

# <sup>1</sup>H-NMR SPECTRA AND NUCLEAR OVERHAUSER EFFECT IN E AND Z ISOMERS OF 3-SUBSTITUTED 3-AMINOACRYLONITRILES\*

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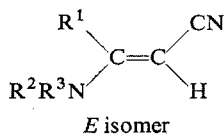
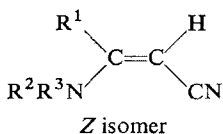
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Measurements of nuclear Overhauser effects (NOE) in a representative series of 3-substituted 3-aminoacrylonitriles establish that the olefinic proton is more shielded and that the proton-proton long-range coupling constants  $^4J(\text{HC}=\text{CCH}_3)$  and  $^4J(\text{HC}=\text{CNH})$  are larger in the Z isomer than in the E isomer. Extending the validity of this finding to other closely related compounds, some of which were prepared for the first time, permits <sup>1</sup>H-NMR study of the E-Z equilibria in this type of compounds. It was found that in solution all crotononitriles studied were predominantly in the E form, while in 3-phenyl derivatives the Z isomer was prevailing. NOE results elucidate the configuration of the model compounds in some detail.

3-Substituted 3-aminoacrylonitriles, occurring as E and Z isomers, form an interesting class among enamines in which *cis-trans* isomerism on the C=C double bond can be conveniently studied.



However, our knowledge of the configuration of these compounds and of the factors affecting it is rather limited. Of the two forms in which the simplest of these compounds (3-aminocrotonitrile (I)) exists<sup>1,2</sup>, the high-melting one was assigned<sup>3</sup> the E configuration. The assignment was based on the melting point and solubility data, only. Analogous reasoning cannot, however, be applied to other compounds of this type. Results of subsequent measurements of dipole moments<sup>4</sup> were in agreement with the suggested assignment but for some other derivatives the measurements of dipole moments were shown to be inconclusive. In contrast, NMR spectroscopy generally appears to be conclusive in such studies providing the structure-spectrum relations are established in the spectra of some typical compounds. <sup>1</sup>H-NMR spectra of the two isomers of compound I were reported<sup>5</sup> and, using the above assignment, both olefinic and methyl protons were found to be more shielded and the long-range coupling between them was larger in the Z isomer than in the E isomer. These findings cannot be quoted as a supporting evidence for the assignment

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but, if verified, they can be utilized in the intended study. In trisubstituted ethylenes the relationship between the long-range coupling and spatial arrangement of the substituents is not clear and several anomalies have been reported<sup>6</sup>. Direct additivity rules which apply well to the shifts of olefinic protons<sup>7,8</sup> cannot be used in this case as the shielding contributions of  $-\text{NH}_2$  and  $-\text{NHR}$  groups have not yet been determined (either because of the lack of the necessary data or because of anomalous behaviour of these groups; the shielding contributions of dialkylamino and diarylamino groups differ considerably<sup>7</sup>). Moreover, it was noted<sup>5</sup> that though the relative shifts of methyl protons in the two isomers agree with the relative shifts in similar compounds, the shifts of the olefinic protons are consistent with the known effects only if it is postulated that the primary amino group reverses the expected order of their shifts.

Therefore we have sought an independent assignment of the NMR spectra to check the assignment made earlier<sup>3,4</sup> in the absence of exact methods. With the assignment verified  $E-Z$  equilibria could conveniently be studied by the NMR technique. The shielding contributions of amino groups can be estimated, and the long-range coupling constants utilized in a study of structure-coupling relationships. Measurement of nuclear Overhauser effect (NOE) offers the possibility of relating pairs of NMR signals to pairs of sterically close protons in the molecule thus permitting the independent assignment of the isomers<sup>9</sup>. For the NOE measurements compounds 1–5 were chosen as representative models. The results should be applicable to the other aminoacrylonitriles 6–15 of which 12–15 are new compounds not previously studied.

No	R <sup>1</sup>	R <sup>2</sup>	R <sup>3</sup>
1	CH <sub>3</sub>	H	H
2	CH <sub>3</sub>	CH <sub>3</sub>	H
3	CH <sub>3</sub>	CH <sub>3</sub>	CH <sub>3</sub>
4	CH <sub>3</sub>	C <sub>6</sub> H <sub>5</sub>	H
5	C <sub>6</sub> H <sub>5</sub>	H	H
6	<i>p</i> -CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub>	H	H
7	<i>p</i> -CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>	H	H
8	<i>p</i> -ClC <sub>6</sub> H <sub>4</sub>	H	H
9	<i>m</i> -ClC <sub>6</sub> H <sub>4</sub>	H	H
10	CH <sub>3</sub>	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub>	H
11	CH <sub>3</sub>	C <sub>2</sub> H <sub>5</sub>	H
12	CH <sub>3</sub>	<i>n</i> -C <sub>3</sub> H <sub>7</sub>	H
13	CH <sub>3</sub>	<i>i</i> -C <sub>3</sub> H <sub>7</sub>	H
14	CH <sub>3</sub>	C <sub>6</sub> H <sub>11</sub>	H
15	CH <sub>3</sub>	C <sub>2</sub> H <sub>5</sub>	C <sub>2</sub> H <sub>5</sub>

