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Studies on Geometric Isomerism by Nuclear Magnetic Resonance. IV.[*1] Structure of α-Cyano-β-amino-β-alkylacrylic Esters

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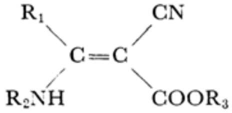
The NMR spectra of α-cyano-β-amino-β-alkylacrylic esters prepared from α-cyano-β-methoxy-β-alkylacrylic esters and simple amines have been studied. It has been found that these aminoesters, in a variety of solvents, are all present in an intramolecular hydrogen-bonded enamine form with a chelate ring.

In the first paper of this series[1] the authors discussed the geometrical configurations of the compounds of the $R_1(R_2O)C=C(CN)COOR_3$ type. In the present work, the structures of α-cyano-β-amino-β-alkylacrylic esters, prepared easily by the condensation of α-cyano-β-methoxy-β-alkylacrylic esters with simple amines, such as ammonia, methylamine, and benzylamine, will be described. These aminoesters possess two possible geometrical isomers (1 and 2)[2] and four possible tautomers (3, 4, 5 and 6). Therefore, it appears attractive to examine in which species the esters exist in the solution.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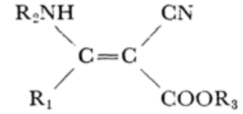
trans form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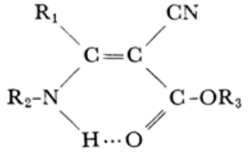
cis form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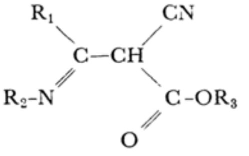
enamine form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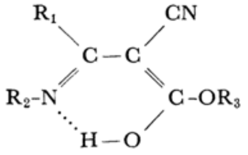
ketimine form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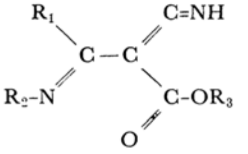
keteneacetal form


6
keteneimine form

The ketimine-enamine tautomerism has been extensively investigated by several workers, using the infrared,[3-6] and ultraviolet[7,8] spectra. Recently, Dudek *et al.*[9,10] and Ostercamp[11] have studied the NMR spectra of a number of α, β-unsaturated aminoketones; they concluded that the aminoketones studied exist essentially in the enamine form, which possesses a chelate-ring structure resulting from the hydrogen-bond formation between the amino and the ester carbonyl groups. However, the ketimine-enamine equilibrium of these aminoketones depends to some extent upon the nature of the substituent and the solvent. Dudek *et al.*[10] also showed that ethyl β-benzylaminocrotonate exists predominantly in the enamine form. However, no investigation has been made concerning α-cyano-β-amino-β-alkylacrylic esters.

Results and Discussion

The NMR data for the α-cyano-β-amino-β-alkylacrylic esters examined in this work are set out in Table 1, while representative NMR spectra of the esters are shown in Figs. 1, 2, and 3. For purposes of comparison, the NMR spectra of several α-cyano-β-aminocrotononitriles have been measured; the results are listed in Table 2.

As a typical example, the present authors analyzed the spectrum of ethyl α-cyano-β-benzylaminocrotonate (II, Fig. 1) in a deuteriochloroform solution. A triplet at 1.30 ppm and a quartet at 4.21

[*1] Presented partly at the 19th Annual Meeting of the Chemical Society of Japan, Yokohama, 1966.

[1] T. Hayashi, I. Hori, H. Baba and H. Midorikawa, *J. Org. Chem.*, **30**, 695 (1965).

[2] By a trans isomer is meant the form in which the β-methyl and the alkoxycarbonyl groups are on opposite sides of the C=C bond. The notations used here to distinguish the methyl groups are according to the preceding papers.

[3] S. Baldwin, *J. Org. Chem.*, **26**, 3288 (1961).

[4] B. Witkop, *J. Am. Chem. Soc.*, **78**, 2873 (1956).

