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NMR STEREOSPECIFIC LONG-RANGE COUPLING AND PREFERRED CONFORMATIONS IN SOME (*E*)- AND (*Z*)-α-PHENYL-β-[2-(N-METHYL)NITROPYRROLYL] ACRYLIC ACIDS

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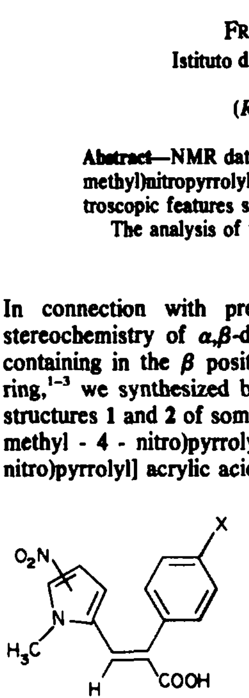
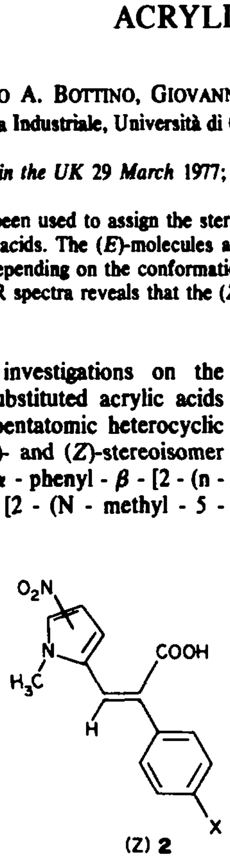
Abstract—NMR data have been used to assign the stereochemistry to some new (*E*)- and (*Z*)-α-phenyl-β-[2-(N-methyl)nitropyrrolyl]acrylic acids. The (*E*)-molecules are biased in the *s-cis* conformation showing NMR spectroscopic features strictly depending on the conformation.

The analysis of the NMR spectra reveals that the (*Z*)-isomers exist also in the *s-cis* conformation.

In connection with previous investigations on the stereochemistry of α,β-diaryl substituted acrylic acids containing in the β position a pentatomic heterocyclic ring,[1-3] we synthesized both (*E*)- and (*Z*)-stereoisomer structures 1 and 2 of some new α - phenyl - β - [2 - (n - methyl - 4 - nitro)pyrrolyl] and [2 - (N - methyl - 5 - nitro)pyrrolyl] acrylic acids.



(E) 1

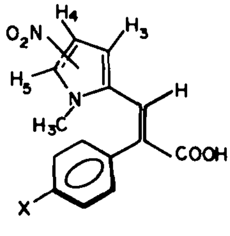


X = H, CH_3, Cl.

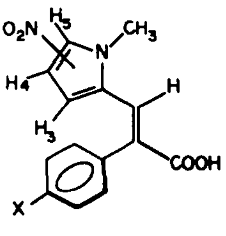
(Z) 2

Differently from the (*E*) - α - phenyl - β - (2 - furyl)acrylic acids[2,3] which exist in the *s-cis* conformation because of an electrostatic repulsive factor,[3] the (*E*)- acids 1 are biased in the *s-cis* conformation by steric reasons as clearly evidenced by molecular models.

Therefore these molecules represent an interesting molecular model to observe the relation between the NMR spectroscopic features and the conformational behaviour, in all the series of the (*E*)-α,β-diaryl acrylic acids.[3]



s-trans



s-cis

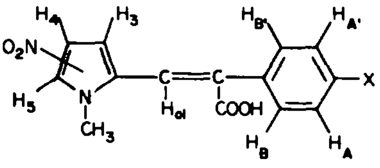
RESULTS AND DISCUSSION

The assignments of the configuration of the acids 1 and 2 have been accomplished by the position of the olefinic proton in the NMR spectrum. As previously observed for the α,β-di-(2-thienyl)acrylic acids[4] and for the α-phenyl-β-(2-thienyl)[1] and β-(2-furyl)acrylic acids,[2] the resonance lines of ethylene proton in the (*Z*)- acids 2 lie at higher fields compared with the corresponding proton in the (*E*)-isomers 1 (Table 1), in both series of 4-nitro and 5-nitro derivatives, this being due to an anisotropic deshielding effect of the CO group on the near ethylene proton in the (*E*)-isomers 1.[1,2,4,5]