## EXPERIMENTAL

### COMPOUNDS AND THEIR IDENTIFICATION

Physical and spectral properties of the compounds prepared in this study are summarized in Table I and II, the melting and boiling points are uncorrected, all the values refer to freshly prepared

compounds. Melting points were determined on a Boetius block. IR spectra were recorded in chloroform solution on a Perkin-Elmer 325 spectrometer. UV spectra of ethanolic solutions were measured on an Optica Milano NI 4CF instrument. NMR spectral measurements, summarized in Table III were recorded on a Varian XL 100 spectrometer at 37°C in different solvents noted in the Table. Typical concentration was 30 mg of the compound in 0.8 ml of the solvent. Though the assignment of the lines to the isomers is the subject of this work, the chemical shifts are, for the sake of simplicity, presented in Table III as assigned in the following discussion of NOE results. The assignments of long-range couplings were verified by decoupling experiments. All the employed solvents were of Uvasol quality (Merck). 3-Aminocrotonitrile (*I*) was prepared by treating acetonitrile with sodium powder<sup>2,5,10</sup> in 65–70% yield (b.p. 138–140°C/14 Torr). The melting point of the freshly distilled synthetic mixture of the two isomers *I*(*Z*) and *I*(*E*) was 52–54°C. After a few days' storage at room temperature the melting point rose to 70–78°C. Repeated crystallization of this sample from benzene solutions gave a pure isomer melting at 80–81°C. This proved to be the *E* isomer by the NOE method. 3-Aryl-3-aminoacrylonitriles (*5*–*9*) were prepared and described previously<sup>4</sup>.

TABLE I

Physical Properties of Substituted 3-Aminocrotonitriles 2–4 and 10–15

Compd.	Yield, % (procedure <sup>a</sup> )	M.p., °C b.p., °C/Torr	Formula (m. wt.)	Calcd./Found		
				% C	% H	% N
2	55 (A)	54–55 <sup>b</sup>	C <sub>5</sub> H <sub>8</sub> N <sub>2</sub> (96.2)	—	—	—
	67 (B)	146–148/15				
3	60 (A)	—	C <sub>6</sub> H <sub>10</sub> N <sub>2</sub> (110.2)	65.41	9.16	25.43
		135–137/9 <sup>c</sup>		65.20	9.13	26.10
4	37 (C)	116–117 <sup>d</sup>	C <sub>10</sub> H <sub>10</sub> N <sub>2</sub> (158.1)	—	—	—
		—				
10	79 (C)	78–79 <sup>e</sup>	C <sub>11</sub> H <sub>12</sub> N <sub>2</sub> (172.2)	76.71	7.02	16.27
		—		76.66	7.36	16.25
11	87 (A)	45–46	C <sub>6</sub> H <sub>10</sub> N <sub>2</sub> (110.2)	65.41	9.16	25.43
	89 (B)	117–118/13		65.37	9.45	25.40
12	72 (A)	25–26	C <sub>7</sub> H <sub>12</sub> N <sub>3</sub> (124.3)	67.65	9.72	22.63
		150–151/10		67.58	9.84	22.48
13	60 (A)	—	C <sub>7</sub> H <sub>12</sub> N <sub>3</sub> (124.3)	67.65	9.72	22.63
	67 (B)	137–138/10		67.56	9.87	22.54
14	96 (C)	88–89	C <sub>10</sub> H <sub>16</sub> N <sub>2</sub> (165.1)	73.22	9.75	17.03
		—		73.02	9.91	17.62
15	72 (A)	—	C <sub>8</sub> H <sub>14</sub> N <sub>2</sub> (138.2)	69.46	10.24	20.35
		126–128/2		69.52	10.21	20.27

<sup>a</sup> See Experimental part; <sup>b</sup> m.p. 52–56°C (ref.<sup>11</sup>); <sup>c</sup> b.p. 70–77°C/0.05 Torr (ref.<sup>12</sup>); <sup>d</sup> m.p. 113–117°C (ref.<sup>11–13</sup>); <sup>e</sup> m.p. 79°C (ref.<sup>13</sup>).

N-Substituted 3-aminocrotonitriles (2–4, 10–15) were prepared by the following procedures in yields given in Table I:

Procedure A: a solution of 0.1 mol of enamionitrile *I* and of 0.2 mol of the corresponding amine in 20 ml of ethanol was kept at 130–160°C for 5–8 hours in an autoclave. The product was fractionated on a distilling column.

Procedure B: 0.6 ml of 6M solution of HCl in ethanol was added to 50 ml of dioxane solution of 0.15 mol enamionitrile *I* and 0.3 mol of the corresponding amine. The mixture was heated for

TABLE II  
Spectral Properties of Substituted 3-Aminocrotonitriles 2–4 and 10–15

Compd.	$\lambda_{\max}$ , nm <sup>a</sup> (log $\epsilon$ )	$\nu$ , cm <sup>-1b</sup>				
		N—H	CH <sub>3</sub>	=CH—	C≡N	C=C, C—N
2	258 (4.38)	3 465	2 930	3 005	2 190	1 610
		3 350	1 385			1 230
		1 530				
3	268 (4.31)	—	2 925	3 000	2 198	1 625 1 210
4	250; 290 (3.61; 4.22)	3 430	2 920	3 060 <sup>c</sup>	2 200	1 615
		3 300	1 385	3 005		<sup>c</sup>
		1 520				<sup>c</sup>
10	260 (4.36)	3 440	<sup>c</sup>	3 040 <sup>c</sup>	2 200	1 605
		3 325		3 000		1 205
		1 510				
11	258 (4.34)	3 450	2 980	3 005	2 198	1 605
		3 320	2 920			1 210
		1 540	1 380			
12	260 (4.26)	3 450	2 960	3 000	2 200	1 605
		3 320	2 925			1 215
		1 530	1 380			
13	260 (4.16)	3 450	3 960	3 000	2 200	1 605
		3 320	2 925			1 215
		1 530	1 380			
14	265 (4.31)	3 440	2 938	3 005	2 200	1 603
		3 340	1 365			<sup>c</sup>
		1 520				
15	270 (4.21)	—	2 978	3 005	2 195	1 630
			2 925			1 210

<sup>a</sup> In ethanol; <sup>b</sup> in chloroform; <sup>c</sup> absorption maximum could not be unambiguously located either because of its low intensity or because of an overlap with more intense bands.