[5] J. Dabrowski, *Spectrochim. Acta*, **19**, 475 (1963).

[6] K. L. Wierzchowski and D. Shugar, *ibid.*, **21**, 943 (1965).

[7] K. L. Wierzchowski and D. Shugar, *ibid.*, **21**, 931 (1965).

[8] K. Ueno and A. E. Martell, *J. Phys. Chem.*, **61**, 257 (1957).

[9] G. O. Dudek and R. H. Holm, *J. Am. Chem. Soc.*, **84**, 2691 (1962).

[10] G. O. Dudek and G. P. Volpp, *ibid.*, **85**, 2697 (1963).

[11] D. L. Ostercamp, *J. Org. Chem.*, **30**, 1169 (1965).

ppm are evidently to be ascribed to the ethoxycarbonyl protons. On the basis of the chemical shifts and relative peak areas, a singlet at 2.30 ppm, a doublet at 4.54 ppm, and a multiplet near 7.30 ppm are attributable to the β-methyl, benzyl methylene, and phenyl protons respectively. The fact that the spectrum shows only one β-methyl signal indicates that the ester (II) exists practically

TABLE 1. NMR DATA FOR THE COMPOUNDS OF THE TYPE $\begin{matrix} R_1 \\ R_2NH \end{matrix}\!\!>\!C{=}C(CN)COOR_3$ IN ppm DOWNFIELD FROM TMS

	Compound			Solvent	R_1			R_2	NH	R_3
	R_1	R_2	R_3		β-CH_3	β-CH_2	γ-CH_3			
I	Me	$PhCH_2$	Me	$CHCl_3$	2.34			4.60a)	10.33	3.77
II	Me	$PhCH_2$	Et	$CDCl_3$	2.30			4.54a)	10.22	4.21 1.30
				CD_3COCD_3	2.31			4.67a)	10.33	4.21 1.21
				C_6H_6	1.69			3.63a)	10.30	4.06 1.03
				C_5H_5N	2.25			4.56a)		4.19 1.16
				$C_5H_5N+D_2O$	2.33			4.66b)	—	4.20 1.16
III	Et	$PhCH_2$	Me	$CDCl_3$		2.69	1.28	4.62a)	10.23	3.77
IV	Me	Me	Me	CD_3COCD_3	2.30			3.14c)	9.80	3.66
				C_5H_5N	2.15			2.81c)		3.69
				$C_5H_5N+D_2O$	2.19			2.98d)	—	3.73
V	Et	Me	Me	$CDCl_3$		2.69	1.28	3.12c)	9.80	3.77
VI	*i*-Pr	Me	Me	$CDCl_3$		3.26e)	1.43	3.15c)	10.19	3.77
VII	Ph	Me	Me	$CDCl_3$		(7.20—7.60)f)		2.85c)	9.82	3.84
VIII	Me	H	Me	$CHCl_3$	2.31			5.85	9.20	3.79
IX	Me	H	Et	C_5H_5N	2.31			5.90	9.60	4.25 1.18
				$C_5H_5N+D_2O$	2.35			—	—	4.25 1.21
X	Et	H	Me	$CDCl_3$		2.59	1.29	6.10	9.20	3.78
XI	*i*-Pr	H	Me	$CDCl_3$		3.19e)	1.28	6.05	9.29	3.79
XII	*t*-Bu	H	Me	$CDCl_3$			1.46	6.07	10.02	3.79

a) Benzyl methylene (doublet, 6 cps)
b) Benzyl methylene (singlet)
c) Doublet, 5.4 cps
d) Singlet
e) β-Methine
f) Phenyl (multiplet)

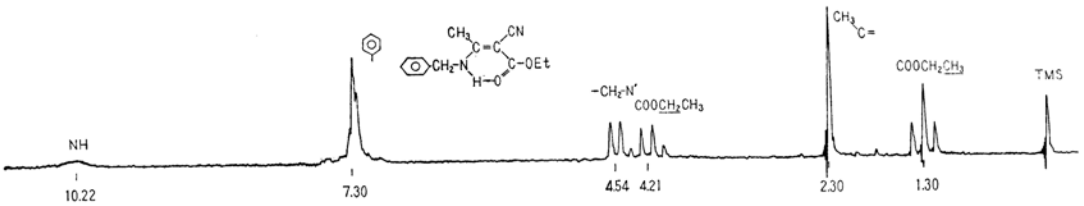


Fig. 1. The NMR spectrum of ethyl α-cyano-β-benzylaminocrotonate (II) in $CDCl_3$.

