MAGNETIC RESONANCE IN CHEMISTRY, VOL. 36, 154–162 (1998)

^{1}H and ^{13}C NMR Spectra and Isomerism of 3-Aminoacroleins

Antonio Gómez-Sánchez[1]*, Rocío Paredes-León[1] and Juan Cámpora[2]

[1] Departamento de Química Orgánica 'Profesor García González,' Universidad de Sevilla, Apartado de Correos No. 553, E-41071 Seville, Spain
[2] Departamento de Química Inorgánica, Instituto de Investigaciones Químicas, Universidad de Sevilla, Consejo Superior de Investigaciones Científicas, Avenida de Américo Vespucio, s/n, E-41092 Seville, Spain

Received 10 July 1997; Accepted 30 August 1997

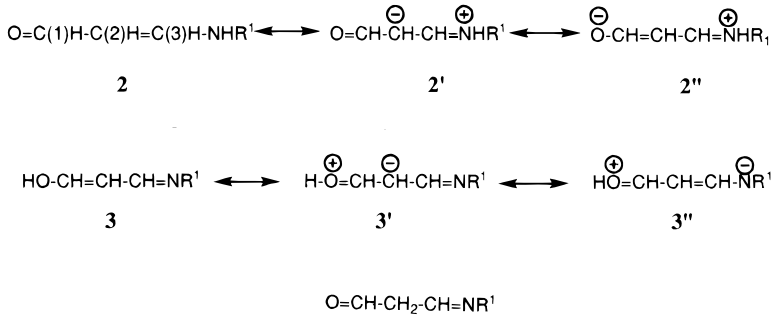
ABSTRACT: A set of 3-alkylaminoacroleins ($R^1NHCH{=}CHCH{=}O$, R^1 = alkyl) were studied by ^{13}C and ^{1}H NMR spectroscopy in solutions of different solvents and, for the simplest representative of the series, 3-methylaminoacrolein, at different temperatures. The equilibrium solutions of these compounds consists of mixtures of the chelated *ZZE* form (*Z* geometry around the =C—C=O single bond and the C=C bond, and *E* geometry around the C—N bond) and the two *E* configurational isomers having the *E* disposition around the =C—C=O single bond and differing in the disposition around the C—N bond (*EEZ* and *EEE* forms). The relative proportions of the three isomers depend on solvent polarity, concentration, bulk of substituent R^1 and temperature. The *EEZ* isomer is the most abundant in polar solvents, while the concentration of the *ZZE* form increases in non-polar solvents and when increasing the bulk of R^1. A lineshape ^{1}H NMR study for 3-methylaminoacrolein in $CDCl_3$ gave a $\Delta G^{\ddagger}$ value of 66.0 kJ mol^{-1} at 303 K for the *EEZ* → *EEE* conversion. The presence of other tautomeric forms was not observed. © 1998 John Wiley & Sons, Ltd.

KEYWORDS: NMR; ^{13}C NMR; ^{1}H NMR; 3-aminoacroleins; isomeric equilibrium solvent dependence; hindered rotation about C—N bond

INTRODUCTION

The functionalities and reactivity of enaminones ($R^1CO{-}CR^2{=}CR^3{-}NR^4R^5$, **1**) makes them attractive intermediates in organic synthesis.[1] These compounds are typical push–pull ethylenes, with low energy barriers around the formal carbon–carbon double bond, and increased energy barriers around the O=C—C= and the C—N single bonds which allows the existence of several configurational and conformational isomers. Thus, the stereochemistry of their reactivity can be controlled to some extent by isomeric equilibria. A knowledge of the electron distribution inside these mesomeric compounds, the relative energies of their isomeric forms and the energy barriers between them is therefore of importance in understanding their reactivity. Spectroscopic techniques combined with theoretical studies are well suited to provide an insight into this matter and have been applied extensively to the investigation of enaminoketones **1** ($R^1 \neq H$).[2] The data available for the simplest representatives of this class of compounds, 3-aminoacroleins (**2**), are scarce and conflicting. Compounds **2** can exist in four isomeric forms (**A**–**D**, Scheme 1) when the two R^1 substituents on the nitrogen are the same (e.g. 3-aminoacrolein, 3-dialkylaminoacroleins), or eight (**E**–**L**) when the two R^1 are different (3-alkylaminoacroleins). The compounds with a primary or secondary amino group could also exist in the tautomeric iminoenol form (**3**) and the oxoimino form (**4**). The

* *Correspondence to*: A. Gómez-Sánchez Departamento de Química Orgánica 'Profesor García González,' Universidad de Sevilla, Apartado de Correos No. 553, E-41071 Seville, Spain
Contract/grant sponsor: Dirección General de Investigación Científica y Técnica; *Contract/grant number*: PB91-0615.
Contract/grant sponsor: Junta de Andalucia.