TABLE III  
<sup>1</sup>H-NMR Spectra of Enaminonitriles 1—15<sup>a</sup>

Nitrile	Solvent	Prevailing isomer (relative population, %)	Chemical shifts in isomers											
			HC≡		H <sub>3</sub> CC≡		HN <sup>b</sup>		R <sup>2c</sup>					
			Z	E	Z	E	Z	E	Z	E	Z	E		
1 <sup>d</sup>	(CD <sub>3</sub> ) <sub>2</sub> SO	E	—	3.94 <sup>e</sup>	—	1.94 <sup>e</sup>	6.48	6.48	—	—	—	—		
	CDCl <sub>3</sub>	Z <sup>f</sup> (70)	3.89 <sup>g</sup>	4.10	1.92 <sup>g</sup>	2.09	4.68	4.68	—	—	—	—		
	C <sub>6</sub> D <sub>6</sub>	E (66)	3.22 <sup>g</sup>	3.49 <sup>e</sup>	0.90 <sup>g</sup>	1.37	—	—	—	—	—	—		
2 <sup>d</sup>	CDCl <sub>3</sub> <sup>h</sup>	E (85)	3.39	3.65	1.70	2.03	5.42	2.96 (d) <sup>i</sup>	2.62 (d) <sup>i</sup>	—	—	—		
	C <sub>6</sub> D <sub>6</sub>	E (95)	3.44 <sup>g</sup>	3.51	1.36 <sup>g</sup>	1.86	—	2.52 (d) <sup>i</sup>	2.21 (d) <sup>i</sup>	—	—	—		
3 <sup>j</sup>	C <sub>6</sub> D <sub>6</sub>	E	—	3.48	—	1.80	—	—	—	—	—	2.27		
4 <sup>d</sup>	CDCl <sub>3</sub> <sup>h</sup>	E (90)	3.93	4.35	1.90	2.17	6.65	6.9—7.4 (m)	—	—	—	—		
	C <sub>6</sub> D <sub>6</sub>	E (95)	k	4.06	1.09	1.50	4.70	6.4—6.9 (m)	—	—	—	—		
5 <sup>d</sup>	CDCl <sub>3</sub>	Z (85)	4.14	4.35	l	l	5.12	5.12	—	—	—	—		
	mix (75) <sup>m</sup>	Z (99)	4.19 <sup>n</sup>	4.50 <sup>o,p</sup>	l	l	6.80	6.80	—	—	—	—		
	mix (50) <sup>m</sup>	Z (100)	4.16	—	l	l	6.54	6.54	—	—	—	—		
	mix (25) <sup>m</sup>	Z (99)	4.11 <sup>n</sup>	4.60 <sup>o,p</sup>	l	l	6.62	6.62	—	—	—	—		
	C <sub>6</sub> D <sub>6</sub>	Z	3.90	—	l	l	4.52	4.52	—	—	—	—		
6	mix (50) <sup>n</sup>	Z	4.11 <sup>n</sup>	—	l,q	l,q	6.45	6.45	—	—	—	—		
	C <sub>6</sub> D <sub>6</sub>	Z	3.91 <sup>n</sup>	—	l,q	l,q	4.10	4.10	—	—	—	—		
7	C <sub>6</sub> D <sub>6</sub>	Z	3.92 <sup>r</sup>	—	l,s	l,s	4.26	4.26	—	—	—	—		
8	C <sub>6</sub> D <sub>6</sub>	Z	3.77	—	l	l	3.92	3.92	—	—	—	—		
9	C <sub>6</sub> D <sub>6</sub>	Z	3.72	—	l	l	4.46	4.46	—	—	—	—		
10	CDCl <sub>3</sub> <sup>h</sup>	E	—	3.80	—	2.07	4.87	4.10 (d) <sup>i,t</sup>	—	—	—	—		
	C <sub>6</sub> D <sub>6</sub>	E	—	3.44	—	1.43	—	3.26 (b) <sup>i</sup>	—	—	—	—		

11	CDCl <sub>3</sub>	E (99)	3.61 <sup>p</sup>	3.74 <sup>o</sup>	1.90	2.10	4.80	1.20 (t) <sup>u,v</sup>
	C <sub>6</sub> D <sub>6</sub>	E (99)		3.54		1.86	4.90	0.84 (t) <sup>u</sup> 2.46 (t) <sup>v</sup>
12	CDCl <sub>3</sub>	E (77) <sup>x</sup>	3.62	3.71 <sup>o</sup>	1.88	2.09	5.27	0.97 (t) <sup>u,y</sup> 1.60 (m)
	C <sub>6</sub> D <sub>6</sub>	E (99)		3.58		1.91		0.75 (t) <sup>u</sup> 1.30 (m) 2.50 (q)
13	C <sub>6</sub> D <sub>6</sub>	E (93)	3.32	3.59	1.29 <sup>g</sup>	1.78	4.73	0.77 (d) <sup>u</sup> 2.91 (h) <sup>u</sup>
14	CDCl <sub>3</sub> <sup>h</sup>	E (80)	3.56	3.77	1.85	2.05	4.28	0.8—1.9 (m)
	C <sub>6</sub> D <sub>6</sub>	E (99)	3.42 <sup>p</sup>	3.64		1.88	4.75	0.9—2.8 (m)
15	CDCl <sub>3</sub> <sup>h</sup>	E		3.70		2.14		1.02 (t) <sup>u</sup> 3.22 (q) <sup>u</sup>
	C <sub>6</sub> D <sub>6</sub>	E		3.58		1.85		0.78 (t) <sup>u</sup> 2.70 (q) <sup>u</sup>