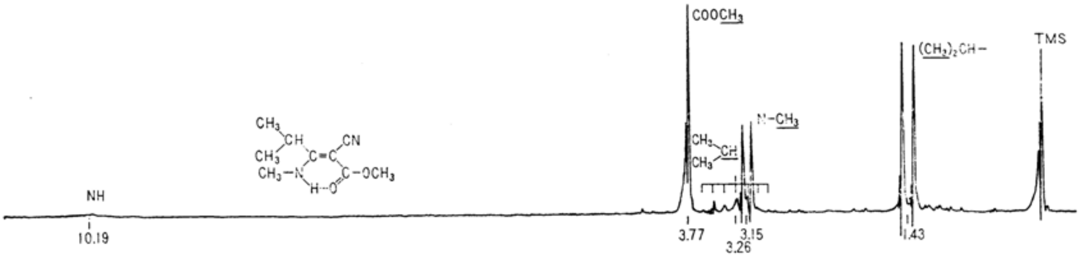


Fig. 2. The NMR spectrum of methyl α-cyano-β-methylamino-β-isopropylacrylate (VI) in $CDCl_3$.

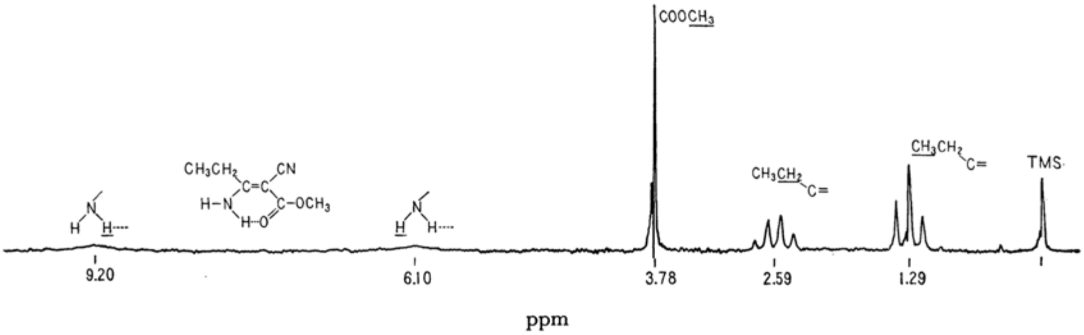
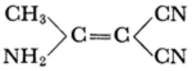
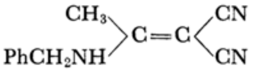


Fig. 3. The NMR spectrum of methyl α-cyano-β-amino-β-ethylacrylate (X) in $CDCl_3$.

TABLE 2. NMR DATA FOR β-AMINOCROTONONITRILE AND α-CYANO-β-AMINOCROTONONITRILES IN ppm DOWNFIELD TMS

	Compound	Solvent	β-CH_3	NH	
XIII	β-Aminocrotonitrile (equilibrium mixture)	$CDCl_3$	1.91 2.07	4.90	3.77[a] 4.10
		C_6H_6[b]	1.03 1.50	4.65	3.36[a] 3.63
XIV	 $(CH_3)(NH_2)C{=}C(CN)_2$	CD_3COCD_3	2.25	7.72	
		C_5H_5N	2.22		
XV	 $(CH_3)(PhCH_2NH)C{=}C(CN)_2$	$CDCl_3$	2.16	7.29	4.46[c]
		CD_3COCD_3	2.25	8.15	4.71[c]