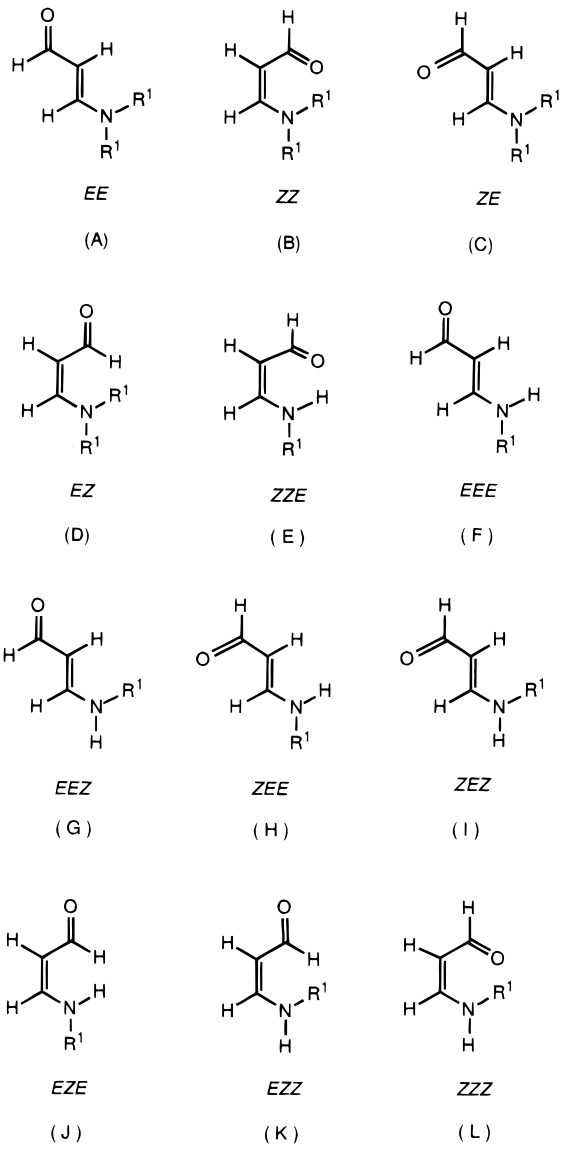


2 **2'** **2"**

3 **3'** **3"**

4

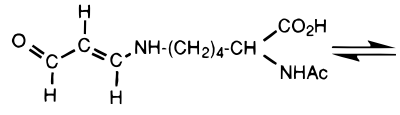
© 1998 John Wiley & Sons, Ltd. CCC 0749-1581/98/030154–09 $17.50



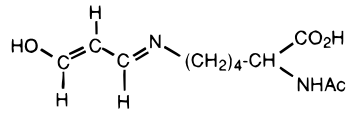
Scheme 1

former, a delocalized system to which ionic structures bearing a positive charge on the oxygen contribute, must be less stable than **2**. The non-conjugated oxo-imino form must be the most unfavourable.

The solvent dependence of the UV spectra of 3-ethylaminoacrolein has been attributed[3] to the existence of an equilibrium involving the isomers having the *E* configuration around the C=C bond and differing in the *Z* or *E* conformation around the =C—C=O single bond. The IR spectral data[4] for 3-aminoacrolein and several of its *N*-monoalkyl derivates indicate that, in the solid state, they adopt the *E* geometry around the C=C bond and probably also around the =C—C=O single bond (i.e. **A**), and that in solution a solvent-dependent equilibrium is established between this form and the intramolecularly bonded form with the *ZZ* (**B**) or *ZZE* (**E**) geometry. The NMR spectra at low field (60 or 100 MHz for protons) have been investigated by several workers,[4–8] with results agreeing with those obtained from IR studies and excluding the presence of tautomeric forms. No consideration seems to have been given to the possibility of a double conformation around the



5a

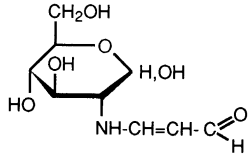


5b

C—N bond. On the other hand, McGirr *et al.*[9] found that the 400 MHz ^{1}H NMR spectrum of the lysine derivative **5** in D_2O solution exhibits two sets of signals, in the ratio 2:1, which were considered to be due to one of the *EE* forms (**5a**) in equilibrium with its tautomer, the iminoenol form (**5b**), with the *E* configuration around the C(1)=C(2) and C(3)=N bonds; the resonances attributed to the iminoenol form were not distinguishable at low magnetic fields (60 MHz). Several sugar aminoacroleins, such as **6**, have been described[10,11] and their structures and stereochemistry investigated by ^{1}H and ^{13}C NMR spectroscopy in D_2O solution. The aminoacrolein moiety of these compounds was found to exist as an equilibrium mixture of two forms considered to be the *EEZ* (**G**; R^1 = sugar group) and *EEE* (**F**) conformational isomers. In all cases the two isomers could be readily distinguished by their NMR spectra and the conformational assignment was made on the basis of the different chemical shifts of C-2 and H-2. The shielding effect observed for C-2, and the deshielding effect observed for H-2, in the *EEZ* form was attributed[11] to a γ-shielding effect[12] produced by the sugar moiety (the *N*-substituent) on C-2, and the concomitant γ-deshielding effect on H-2, in the sterically more crowded *EEZ* form. The ^{1}H NMR spectra of the aminoacrolein moiety of these sugar derivatives are very similar to the published[9] 400 MHz ^{1}H NMR spectrum of the lysine derivative **5**.

The NMR data[2d,2g,13] for 3-dimethylaminoacrolein (**2**, R^1 = Me) are consistent with the compound existing in solution as an equilibrium mixture of the predominating *EE* (**A**) (>85%) form and the *ZE* (*C*) form.

The purpose of this investigation was to obtain a better knowledge of the isomerism affecting 3-alkylaminoacroleins in solution, to measure the energy barrier to rotation around the C(3)—N bond for a representative compound and to achieve a better NMR characterization of the different isomeric forms. ^{1}H and ^{13}C NMR spectral data for some of the compounds studied here were included and briefly discussed in a more general context.[14] Additional data and a more thorough discussion are presented here.



6

© 1998 John Wiley & Sons, Ltd.