<sup>a</sup> Chemical shifts in  $\delta$  scale (p.p.m. relative to TMS, paramagnetic shifts positive). Approximate error  $\pm 0.02$  p.p.m. For the assignment to the isomers see Discussion. Coupling constants, if determined, are given in the legend. <sup>b</sup> One broad line common for both isomers. <sup>c</sup> First order analysis of multiplets which are labelled: (d) — doublet, (t) triplet, (q) quartet, (m) multiplet in the ranges indicated not resolved for isomers, (h) heptaplet, (b) broad singlet. <sup>d</sup> For the data on (CD<sub>3</sub>)<sub>2</sub>SO solution measured at 60 MHz and 24°C see Table IV. <sup>e</sup> <sup>4</sup>J(HC=CCH<sub>3</sub>) < 0.1 Hz. <sup>f</sup> Z enriched sample. <sup>g</sup> <sup>4</sup>J(HC=CCH<sub>3</sub>) = 0.75  $\pm$  0.2 Hz. <sup>h</sup> Measured at 60 MHz and 26°C. <sup>i</sup> <sup>3</sup>J(HNCH<sub>3</sub>) = 5.0  $\pm$  0.5 Hz. <sup>j</sup> For the data on CDCl<sub>3</sub> solution measured at 60 MHz and 24°C see Table IV. <sup>k</sup> If present, the line overlapped by other lines in the spectrum. <sup>l</sup> Multiplet of phenyl protons around  $\delta$  = 6.9 not resolved for isomers. <sup>m</sup> C<sub>6</sub>D<sub>6</sub> solution of ( ) % of (CD<sub>3</sub>)<sub>2</sub>SO. <sup>n</sup> <sup>4</sup>J(HC=CNH) = 1.0  $\pm$  0.2 Hz. <sup>o</sup> <sup>4</sup>J(HC=CNH) < 0.15 Hz. <sup>p</sup> Signal becomes apparent only after two days' storage of the solution. <sup>q</sup> CH<sub>3</sub> proton line at  $\delta$  = 2.02. <sup>r</sup> <sup>4</sup>J(HC=CNH) = 0.9  $\pm$  0.2 Hz. <sup>s</sup> CH<sub>3</sub> proton multiplet around  $\delta$  = 7.3. <sup>t</sup> <sup>3</sup>J(HCCH) = 7.3  $\pm$  1 Hz. <sup>v</sup> NCH<sub>2</sub> protons appear as an overlapping pair (<sup>3</sup>J(HNCH)) of triplets giving the net appearance of a quartet centered at  $\delta$  = 2.95; in the Z isomer the quartet, is visible at  $\delta$  = 3.4 after two days' storage. <sup>x</sup> Population in the fresh sample, after two days in the solution the concentration of the E isomer is increased to 96%. <sup>y</sup> The same as <sup>v</sup>, the quartet is at  $\delta$  = 2.91 in the E isomer, and at  $\delta$  = 3.29 in the Z isomer.

TABLE IV  
<sup>1</sup>H-NMR Spectra of Solutions Used in NOE Measurements of Enaminonitriles 1-5

Solution <sup>a</sup> of enamino- nitrile	Population % of isomer I <sup>c,d</sup>	Chemical shifts <sup>b</sup>							
		isomer I <sup>c</sup>			isomer II <sup>c</sup>				
		HC=	H <sub>3</sub> CC=	HN	H <sub>3</sub> CN	HC=	H <sub>3</sub> CC=	HN	H <sub>3</sub> CN
1	65	3.91 <sup>e,f</sup>	1.91 <sup>e</sup>	6.49 <sup>f,g</sup>	—	3.61 <sup>h,i</sup>	1.77 <sup>h</sup>	6.49 <sup>g,i</sup>	—
2	99	3.69 <sup>j,k</sup>	1.96 <sup>j</sup>	6.91 <sup>l</sup>	2.59 <sup>k,l</sup>	<i>m</i>	<i>m</i>	<i>m</i>	<i>m</i>
3	94	3.68 <sup>n,o</sup>	2.17 <sup>n</sup>	—	2.91 <sup>o</sup>	<i>m</i>	2.35	—	2.73
4	99	4.42 <sup>p</sup>	2.16 <sup>p</sup>	8.83	— <sup>q</sup>	4.04	1.92	<i>m</i>	— <sup>q</sup>
5	68	4.18 <sup>r</sup>	— <sup>s</sup>	6.81 <sup>g,r</sup>	—	4.27 <sup>f</sup>	— <sup>s</sup>	6.81 <sup>g,t</sup>	—

