Reactions of *N*-Aryl-*N*-(4,5-dihydro-1*H*-imidazol-2-yl)hydroxylamines with Electron-Deficient Acetylenes. Synthesis and Structure of Novel Heterocyclic Ketene Aminals

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Reactions of the title hydroxylamine hydrochlorides **1** with electron-deficient acetylenes **3** are described. Compounds **1a** reacts with ethyl propiolate (**3a**) to give the expected indole **7**. Similar reactions of **1a**−**e** with disubstituted acetylene derivatives such as diethyl acetylenedicarboxylate (**3b**), dimethyl acetylenedicarboxylate (**3c**), or ethyl phenylpropiolate (**3d**) lead to the formation of novel heterocyclic ketene aminals **9a**−**m**. X-ray crystal structure and NMR spectra of **9a** are described in detail.

N-Aryl-*N*-(4,5-dihydro-1*H*-imidazol-2-yl)hydroxylamine hydrochlorides **1** are readily prepared by reacting 2-chloro-4,5-dihydroimidazole with suitable *N*-aryl-hydroxylamines[1,2] and could be converted to the free bases **2** on treatment with methanolic NaOH.[3] Our detailed studies on the structure of **2** revealed that in the crystalline phase the compound **2a** (R = H) exists as a 1:1 mixture of two tautomeric forms: **A** (α-iminohydroxylamine) and **B** (α-aminonitrone). On the other hand, NMR spectra suggested that in solution the nitrone form **B** prevails[3] (Scheme 1).

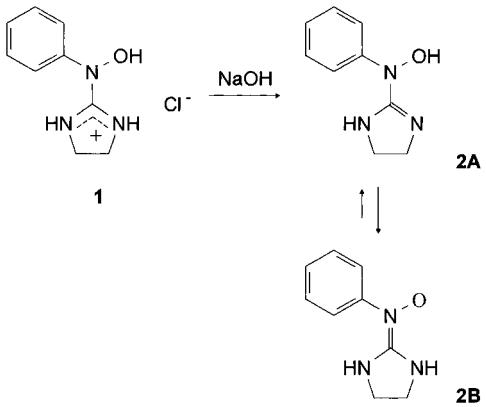
The reactions of various *N*-arylnitrones or *N*-arylhydroxylamine derivatives with acetylenes bearing electron-withdrawing groups have been studied in a number of laboratories. Thus, it has been reported that the reaction of α-aryl-*N*-phenylnitrone with hexafluoro-2-butyne leads to 2,3-bis(trifluoromethyl)indole[4] and the treatment of *N*-arylhydroxylamines or hydroxamic acids with activated monosubstituted acetylenes gives rise to the formation of indoles functionalized at the C-3 carbon *via* tandem Michael addition−[3,3]sigmatropic rearrangement reaction.[5,6]

As an extension of our study on the reactivity of hydroxylamines **1**,[1] this paper deals with the reactions of the hydrochlorides **1** or corresponding free bases **2** with a variety of electron-deficient acetylene derivatives **3**.

Results and Discussion

First, the hydrochloride **1a** was subjected to the reaction with ethyl propiolate **3a** in the presence of a 2-fold excess of Et_3N, and the expected indole **7** was obtained in 65% yield (Scheme 2). To examine what effect acetylene substituents would have on the reaction course, we attempted a similar reaction of **1a** with diethyl acetylenedicarboxylate **3b**. The only product that could be isolated in pure form (31% yield) from the complex mixture of products was the ketene aminal **9a** (Scheme 2). When the free base **2** was used instead of salt **1a**, the compound **9a** was obtained in 22% yield only, and therefore, the hydrochlorides **1a**−**d** were found to be more suitable substrates for preparation of a series of novel ketene aminals **9a**−**m**. In general, the reactions of **1** with activated acetylenes were performed in polar aprotic solvents such as THF or acetone at room temperature and gave the desired products in 10−39% yields.

Scheme 1



Plausible routes to the formation of **7** or **9** are shown in Scheme 2. We assume that the mechanism of the reaction leading to the indole **7** is analogous to those previously described[2,3] and consists of loss of a water molecule from the intermediate **6**. Alternatively, **6** can undergo a retro-ene reaction leading to reopening of the indoline ring with formation of **8**. In the presence of Et_3N, the intermediate **8** can subsequently undergo an intramolecular nucleophilic substitution reaction, giving rise to the formation of final ketene aminals **9**.