Table 1. 3-Aminoacroleins, O=C(1)H—C(2)H=C(3)H—NHR[1] (**2**)

Compound	R^1	UV (nm) (ε)[a]	M.p. (°C)	R_F	Molecular weight[b] Calculated	Found	Formula
2a	H	272.8 (18 521)	103	0.40[d]	71.0371	71.0368	C_3H_5NO
2b	Me	276.8 (27 875)	–[c]	0.37[e]	85.0528	85.0526	C_4H_7NO
2c	Et	278.4 (27 868)	—[c]	0.37[e]	99.0684	99.0685	C_5H_9NO
2d	*i*-Pr	279.2 (31 057)	—[c]	0.22[e]	113.0841	113.0848	$C_6H_{11}NO$
2e	*c*-C_6H_{11}	280.0 (20 912)	—[c]	0.38[e]	153.1154	153.1152	$C_9H_{15}NO$
2f	*t*-Bu	287.2 (32 049)	80	0.39[e]	127.0997	127.0999	$C_7H_{13}NO$

[a] In MeOH.
[b] By high-resolution mass spectrometry.
[c] Oils.
[d] In acetone–toluene (4 : 1).
[e] In acetone–CH_2Cl_2 (:4).

EXPERIMENTAL

Compounds **2a–e** are listed in Table 1 and were obtained by treating a solution of malondialdehyde [prepared by shaking aqueous 1,1,3,3-tetramethoxypropane with Dowex 50W X8 resin (H^+)] with an excess of ammonia or the appropriate amine. Evaporation and column chromatography (silica gel 60; eluent, acetone–dichloromethane) of the residue afforded the pure products which gave high-resolution mass spectra in agreement with their structures.

The solvents used were of commercial purity, with the lowest water content available. The ^1H and the proton decoupled ^{13}C NMR spectra were measured for solutions of concentration 0.1–0.2 mol dm^{-3}, unless specified unless, on a Bruker AM 500 spectrometer with the standard data system, using a 5 mm ^1H/broadband switchable probe, or on a Bruker AMX-300 spectrometer, and were referenced against internal TMS. The ^{13}C NMR spectra were acquired using a 3 μs pulse width, 1.6 s acquisition, 2 s delay for NOE building and 0.6 Hz per point digital resolution. The assignments of signals and couplings were confirmed by using selective irradiation and deuteration of the NH proton. The variable temperature was computer controlled using a BVT 1000 unit (Bruker), and the internal temperature calibrated with a methanol 'thermometer' using the Bruker Batman program. The rate constants for 3-methylaminoacrolein (**3b**) were obtained by fitting the 300 MHz ^1H NMR spectra to the lines calculated using the gNMR 2.3.6 program.[15] The spectra were recorded in the temperature range 213–328 K in 5 K steps.

RESULTS AND DISCUSSION

The ^1H and ^{13}C NMR spectral data for compounds **2a–f** are presented in Tables 2 and 3, respectively. As shown in the following discussion, consideration of these data provides a fairly complete picture of the isomeric equilibria.

The spectra of 3-methylaminoacrolein (**2b**) are typical and will be commented upon in detail. The reported[6] 100 MHz ^1H NMR spectrum in DMSO-d_6 revealed single AMX system signals of an aldehyde proton, H-1, and two olefinic protons, H-2, H-3, with coupling constants ^3J(H-1,H-2) = 9 Hz and ^3J(H-2,H-3) = 14 Hz, in addition to a three-proton doublet, ^3J(N-H,CH_3) = 5 Hz, due to the NMe group; no value for ^3J(H-3,NH) was given in the cited paper,[6] presumably because the H-3 and NH signals observed were broad. These results suggested the presence of the enamine form having the *E* geometry with respect to both the =C—C=O single bond and the C=C bond, and excluded the presence of the enaminol form. When, in the present study, the spectrum was taken at 500 MHz in the same solvent, the above spectrum was split into two very similar subspectra, the intensity ratio of which is temperature and concentration dependent, being approximately 89 : 11 at 298 K and 2.5 M concentration. The two subspectra differ mainly in the coupling between H-3 and the N-H proton, which is 7.0 Hz for the major form and 13.1 Hz for the minor form. As both ^3J(H-1,H-2) and ^3J(H-2,H-3) are large and almost the same (see Table 2), it is reasonable to assume that an equilibrium existed between a major isomer having the *Z* conformation around the C—N bond (i.e. the *EEZ* form, **G**) and a minor isomer with the *E* conformation (the *EEE* form, **F**). The spectrum also showed very weak multiplets at δ 4.85 ppm, with ^3J(H-1,H-2) = 2.5 Hz and ^3J(H-2,H-3) = 7.0 Hz, and at δ 6.94 ppm, with ^4J(H-1,H-3) = 2.8 Hz and ^3J(H-2,H-3) and ^3J(H-3,NH) = 13.1 Hz, assigned to H-2 and H-3, respectively, of the *ZZE* isomer, also present in trace amounts under these conditions. On raising the temperature, the signals due to the *EEE* and the *ZZE* forms increased in intensity at the expenses of

© 1998 John Wiley & Sons, Ltd.

the signals of the *EEZ* form and all widened, until at 323 K the signals due to the *EEZ* and *EEE* forms collapsed into single signals; above this temperature the spectrum observed was similar (not considering the very weak signals attributed to the *ZZE* form) to that reported[6] taken at 100 MHz and room temperature. Likewise, the ^{13}C NMR spectra taken at 126 MHz with the same solvent and concentration were also temperature dependent; at 298 K two very similar sets of signals were observed, in the approximate ratio 85:15, which by consideration of the chemical shifts and coupling constants (see Table 3), and the ^{1}H NMR spectra discussed above, are assigned to a predominant enaminal form with the *EEZ* geometry in equilibrium with the corresponding *EEE* form. Confirmation of the geometry of the two rotamers was obtained by measuring the coupling ^{3}J(C,H) between H-3 and the carbon of the NCH_3 group; the value found for the *EEZ* form, with this carbon and H-3 in a **W** disposition, was larger (7.6 Hz) than for the *EEE* form (4.2 Hz). The two subspectra collapsed into a single spectrum at 328 K. Similar results were obtained using D_2O as solvent; the ratio between the two conformers was 87:13 at 298 K and 2.5 M concentration.