<sup>a</sup> For the description of the solutions see Experimental. <sup>b</sup> Chemical shifts in  $\delta$  scale (in p.p.m. relative to TMS line, paramagnetic shifts positive) were calculated using the chemical shift of internal reference line of HMDSS  $\delta = 0.03$ . <sup>c</sup> The isomer prevailing in the solution is denoted as isomer I the other one as isomer II. <sup>d</sup> Relative population of isomers as present in the measured solutions was determined from the ratio of integrals of corresponding lines in the two isomers. <sup>e</sup> <sup>4</sup>J(HC : CCH<sub>3</sub>) < 0.2 Hz. <sup>f</sup> <sup>4</sup>J(HC : CNH) < 0.2 Hz. <sup>g</sup> Half-width 10 Hz. <sup>h</sup> <sup>4</sup>J(HC : CCH<sub>3</sub>) = 0.6 ± 0.1 Hz. <sup>i</sup> <sup>4</sup>J(HC : CNH<sub>2</sub>) = 1.0 ± 0.2 Hz. <sup>j</sup> <sup>4</sup>J(HC : CCH<sub>3</sub>) < 0.1 Hz. <sup>k</sup> <sup>5</sup>J(HC : CNCH<sub>3</sub>) = 0.3 ± 0.1 Hz. <sup>l</sup> <sup>3</sup>J(H<sub>3</sub>CNH) = 4.7 ± 0.3 Hz. <sup>m</sup> The line could not be found in the spectrum. <sup>n</sup> <sup>4</sup>J(HC : CCH<sub>3</sub>) < 0.1 Hz. <sup>o</sup> <sup>5</sup>J(HC : CNCH<sub>3</sub>) = 0.35 ± 0.05 Hz. <sup>p</sup> <sup>4</sup>J(HC : CCH<sub>3</sub>) < 0.2 Hz. <sup>q</sup> C<sub>6</sub>H<sub>5</sub>N around  $\delta = 7.2$ . <sup>r</sup> <sup>4</sup>J(HC : CNH) = 0.85 ± 0.05 Hz. <sup>s</sup> C<sub>6</sub>H<sub>5</sub> around  $\delta = 7.5$ . <sup>t</sup> <sup>4</sup>J(HC : CNH) < 0.1 Hz.

TABLE V  
Experimental NOE Enhancements for Protons of 3-Substituted 3-Aminoacrylonitriles

Aminoacrylo- nitrile	Saturated line <sup>e</sup>	Observed line <sup>a</sup>						
		HC= (I)	H <sub>3</sub> CC= (I)	HN <sup>b</sup>	HC= (II)	H <sub>3</sub> CC= (II)	C <sub>6</sub> H <sub>5</sub>	
1	H <sub>3</sub> CC= (I)	2.6 ± 3.0	—	-0.9 ± 1.2	3.4 ± 4.9	0 + 8 <sup>c</sup>	—	
	HN <sup>b</sup>	29.2 ± 1.8	5.0 ± 3.6 <sup>c</sup>	—	-9.0 ± 3.0 <sup>d</sup>	4.6 ± 3.1	—	
	H <sub>3</sub> CC= (II)	2.0 ± 2.6	0 + 8 <sup>c</sup>	0.6 ± 1.7	32.6 ± 6.1	—	—	
2	H <sub>3</sub> C—C=	3.8 ± 1.3	—	6.6 ± 2.6	—	—	—	
	H <sub>3</sub> C—N	29.9 ± 1.8	—	7.7 ± 3.0	—	—	—	
	HC=	—	0.3 ± 1.8	—	—	—	—	
3	H <sub>3</sub> C—C=	2.1 ± 0.8	—	—	—	—	—	
	H <sub>3</sub> CN	31.1 ± 1.4	<sup>e</sup>	—	—	—	—	
	HC=	—	0 ± 0.5	0.2 ± 2.0	—	—	2.4 ± 0.8	
4	H <sub>3</sub> CC=	6.5 ± 1.0	—	11.9 ± 1.8	—	—	1.8 ± 1.0	
	HN	7.7 ± 0.8	<sup>f</sup>	—	—	—	1.5 ± 0.8	
	C <sub>6</sub> H <sub>5</sub>	21.1 ± 1.2	<sup>f</sup>	1.8 ± 1.6	—	—	—	
5	HC= (I)	—	—	0.1 ± 1.0 <sup>g</sup>	0 ± 3 <sup>c</sup>	—	2.1 ± 0.4 <sup>h</sup>	
	HN <sup>b</sup>	<sup>e</sup>	—	—	26.5 ± 1.8	—	<sup>e</sup>	
	C <sub>6</sub> H <sub>5</sub> <sup>b</sup>	28.3 ± 0.9	—	<sup>e</sup>	—	—	—	
HC= (II)	0 ± 3 <sup>c</sup>	—	2.3 ± 0.9 <sup>g</sup>	—	—	—	0.9 ± 0.6 <sup>h</sup>	

<sup>a</sup> Lines are labelled according to Table IV, roman numeral denoting the isomer; <sup>b</sup> overlapping lines of the two isomers; <sup>c</sup> estimated from peak heights; <sup>d</sup> distortion apparently due to the spectrometer; <sup>e</sup> could not be measured; <sup>f</sup> was not measured; <sup>g</sup> total compounded NOE enhancement in the two isomers. According to the population of the isomers and according to the two effects observed on HN line the enhancements in isomers I and II are 0.1 ± 1.5% and 4.6 ± 1.8%, resp.; <sup>h</sup> as in note<sup>g</sup>, the enhancements in isomers I and II are 3.1 ± 0.6% and 1.8 ± 1.2%, resp.



5–6 hours in a pressure tube at 120–140°C. The reaction product was worked up by fractional distillation.

Procedure C: a mixture of 0.1 mol enaminonitrile *I* and 0.2 mol of the corresponding amine was refluxed for 2–4 hours till the generation of ammonia was completed. After cooling the precipitate was filtered off and purified by crystallization from ethanol.

#### NOE MEASUREMENTS

The spectrometer (Tesla BS 477) and the measuring technique were described previously<sup>14,15</sup>. The measured samples were degassed by the standard freeze-pump-thaw cyclic procedure (using vacuum better than  $10^{-3}$  Torr). The samples were 0.35–0.45M solutions of enaminonitriles and 0.04–0.06M solutions of hexamethyldisilane (HMDSS, prepared in this laboratory). Deuteriochloroform (Merck, Uvasol quality, isotopic purity 99%) was used as a solvent for compound 3, all the other compounds were dissolved in perdeuterated dimethyl sulphoxide (Lachema, Lachesol set, isotopic purity 99.5%). The <sup>1</sup>H-NMR data, measured (at 24°C) in these solutions under the same conditions and on the same spectrometer as used for the NOE experiments, are assembled in Table IV. The long-range couplings were assigned according to decoupling experiments. The results of NOE measurements are given in Table V as the percentage of enhancement. The errors indicated are 95% confidence limits (assuming *t*-distribution).