These results indicate that adding a second electron-withdrawing group to the acetylene moiety has caused a change in mechanism of the reaction. The nucleophilic attack of the exocyclic nitrogen atom at the C=O group in **5** may occur with high diastereofacial selection (Scheme 2). In the case of ethyl propiolate (R_1 = H), the nucleo-

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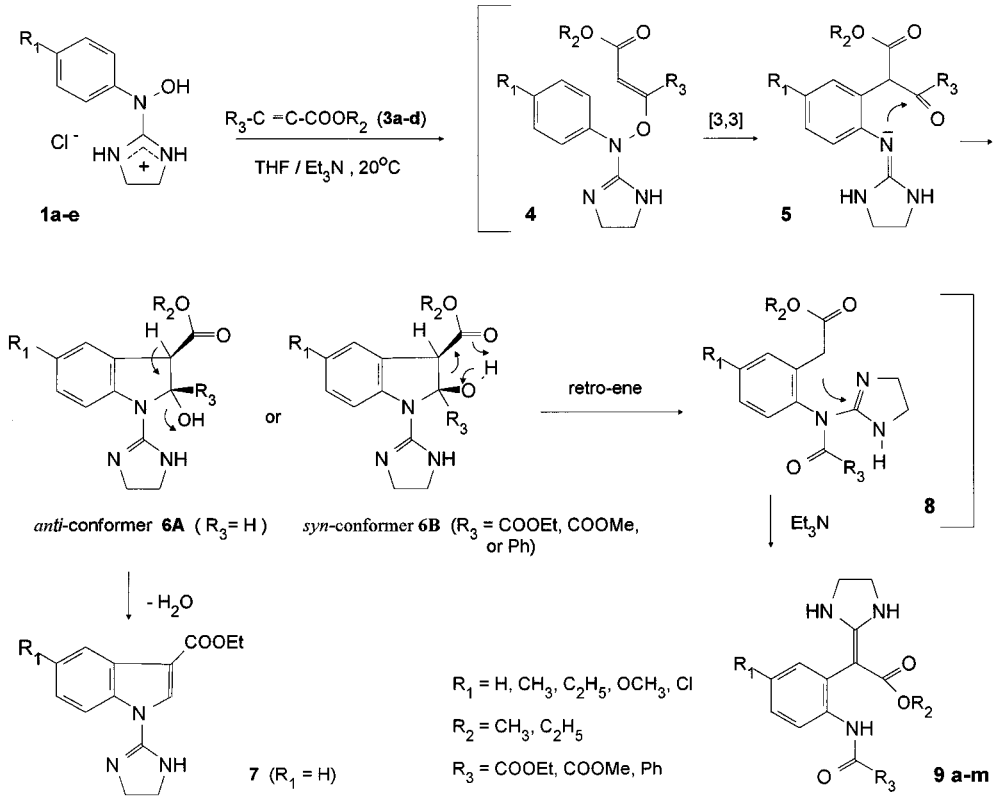
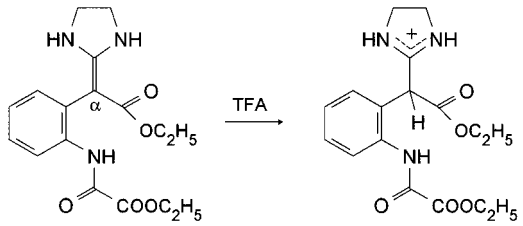
Scheme 2



Scheme 3



philic addition to C=O shows a high preference for the *anti*-configured product **6A**, which can be stabilized by an aromatization process upon loss of a water molecule. On the other hand, when a bulky substituent is present at the prochiral carbon atom of **5** (R_1 = COOMe, COOEt or Ph), the conformational preference of *syn*-diastereoisomer **6B** over *anti*-configured **6A** may result from vicinal repulsion between R_1 and the ester group. Hence, the hydroxyl and ester groups are brought into close proximity, enabling spontaneous retro-ene reaction to take place.

Heterocyclic ketene aminals, also known as cyclic 1,1-enediamines, are valuable substrates for the construction of fused heterocycles and have been recently reiewed.[7] The characteristic feature of these push−pull olefins is the highly polarized double C=C bond due to the conjugation of two electron-donating amino groups and electron-withdrawing groups. Consequently, the nucleophilicity of the α-carbon is much stronger than that of the nitrogen. We therefore felt it necessary to examine in detail both the crystal structure and the NMR spectra of the sterically hindered 1,1-enediamine derivative **9a** and the corresponding immonium salt **10** (Scheme 3).

Crystal structure of 9a. The X-ray crystal structure with the atom numbering scheme of compound **9a** is shown in Figure 1. Experimental data for the X-ray analysis are given in Table 1.

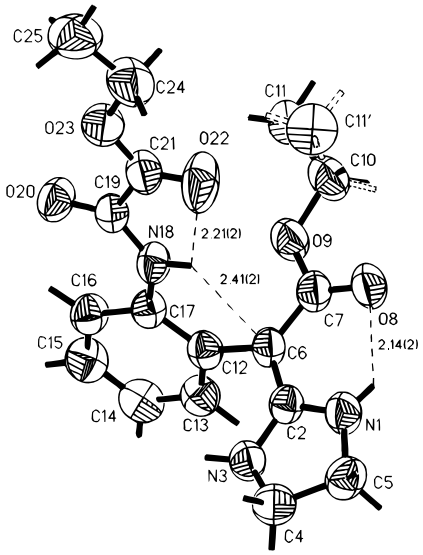


Figure 1. Atom labeling in **9a** (elipsoids drawn at the 50% probability level).