The complexity of the isomeric equilibria of **2b** is more apparent in $CDCl_3$ solutions. The reported[6] 100 MHz ^{1}H NMR spectrum in this solvent indicated the presence of two isomers of the enaminal form, in the ratio 1:2, which were considered to be the *ZZE* form in equilibrium with a form having the *E* geometry with respect to the =C—C=O single bond and the C=C bond. The ^{1}H NMR spectrum taken in this investigation at 500 MHz, 2.5 M concentration and 298 K shows an AMX system of very sharp signals, which by consideration of the chemical shifts and coupling constants (see Table 2) was straightforwardly assigned to the chelated *ZZE* form, and two sets of signals assigned to the *EEZ* and *EEE* conformers in a situation of slow exchange. Under these conditions, the spectra of these two conformers differ only in the chemical shifts of the H-3 signals, which are broad and have values of δ 7.26 and 7.01 ppm, respectively. The *ZZE*, *EEZ* and *EEE* isomers were in the approximate ratios 28:64:8. The spectrum is temperature dependent; at 248 K it exhibits well resolved, clean signals for the three isomers *ZZE*, *EEZ* and *EEE* in the approximate ratios 13:81:6. In agreement with these results, the 126 MHz ^{13}C NMR spectrum of the same solution, taken at 298 K, shows the presence of the three forms in the approximate ratios 30:62:8. A C,H chemical shift correlation experiment confirmed that the isomer at *ca.* 22% concentration is the *ZZE* form.

The presence of the three isomeric forms of **2b** in $CDCl_3$ solution can be clearly observed also in the ^{1}H NMR spectra taken at 300 MHz at temperatures below 280 K (see Table 2); under these conditions the coalescence temperature for the H-3 protons of the *EEZ* and *EEE* forms was 303 K, and a bandshape analysis of the spectra taken between 246 and 328 K gave the values of the energy activation parameters for the *EEZ* → *EEE* conversion: $\Delta H\ddagger = 63.5 \pm 6.7$ kJ mol^{-1}, $\Delta S\ddagger = 8.4 \pm 8.4$ J mol^{-1} K^{-1} and $\Delta G\ddagger$ (at 303 K) $= 66.0 \pm 2.1$ kJ mol^{-1}.

The NMR spectra of the remaining compounds were only recorded at 295 K. The ^{13}C NMR spectra for compounds **2c–f** in $CDCl_3$ solutions (see Table 3) show the presence of the *ZZE*, *EEE* and *EEZ* isomers. The proportion of the *ZZE* form increases with increasing bulk and decreasing polarity of R^1 in the order Me < Et < *i*-Pr = *c*-C_6H_{11} < *t*-Bu, the *ZZE* isomer being the less favoured (by ΔG° of at least 2.7 kJ mol^{-1}) when R^1 = Me and the most favoured (by ΔG° of at least 4.2 kJ mol^{-1}) with respect to the *EEZ* and *EEE* isomers when R^1 = *t*-Bu. From the data in Table 3 it can also be seen that the ratio of the *EEZ* and *EEE* populations decreases with increasing bulk of R^1 in the same order, the *EEZ* being the most favoured from (by $\Delta G^\circ \approx 5.4$ kJ mol^{-1}) when R^1 = Me and absent when R^1 = *t*-Bu. The same trends can be observed in the more polar and solvating DMSO-d_6 and D_2O solvents; for the former, the *ZZE* form is only observed for **2e** and **2f** with the bulkiest R^1, and for D_2O it was not observed for any of the compounds. Furthermore, the *EEE* conformation is stabilized relative to the *EEZ* conformation in D_2O and the isomer having the former conformation is the only one observed when R^1 = *t* = Bu. These results suggest that the isomeric equilibria of these compounds are mainly governed by three factors: (1) the tendency for formation of the intramolecular hydrogen bond more apparent in non-polar solvents and when the size of R^1 reinforces the strength of the bond by a buttressing effect, (2) the tendency for the N-R^1 group to be *syn*-periplanar to the enamine C=C bond and (3) the tendency of the compounds to adopt the strainless, most extended and polar *EEE* geometry, which tends to balance the other factors. These factors are operative in similar enamines (e.g. nitroenamines, $R^1NHCH{=}CHNO_2$),[16] the only difference being their relative weights.

The different isomeric forms of 3-alkylaminoacroleins have characteristic NMR spectra. The *ZZE* isomer can be readily distinguished by its typical set of ^{3}J[H-*i*,H-(*i* + 1)] coupling constants, the rather long-range ^{4}J(H-1,H-3) coupling [larger than the ^{3}J(H-1,H-2)] and the large ^{3}J(H-3,NH) and δ(NH) values indicative of the intramolecular hydrogen bond and the fixed *E* conformation around the C(3)—N bond. Isomers differing in the conformation around the C(1)—C(2) bond have very different ^{3}J(H-1,H-2) coupling (2.1–2.3 Hz for the *Z*-conformation; 8.5–9.6 Hz for the *E*-conformation). Comparison of the ^{3}J(H-1,H-2) values for the *EEZ* and *EEE* isomers with the value found (8.1 Hz)[2d,2g,13] for ^{3}J(H-1,H-2) of 3-dimethylaminoacrolein (which exists in solution as an equilibrium mixture containing more than 95% of the *EE* form) can be taken as indicative that the *ZEZ* (**I**) and *ZEE* (**H**) forms do not contribute significantly to the isomeric equilibria of compounds **2**. Isomers having different configurations around the C(2)=C(3) bond differ in the ^{3}J(H-2,H-3) and ^{3}J(C-1,H-3) coupling constants: the *ZZE* isomer, with C-1 and

© 1998 John Wiley & Sons, Ltd.