In the experimental spectra, the lines were assigned to isomers *I* and *II* according to the intensities. In the pairs of HC=, H<sub>3</sub>CC=, and H<sub>3</sub>CN proton lines the stronger one was assigned to the isomer arbitrarily designated as *I*. The relative intensity ratio of the lines in the pairs are given in Table IV as a percentage of the prevailing isomer *I*. The NOE experiments served to relate the isomers *I* and *II* to the isomers *E* and *Z*.

In contrast to Tables I–III the data in Tables IV and V were obtained a few months after the preparation of the compounds and also several weeks after the solutions had been prepared. The solutions were checked for variations in the isomer ratio. The NOE experiments were performed on virtually equilibrated samples since the ratio of the isomers was the same at the time of measurement as it was ten days before. Therefore, the populations given in Table IV can serve as estimates of the distribution at equilibrium.

#### CALCULATIONS

Theoretical NOE enhancement were calculated on a Tesla 200 computer according to the method described elsewhere<sup>16</sup>. Unless otherwise indicated all bond angles were taken as 120°C except H–C–H and H–C–C angles in methyl groups which were taken as 109.5°. Selected best bond lengths were taken from ref.<sup>17</sup>.

#### RESULTS AND DISCUSSION

Before evaluating the NOE data in structural terms attention must be paid to other<sup>9</sup> relaxation mechanisms (in addition to the dipole-dipole relaxation) since these would make the interpretation uncertain.

##### *Effect of Scalar Relaxation*

In addition to the lines listed in Table IV there was also the line of H<sub>2</sub>O protons ( $\delta = 3.37–3.40$ ) visible in the spectra of enaminonitriles *1*, *2*, *4*, and *5* (*i.e.* in com-

pounds containing NH proton) which were measured in dimethyl sulphoxide. Owing to the well known properties of the solvent, the H<sub>2</sub>O line was separated from the NH line. Measurements of NOE on the NH line when the H<sub>2</sub>O line was saturated gave no enhancement ( $f_{\text{HN}}\{\text{H}_2\text{O}\} = 0 \pm 3\%$ , in the notation of ref.<sup>9</sup>) in the samples. Therefore the inverse value ( $\tau$ ) of the rate constant of the proton exchange between the NH and OH groups is  $\tau \geq 30/R_{\text{HN}}$ , where  $R_{\text{HN}}$  is the total direct relaxation rate of the NH proton<sup>9,18</sup>. As follows from this relation and from equations of ref.<sup>19</sup> the ratio of the relaxation rate due to the scalar relaxation ( $\rho_{\text{HC}}^{\text{SC}}$ ) to the total direct relaxation rate ( $R_{\text{HC}}$ ) of the proton bonded to a carbon atom is

$$\rho_{\text{HC}}^{\text{SC}}/R_{\text{HC}} \leq (J/\Delta\nu)^2 R_{\text{HN}}/(R_{\text{HC}} \cdot 60),$$

where  $J$  is the coupling constant between the HC and HN proton and  $\Delta\nu$  is the difference in their chemical shifts (in Hz). Since it is apparent from Table IV that the ratio  $J/\Delta\nu$  is less than  $10^{-2}$ , the total direct relaxation rate of the NH proton would have to be (according to the above relation)  $10^4$  times faster than that of the HC proton in order that the scalar relaxation of the HC proton would amount to 2% of the total relaxation rate of this proton. As follows from the observed line-widths,  $R_{\text{HN}}$  could not be more than  $300 R_{\text{HC}}$ . The effect of scalar relaxation on the NOE observed on the HC protons is therefore negligible.

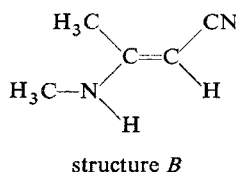
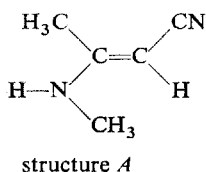
Because of the low concentration of the less abundant isomer (*II*) the NOE could be measured only in compounds *1* and *5* for both isomers. Since in none of the four NOE experiments where the enhancement was detected on the line of one isomer while the line of the same type in the other isomer was saturated gave NOE values that would significantly differ from zero (e.g. the value of  $f_{\text{H}_3\text{CC}=(\text{I})}\{\text{H}_3\text{CC}=(\text{II})\}$ ), the average life-time of each isomer must be considerably longer than the relaxation times of the protons in the isomers. Therefore, from the point of view of NOE the two isomers can be considered as independent compounds<sup>20</sup>.

A simplified model which takes into account only dipole-dipole relaxation and its dependence on interprotonic distance and neglects all other possible relaxation pathways would predict that in the *E* isomers appreciable NOE enhancements should be observed between amino and olefinic protons which are in *cis* arrangement. Protons of the R<sup>1</sup> substituents are too remote from the olefinic protons to give a significant NOE. In the *Z* isomer the situation is reversed since the olefinic proton is close to the protons of R<sup>1</sup> substituents. In the case of enaminonitrile *1*, this qualitative picture was, confirmed by calculations which took into account all the protons in the molecule.