Two approximately planar groups of atoms, N1 to C10 and C12 to C25, forming a dihedral angle of 64.8(1)° and twisted around the C6−C12 bond, can be distinguished within this molecule. The free rotation around the C6−C12 bond is hindered due to steric interaction between the two bulky substituents at the phenyl ring. The "near-to-planar" arrangement of the N1−C10 part of the molecule is stabilized by the N1−H···O8=C hydrogen bond, which is a part of a six-membered conjugated ring system. π-Electron delocalization within this fragment is reflected in molecular geometry where formally single C7−C6 and formally double C6−C2 bonds have similar lengths [1.420(2) and 1.397(2) Å, respectively]. Similar

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Table 1. Experimental Data for the X-ray Analysis of 9a

compd	9a
emp form	$C_{17}H_{21}N_3O_5$
form wt	347.37
T (K)	293(2)
wavelength	Cu Kα (1.541 78 Å)
cryst syst	monoclinic
space grp	$P2_1/n$
unit cell dimens	$a = 10.268(2)$ Å $b = 13.664(3)$ Å $\beta = 91.35(1)°$ $c = 12.436(1)$ Å
volume	1744.3(5) Å^3
Z	4
density (calcd)	1.323 g·cm^{-3}
max cryst dimens	0.45 × 0.2 × 0.05 mm
cryst color, habit	colorless, plate
diffractometer/scan	Kuma Diffraction KM-4/w-2q
decay of standards	2.5%
$2q_{max}$ for data collectn	130°
index ranges	$h = -12 \rightarrow 12$, $k = 0 \rightarrow 15$, $l = 0 \rightarrow 14$
reflns collected	2958
ind reflns	2838 ($R_{int} = 0.019$)
absorptn correctn	not applied
computer programs	SHELXS-86, SHELXL-93
refinement method	full-matrix least-squares on F^2
data/restrains/parameters	2838/2/296
goodness-of-fit on F^2	1.099
extinctn coeff	0.009(1)
final R indices [$I > 2s(I)$]	$R_1 = 0.044$, $wR_2 = 0.133$
R indices (all data)	$R_1 = 0.061$, $wR_2 = 0.141$
largest diff peak and hole	0.21 and −0.25 e Å^{-3}

structural behavior has been observed earlier for other compounds of the push−pull type.[7−9]

Coplanar arrangement of the phenyl ring and the amide group allows for maximum conjugation of their π-electron systems; however, it also gives rise to two short intramolecular contacts, C6···H18 and O20···H16 (Figure 1). Since, as evidenced by ^{13}C-NMR, C6 is the main nucleophilic center within this molecule, the N18−H18··· C6 close contact can, to a great part, arise also from attractive interaction (an intramolecular hydrogen bond) between the amide N(18)−H group and π-electrons of a cyclic 1,1-enediamine system. Nevertheless, to reduce repulsive interactions between substituents the amide group is slightly twisted about the C17−N18 bond (9.3°).

The oxamic acid ethyl ester fragment of the molecule has two carbonyl oxygen atoms trans to each other, an arrangement that has been shown to be the energy minimum conformation for this group.[10] The bond length between the two sp^2-hybridized carbon atoms C19 and C21, 1.522(3) Å, indicates that there is practically no conjugation between the π-electron systems of the amide and ester groups. In benzyl *N*-(*tert*-butoxycarbonyl)-oxamate,[11] where these two groups were twisted by 90°, the analoguous bond was only slightly elongated [1.533(2) Å]. The ethyl group is in a staggered conformation with respect to the carboxy group.

NMR Studies on 9a. Structural differences between the free 1,1-enediamine **9a** and its salt **10** are accompained by several spectral changes. The results of ^{1}H NMR experiments are summarized in Table 2. The plots of the 3.0−5.5 ppm region of ^{1}H NMR spectra of **9a** recorded in DMSO-d_6 and $CDCl_3$ are shown in Figure 2a and b, respectively.

