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N,N-Disubstituted α-Amino-α,β-unsaturated Aldehydes and their Derivatives: ^{1}H and ^{13}C NMR Study

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^{1}H and ^{13}C NMR spectra of *N,N*-disubstituted α-amino-α,β-unsaturated aldehydes and their azomethines and enammonium salts were studied. The spectra reflect the degree of p–π conjugation between the nitrogen lone pair and the π-electrons of the carbon–carbon double bond. In this respect, the title 2-aminoenals are shown to be in an intermediate position between α-unsubstituted aminoalkenes and α,β-unsaturated aldehydes. The degree of conjugation depends on the nature of the amine moiety and the activating group. © **1997 by John Wiley & Sons, Ltd.**

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INTRODUCTION

The study of the π-electron distribution in push–pull alkenes and, especially, the polarization of the central C=C double bond is of major interest in the chemistry of these compounds.[1,2] Olefinic systems bearing vicinal substituents (structure **A**) have received considerable attention. For example, β-enaminoketones **A** [X = NR_2, Y = C(O)R] have been widely studied by ^{1}H and ^{13}C NMR spectroscopy.[3–8] However, *gem*-substituted push–pull alkenes (structure **B**) have been studied much less intensively.[9,10] Nevertheless, the investigation of the latter compounds is very promising from both the chemical and the spectroscopic points of view. Compounds with a combination of different reaction centres (double bond, carbonyl and protected amino functions) at the same carbon atom in the molecule of 2-aminoenals **B** (X = NR_2, Y = CHO) provide valuable information on structure–reactivity relationships. These compounds seem to play an important role in living systems.[11]. Furthermore, the high chemical reactivity of 2-aminoenals makes them useful synthons in modern organic synthesis.

In this paper, ^{1}H and ^{13}C NMR spectra of recently synthesized[11,12] α-amino-α,β-unsaturated aldehydes and their derivatives are reported.

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EXPERIMENTAL

Compounds

2-Aminoenals (**1–7**, **11**) were prepared by nucleophilic substitution of 2-haloenals by secondary amines.[12–14] Azomethines (**12–14**) and enammonium salts of 2-aminoenals (**15–18**) were obtained as described previously.[15,16] The new compounds gave satisfactory analyses. The NMR data of known compounds were taken from the literature for identification.

Measurements

^{1}H and ^{13}C NMR spectra were recorded at ambient temperature in $CDCl_3$ on a JEOL FX 90Q spectrometer at 89.90 and 22.5 MHz. Hexamethyldisiloxane (HMDS) and chloroform were used as internal references. The errors of the measured chemical shifts were less than 0.05 ppm for ^{1}H and 0.1 ppm for ^{13}C shifts. ^{13}C NMR assignments were based on the results of the

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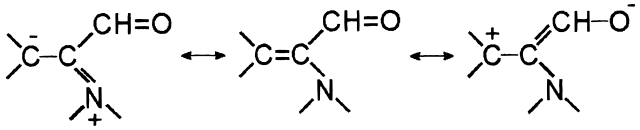
off-resonance and selectively ^{1}H-decoupled spectra, and also on ^{1}H nuclear Overhauser effects (NOE) and *J*-modulated spin-echo techniques.[17]

The configuration of *E*- and *Z*-isomers was derived from NOE measurements. The ^{1}H NOE experiments were performed in $CDCl_3$ on Bruker 200 and 400 MHz spectrometers. The assignments of ^{13}C NMR resonances to particular isomers in a mixture of *E,Z*-isomers were based on relative signal intensities, in parallel with ^{1}H NMR data.

RESULTS AND DISCUSSION

N,N-Disubstituted α-amino-α,β-unsaturated aldehydes represent a superposition of structural moieties of two classes of organic compounds: enamines and α,β-unsaturated aldehydes. Therefore, these compounds may be treated either as α,β-unsaturated carbonyl systems with a protected amino function in the α-position or as α-formyl enamines. Such an approach gives rise to the description of their chemical reactivity and distribution of electron density by three canonical structures:



I II III

If the resonance hybrid structure **I** has a greater weight than structure **III**, the compound would be expected to possess a highly nucleophilic β-carbon atom of the double bond. In contrast, if the polar canonical form **III** predominates, the chemical behaviour of 2-aminoenals would be similar to that of the ordinary α,β-unsaturated carbonyl systems.