IR CO stretching frequencies are in agreement with these assignments (Table 2). In fact, because of the conjugation with the pyrrole ring through the ethylene bond, in all the (*E*)-compounds, the CO stretching frequencies appear at lower wavenumbers[1,2,4,6] compared with the corresponding (*Z*)-isomers where the CO group is twisted out of the molecular plane.[7]

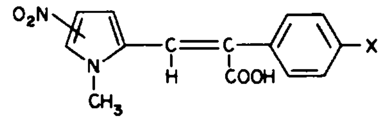
The (*E*)-acrylic derivatives 1 are an interesting *s-cis* molecular model which should exhibit the postulated diamagnetic shift of the proton in position 3- of the

Table 1. Chemical shifts (δ, ppm) of the protons of the acids 1 and 2



		H_α	H_5	H_3	$H_{BB'}$	$H_{AA'}$
	$4\text{-}NO_2$					
X=H	(*E*)	7.65	8.09	5.60	(7.12–7.55)	
	(*Z*)	6.97	8.10	6.95	(7.35–7.63)	
CH_3	(*E*)	7.63	8.08	5.73	7.30	7.11
	(*Z*)	6.90	8.08	6.91	7.45	7.26
Cl	(*E*)	7.70	8.10	5.73	7.55	7.30
	(*Z*)	6.96	8.10	6.93	7.55	7.55
	$5\text{-}NO_2$					
X=H	(*E*)	7.68	7.00	5.31	(7.12–7.50)	
	(*Z*)	7.01	7.28	6.48	(7.33–7.63)	
CH_3	(*E*)	7.63	7.00	5.37	7.20	7.08
	(*Z*)	7.00	7.31	6.50	7.48	7.30
Cl	(*E*)	7.68	7.03	5.40	7.43	7.26
	(*Z*)	7.08	7.30	6.50	7.63	7.52

Table 2. Some[a] physical properties of the acids 1 and 2



		$IR(\nu_{C=O}, cm^{-1})$	m.ps. (°C)	Crystallization solv.
	4-NO_2			
X=H	(*E*)	1660	246-7	ETOH/H_2O
	(*Z*)	1700	207-8	ETOH/H_2O
CH_3	(*E*)	1660	257-8	ETOH/H_2O
	(*Z*)	1710	189-90	ETOH/H_2O
Cl	(*E*)	1665	261-2	ETOH/H_2O
	(*Z*)	1710	179-80	benzene/cyclohexane
	5-NO_2			
X=H	(*E*)	1680	203-4	toluene/cyclohexane
	(*Z*)	1725	134-5	toluene/cyclohexane
CH_3	(*E*)	1670	213-4	ETOH/H_2O
	(*Z*)	1730	164-5	ETOH/H_2O
Cl	(*E*)	1680	209-10	benzene/cyclohexane
	(*Z*)	1725	169-71	benzene/cyclohexane

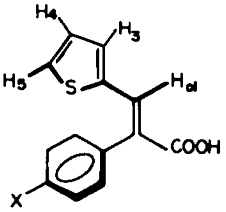
[a] Satisfactory combustion analytical data for C, H and N were found for these compounds.

heterocyclic ring[3,4] owing to the anisotropic shielding effect of the circulating π-electrons of the phenyl ring. As observed from the inspection of the room temperature NMR data of the (*E*)-acids 1 (Table 1) the 3-heterocyclic proton is remarkably shielded. This shielding effect is strongly evidenced by comparison with the chemical shift values of the same proton in the corresponding (*Z*)-isomers, where no interaction with the phenyl electronic current is possible.

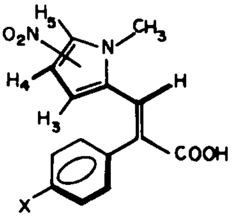
Moreover the inspection of the Table 1 reveals no substantial differences in each pair of (*E*)- and (*Z*)-stereoisomers on the chemical shift values of the 4-proton as well as of the 5-proton and of those of the corresponding benzene protons (Table 1). This indicates that the observed diamagnetic shift on the 3-proton of the (*E*)-isomers is due exclusively to a steric and conformational factor.