For 3-aminocrotononitrile *1* comparison of the calculated and experimental enhancements (Tables V and VI) of the olefinic proton line results in assigning structure *E* to isomer *I* (the more abundant isomer with less shielded olefinic and methyl protons and smaller long-range coupling between them). This assignment is

correct beyond any doubts since the relevant enhancements are not only in the right ratios but they also agree numerically with the theoretically predicted enhancements for the *E* and *Z* isomers. The negative value of  $f_{\text{HC}=\{\text{HN}\}}$  is most likely due to electronic interference in the spectrometer. Since it is not relevant for the assignment no effort was made to overcome this distortion.

In *N*-methyl-3-aminocrotonitrile 2 the prevailing isomer is, according to the above reasoning and the data of Table V, also in the *E* configuration. Similar values of enhancements observed on the HN proton line ( $f_{\text{HN}\{\text{H}_3\text{CN}\}}$  and  $f_{\text{HN}\{\text{H}_3\text{CC}=\}}$ ) suggest that the dihedral angle  $\vartheta$  of the C=C and H—N bond is  $180^\circ$  (i.e. structure *A* with the HN proton in between the two methyl groups  $\text{H}_3\text{CC}=\$  and  $\text{H}_3\text{CN}$ ).



Calculations show that in the arrangement with the dihedral angle  $\vartheta_1 = 0^\circ$  (structure *B*) in which the two methyl groups are sterically close, the maximum observable NOE on the HN proton line from  $\text{H}_3\text{CC}=\$  saturated protons would be 1%. Exact calculations of all theoretical NOE are not possible since the ratio of the rates of methyl group rotation and molecular reorientation is not available. The only safe conclusion from these considerations is that enaminonitrile 2 is not exclusively in a conformation with  $0^\circ$  dihedral angle; it is very likely that in the prevailing conformation this angle is close to  $180^\circ$ .

Similarly, the NOE results undoubtedly confirm that in enaminonitriles 3 and 4 the prevailing isomers have structure *E*. Despite the fact that several NOE enhancements were measured with needed precision in these compounds, the detailed geometry of the molecules cannot be ascertained since nothing is known about the rotation of the groups in the molecules.

In contrast to compounds 1–4, the NOE data for the HC= proton in 3-phenyl-3-aminoacrylonitrile 5 clearly prove that in this compound the prevailing isomer has the structure *Z*.

Calculations of theoretical NOE values for the undistorted (all bond angles  $120^\circ$ ) coplanar arrangement of the *Z* isomer of compound 5 lead to larger value of enhancement  $f_{\text{C}_6\text{H}_5\{\text{HC}=\}}$  than observed. The experimental values of NOE are best reproduced when  $\rho^*/\hbar\gamma^2\tau_c = 1.9 \cdot 10^{-6}$  (notation of ref.<sup>9</sup>), the calculated theoretical NOE values are  $f_{\text{HC}=\{\text{C}_6\text{H}_5\}} = 28.2\%$  and  $f_{\text{C}_6\text{H}_5\{\text{HC}=\}} = 5.1\%$  which should be compared with the experimental values of Table V. Apparently the true geometry of this isomer is different; either the phenyl group is twisted out of the plane of the C=C double bond

TABLE VI  
Theoretical NOE Enhancements for Protons of 3-Aminocrotononitrile<sup>a</sup>

Saturated line	Observed line					
	isomer <i>E</i>			isomer <i>Z</i>		
	HC=	H <sub>3</sub> CC	HN	HC=	H <sub>3</sub> CC	HN
H <sub>3</sub> CC=	3.7 (3.4)	—	2.1 (3.0)	28.7 (25.3)	—	2.2 (3.1)
HN	29.3	2.1 (3.2)	—	2.2 (2.9)	2.1 (3.2)	—

<sup>a</sup> Values for "eclipsed" conformation of methyl group relative to the double bond. If the value for "staggered" conformation is different it is indicated in parenthesis. The rate of overall tumbling of the molecule was assumed to be much smaller than the rate of methyl group rotation.

or the bond angles are considerably different from the assumed  $120^\circ$  or both. In either case the HC= proton would be more remote from the closest proton of the phenyl group and this would bring the theoretical values closer to the experimental ones. For example, the geometry shown in Fig. 1 yields  $f_{\text{HC}=\{\text{C}_6\text{H}_5\}} = 28.2\%$  and  $f_{\text{C}_6\text{H}_5\{\text{HC}=\}} = 3.9\%$  (for  $\rho^*/\hbar\gamma^2\tau_c = 2.2 \cdot 10^{-6}$ ), which agree reasonably with the experiment. In the *E* isomer of this compound the NOE enhancement  $f_{\text{HN}\{\text{HC}=\}}$  is larger than that calculated for an undistorted model similar to that described above. This suggests, in accord with the depicted structure, that the proton of the NH<sub>2</sub> group is closer to the HC= proton than assumed by the undistorted model.

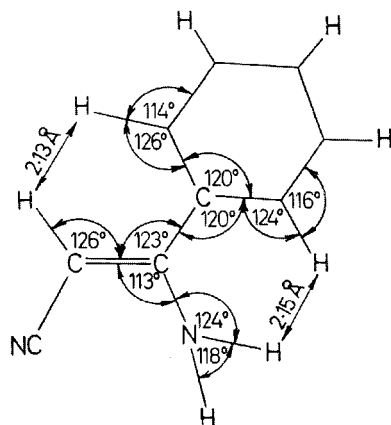


FIG. 1

Structure of Enaminonitrile 5 which Leads to Theoretical NOE Values Close to Those Determined Experimentally

### *Structure-Spectra Relationships in Enaminonitriles*

On the basis of the above assignments the following generalizations emerge from the data of Table IV: 1) the olefinic proton ( $\text{HC}=\text{C}$ ) is more shielded, 2) the long-range coupling constant  ${}^4J(\text{HC} : \text{CCH}_3)$  is larger, and 3) the long-range coupling constant  ${}^4J(\text{HC} : \text{CNH})$  is also larger in the *Z* isomer than in the *E* isomer. (Of these conclusions, 1) and 2) confirm the earlier assignment of Bullock and Gregory<sup>5</sup>. Their finding that also the methyl protons ( $\text{H}_3\text{CC}=\text{C}$ ) are more shielded in the *Z* isomer is not supported by the present results).