The reactivity of 2-aminoenals is dependent on the degree of conjugation of the π-electrons of the carbon–carbon double bond with the nitrogen lone pair and also with the π-system of the carbonyl group. It is well known that the degree of p–π overlap in alkenes is manifested by the chemical shift of the vinylic proton; accordingly, ^{13}C chemical shifts of the olefinic carbons are mainly controlled by both π- and σ-electron density and are more indicative with respect to the degree of conjugation and charge separation.[3,18,19]

^{1}H NMR chemical shifts are presented in Table 1. They show that in general 2-aminoenals exist as a mixture of two geometric isomers. The *Z*-isomer dominates in both β-alkyl- and β-aryl-substituted α-aminoacroleins. On the other hand, 2-aminoenals with an acyclic amine moiety (**3**, **4**) exist only in the *Z* configuration. These facts were taken into account in the comparative study of spectral parameters of the latter compounds with those of corresponding 2-enals and ordinary enamines.

The analysis of ^{1}H chemical shifts of 2-aminoenals **1**–**11** shows that they occupy an intermediate position between α-unsubstituted aminoalkenes and α,β-unsaturated aldehydes. First, this is suggested by the lower field shift of the β-olefinic proton signal in 2-aminoenals compared with that in enamines. Further, the magnitude of δ(CH=) for the compounds studied does not exceed the value for unsubstituted enals in the series of both β-alkyl- and β-arylacroleins. Roughly this may be accounted for by a substantial rise in deshielding of the 2-aminoenal β-olefinic proton similar to that of the corresponding enamines as a result of the introduction of an acceptor formyl group in the α-position of the enamine. It is noteworthy that the α-amino group of the conjugated acrylic system takes part in the conjugation of α,β-unsaturated aldehydes. The extent of weakening of the conjugation of the carbon–carbon double bond in 2-aminoenals is indicated by the chemical shift of the aldehyde proton and depends on the nature of the amine moiety. For example, in the β-position the electrophilicity of the double bond in 2-aminoenals **1E**–**4E** with the same configuration increases on going from α-piperidino- (**1**) to α-diethylaminocrotonaldehyde (**3**).

The low-field shifts of β-olefinic and aldehyde protons of these compounds may be connected with the increase in canonical structure **III** sharing characteristics for unsaturated carbonyl compounds. The change of the extent of p–π interaction of the nitrogen lone pair and double bond is caused by both steric and electronic effects. The smaller delocalization of π-electrons in aldehyde **2** compared with the analogous piperidine **1** may be due to the significant $-I$ effect of the ether group $(CH_2CH_2)_2O$ ($\delta^* = +0.67$) compared with the $+I$ effect of the pentamethylene group $(CH_2)_5$ ($\delta^* = -0.18$).[20]

Since ^{13}C chemical shifts are less susceptible to the influence of anisotropic effects, they can serve as more reliable parameters of the degree of conjugation and double bond polarization (Table 2). Correlation of the chemical shifts of the β-carbon atom ^{13}C nuclei in 2-aminoenals, corresponding enamines and unsaturated aldehydes confirms the conclusions derived from the analysis of the ^{1}H NMR spectra. The signals of the C_β-atom in aminoaldehydes **1**–**11** appear at considerably lower fields than those of enamines; these signals are close to the chemical shifts of the β-carbon atom of the double bond in unsaturated aldehydes. In contrast to unsubstituted 2-enals, the α-carbon atom of 2-aminoenals resonates at lower field than the β-atom. Spectral characteristics of the discussed compounds are compiled in Table 3.

It is widely known that the ^{13}C NMR chemical shift difference of the two carbon atoms is a sensitive indicator of double bond polarization. The relationship between chemical shift differences of α- and β-olefinic carbon atoms and the nature of the amine fragment can be seen from the data in Table 4.

It should be pointed out that in contrast to 3-enaminones, the signal of the β-carbon atom in 2-amino-2,3-unsaturated carbonyl compounds is at higher field compared with the α-carbon atom.[4]

As expected, the passage from the strongly electron-withdrawing formyl group to the weaker electron-accepting azomethine results in strengthening of the p,π-interaction of the nitrogen atom with the double bond and also in an increase in the contribution of the canonical structure with negative charge at the

Table 1. H chemical shifts of 2-aminoenals, their derivatives and corresponding enamines