The availability of molecules in opposite conformations, i.e. the (*E*) - α - phenyl - β - (2 - thienyl)acrylic acids in the *s-trans* conformation[3] and the (*E*) - α - phenyl - *b* - [2 - (N - methyl)nitropyrrolyl] acrylic acids 1 in the *s-cis* conformation, allowed us to observe the stereospecificity of the coupling (W_5-plan) between the ethylene proton and the heterocyclic protons which are separated by five bonds ($J^5_{H,H}$), i.e. H_5 or H_4.

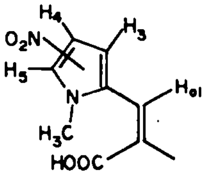
As observed for the aromatic[8,9] and heterocyclic aldehydes,[9,10] we have noticed the necessity of a *trans* coplanar disposition (dihedral angle 180°)[9] for the coupling to occur.



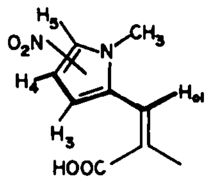
$J^5_{H_{ol},H_5} = 0{\cdot}6Hz$



$J^5_{H_{ol},H_4} = 0{\cdot}5Hz$



s-trans



s-cis

In fact in the case of (*E*) - α - phenyl - β - (2 - thienyl)acrylic acids we have observed the coupling between the ethylene proton and H_5 ($J^5_{H,H} = 0.6$ Hz), whereas no coupling is present between ethylene proton and H_4 ($J^5_{H,H} = 0$ Hz).

On the contrary in the case of (*E*) - α - phenyl - β - [2 - (N - methyl - 4 - nitro)pyrrolyl]acrylic acids no coupling is noticed between ethylene proton and H_5 according to the *cis* coplanar disposition (dihedral angle 0°) of the two protons, whereas in the corresponding 5-nitro derivatives a coupling H_4-ethylene proton ($J^5_{H,H} = 0.5$ Hz) is observed. Likewise, in the case of the (*E*) - α - phenyl - β - (2 - furyl)acrylic acids populating only the *s-cis* conformation we have observed a spin–spin coupling ($J^5_{H,H} =$ 0.6 Hz) between the olefinic proton and the 4-heterocyclic proton, whereas no coupling occurs with the 5-proton.

The compounds 1 and 2 show a long-range spin–spin coupling between H_3 and the ethylene proton (0.5 Hz); consequently this latter signal appears as an unresolved multiplet (doublet of doublet).

In the case of the (*Z*) - α - phenyl - β - [2 - (N - methyl)nitropyrrolyl]acrylic acids 2 the inspection of the molecular models reveals that the *s-trans* conformation is more hindered than the *s-cis* because of the steric interaction between the N-Me and the adjacent carboxyl group. Because of the very low solubility of these products it was impossible to perform NMR low temperature spectra to investigate on the population ratio of the two rotamers.

However in the (*Z*)-4-nitro-derivatives 2 no stereospecific long-range coupling is observed in the NMR room temperature spectrum between the 5-proton and the olefinic proton, whereas in the (*Z*)-5-nitro corresponding compounds the signal of the 4-heterocyclic proton shows a stereospecific coupling ($J^5_{H,H}$) of 0.5 Hz.

This value is identical to that observed in the series of the corresponding (*E*)-5-nitro isomers 1. Since the value of the coupling constant is averaged depending on the population ratio of the two rotamers, the presence of the only *s-cis* rotamer can be suggested.

EXPERIMENTAL

The samples of the (*E*)- and (*Z*) - α - phenyl - β - [2 - (N - methyl)nitropyrrolyl]acrylic acids were prepared with the Perkin reaction by refluxing (1 hr) equimolar amounts of the 5- or 4-nitrosubstituted N-methyl-2-formyl-pyrrole and the *para*-substituted phenylacetic acid in Ac_2O with tri-ethylamine as catalyst. In the case of the 4-nitro-pyrrolyl derivatives the product was treated as described.[1]

Isomeric ratio (*E*)/(*Z*) was 3:1. The mixture of the reaction of the 5-nitropyrrolyl compounds was poured into diluted HCl aq. The separated solid after filtration was absorbed on alumina column and eluted with acetone-H_2O 1:1. Isomeric ratio (*E*)/(*Z*) was about 10:1.

M.ps and crystallization solvents are reported in the Table 2. NMR spectra were performed on 4% solns with *ca.* 1% of TMS as internal standard. A Varian A-60 D spectrometer was used. In all cases DMSO-d_6 of commercial quality was employed.

IR spectra were measured on a Perkin Elmer 237 spectrophotometer in KBr.

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