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H-N-C-H COUPLING IN THE NMR SPECTRA OF 3-AMINOACRYLIC ESTERS

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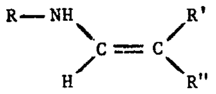
Huisgen *et al*[2] have reported the NMR spectra of some 3-aminoacrylic ester derivatives and shown that a relatively large coupling exists between the proton of the amino group and that of the adjacent methine. We have examined the effect of substituents and stereochemistry on the magnitude of this coupling in an extended series of 3-aminoacrylic esters and nitriles (Table 1).

H-N-C-H coupling constants in compounds of this series in which the amino and ester groups are *cis* to one another are generally higher and less variable (12-15 cps) than in compounds in which the groups are *trans* (7.5 - 14 cps). This may be interpreted in terms of the configuration of the amino and methine protons with respect to each other.



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Conjugation of the nitrogen lone pair with the acrylic ester moiety will induce a partial double bond character in the $-\ddot{N}-C=$ bond so that the amino and methine protons will tend to take up either a *syn* or an *anti*-configuration with respect to each other. In the *cis* compounds intramolecular hydrogen bonding will force these protons into an

TABLE I[3]

Variation in H-N-C-H coupling constants and chemical shifts with variation in substituents in Structure I

R	R'	R"	$J^{4}_{H\text{-}N\text{-}C\text{-}H}$ (cps)	Chemical Shift p.p.m.	
				=CH	-NH-
Methyl	H	CO_2CH	7.5	7.58	5.3
n-propyl	"	"	8.0	7.50	5.8
n-butyl	"	"	8.2	7.39	5.6
iso-propyl[2]	"	"	9.0	7.33	5.4
tert-butyl[2]	"	"	13.0	7.41	5.7
cyclohexyl	"	"	10.0	7.47	4.9
benzyl	"	"	8.0	7.59	5.6
phenyl	"	"	13.0	7.87	9.6
p-tolyl[2]	"	"	13.1	7.91	-
p-anisyl[2]	"	"	13.0	7.84	-
methyl	CO_2CH_3	H	14.0	6.61	-
n-propyl	"	"	13.0	6.63	7.6
n-butyl[2]	"	"	13.0	6.53	7.7
iso-propyl[2]	"	"	13.1	6.56	7.3
tert-butyl[2]	"	"	13.5	6.73	8.0
cyclohexyl	"	"	13.0	6.73	7.8
benzyl	"	"	13.0	6.69	8.0
p-anisyl[2]	"	"	13.0	7.16	-
methyl	"	$CH=CH-CO_2CH_3$	14.0	7.23	8.8
cyclohexyl	"	"	14.0	7.37	9.0
benzyl	"	"	13.5	7.27	9.2
cyclohexyl	$CO_2C_2H_5$	CN	15.0	7.95	6.6
O-chlorphenyl	"	$CO_2C_2H_5$	13.5	8.53	11.3

TABLE I cont'd.

R	R'	R"	$J_{H-N-C-H}$ (cps)	Chemical Shift p.p.m.	
				=CH	-NH-
m-chlorphenyl	$CO_2C_2H_5$	$CO_2C_2H_5$	13.5	8.33	11.0
p-chlorphenyl	"	"	14.0	8.31	11.1
2:3-dichlorphenyl	"	"	13.5	8.5	11.3
2:4-dichlorphenyl	"	"	13.5	8.45	11.3
2:5-dichlorphenyl	"	"	13.5	8.5	11.3
o-tolyl	"	"	13.5	8.55	11.3
m-tolyl	"	"	13.5	8.36	11.0
p-tolyl	"	"	14.0	8.5	11.0
o-aminophenyl	"	"	13.5	8.42	10.8
m-trifluoromethylphenyl	"	"	13.5	8.61	11.3
m-carboxyphenyl	"	"	13.5	8.61	11.3
5-chloro-2-pyridyl	"	"	13.0	9.05	11.2
3-methyl-2-pyridyl	"	"	13.0	9.33	11.3
4-methyl-2-pyridyl	"	"	13.0	9.13	11.1
5-methyl-2-pyridyl	"	"	13.0	9.15	11.1
phenyl	CO_2CH_3	$CH=CH-CO_2CH_3$	13.0	7.73	10.7
2-pyridyl	"	"	12.5	8.55	10.9
3-methyl-2-pyridyl	"	"	12.5	8.65	11.1
4-methyl-2-pyridyl	"	"	12.5	8.5	10.8
5-methyl-2-pyridyl	"	"	12.0	8.45	10.8
phenyl	$CO_2C_2H_5$	CN	13.5	7.87	10.8
p-chlorphenyl	"	"	13.5	7.87	10.8
2:3-dichlorphenyl	"	"	13.0	7.87	11.3
o-tolyl	"	"	13.5	7.87	10.9
m-tolyl	"	"	13.5	7.87	10.8
p-tolyl	"	"	14.0	7.83	10.8