$R'R''C{=}C(NR_2){-}Y$

Compound	R″	R′	NR_2	Y	Isomer	*Z*/*E* ratio	Chemical shift, δ (ppm) CH=	CHO	Ref.
1	Me	H	$N(CH_2)_5$	CHO	*Z*	80:20	5.48 q	9.24 s	
					E		5.15 q	9.87 s	
2	Me	H	$N(CH_2CH_2)_2O$	CHO	*Z*	75:25	6.20 q	9.25 s	
					E		5.80 q	9.93 s	
3	Me	H	NEt_2	CHO	*Z*	100:0	6.50 q	9.95 s	
4	Me	H	NBu_2	CHO	*Z*	100:0	6.39 q	9.32 s	
5	Me	Me	$N(CH_2)_5$	CHO	—	—	—	10.03 s	
6	Me	Me	$N(CH_2CH_2)_2O$	CHO	—	—	—	10.06 s	
7	*n*-Pr	H	$N(CH_2)_5$	CHO	*Z*	85:15	5.92 t	9.26 s	
					E		5.61 t	9.85 s	
8[a]	Ph	H	$N(CH_2)_5$	CHO	*Z*	70:30	6.50	9.50	21
					E		6.75	9.60	
9[a]	Ph	H	$N(CH_2CH_2)_2O$	CHO	*Z*	70:30	6.10	9.20	21
					E		6.50	9.40	
10[a]	Ph	H	NMe_2	CHO	*Z*	70:30	6.37	9.40	21
					E		6.45	9.50	
11[a]	Ph	H	NEt_2	CHO	*Z*	70:30	6.45	9.50	21
					E		6.65	9.70	
12	Me	H	$N(CH_2)_5$	CH=NMe	*Z*	55:45	5.49 q	7.66 q	
							J = 7.3 Hz		
					E		5.11 q	8.03 q	
							J = 7.1 Hz		
13	Me	H	$N(CH_2CH_2)_2O$	CH=NMe	*Z*	55:45	5.58 q	8.11 q	
							J = 7.3 Hz		
					E		5.20 q	7.67 q	
							J = 7.1 Hz		
14	Me	H	$N(CH_2)_5$	CH=NBu	*Z*		5.51 q	7.67 q	
					E		5.10 q	8.07 q	
15[b]	Me	H	$HN^+(CH_2)_5$	CHO	*Z*	20:80	7.20 q	9.42 s	
					E		8.46 q	9.96 s	
16[b]	Me	H	$HN^+(CH_2CH_2)_2O$	CHO	*Z*	10:90	6.96 q	9.46 s	
					E		8.62 q	10.11 s	
17[c]	Me	H	HN^+Bu_2	CHO	*Z*	75:25	7.35 q	9.38 s	
					E		7.48 q	9.99 s	
18[c]	Ph	H	HN^+Et_2	CHO	*Z*	50:50	8.13 s	9.57 s	
					E		8.34 s	9.81 s	
19	Me	H	$N(CH_2)_5$	H	*E*		4.23	—	22
					Z		4.37	—	
20	Me	H	$N(CH_2CH_2)_2O$	H	*E*		4.34	—	22
					Z		4.75	—	
21	Me	H	NEt_2	H	*E*		4.10	—	22
					Z		4.46	—	
22	Ph	H	NEt_2	H	*E*		6.02	—	23
23	Me	H	H	CHO	*E*		6.79		24, 25
					Z		6.70		
24	Ph	H	H	CHO	*E*		7.36		26, 27
					Z		7.0–7.6		

[a] Solvent CCl_4.
[b] Counterion is Cl^-.
[c] Counterion is CF_3COO^-.

β-carbon atom. For instance, on going from aldehyde **2** to the azomethine derivative **13** a decrease in δ(CH=) by about 0.6 ppm both for *E*- and *Z*-isomers is observed.

The ^{13}C chemical shifts change in parallel with the proton shifts, as follows from the ^1H and ^{13}C NMR spectra of this series. Thus, the β-carbon of azomethine **12** resonates at *ca.* 11.5–15.5 ppm to higher field compared with the corresponding aldehyde **1** whereas the chemical shift of the α-carbon atom remains virtually the same. The data obtained show that azomethines possess enamine properties to a greater extent than their carbonyl analogues.

On the other hand, the protonation of 2-aminoenals removes the nitrogen lone pair from conjugation with the double bond. As a result, the conjugation characteristics of α,β-unsaturated aldehydes are restored completely. This follows from both the ^1H and ^{13}C NMR

Table 2. ^{13}C chemical shifts of 2-aminoenals, their derivatives and corresponding enamines