a) Vinyl methine b) Ref. 13 c) Benzyl methylene (doublet, 6 cps)

in one form. The doublet of the benzyl methylene signal suggests that one proton attaches to the amino nitrogen. Therefore, the remaining broadened, unresolved signal at 10.22 ppm may be attributed to the hyrogen-bonded NH proton. In fact, examination showed that the spin-spin decoupling between the benzyl methylene and the NH protons resulted in the collapse of the doublet of the benzyl methylene protons into the singlet. The position of the NH signal is substantially independent of the variation in the concentration. This fact suggests that the intramolecular hydrogen bond is formed between the amino group and the ester carbonyl or the cyano group.

In the case of β-aminocrotononitrile (XIII), Conn and Taurins[12] have interpreted the relative stability of the geometric isomers on the basis of the hydrogen bond formation between the amino and the cyano groups. However, the NMR spectra of the stereoisomeric mixture of the nitrile (XIII) in benzene[13] and deuteriochloroform solutions showed that the NH signals of the cis and trans isomers are located at almost the same position, in a much higher field than that of the α-cyano-β-aminocrotonic esters (Table 2). The NH signals of α-cyano-β-aminocrotononitriles (XIV and XV) showed similar results (Table 2). These facts indicate that the possibility of a hydrogen bond formation between the amino and the cyano groups can be ruled out.

Consequently, it may be concluded that the ester (II) exists in only one form, the enamine form 3, with an intramolecular hydrogen bond between the amino and the ester carbonyl groups. The examination of molecular models supports the above conclusion. The NMR spectra in deuterioacetone and pyridine solutions are very similar to that in a deuteriochloroform solution. Thus, the same tautomeric species predominates overwhelmingly under these circumstances. The NMR spectrum in a benzene solution showed the β-methyl and benzyl methylene signals at a much higher field than that in a deuteriochloroform solution. Since, however, the NH signal of the former was located at almost the same position as that of the latter, the above facts should not be interpreted as due to the presence of any species different from the enamine form, but only to the solvent effect in a benzene solution.

The NMR spectra of α-cyano-β-methylamino-β-alkylacrylic esters, similar to those of the above β-benzylamino esters, showed the very broad

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[12] J. J. Conn and A. Taurins, *Can. J. Chem.*, **31**, 1211 (1953).

[13] E. Bullock and B. Gregory, *ibid.*, **43**, 332 (1965).

TABLE 3. PROPERTIES OF α-CYANO-β-AMINO-β-ALKYLACRYLIC ESTERS AND β-AMINOCROTONONITRILES

Compound	Mp, °C (Bp, °C/mmHg)	Formula	Found			Calcd		
			C, %	H, %	N, %	C, %	H, %	N, %
I	153	$C_{13}H_{14}O_2N_2$	67.98	5.81	12.13	67.81	6.13	12.17
II	96—97	$C_{14}H_{16}O_2N_2$	68.57	6.39	11.23	68.83	6.60	11.47
III	64	$C_{14}H_{16}O_2N_2$	68.73	6.33	10.86	68.83	6.60	11.47
IV	124[a)]	$C_7H_{10}O_2N_2$	54.53	6.23	18.19	54.53	6.54	18.17
V	63	$C_8H_{12}O_2N_2$	57.22	6.92	16.50	57.13	7.19	16.66
VI	(165—166/5)	$C_9H_{14}O_2N_2$	59.69	7.90	15.51	59.32	7.74	15.37
VII	159	$C_{12}H_{12}O_2N_2$	66.42	5.23	12.41	66.65	5.59	12.96
VIII	180[b)]	$C_6H_8O_2N_2$	51.57	5.60	20.09	51.42	5.75	19.99
IX	185—186.5[c)]	$C_7H_{10}O_2N_2$	54.52	6.26	17.86	54.53	6.54	18.17
X	146	$C_7H_{10}O_2N_2$	54.61	6.27	18.11	54.53	6.54	18.17
XI	128	$C_8H_{12}O_2N_2$	57.04	7.08	16.47	57.13	7.19	16.66
XII	135	$C_9H_{14}O_2N_2$	58.85	7.36	14.94	59.32	7.74	15.37
XIII	65—72[d)]	$C_4H_6N_2$	58.39	7.31	34.22	58.51	7.37	34.12
XIV	218—220	$C_5H_5N_3$	56.15	4.60	39.16	56.06	4.71	39.23
XV	115—116	$C_{12}H_{11}N_3$	72.88	5.56	21.28	73.07	5.62	21.31