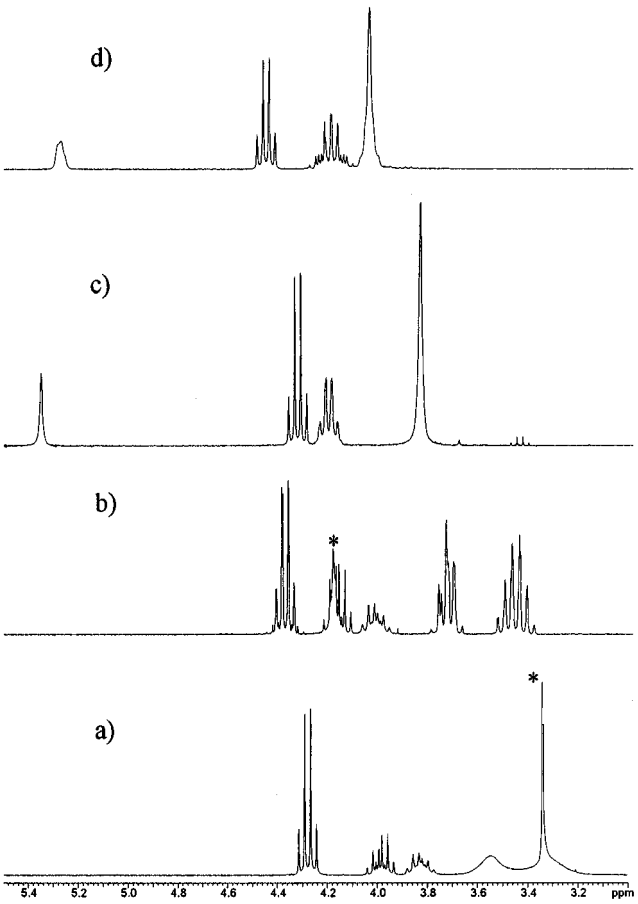

Figure 2. 3.0−5.5 ppm region of the ^{1}H NMR spectrum of **9a** (a) recorded in DMSO-d_6 and (b) in $CDCl_3$. Signal marked * originates from water in DMSO-d_6. The same region of **10** recorded in (c) DMSO-d_6 and (d) $CDCl_3$. In spectrum b the H3 signal at 4.05 ppm overlaps with a low-field H10 resonance.

Table 2. ^{1}H NMR Chemical Shifts (ppm) of Compounds 9a and 10 Recorded in DMSO-d_6 and $CDCl_3$

	9a		10	
	DMSO-d_6	$CDCl_3$	DMSO-d_6	$CDCl_3$
H(1)	8.11 br	8.10 br	10.06 s	8.75 s
H(3)	6.08 br	4.19 s	10.06 s	8.75 s
H(4)	3.33 br	3.53−3.39 m	3.85 s	4.05 s
H(5)	3.54 br	3.80−3.68 m		
H(6)			5.39	5.25 s
H(10a)	4.04−3.93 m	4.22−4.12 m	4.21 q	4.22 m
H(10b)	3.88−3.77 m	4.07−3.96 m		4.17
H(11)	0.99 t	1.14 t	1.19 t	1.16 t
H(ar)	8.11 d	8.25 dd	7.50−7.37 m	7.57 −7.34 m
	7.28−7.08 m	7.34−7.12 m		
H(18)	9.33 s	9.33 s	10.65 s	9.78 s
H(24)	4.28 q	4.38 m	4.33 q	4.45 q
H(25)	1.29 t	1.40 t	1.34 t	1.42 t

In Figure 2a two broad resonances at 3.54 and 3.33 ppm have been assigned to H5 and H4 protons of the imidazolidine ring, respectively. After the sample was heated to 40 °C, imidazolidine H4 and H5 signals coalesced into a signal at 3.44 ppm. In chloroform, at room temperature, these resonances reveal their multiplet structure. The temperature dependence of H4 and H5 signals on the spectrum recorded in DMSO-d_6 indicates a low barrier to rotation about the formally double C2−C12 bond.

Free rotation about the C6−C12 bond is hindered due to steric interactions between substituents, and therefore

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Table 3. ^{13}C NMR Chemical Shifts (ppm) of Compounds 9a and 10 Recorded in DMSO-d_6 and $CDCl_3$

	9a		10	
	DMSO-d_6	$CDCl_3$	DMSO-d_6	$CDCl_3$
C-2	163.40	163.72	166.80	167.50
C-4	42.66	42.94	45.12	44.93
C-5	43.47	44.14	45.12	44.93
C-6	69.19	71.18	45.63	43.74
C-7	166.76	168.41	167.17	167.68
C-10	57.32	58.86	63.12	65.28
C-11	14.66	14.76	13.91	13.26
C-19	153.29	153.98	157.32	158.75
C-21	160.41	160.94	160.76	159.23
C-24	62.74	63.37	63.03	64.46
C-25	13.67	14.03	14.06	13.48
phenyl	136.00	136.25	135.90	132.89
	133.44	132.97	130.26	131.52
	128.17	127.87	129.42	130.33
	126.66	127.71	128.85	128.29
	124.71	125.43	128.80	128.29
	119.66	121.22	128.56	127.59

9a is asymmetric in all possible stable conformations. In such a case, chemical shift nonequivalence for methylene protons of both ethyl ester groups can be expected.[12] Indeed, as shown in Figure 2a two sets of signals, at 3.99 and 3.83 ppm, have been observed for methylene H10 protons. In the spectrum at 150 °C these protons give rise to a broadened quartet. A further increase of the temperature led to decomposition of the compound **9a**.

In DMSO-d_6 geminal nonequivalence has been observed for one methylene group only; however, in $CDCl_3$ solution a small chemical shift nonequivalence of geminal H24 protons has also been revealed.

The assignment of ^{13}C NMR spectra of **9a** and immonium salt **10** was based on the analysis of one-bond and long-range coupling carbon−proton shift correlations. The inversly detected HMQC spectrum revealed the NMR frequencies of proton and carbons that are connected through one bond, while the HMBC spectrum gave the frequencies of protons and carbons connected through two and three bonds. The results of the ^{13}C NMR experiments are summarized in Table 3.