TABLE I cont'd.

R	R'	R"	$J_{H-N-C-H}$ (cps)	Chemical Shift p.p.m.	
				=CH	-NH-
m-tolyl	CN	$CO_2C_2H_5$	14.0	8.48	8.6
phenyl	"	CN	0	8.47	3.4
o-chlorphenyl	"	"	0	8.37	3.4
m-chlorphenyl	"	"	0	8.43	3.5
2:3-dichlorphenyl	"	"	0	8.33	3.1
2:5-dichlorphenyl	"	"	0	8.47	3.1
m-tolyl	"	"	0	8.43	3.4
o-hydroxyphenyl	"	"	0	8.40	3.7
p-hydroxyphenyl	"	"	0	8.25	3.7

anti configuration[2] whereas in the trans compounds one might expect an equilibrium mixture of syn and anti forms. In the n-alkyl series, where there is unlikely to be significant steric interaction between the alkyl group and the acrylic ester moiety, the contribution from the syn and anti forms in the trans compounds will tend to be equal. The lower J values for these compounds relative to the anti oriented cis compounds indicate that a higher coupling constant is associated with the anti than with the syn configuration.

The greater variability of the coupling constants in the trans as compared with the cis series is consistent with the predicted effect of steric factors on the syn/anti equilibrium. J values for trans-3-alkylaminoacrylic esters tend to increase with increasing substitution on the carbon atom adjacent to the nitrogen atom e.g., 1; R = methyl, J = 7.5 cps; R = n-propyl, J = 8.0 cps; R = isopropyl, J = 9.0 cps; R = cyclohexyl, J = 10.0 cps; R = tertbutyl, J = 13.2 cps. Models show that in the syn-configuration the more substituted this carbon atom becomes, the greater is the steric interaction between the alkyl group and the substituent in the 2-position of the acrylic ester. Thus the effect of increasing substitution will be to shift the equilibrium in favour of the anti form leading to the observed increase in coupling constant.

In arylamino acrylic esters the aryl group will be cross conjugated to the α,β-unsaturated ester through the nitrogen lone pair and a co-planar conformation will be induced. In this co-planar situation the amino and methine protons are unable to assume a *syn* configuration because of repulsive interaction between the *ortho* substituent of the aryl nucleus and the 2-substituent of the acrylic esters. It is therefore not surprising that J values for the *trans* arylamino series, where the *anti* configuration is stabilized by steric factors, are of the same order of magnitude (12-14 cps) as those for all *cis* compounds, where the *anti* configuration is stabilized by intramolecular hydrogen bonding.

H-N-C-H coupling is only observed when the exchange rate of the N-H proton is slow relative to the magnitude of the coupling constant, a condition commonly encountered with amide type compounds. In the series studied coupling was observed in the 3-aminoacrylic, aminomethylene malonic and aminomethylene cyanoacetic esters but not in the aminomethylene malononitriles. It would appear that slow N-H proton exchange rates are associated with the presence of an ester group in the molecule i.e. with the vinylogous urethane structure.

The orientations of the groups about the double-bond were determined either from the vinyl coupling constants in the cases where R' or R" = H or from the infra-red frequency of the ester carbonyl (*cis* = 1670 - 1665 cm^{-1}, *trans* = 1710 - 1695 cm^{-1})[2,5].

References

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2. R. Huisgen, Herbig, K., Siegl, A., and Huber, H., *Chem. Ber.* *99*, 2526 (1966).
3. N.M.R. Spectra were determined in deuteriochloroform solution on a Varian A-60 spectrometer.
4. Coupling constants in the present work were determined to the nearest 0.5 cps.
5. W. Bottomley, *Tetrahedron Letters*, In press.