$$R'R''C{=}C(NR_2){-}Y$$

Compound	R″	R′	NR_2	Y	Isomer	Chemical shift δ (ppm) C_β	C_α	CHO	Ref.
1[a]	Me	H	$N(CH_2)_5$	CHO	*Z*	140.4	151.8	193.1	
					E	122.7	148.8	189.4	
2[a]	Me	H	$N(CH_2CH_2)_2O$	CHO	*Z*	141.8	150.3	192.5	
					E	124.2	147.4	188.0	
3	Me	H	NEt_2	CHO	*Z*	146.6	149.2	193.3	
4	Me	H	NBu_2	CHO	*Z*	146.8	150.0	194.1	
5	Me	Me	$N(CH_2)_5$	CHO	—	145.9	151.7	189.8	
6	Me	Me	$N(CH_2CH_2)_2O$	CHO	—	144.3	154.7	189.3	
11	Ph	H	NEt_2	CHO	*Z*	139.3	146.9	194.3	
12	Me	H	$N(CH_2)_5$	CH=NMe	*Z*	125.1	148.8	163.0	
					E	111.2	147.3	158.9	
13	Me	H	$N(CH_2CH_2)_2O$	CH=NMe	*Z*	127.5	147.5	162.4	
					E	112.9	146.1	157.4	
15	Me	H	$HN^+(CH_2)_5$	CHO	*Z*	145.2	138.9	182.5	
					E	150.5	133.7	186.3	
19	Me	H	$N(CH_2)_5$	H	*E*	94.77	141.69	—	28
					Z	108.24	141.20	—	
20	Me	H	$N(CH_2CH_2)_2O$	H	*E*	96.18	141.23	—	28
					Z	109.76	140.61	—	
21	Me	H	NEt_2	H	*E*	91.81	137.59	—	
					Z	109.55	139.22	—	28
22	Ph	H	NEt_2	H	*E*	98.93	140.37	—	29
23	Me	H	H	CHO	*E*	153.7	134.9	193.4	30
					Z	146.3	129.5	189.0	
24	Ph	H	H	CHO	*E*	152.49	128.54		29
25	Me	Me	H	CHO	—	159.6	127.2	189.8	
26	Me	Me	$N(CH_2)_5$	H	—	123.07	137.20	—	28
27	Me	Me	$N(CH_2CH_2)_2O$	H	M	124.62	136.22	—	28

[a] The olefinic carbon signals were wrongly attributed in our previous paper.[31]

Table 3. The chemical shift differences of β—CH= (^1H NMR) and C_β atom (^{13}C NMR) of 2-aminoenals, α,β-unsaturated aldehydes and aminoolefins.

Compound	^1H NMR Δ_1[a]	Δ_2[b]	^{13}C NMR Δ_1	Δ_2
1Z	−1.31	+1.11	−13.3	+32.2
1E	−1.55	+0.92	−23.6	+27.9
2Z	−0.59	+1.45	−11.9	+32.0
2E	−0.90	+1.46	−22.1	+28.0
3Z	−0.29	+2.04	−7.1	+37.0
5	—	—	−13.7	+22.8
6	—	—	−15.3	+19.7
11Z	−0.91		−13.2	

[a] δ(2-aminoenal) − δ(α,β-unsaturated aldehyde)
[b] δ(2-aminoenal) − δ(aminoolefin)

Table 4. The relationship between the chemical shift differences between the α- and β-olefinic carbon atoms and the nature of the amine fragment

Compound	$\delta(C_\beta) - \delta(C_\alpha)$
1Z	−11.4
1E	−26.1
2Z	−8.5
2E	−23.2
3Z	−2.6
4Z	−3.2
23Z	+16.8
23E	+18.8

data. For instance, the protonation of 2-aminoenals **1**–**4** results in the low-field shifts of the olefinic proton (Table 1). Double bond protons resonate at even lower field than those of unsubstituted 2-alkenals. The same effect can easily be seen from the ^{13}C NMR spectra, which results in a dramatic low-field shift of C_β carbons of up to 30 ppm and inversion of the C_α and C_β carbon signals. This phenomenon can easily be explained by conversion of the NR_2 group with a $+M$ effect into a strongly electron-accepting group HNR_2^+. Analysis of the ^1H and ^{13}C NMR spectra leads to the conclusion that for enammonium salts, the polar canonical form **III** that is peculiar to acrylic systems becomes predominant.

CONCLUSION

The following general conclusions can be derived from this NMR study of 2-aminoenals and their azomethine and enammonium derivatives. The ^{1}H and ^{13}C NMR spectra of 2-aminoenals reflect the extent of the competing conjugation of substituted amine and carbonyl groups with the carbon–carbon double bond. The charge delocalization and the double bond polarization are defined by both the configuration and the nature of the amine moiety. The polarization of the central double bond of 2-aminoenals is opposite to that of 3-enaminones. The p–π interaction of the lone nitrogen pair and the double bond competes with the conjugation of the double bond and the carbonyl group. Thus the 2-aminoenals have an intermediate position between α,β-unsaturated aldehydes and ordinary enamines. The decrease in the electron-accepting ability of the activating group on going from aldehydes to azomethine derivatives causes the latter to show enamine properties. In contrast, the removal of the lone nitrogen pair from conjugation on protonation makes these compounds similar to ordinary acrylic systems. The observed effects were confirmed experimentally by the investigation of the interaction of these compounds with nucleophilic[15] and electrophilic[16,32,33] reagents.

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