Application of these rules to the assignments in the spectra of solutions in which both isomers are present would be simple. When only one isomer is present then a recourse to numerical values would be necessary. In the *Z* isomer, the coupling constant  ${}^4J(\text{HC} : \text{CCH}_3)$  is close to 0.5 Hz and  ${}^4J(\text{HC} : \text{CNH})$  is about 0.9 Hz while they are both less than 0.2 Hz in the *E* isomer. Chemical shifts are hard to predict with the necessary accuracy, but a comparison with the assigned spectrum of a model compound which must be structurally very similar and measured under identical conditions (solvent, concentration and temperature) might be conclusive.

### *Applications*

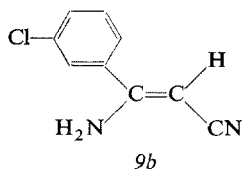
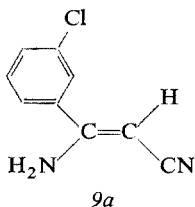
In order to facilitate the applications of the above rules to the intended study of the *E-Z* equilibria and to the other enaminonitriles, the spectra of compounds 1–5 were measured also in solvents in which the study will be carried out. The results of these measurements, which are also given in Table III, clearly indicate considerable solvent dependence of the chemical shifts. The validity of the rules 2) and 3) does not seem to be affected by the solvents.

In hexadeuteriobenzene the olefinic proton is always diamagnetically shifted relative to its shielding in hexadeuteriodimethyl sulphoxide or deuteriochloroform solutions. The relative solvent shifts in the last two mentioned solvents do not show a regular pattern. The limited data on the shifts of enaminonitrile 5 in the mixture solvent ( $(\text{CD}_3)_2\text{SO} : \text{C}_6\text{D}_6$ ) demonstrate that in this compound the difference between the shifts of olefinic protons in the two isomers is increased if the compound is dissolved in hexadeuteriobenzene.

*Compounds 6–9.* The model compound, 3-phenyl-3-aminoacrylonitrile (5), is structurally very similar to these compounds. They differ only by substitution of the phenyl ring which is unlikely to cause any major changes in the NMR spectrum except for the trivial appearance of the lines of the substituents and a change in the symmetry of the spectrum of the phenyl protons. On the basis of literature data<sup>8,21</sup> a small change in the chemical shift of the olefinic proton with the ring substituent has also to be expected. Employing deuteriobenzene as a solvent the difference between the shifts of *E* and *Z* isomers would be increased as it is in the spectrum of the model

compound. The shifts of olefinic protons of compounds 6–9 clearly indicate that these compounds are present as *Z* isomers in the studied solutions similarly as is the model compound in which, however, the other isomer could be seen. This assignment is verified by the observed long-range couplings. The chemical shift of the olefinic proton shows an interesting linear dependence on Hammett constant of the substituent on the phenyl ring. The olefinic proton becomes more shielded as the substituent constant increases. Such a trend is opposite to the trend observed in substituted styrenes<sup>8</sup> or cinnamic nitriles<sup>21</sup>.

**Compounds 10–14.** In the spectra of these compounds the lines of the less abundant isomer are very weak, and they are close to the lines of the prevailing isomer. It was not possible to observe long-range couplings on these weak lines. The structure of the prevailing isomers was determined from the comparison of the shifts of the olefinic protons with that in the model compound 2 and from the absence of long-range couplings. All these observations point to the *E* isomer to be the prevailing one in these compounds. (In the cyclohexyl derivative (14) the olefinic proton line is slightly broadened (linewidth c. 1.5 Hz). If HN proton doublet is saturated in dimethyl sulphoxide solution, the olefinic proton appears as a pair of (1 : 1) overlapping lines separated by 0.6 Hz. Though there are several possibilities, the origin of this doublet is not yet clear.)



**Compound 15.** According to the comparison of the chemical shifts in this and in the model compound 3 the compound is most likely the *E* isomer.

The above determinations of the structures of the isomers of enaminonitriles confirm the structure proposed earlier by Conn and Taurins<sup>3</sup> and accepted by Bullock and Gregory<sup>5</sup> for compound 1. The present results are also in accord with the determinations based on dipolemoment data<sup>4</sup> in the case of compounds 5 and 8. Large dipole moments observed in compounds 6 and 7 (4.98 and 5.16 D, resp.) were interpreted<sup>4</sup> as proving the *E* structure for the dominant isomers of these compounds. In the view of the present findings that conclusion must be reversed. In the case of compound 9 the dipolemoment study was not conclusive since the rotation around  $C_{\text{aryl}}-C_{\text{olefin}}$  bond considerably affected the calculated dipole moments. At the temperature of 37°C the NMR spectrum shows only one type of olefinic proton

(Table III), at 60°C, however, two more lines are apparent in the spectrum ( $\delta = 3.80$  and  $\delta = 4.92$ ). It is possible that at this higher temperature both rotamers 9a and 9b (lines at  $\delta = 3.72$  and 3.80) and, in addition to them, the *E* isomer (line at  $\delta = 4.92$ ) are all present in the solution.

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