In the ^{13}C NMR spectrum recorded in DMSO-d_6 we have observed two broad resonances at 42.66 and 43.47 ppm, attributed to C4 and C5 imidazolidine carbon atoms, respectively. At the ^{13}C spectrum recorded in $CDCl_3$ both these signals were sharp.

High electron density on carbon atom C6 reflected in an unusually small value for its chemical shift (69.19 ppm) prompted us to perform an experiment with addition of TFA to check the protonation site in this molecule. An excess of TFA was added directly to the NMR tube with the sample dissolved in DMSO-d_6, and ^1H and ^{13}C NMR spectra were collected. Some new features were seen in the ^1H NMR spectrum of **10**: a new signal integrated to one proton has appeared at 5.39 ppm, imidazolidine H4 and H5 protons gave rise to a singlet at 3.85 ppm, and the geminal H10 protons appeared as a slightly broadened quartet at 4.21 ppm (Figure 2c). As in **9a**, larger chemical shift nonequivalence was observed for geminal H10 protons in $CDCl_3$ (Figure 2d).

In the ^{13}C NMR spectrum recorded in DMSO-d_6 with addition of TFA carbon atoms C4 and C5 give rise to a signal at 45.12 ppm. The signal at 69.19 ppm disappears and a new signal at 45.63 ppm arises. This resonance is correlated to the proton at 5.39 ppm on HMQC spectrum. Analysis of the long-range $^1H-^{13}C$ coupling pattern obtained from the HMBC experiment allowed us to attribute this signal to the carbon atom C6. Thus, the results of NMR experiments prove that C6 is the main nucleophilic center in the molecule **9a**.

In conclusion, an interesting rearrangement has been discovered. This provides a synthetic route for the assembly of arylimidazolin-2-ylideneacetic acid esters in one step. Since the starting *N*-aryl-*N*-(4,5-dihydroimidazol-2-yl)hydroxylamines are readily available, these results point to a potentially useful rearrangement.

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Experimental Section

Melting points are uncorrected. All compounds were elementally analyzed within 0.3% of theoretical values. Mass spectra were recorded at 70 eV. Infrared spectra were recorded in KBr. The ^1H and ^{13}C NMR spectra were recorded in DMSO-d_6 at 300 and 75.4 MHz, respectively, and the proton and carbon chemical shifts were referenced to TMS.

Reaction of Hydroxylamine Hydrochloride 1a with Ethyl Propiolate. Preparation of Indole Derivative 7. To a stirred suspension of **1a** (1 g, 4.7 mmol) in anhydrous acetone (20 mL) were added dropwise ethyl propiolate (0.47 mL, 4.9 mmol) and Et_3N (1.3 mL, 9.4 mmol). The reaction mixture was refluxed for 1.5 h and then cooled to room temperature. The organic solvent was evaporated to dryness in vacuo to give a syrup that was washed with diethyl ether. Trituration of the residue with water gave a solid product that was separated by suction and purified by recrystallization from aqueous methanol: yield 0.78 g of **7** (65%); mp 154−155 °C; IR (KBr) 3152, (NH) 1708 (C=O), 1636 (C=N)cm^{-1}; ^1H NMR δ 1.35 (t, 3H), 3.7 (br s, 4H), 4.3 (q, 2H), 7.3−7.4 (m, 2H), 8.0−8.1 (m, 1H), 8.4 (s, 1H), 8.5−8.6 (m, 1H); ^{13}C NMR δ 14.36, 48.56, 59.79, 109.65, 115.83, 120.69, 123.34, 124.33, 126.48, 132.06, 135.51, 155.44, 163.55 ppm; MS *m*/*z* 257 (M^+). Anal. Calcd for $C_{14}H_{15}N_3O_2$: C, 65.35; H, 5.87; N, 16.33, Found: C, 65.42; H, 5.81; N 16.09.

Reaction of Hydroxylamine Hydrochloride 1a with Diethyl Acetylenedicarboxylate 3b. Preparation of Ethyl [[2-(Ethoxalylamino)phenyl]imidazolidin-2-ylidene]-acetate (9a). To a stirred suspension of **1a** (1 g, 4.7 mmol) in anhydrous THF (15 mL) were added dropwise diethyl acetylenedicarboxylate (**3b**) (0.74 mL, 4.7 mmol) and Et_3N (1.3 mL, 9.4 mmol). After the exothermic reaction had subsided the reaction mixture was stirred for 2 h at room temperature. The solid that precipitated (triethylamine hydrochloride) was separated by suction and washed with THF (20 mL), and the filtrate was evaporated to dryness in vacuo. Then, the residue was recrystallized from methanol to give **9a** (0.5 g, 31% yield): mp 184−188 °C dec; IR (KBr) 3344 (NH), 1696 (C=O), 1644 (C=O) cm^{-1}; ^1H and ^{13}C NMR spectra are given in Tables 2 and 3, respectively. Anal. Calcd for $C_{17}H_{21}N_3O_5$: C, 58.77; H, 6.09; N, 12.09. Found: C, 59.01; H, 6.07; N, 12.15.