Table 2. Proton chemical shifts (δ in ppm) and spin-spin coupling constants (J in Hz) in isomeric 3-aminoacroleins[a]

Compound	Solvent	Isomer (%)	^{1}H chemical shifts					Coupling constants				
			H-1	H-2	H-3	NH	H-1′ [b]	J(H-1,H-2)	J(H-2,H-3)	J(H-3,NH)	J(NH,H-1′)	J(H-1,H-3)
2a	DMSO-d_6	*EE* (100)	8.91	5.11	7.22	7.07[c] 7.35[c]		8.8	12.5			
	D_2O	*EE* (100)	8.69	5.43	7.54			9.6	12.3			
	$CDCl_3$	*EE* (41)	9.16	5.45	7.16	5.08[c]		8.4	13.0			
		ZZ (59)	9.25	5.09	6.87	9.23[c]		2.0	7.3	14.7		3.2
2b	DMSO-d_6	*EEE* (11)	8.85	5.04	7.20	7.63[c]	2.87	8.8	12.3	13.1	4.6	
		EEZ (89)	8.96	5.00	7.34	7.54[c]	2.65	8.6	12.8	7.0	4.9	
		ZZE		4.85	6.94			2.5	7.0	13.1		2.8
	D_2O	*EEE* (18)	8.58	5.34	7.45		3.02	9.3	11.8			
		EEZ (82)	8.69	5.34	7.56		2.84	8.7	13.8			
	$CDCl_3$	*EEE* (8)			7.01[c]							
			9.07[d]	5.25[d]		6.07[c,d]	2.82	9.2	12.8		4.6	
		EEZ (64)			7.26[c]							
		ZZE (28)	9.04	4.97	6.75	9.85[c]	3.03	2.3	7.0	13.0	5.1	3.1
2b[e]	$CDCl_3$	*EEE* (6)	9.15	5.29	7.12	6.68[c]	3.15	8.8	12.8	14.0	4.9	
		EEZ (81)	9.07	5.29	7.36	6.68[c]	2.90	8.9	12.8	7.2	5.1	
		ZZE (13)	8.98	5.06	6.90	10.0[c]	3.13	2.3	6.9	13.2	5.3	3.1
2c	DMSO-d_6	*EEE* (21)	8.87	5.04	7.26	7.82[c]	3.19	8.9	12.9	12.8		
		EEZ (79)	8.96	5.04	7.26	7.58[c]	3.03	8.5	13.0	7.41		
	D_2O	*EEE* (27)	8.54	5.34[d]	7.50		3.30	9.8	12.7			
		EEZ (73)	8.64	5.34[d]	7.49		3.18	9.4	12.7			

© 1998 John Wiley & Sons, Ltd.

	$CDCl_3$	*EEE* (17)			≈7.15[c,d]								
			9.11[d]	5.31[d]		5.61[c,d]	3.31[d]	9.15	13.0				
		EEZ (61)			7.22[c]								
		ZZE (22)	9.12	4.98	6.83	9.97[c]	3.20	2.3	7.0	13.1			3.1
2d	DMSO-d_6	*EEE* (33)	8.86	5.03	7.29	7.82[c]	3.44	8.8	13.2	12.9			
		EEZ (67)	8.92	5.03	7.15	7.54[c]	3.44	8.5	12.9	6.6			
	D_2O	*EEE* (45)	8.53	5.31	7.53		3.64	9.7	12.0				
	D_2O	*EEZ* (55)	8.61	5.34	7.40		3.64	9.4	12.6				
	$CDCl_3$	*EEE*[f]											
			8.94	5.21[c,d]	7.08[c,d]	6.52[c,d]	3.49[c,d]	8.2					
		EEZ[f]											
		ZZE (31)	9.0	4.91	6.81	9.83[c]	3.43	2.3	7.1	13.2			3.1
2e	DMSO-d_6	*EEE* (38)	8.85	5.08	7.29	7.84[c]	3.08	8.9	12.6	12.9			
		EEZ (62)	8.92	5.07	7.14	7.56[c]	3.15	8.6	13.1	6.4			
	$CDCl_3$	*EEE*[g]				5.46[c]							
			9.06[d]	5.31[d]	7.09[c,d]		3.21[d]	8.4	13.0				
		EEZ[g]				5.23[c]							
	$CDCl_3$	*ZZE* (42)	9.08	4.95	6.85	10.04[c]	3.1	2.3	7.0	13.2			3.1
2f	DMSO-d_6	*EEE* (94)	8.90	5.09	7.40	7.94		8.9	12.2	13.1	13.6		
		ZZE (6)		4.93	7.23				6.6	13.5			3.1
	D_2O	*EEE* (100)	8.57	5.34	7.64			9.3	11.3				
	$CDCl_3$	*EEE* (26)	9.09	5.33	7.12[c]	5.45[c]		8.5	12.5				
		ZZE (74)	9.08	4.98	6.94	10.30[c]		2.3	7.1	13.4			3.1

[a] Measured at 500 MHz and 298 K unless indicated otherwise.
[b] H-1′ refer to the hydrogen nuclei of R^1 in the α-position with respect to the N.
[c] Broad signal.
[d] Averaged signals for the *EEE* and *EEZ* isomers.
[e] Measured at 300 MHz and 248 K.
[f] 69% of the *EEE* and *EEZ* isomers.
[g] 58% of the *EEE* and *EEZ* isomers.

