadiazole (**6a**).

5-Isopropyl-3-phenyl-4,5-dihydro-1,2,4-oxadiazole (0.40 g, 0.0021 mole) was dissolved in *N*,*N*-dimethylformamide (2 ml) at 25-30° in a 10-ml beaker. Solid *N*-chlorosuccinimide (0.28 g, 0.0021 mole) was added in small portions with stirring to the solution. The first addition resulted in a slight decrease in temperature followed by a slight increase in temperature within the first ten minutes, which confirmed the initiation of the reaction. The reaction mixture was heated to 50°. The temperature of the reaction mixture was maintained at 50° by controlling the rate of addition of *N*-chlorosuccinimide and by intermitent cooling of the beaker. Completion of the reaction was noted by the cessation of the exotherm and the spontaneous cooling of the beaker to room temperature. The solution was poured into ice water (10 ml) and extracted with ether (4 X 5 ml). The combined ether extracts were then washed with cold water (3 X 5 ml). The organic layer was dried over anhydrous magnesium sulfate and the ether was removed in rotary evaporator at aspirator pressure to give 0.32 g (0.0017 mole, 81%) of 5-isopropyl-3-phenyl-1,2,4-oxadiazole [13] as a colorless liquid. The liquid was microdistilled in a short path distillation apparatus (Kontes No. 548250) to give the analytical sample; gc-ms: m/e 188 (42), 119 (100), 103 (20), 91 (31), 76 (11), 64 (16); ^{1}H nmr (90 MHz, deuteriochloroform): δ 8.00-8.24 (m, 2H, aromatic H), 7.39-7.62 (m, 3H, aromatic H), 3.05-3.49 [septet, J = 6 Hz, 1H, C*H*$(CH_3)_2$], 1.42 [d, J = 6 Hz, 6H, $(CH_3)_2$] ppm; ^{13}C nmr (50 MHz, deuteriochloroform): δ 183.9 (N=C-O), 167.9 (C=N-O), 130.7 (aromatic CH), 128.5 (aromatic CH), 127.1

(aromatic CH), 27.3 ($ArCH_3$), 23.9 [$C(CH_3)_2$], 19.9 [$(CH_3)_2$] ppm; ir (neat liquid): 1742, 1568 cm^{-1}.

Anal. Calcd. for $C_{11}H_{12}N_2O$: C, 70.19; H, 6.43; N, 14.88; Found: C, 70.29; H, 6.39; N, 14.78.

5-Isopropyl-3-(4-methylphenyl)-1,2,4-oxadiazole (**6c**).

This compound was obtained as a colorless oil (85%) after microdistillation; gc-ms: m/e 202 (61), 133 (100), 104 (14), 91 (12), 77 (13); ^1H nmr (90 MHz, deuteriochloroform): δ 8.01 (d, J = 8 Hz, 2H, aromatic H), 7.29 (d, J = 8 Hz, 2H, aromatic H), 3.01-3.51 [septet, J = 7 Hz, 1H, $CH(CH_3)_2$], 2.41 (s, $ArCH_3$), 1.45 [d, J = 7 Hz, 6H, $(CH_3)_2$] ppm; ^{13}C nmr (50 MHz, deuteriochloroform): δ 183.7 (N=C-O), 168.2 (C=N-O), 141.2 (aromatic *C*-C=N), 129.5 (aromatic CH), 127.3 (aromatic CH), 124.2 (aromatic CH), 27.5 ($ArCH_3$), 21.5 [$C(CH_3)_2$], 20.3 [$(CH_3)_2$] ppm; ir (neat liquid): 1589 cm^{-1}.

Anal. Calcd. for $C_{12}H_{14}NO_2$: C, 71.26; H, 6.98; N, 13.85; Found: C, 71.38; H, 7.04; N, 13.90.

Acknowledgements

We gratefully acknowledge the financial support of this work by a grant from the National Science Foundation (RUI grant number CHE-921-1435). We also acknowledge the support for D.N., M.H., and N.S. by a Minority Biomedical Research Support Program grant from the National Institutes of Health (NIH-MBRS Grant GM08256).

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