The following ketene aminals were prepared analogously by reacting hydroxylamine hydrochlorides **1a**−**e** with diethyl or dimethyl acetylenedicarboxylates **3b,c**.

Ethyl [[2-(ethoxalylamino)-5-methylphenyl]imidazolidin-2-ylidene]acetate (9b): 39% yield; mp 171−174 °C (methanol); IR (KBr) 3360 (NH), 1696 (C=O), 1648 (C=O) cm^{-1}; ^1H NMR δ 1.0 (t, 3H), 1.3 (t, 3H), 2.3 (s, 3H), 3.2−3.7 (m, 4H), 3.7−3.9 (m, 1H), 3.9−4.1 (m, 1H), 4.3 (q, 2H) 6.1 (br s, 1H, NH), 6.9−7.1 (m, 2H), 8.0 (d, 1H), 8.1 (br s, 1H, NH), 9.3 (s, 1H, NH); ^{13}C NMR δ 13.7, 14.7, 20.6, 43.4, 57.3, 62.7, 69.3, 119.7, 125.0, 127.2, 128.0, 130.1, 133.7, 153.1, 160.5, 163.4, 166.8 ppm. Anal. Calcd for $C_{18}H_{23}N_3O_5$: C, 59.82; H, 6.41; N, 11.62. Found: C, 59.64; H, 6.33; N, 11.41.

Ethyl [[2-(ethoxalylamino)-5-ethylphenyl]imidazolidin-2-ylidene]acetate (9c): 19% yield; mp 172−175 °C (methanol); IR (KBr) 3360 (NH), 1704 (C=O), 1648 (C=O) cm^{-1}; ^1H NMR δ 1.0 (t, 3H), 1.2 (t, 3H), 1.3 (t, 3H), 2.55 (q, 2H), 3.3 (br s, 2H), 3.5 (br s, 2H), 3.7−3.9 (m, 1H), 3.9−4.1 (m, 1H), 4.3 (q, 2H), 6.1 (br s, 1H, NH), 7.0 (d, 1H), 7.1 dd, 1H), 8.0 (d, 1H), 8.1 (br s, 1H, NH), 9.3 (br s, 1H, NH). Anal. Calcd for $C_{19}H_{25}N_3O_5$: C, 60.78; H, 6.71; N, 11.19. Found: C, 61.01; H, 6.55; N, 11.38.

Ethyl [[2-(ethoxalylamino)-5-methoxyphenyl]imidazolidin-2-ylidene]acetate (9d): 23% yield; mp 181−183 °C (methanol); IR (KBr) 3344 (NH), 1696 (C═O), 1648 (C═O) cm^{-1}; ^1H NMR δ 1.0 (t, 3H), 1.3 (t, 3H), 3.3 (br s, 2H), 3.5 (br s, 2H), 3.7 (s, 3H), 3.8−3.9 (m, 1H), 3.9−4.1 (m, 1H), 4.3 (q, 2H), 6.2 (br s, 1H, NH), 6.7 (d, 1H), 6.8 (dd, 1H), 8.0 (d, 1H), 8.1 (br s, 1H, NH), 9.2 (s, 1H, NH). Anal. Calcd for $C_{18}H_{23}N_3)_6$: C, 57.28; H, 6.14; N, 11.13. Found: C, 57.55; H, 6.22; N, 11.02.

Ethyl [[2-(ethoxalylamino)-5-chlorophenyl]imidazolidin-2-ylidene]acetate (9e): 26% yield; mp 176−180 °C (ethanol); IR (KBr) 3360 (NH), 1704 (C═O), 1648 (C═O) cm^{-1}; ^1H NMR δ (DMSO-d_6) 1.0 (t, 3H), 1.3 (t, 3H), 3.3 (br s, 2H), 3.5 (br s, 2H), 3.7−4.1 (m, 2H), 4.3 (q, 2H), 6.4 (br s, 1H, NH), 7.2 (d, 1H), 7.4 (dd, 1H), 8.1 (d, 1H), 8.2 (br s, 1H, NH), 9.4 (s, 1H, NH); ^{13}C NMR δ 13.6, 14.6, 43.1, 53.5, 57.5, 62.8, 68.7, 121.2, 126.5, 128.2, 130.6, 132.9, 135.0, 153.5, 160.2, 163.3, 166.4 ppm. Anal. Calcd for $C_{17}H_{20}ClN_3O_5$: C, 53.47; H, 5.28; N, 11.01. Found: C, 53.27; H, 5.71, N, 10.87.