© 1998 John Wiley & Sons, Ltd.

Table 3. Carbon chemical shifts (δ in ppm) and spin–spin coupling constants (J in Hz) in isomeric 3-aminoacroleins[a]

Compound	Solvent	Isomer (%)	^{13}C chemical shifts [^1JC(i)H(i)] C-1	C-2	C-3	C-1′ [b]	Other couplings ^2J(C-1,H-2)	^2J(C-2,H-1)	^2J(C-2,H-3)	^3J(C-1,H-3)
2a	DMSO-d_6	*EE*	188.82	103.21	159.95			22.6		
		(100)	(161.0)	(156.0)	(161.0)					
	D_2O	*EE*	191.68	102.21	163.67			20.1	2.5	
		(100)	(166.0)	(158.4)	(164.7)					
2b	DMSO-d_6	*EEE*	187.89	101.46	163.01	34.33		20.1		5.22
		(15)	(162.2)	(152.1)	(162.2)	(137.4)				
		EEZ	188.84	100.00	158.88	29.52		22.6		3.15
		(85)	(159.7)	(157.2)	(164.7)	(137.7)				
	D_2O	*EEE*	189.36	100.44	165.95	34.28	5.0	17.6	1.7	
		(13)	(164.7)	(158.4)	(164.7)	(139.1)				
		EEZ	190.90	98.68	162.17	29.11	6.3	19.5	2.14	
		(87)	(164.7)	(158.4)	(167.2)	(139.0)				
	$CDCl_3$	*EEE*	188.80	101.75	162.70	34.79		16.7		
		(8)	(165.9)	(157.8)	(162.2)	(137.9)				
		EEZ	189.61	99.83	159.10	29.68		20.7		
		(62)	(162.2)	(158.4)	(163.4)	(137.6)				
		ZZE	187.18	94.09	155.09	35.01	5.0	20.1		8.8
		(30)	(165.9)	(164.7)	(162.1)	(137.3)				
2c	DMSO-d_6	*EEE*	187.48	101.38	161.14	42.52	4.4	22.6		
		(26)	(159.1)	(153.4)	(161.0)	(138.5)				
		EEZ	188.53	99.89	157.45	37.57	4.4	25.1		
		(74)	(160.3)	(157.2)	(162.2)	(137.6)				
	D_2O	*EEE*	189.27	100.34	164.34	43.14	5.6	18.9		
		(25)	(165.4)	(158.4)	(163.7)	(139.5)				
		EEZ	190.85	98.69	160.95	37.81	6.3	19.6	1.8	
		(75)	(166.0)	(158.6)	(166.0)	(139.1)				
	$CDCl_3$	*EEE*	188.88	102.02	160.83	43.33		18.9		
		(14)	(159.7)	(157.2)	(163.5)	(139.1)				
		EEZ	189.75	100.28	157.80	38.06		19.5		
		(59)	(161.0)	(161.6)	(163.5)	(139.1)				
		ZZE	187.34	94.04	153.29	43.51	5.03	19.7		8.8
		(27)	(166.6)	(164.0)	(163.2)	(138.0)				
2d	DMSO-d_6	*EEE*	187.54	101.45	159.63	49.27	5.03	23.9		
		(33)	(158.4)	(154.7)	(161.0)	(138.3)				
		EEZ	188.65	100.00	156.51	44.36	6.3	23.3		
		(67)	(161.0)	(155.3)	(162.2)	(137.7)				
	D_2O	*EEE*	189.26	100.17	163.12	50.31	5.6	18.9		
		(42)	(164.7)	(158.4)	(164.7)	(140.3)				
		EEZ	190.97	98.75	160.31	45.01	5.6	20.1		
		(58)	(165.9)	(159.7)	(165.9)	(142.7)				
	$CDCl_3$	*EEE*	189.09	102.43	158.96	45.13				
		(7)	(160.3)		(155.9)	(135.7)				
		EEZ	189.99	100.92	156.71	45.13		21.0		
		(19)	(159.7)	(160.9)	(162.2)	(135.7)				
		ZZE	187.46	94.06	151.61	50.26	5.03	22.1		8.8
		(74)	(165.9)	(163.9)	(162.2)	(137.9)				
2e	DMSO-d_6	*EEE*	187.42	101.46	159.58	56.25	5.03	22.6		
		(35)	(159.7)	(155.9)	(170.0)	(137.7)				
		EEZ	188.48	99.81	156.30	51.29	5.7	23.3		
		(61)	(160.3)	(156.6)	(162.2)	(136.4)				
		ZZE	186.31	93.83	152.33					
		(4)								
	$CDCl_3$	*EEE*	188.76	102.17	159.06	57.12		20.7		
		(8)	(166.0)	(157.8)	(158.4)	(135.9)				
		EEZ	189.64	100.45	156.62	52.15		22.0		
		(23)	(162.0)	(157.8)	(162.2)	(135.9)				
		ZZE	187.12	93.93	151.58	57.12	5.03	19.8	2.4	8.8
		(69)	(166.0)	(163.9)	(162.2)	(135.9)				
2f	DMSO-d_6	*EEE*	187.70	102.16	157.04	51.89				
		(86)	(161.0)	(155.9)	(159.7)					
		ZZE	186.27	94.01	150.31	52.05		23.9		
		(14)								
	D_2O	*EEE*	189.09	100.68	160.5	52.90				
		(100)	(164.7)	(157.8)	(163.5)					
	$CDCl_3$	*EEE*	188.96	102.81	156.03	52.31				
		(14)	(167.2)	(157.2)	(157.2)					
		ZZE	187.02	94.01	149.07	52.08	5.03	19.3	4.2	8.8
		(86)	(166.0)	(163.9)	(161.8)					

[a] Measured at 126 MHz and 298 K.
[b] C-1′ refer to the carbon nucleus of R^1 in the α-position with respect to the N.