a) Lit., mp 123°C, M. C. Schmitt, *Bull. soc. chim. France*, (**3**) **31**, 341 (1904).

b) Lit., mp 182—183°C, F. Arndt, H. Scholz and E. Frobel, *Ann.*, **521**, 95 (1935).

c) Lit., mp 190°C, R. Hull, B. J. Lovell, H. T. Openshaw and A. R. Todd, *J. Chem. Soc.*, **1946**, 357.

d) Lit.,[15)] mp 63—71°C.

signal corresponding to the NH protons in the highly deshielded region, and the doublet of the *N*-methyl protons which was converted into the singlet by the spin-spin decoupling with the NH proton. Also, the addition of deuterium oxide to the pyridine solution of methyl α-cyano-β-methylaminocrotonate (IV) resulted in the collapse of the doublet of the *N*-methyl protons into the singlet. Therefore, on the basis of arguments similar to those set forth above, it is evident that the β-methylamino esters exist exclusively in the chelated enamine form 3.

All the NMR spectra of the α-cyano-β-amino-β-alkylacrylic esters showed two broadened signals, with an equal intensity, in the 9.20—10.02 and 5.85—6.10 ppm ranges. The signal in the lower field is evidently due to the hydrogen-bonded NH proton. Since the signal of the β-alkyl protons suggests the existence of only one species, the broad signal in the higher field cannot be considered as being due to the NH proton of other species. Presumably, this is to be attributed to the non-equivalence of two protons on a nitrogen atom resulting from restricted rotation about the C–N single bond. Consequently, the β-amino esters also exist in the chelated enamine form 3 in solution.

It is interesting to note that the shielding of the hydrogen-bonded NH proton is almost independent of the size of the β-substituted alkyl groups, but decreases with the bulkiness of the substituent on the β-amino groups.

Experimental

NMR Spectra. All the NMR spectra were obtained on a JNM-C-60 high-resolution NMR spectrometer operating at 60 Mc at a temperature of 19—20°C. Proton spin-decoupling experiments at 60 Mc were made by using a Model JNM-SD-20B spin decoupler in the frequency sweep. The chemical shift values are reported in ppm downfield from tetramethylsilane, used as the internal zero of reference. The values are accurate to ±0.025 ppm. Samples were examined in a *ca.* 8% (w/v) solution.

Materials. All the α-cyano-β-amino-β-alkylacrylic esters studied in the present work were prepared from the corresponding α-cyano-β-methoxy-β-alkylacrylic esters[1,14)] and amines. β-Aminocrotononitrile (XIII) was prepared as a stereoisomeric mixture according to the method of Adkins and Whitman,[15)] while α-cyano-β-aminocrotononitriles (XIV and XV) were prepared by the condensation of α-cyano-β-ethoxycrotononitrile[16)] with the corresponding amines. Their physical properties and analytical data are listed in Table 3.

The authors are much indebted to Mr. Jun Uzawa of this Institute for running many of the NMR spectra and Mr. Yasuhiro Hoshino for his technical assistance. This work was supported in part by a grant from the Ministry of Education.

[14)] A. Dornow and E. Schleese, *Chem. Ber.*, **91**, 1830 (1958).

[15)] H. Adkins and G. M. Whitman, *J. Am. Chem. Soc.*, **64**, 150 (1942).

[16)] Y. Urushibara and M. Takebayashi, This Bulletin, **11**, 557 (1936).