Methyl [[2-(methoxalylamino)phenyl]imidazolidin-2-ylidene]acetate (9f): 20% yield; mp 179−181 °C (ethanol); IR (KBr) 3352 (NH), 1708 (C═O), 1648 (C═O) cm^{-1}; ^1H NMR δ 3.3 (br s, 2H), 3.4 (s, 3H), 3.5 (br s, 2H), 3.8 (s, 3H), 6.1 (br s, 1H, NH), 7.1−7.3 (m, 3H), 8.1 (s, 1H), 8.2 (br s, 1H, NH), 9.3 (s, 1H, NH); ^{13}C NMR δ 43.0, 49.6, 53.5, 69.1, 119.8, 124.8, 126.8, 128.1, 133.6, 136.0, 153.3, 161.2, 163.3, 167.2 ppm; MS m/z 319 (M^+). Anal. Calcd for $C_{15}H_{17}N_3O_5$: C, 56.41; H, 5.37; N, 13.16. Found: C, 56.13, H, 5.33, N, 12.99.

Methyl [[2-(methoxalylamino)-5-methylphenyl]imidazolidin-2-ylidene]acetate (9g): 27% yield; mp 190−194 °C (ethanol); IR (KBr) 3360 (NH), 1708 (C═O), 1648 (C═O) cm^{-1}; ^1H NMR δ 2.25 (s, 3H), 3.3 (br s, 2H), 3.4 (s, 3H), 3.5 (br s, 2H), 3.8 (s, 3H), 6.0 (br s, 1H, NH), 6.9−7.2 (m, 2H), 8.0 (br s, 1H, NH), 8.1 (d, 1H), 9.3 (s, 1H, NH); ^{13}C NMR δ 20.5, 43.4, 49.5, 53.4, 69.1, 119.8, 127.3, 128.0, 133.4, 133.9, 134.2, 153.2, 161.2, 163.3, 168.5 ppm. Anal. Calcd for $C_{16}H_{19}N_3O_5$: C, 57.65; H, 5.74; N, 12.61. Found: C, 57.39; H, 5.77; N, 12.47.

Methyl [[2-(methoxalylamino)-5-ethylphenyl]imidazolidin-2-ylidene]acetate (9h): 20% yield; mp 170−174 °C (methanol); IR (KBr) 3368 (NH), 1708 (C═O), 1648 (C═O) cm^{-1}; ^1H NMR δ 1.2 (7, 3H), 2.5 (q, 2H), 3.3 (br s, 2H), 3.4 (s, 3H), 3.5 (br s, 2H), 3.8 (s, 3H), 6.1 (br s, 1H, NH), 7.0 (d, 1H), 7.1 (dd, 1H), 8.0 (d, 1H), 8.1 (br s, 1H, NH), 9.3 (s, 1H, NH). Anal. Calcd for $C_{17}H_{21}N_3O_5$: C, 58.78; H, 6.09; N, 12.1. Found: C, 58.5; H, 5.87; N, 12.22.

Methyl [[2-(methoxalylamino)-5-methoxyphenyl]imidazolidin-2-ylidene]acetate (9i): 14% yield; mp 200−208 °C dec (methanol); IR (KBr) 3336 (NH), 1696 (C═O), 1648 (C═O) cm^{-1}; ^1H NMR δ 3.3 (br s, 2H), 3.4 (s, 3H), 3.6 (br s, 2H), 3.7 (s, 3H), 3.8 (s, 3H), 6.2 (br s, 1H, NH), 6.7 (d, 1H), 6.85 (dd, 1H), 8.0 (d, 1H), 8.1 (br s, 1H, NH), 9.2 (s, 1H, NH); ^{13}C NMR δ 43.4, 49.5, 53.4, 55.0, 69.5, 112.0, 118.5, 121.3, 129.3, 129.9, 153.0, 156.0, 161.3, 163.2, 167.1 ppm. Anal. Calcd for $C_{16}H_{19}N_3O_6$: C, 55.01; H, 5.48; N, 12.03. Found: C, 54,82; H, 5.30; N, 12.28.

Methyl [[2-(methoxalylamino)-5-chlorophenyl]imidazolidin-2-ylidene]acetate (9j): 13% yield; mp 178−183 °C (methanol); IR (KBr) 3328 (NH), 1716 (C═O), 1648 (C═O) cm^{-1}; ^1H NMR δ (DMSO-d_6) 3.3 (br s, 2H), 3.45 (s, 3H), 3.5 (br s, 2H), 3.9 (s, 3H), 6.1 (br s, 1H, NH), 7.2 (d, 1H), 7.3 (dd, 1H), 8.1 (d, 1H), 8.15 (br s, 1H, NH), 9.3 (s, 1H, NH); ^{13}C NMR δ 43.1, 49.6, 53.4, 68.4, 121.2, 126.6, 128.2, 130.4, 133.0, 135.0, 153.5, 160.9, 163.2, 166.9 ppm. Anal. Calcd for $C_{15}H_{16}ClN_3O_5$: C, 50.92; H, 4.56; N, 11.88. Found: C, 51.11, H, 4.58, N, 12.05.