© 1998 John Wiley & Sons, Ltd.

H-3 in a *trans* disposition, has a ^3J(C-1,H-3) larger (*ca.* 9 Hz) than the *EEE* and *EEZ* forms (5.8–0 Hz), with C-1 and H-3 *cis*. Isomers *EEE* and *EEZ* differ in the value of the ^3J(H-3,NH) coupling, the chemical shifts of C-1, C-2 and C-3 [$\delta(\text{C-1})_{EEE} < \delta(\text{C-1})_{EEZ}$; $\delta(\text{C-2})_{EEE} > \delta(\text{C-2})_{EEZ}$; $\delta(\text{C-3})_{EEE} > \delta(\text{C-3})_{EEZ}$], and the chemical shifts of H-1 and H-1′[$\delta(\text{H-1})_{EEE} < \delta(\text{H-1})_{EEZ}$; $\delta(\text{H1}')_{EEE} > \delta(\text{H-1}')_{EEZ}$]. As in the similar sugar derivatives (such as **6**), the smaller δ(C-2) of the *EEZ* isomer relative to the value found for the *EEE* form is attributed[11] to the large steric compression (similar to a γ-effect) existing in the former isomer between R^1 and the C(2)H(2) group; C-1′ of substituent R^1 of the *EEZ* isomer also appears, probably for the same reason, at higher field (smaller δ value) than that of the *EEE* isomer. C-1, C-2 and C-3, and H-2 and H-3, of the *ZZE* isomer are shielded relative to the same nuclei of the *EEZ* and *EEE* forms, as usually observed in enaminones.[14] Application of these criteria to the interpretation of the ^{1}H NMR spectrum[9] of the lysine derivative **5** suggests that the major isomer, having the largest δ(H-1), is the *EEZ* form and the minor isomer (considered[9] to be the imino isomer), with the smallest δ(H-1), is the corresponding *EEE* form.

The spectra of 3-aminoacrolein (**2a**) in polar solvents at 298 K show that the compound exists solely in the *EE* form (**A**, R^1 = H), as deduced from the ^3J(H-1,H-2) and ^3J(H-2,H-3) couplings (see Table 2), whereas in $CDCl_3$ solution an equilibrium is established between this form and the intramolecularly bonded *ZZ* form (**B**, R^1 = H).

It is interesting to compare the dynamics of compounds **2** with those of the related enaminones R^1CO—CH=CH—NR^2R^3 (**7**). Whereas dimethylaminoacrolein exists in CH_2=CCl_2 solution almost entirely in the *EE* form (**A**) and the free energy of rotation around the C—N bond amounts to 60.7 kJ mol^{-1} (at 292 K),[2g] the nearest enaminoketones **7** (R^1 = alkyl, R^2 = R^3 = Me) exist in solution as equilibrium mixtures of the two conformational isomers similar to *EE* (**A**) and *ZE* (**C**), with the former decreasing with increasing bulk of R^1, and the energy barrier to rotation about the C—N bond (<60.7 kJ mol^{-1}) also decreasing with increasing bulk of R^1.[2g] This is attributed to the weaker electron-withdrawing capacity of the acyl group (R^1CO) relative to the HCO group,[17] and to the increased ground-state steric hindrance of the *EE* form in the ketones which reduces planarity of the delocalized system; the two factors diminish the electron donation of the NMe_2 group and the energy barrier around the C—N bond. The *E*-configurational isomers of 3-alkylaminoacroleins (**2**) with a secondary amino group show a strong preference for the *E* conformation around the C—C=O single bond, most probably because this extended, planar geometry permits a very efficient electron delocalization that results in increased energy barriers around this bond and the C—N bond, and the easy detection of *E,Z* rotomers around the latter. On the other hand, the *E*-configurational isomers of the corresponding enaminoketones **7** (R^1CO—CH=CH—NHMe) exist in solutions as equilibrium mixtures of a planar form with the *Z* conformation around the C—C=O single bond [similar to *ZEE* (**H**) and/or *ZEZ* (**I**)], and sterically crowded, non-planar forms [similar to *EEE* (**F**) and/or *EEZ* (**G**)], with the plane of the COR^1 group rotated out of the plane of the enamine system;[2g,2i,2k,18,19] no rotational isomers around the C—N bond have been detected in this case, probably because of the weaker electron-withdrawing capacity of the R^1CO group, the reduced electron donation of the amino group and the concomitant low energy barriers around the C—N bond.

CONCLUSIONS

3-Alkylaminoacroleins exist in solution as equilibrium mixtures of the intramolecularly bonded *ZZE* form and the two *E* configurational isomers having the *E* conformation about the =C—C=O single bond and differing in the conformation (*E* or *Z*) about the C—N bond. The relative proportions of the three forms depend on the polarity of the solvent and temperature. Polar solvents (DMSO-d_6, D_2O) favour the *EEZ* form, whereas the concentration of the *ZZE* form increases in non-polar solvents and with increasing bulk of the *N*-substituent; the most extended *EEE* form is favoured in polar solvents when the compound has a bulky *N*-substituent. The three isomeric forms can be readily distinguished and quantified by their ^{13}C NMR spectra and by the ^{1}H NMR spectra at low temperatures. The free energy barrier for the *EEZ* → *EEE* conversion in chloroform solution ($\Delta G‡$ = 66.0 kJ mol^{-1} at 303 K) measured for the *N*-methyl derivative is similar to that of dimethylaminoacrolein.

