Tetrahedron. Vol. 31, pp. 2445 to 2447. Pergamon Press 1975. Printed in Great Britain

CONFORMATIONAL ANALYSIS OF SOME (*E*)-α-PHENYL-β-(2-THIENYL)- AND -(2-FURYL)ACRYLIC ACIDS

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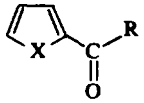
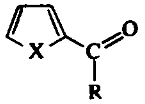
(*Received in UK* 10 *May* 1975; *accepted for publication* 2 *June* 1975)

Abstract—NMR spectral data of some (*E*)-α-phenyl-β-(2-thienyl) acrylic acids indicate that these compounds exist in the preferred *s-trans* conformation. In the case of (*E*)-α-phenyl-β-(2-furyl)acrylic acids and their methyl esters the presence of only *s-cis* rotamer has been established.

INTRODUCTION

Some recent reports[1-12] state that the 2-thienyl carbonyl derivatives exist exclusively in the *s-trans* conformation, and therefore both the presence of the *s-cis* conformation and the free rotation of the CO group may be excluded.


s-trans


s-cis

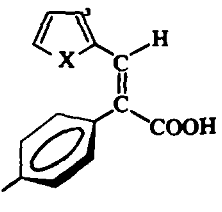
According to some authors[1,10] the reason for this lies both in a greater thermodynamic stability of the C=C–C=O chain in the *s-trans* conformation, and in a repulsive interaction between the double bond $C_2{=}C_3$ of the heterocyclic nucleus and the negatively charged CO oxygen, which seems to reduce the stability of the *s-cis* structure.

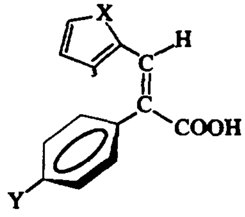
It is also postulated[10] that there is an attractive electrostatic interaction between the thiophene sulfur and the CO oxygen, which is supposed to contribute to the stability of *s-trans* conformation. On the other hand, recent CNDO/2 theoretical calculations[12] on thiophene-2-carboxaldehyde seem to exclude this effect.

In contrast, the 2-carbonyl-furan derivatives show the presence of both the rotamers,[1,3,9,10,13-17] due to electrostatic repulsion between the two O atoms which would produce an increase of the energy of the *s-trans* conformation thus allowing the existence of a *s-cis* rotamer.[10]

In connection with previous studies on 2-carbonyl substituted heterocyclic systems[11] we carried out a NMR study in order to investigate conformational preferences of (*E*)-α-phenyl-β-(2-thienyl)acrylic acids 1 (X = S)[18] and (*E*)-α-phenyl-β-(2-furyl)acrylic acids 1 (X = O).[19] These acids could exist in both $\mathbf{1_a}$ (*s-trans*) and $\mathbf{1_b}$ (*s-cis*) conformations and represent a useful system in verifying whether the above factors affecting the conformational preferences are still operative. Even in these compounds an electrostatic interaction is possible between the heteroatom and the π cloud of the phenyl ring which has been shown to be perpendicular to the molecular plane.[20]

Such interaction could affect the stability of the $\mathbf{1_a}$ conformer with respect to the corresponding $\mathbf{1_b}$.

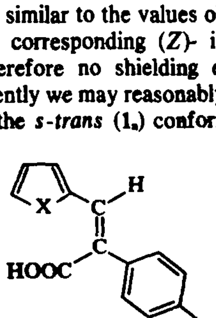

$\mathbf{1_a}$(*s-trans*)


$\mathbf{1_b}$(*s-cis*)

X = O, S
Y = H, CH_3, Cl, NO_2

RESULTS AND DISCUSSION

The NMR spectra of (*E*)-α-phenyl-β-(2-thienyl)acrylic acids 1 (X = S) do not change when the samples are cooled down to −90°. This could be caused either by a fast rotation averaging the signals of the two rotamers or by the presence of a single species. Because of the conjugation between thiophene nucleus and the carboxyl group through the ethylenic bond,[18] the barrier to the rotation is expected to be similar to that observed in the 2-carbonyl thiophene derivatives,[21] and therefore higher than the value required, on the NMR time scale, for an averaging process to occur. This suggests the presence of only one rotational isomer. From the chemical shift values of the proton in position 3 of the thiophene ring it is possible to establish whether $\mathbf{1_a}$ (*s-trans*) or $\mathbf{1_b}$(*s-cis*) is the existing conformation. The $\mathbf{1_b}$ conformation should correspond to a diamagnetic shift of the resonance absorption of the 3-proton compared with the reported values for the same proton in 2-substituted thiophenes owing to the shielding effect of the electronic current of the benzene ring.[22] Actually the 3-proton chemical shift values (Table 1) are included in the normal range for the 3-proton of the variously 2-substituted thiophenes[23] and are similar to the values observed for the same proton in the corresponding (*Z*)- isomers[18] 2 (X = S) (Table 1). Therefore no shielding effect can be noticed, consequently we may reasonably suggest that these acids occur in the *s-trans* ($\mathbf{1_a}$) conformation.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X = O, S
Y = H, CH_3, Cl, NO_2