Reaction of Hydroxylamine Hydrochloride 1a with Ethyl Phenylpropiolate 3d. Preparation of Ethyl [[2-(Benzoylamino)phenyl]imidazolidin-2-ylidene]acetate (9k). To a stirred suspension of **1a** (1 g, 4.7 mmol) in anhydrous acetone (15 mL) was added dropwise ethyl phenylpropiolate (**3d**) (0.82 mL, 4.7 mmol) and

Et_3N (1.3 mL, 9.4 mmol). The reaction mixture was stirred at room temperature for 12 h, and then the solvent was evaporated to dryness in vacuo. The solid residue was washed thoroughly with water and purified by recrystallization from DMF−water: yield 0.16 g of **9k** (10%); mp 173−174 °C; IR (KBr) 3376 (NH), 3288(NH), 1660 (C═O), 1640 (C═O) cm^{-1}; ^1H NMR δ 0.95 (7, 3H), 3.4 (br s, 4H), 3.9 (q, 2H), 6.1 (br s 1H, NH), 7.0−7.3 (m, 3H), 7.4−7.6 (m, 3H), 7.8−8.1 (m, 4H), 8.9 (s, 1H, NH); ^{13}C NMR δ 14.8, 43.3, 57.5, 70.2, 121.5, 124.0, 126.5, 126.7, 128.8, 128.9, 131.7, 133.3, 134.9, 137.5, 163.5, 164.2, 167.3 ppm; MS m/z 351 (M^+). Anal. Calcd for $C_{20}H_{21}N_3O_3$: C, 68.36; H, 6.02; N, 11.96. Found: C, 68.02; H, 5.78; N, 11.65.

The following ketene aminals were prepared analogously by reacting hydroxylamine hydrochloride **1b** or **1e** with ethyl phenylpropiolate (**3d**).

Ethyl [[2-(Benzoylamino)-5-methylphenyl]imidazolidin-2-ylidene]acetate (9l): 24% yield; mp 228−232 °C (DMF−water); IR (KBr) 3380 (NH), 3328 (NH), 1664 (C═O), 1645 (C═O) cm^{-1}; ^1H NMR δ 0.95 (t, 3H), 2.3 (s, 3H), 3.45 (br s, 4H), 3,9 (q, 2H), 6.0 (br s, 1H, NH), 6.95 (d, 1H), 7.05 (dd, 1H), 7.5−7.8 (m, 5H), 7.9 (d, 1H), 8.0 (br s, 1H, NH), 8.8 (s, 1H, NH). Anal. Calcd for $C_{21}H_{23}N_3)_3$: C, 69.02; H, 6.34; N, 11.50. Found: C, 69.30; H, 6.18; N, 11.34.

Ethyl [[2-(benzoylamino)-5-chlorophenyl]imidazolidin-2-ylidene]acetate (9m): 13% yield; mp 207−210 °C (methanol); IR (KBr) 3382 (NH), 3328 (NH), 1666 (C═O), 1636 (C═O) cm^{-1}; ^1H NMR δ 1.0 (t, 3H), 3.4 (br s, 4H), 3.9 (q, 2H), 6.2 (br s, 1H, NH), 7.15 (d, 1H), 7.3 (dd, 1H), 7.5−7.8 (m, 6H), 8.0 (br s, 1H, NH), 8.1 (d, 1H), 8.9 (s, 1H, NH). Anal. Calcd for $C_{20}H_{20}ClN_3O_3$: C, 62.25; H, 5.22; N, 10.89. Found: C, 62.02; H, 4.99; N, 11.10.

Reaction of Nitrone 2a with Diethyl Acetylenedicarboxylate (3b). Preparation of the Ketene Aminal 9a. To a stirred solution of the nitrone **2a** (0.5 g, 2.62 mmol) in anhydrous THF (10 mL) were added **3b** (0.42 mL, 2.62 mmol) and Et_3N (0.36 mL, 2.62 mmol). The reaction mixture was kept at room temperature for 2 h, and then the volatile material was evaporated in vacuo. The solid residue was washed with diethyl ether and purified by recrystallization from methanol: yield 0.21 g (22%).

X-ray Structure Analysis of 9a. Crystal data and some details concerning data collection and structure refinement for **9a** are given in Table 1. The structure was solved by direct methods with the program SHELXS-86.[13] Full-matrix least-squares refinement was carried out on F^2 with SHELXL-93.[14] One of the ester ethyl groups is disordered. The occupancy factor for a major conformer was refined to 73%. Atom labeling is shown in Figure 1.[18]

NMR of Compounds 9a and 10. ^1H detected HMQC[15,16] (heteronuclear multiple quantum coherence) and ^1H detected HMBC[17] (heteronuclear multiple-bond quantum coherence) 2D experiments were accumulated using Varian indirect detection probe. The 2D spectra of **9a** were acquired over an F2 spectral window of 3800 Hz and F1 window of 16 500 Hz. 2D NMR spectra of **10** were acquired with a spectral width of 4000 Hz (^1H) and 16 500 Hz (^{13}C). For HMQC spectra 2048 data points in the $t2$ dimension and 256 complex points in the $t1$ dimension were collected. For HMBC spectra 2048 points in the $t2$ dimension and 128 complex pairs were collected in the $t1$ dimension. The relaxation delay between scans was 2 s.

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(18) The author has deposited atomic coordinates for **9a** with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.