Acknowledgements

This work is a part of a research project supported by the Dirección General de Investigación Científica y Técnica (Project PB91-0615) and the Junta de Andalucia, to whom we express our gratitude. One of us (R.P.-L.) also thanks the Junta de Andalucia for a grant.

REFERENCES

1. J. V. Greenhill, *Chem. Soc. Rev.* **6**, 277 (1977); I. Chaaban, J. V. Greenhill and P. Akhtar, *J. Chem. Soc., Perkin Trans. 1*, 1593 (1979); J. V. Greenhill, M. A. Moten, R. Hanke and E. Breitmeier, *J. Chem. Res (S)*, 66 (1981); N. Takeuchi, S. Handa, K. Koyama, K. Kamata, K. Goto and S. Tobinaga, *Chem. Pharm. Bull.* **39**, 1655 (1991); G. Bartoli, M. Bosco, C. Cimarelli, R. Dalpozzo and G. Palmieri, *Synlett*, 229 (1991).
2. (a) G. O. Dudek and R. H. Holm, *J. Am. Chem. Soc.* **84**, 2691 (1962); (b) G. O. Dudek and G. P. Volpp, *J. Am. Chem. Soc.* **85**, 2697 (1963); (c) G. O. Dudek and E. P. Dudek, *J. Am. Chem. Soc.* **88**, 2407 (1966); (d) J. Dabrowski and K. Kamienska-Trela, *Spectrochim. Acta* **22**, 211 (1966); (e) J. Dabrowski and U. Dabrowska, *Chem. Ber.* **101**, 2365, 3392 (1968); (f) J. Dabrowski and L. Kozerski, *J. Chem. Soc. B*, 345 (1971); (g) J. Dabrowski and L. Kozerski, *Org. Magn. Reson.* **4**, 137 (1972); (h) L. Kozerski and J. Dabrowski, *Org. Magn. Reson.* **5**, 459 (1973); (i) J. Dabrowski, K. Kamienska-Trela and L. Kozerski, *Org. Magn. Reson.* **6**, 499 (1974); (j) E. Czerwinska, L. Kozerski and J. Boksa, *Org. Magn.*

© 1998 John Wiley & Sons, Ltd.

Reson. **8**, 345 (1976); (k) L. Kozerski, K. Kamienska-Trela and L. Kania, *Org. Magn. Reson.* **12**, 365 (1979); (l) P. J. Taylor, *Spectrochim. Acta, Part A* **32**, 1471 (1976); (m) D. Smith and P. J. Taylor, *Spectrochim. Acta, Part A*, **32**, 1477, 1503 (1976); (n) S. Braun, G. Frey and Bachmann, *Org. Magn. Reson.* **7**, 199 (1975); (o). S. Braun, *Org. Magn. Reson.* **11**, 197 (1978); (p) N. M. Brown and D. C. Nonhebel, *Tetrahedron* **24**, 5655 (1968).
3. P. M. Vay, *Chem. Commun.*, 861 (1969).
4. J. Dabrowski, *J. Mol. Struct.* **3**, 227 (1969); J. Terpinski and J. Dabrowski, *J. Mol. Struct.* **4**, 285 (1969).
5. E. Breitmaier, S. Gassenmann, *Chem. Ber.* **104**, 665; C. Skotsch, G. Haffmanns and E. Breitmaier, *Chem. Ber.* **110**, 2872.
6. K. Kikugawa, T. Maruyama, Y. Machida and T. Kurechi, *Chem. Pharm. Bull.* **29**, 1423 (1981).
7. V. Nair, D. E. Vietti and C. S. Cooper, *J. Am. Chem. Soc.* **103**, 3030 (1981).
8. H. McNab, *J. Chem. Soc., Perkin Trans. 2*, 1283 (1981).
9. L. M. McGirr, M. Hadley and H. H. Drapper, *J. Biol. Chem.* **260**, 15427 (1985).
10. A. Gómez-Sánchez, I. Maya and L. Hermosín, *Carbohydr. Res.* **200**, 167 (1990).
11. A. Gómez-Sánchez, I. Hermosín and I. Maya, *Carbohydr Res.* **229**, 307 (1992).
12. D. D. Tavernier and M. J. O. Antennies, *J. Magn. Reson.* **11**, 625 (1978).
13. R. Radeglia and S. Dähne, *J. Mol. Struct.* **5**, 399 (1970); R. Radeglia, *J. Prakt. Chem.* **315**, 1121 (1973).
14. J. L. Chiara and A. Gómez-Sánchez, in *The Chemistry of Enamines, Part 1*, edited by Z. Rappoport, p. 279. Wiley, Chichester (1994).
15. P. H. M. Budzelaar, Cherwell Scientific Publishing, Oxford, 1992–95.
16. J. L. Chiara, A. Gómez-Sánchez and J. Bellanato, *J. Chem. Soc., Perkin Trans. 2*, 787 (1992); L. Kozerski, P. Krajawski and E. Bednarek, *Magn. Reson. Chem.* **33**, 745 (1995).
17. M. Oki, *Applications of Dynamic NMR Spectroscopy to Organic Chemistry*, p. 76, VCH, Weinheim (1985).
18. L. Kozerski and W. von Philipsborn, *Org. Magn. Reson.* **17**, 306 (1981).
19. J. L. Chiara and A. Gómez-Sánchez, in *The Chemistry of Enamines, Part 1*, edited by Z. Rappoport, p. 338. Wiley, Chichester (1994).

© 1998 John Wiley & Sons, Ltd.