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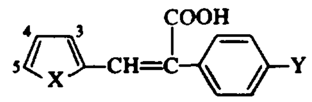
Table 1. Chemical shifts (δ, ppm) of the 3-, 4- and 5-protons of the heterocyclic ring



X	Y	H_3 (*E*)	H_3 (*Z*)	H_4 (*E*)	H_4 (*Z*)	H_5 (*E*)	H_5 (*Z*)
S	H	7·16	(7·3–7·5)	6·92	7·03	(7·3–7·5)	(7·3–7·6)
S	CH_3	(7·10–7·30)	(7·2–7·4)	6·92	7·03	(7·1–7·4)	(7·3–7·5)
S	Cl	7·40	(7·3–7·5)	7·03	7·10	7·53	7·63
S	NO_2	7·41	7·55	7·07	7·19	7·63	7·80
O	H	5·77	6·63	6·12	6·32	7·18	(7·1–7·4)
O	CH_3	5·78	6·60	6·12	6·28	7·20	7·25
O	Cl	5·93	6·67	6·18	6·30	7·20	7·28
O	NO_2	6·33	6·91	6·46	6·58	7·52	7·65

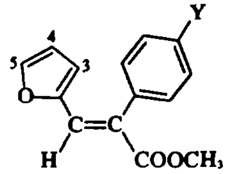
On the other hand the resonance lines of the 3-proton of the (*E*)-α-phenyl-β-(2-furyl)acrylic acids **1** (X = O) exhibit a shielding effect which is strongly evidenced (Table 1) by comparison with resonance absorption of the corresponding proton in the (*Z*)- isomers **2** (X = O). In fact in these latter compounds no interaction with the electronic current of the far benzene ring is possible, thus 3-proton absorptions remain within the normal lower field values. Moreover no substantial differences are noticed in the chemical shifts of the 4-proton as well as of the 5-proton in each pair of (*E*)- and (*Z*)-stereoisomers, thus indicating that the observed shielding effect on the 3-proton of the (*E*) isomers is caused exclusively by a conformational factor. Because of the very low solubility of these acids at temperatures below −70°, we prepared the corresponding methyl esters to investigate low temperature NMR spectra in order to provide insight on the population of the $\mathbf{1_a}$ and $\mathbf{1_b}$ rotamers. NMR spectral features of these esters are in fact strictly similar to their parent acids (Table 2). No broadening of the resonance lines of the heterocyclic ring protons is observed when the samples are cooled down to −120°. This supports the existence of only one rotamer, which reasonably can be indicated as the $\mathbf{1_b}$ (*s-cis*) because of the observed shielding effect on the 3-proton of the furyl ring. The existence only of the $\mathbf{1_b}$ (*s-cis*) conformation for the (*E*)-α-phenyl-β-(2-furyl)acrilic acids and their methyl esters could be justified by a lowering of the $\mathbf{1_a}$ conformation stability because of an electrostatic repulsion between the negative charged heterocyclic oxygen and the π cloud of the benzene nucleus. A similar electrostatic repulsion seems to be responsible for the participation of the *s-cis* rotamer in the conformational equilibrium of the 2-furyl-carbonyl compounds.[10]

EXPERIMENTAL

The samples of the (*E*)- and (*Z*)-α-phenyl-β-(2-thienyl)acrylic acids and α-phenyl-β-(2-furyl)acrylic acids were prepared by a Perkin reaction as described.[18,19] The methyl esters of (*E*)-α-phenyl-β-(2-furyl)acrylic acids were prepared by refluxing (3 hr) the corresponding acids in MeOH in the presence of a trace of H_2SO_4. The mixture was poured into a 2% NaOH aq. The solid was filtered off and crystallized from EtOH-H_2O 1:1. M.ps and chemical shifts values of the heterocyclic protons are reported in Table 2.

NMR spectra were performed on 5% solns with *ca.* 1% of TMS as internal standard. A Varian A-60 D spectrometer was used. In all cases $CDCl_3$ of commercial quality was employed except for the compounds **1** and **2**: X = S, Y = Cl, NO_2 where acetone-d_6 was used, and **1** and **2**: X = O, Y = NO_2 where dimethylsulfoxide was used.

Table 2. M.ps (°C) and heterocyclic proton chemical shifts (δ, ppm) of the methyl esters of **1** (X = O)[a]



	m.p.	H_3	H_4	H_5
Y = H	92	5·78	6·22	7·15–7·45
CH_3	93	5·82	6·22	7·32
Cl	82	5·98	6·30	7·32
NO_2	94	6·22	6·38	7·38

[a] Satisfactory combustion analytical data for C, H (±0·3%) were found for these compounds.

Low temperature NMR spectra of (*E*)-α-phenyl-β-(2-thienyl)acrylic acids were performed on ethanol-d_6, whereas a mixture of acetone-d_6-deuterochloroform-methanol-d_4 respectively 4:2:1 was employed for the methyl esters.

Acknowledgements—The authors are grateful to the Consiglio Nazionale delle Richerche of Italy for financial support.

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