

Available online at www.sciencedirect.com



Journal of Molecular Structure 744-747 (2005) 273-276

Journal of MOLECULAR STRUCTURE

www.elsevier.com/locate/molstruc

Conformations of *E*-2-phenyl-3(2'-furyl)propenoic acid and its methyl ester in various solvents—an NMR study

P. Forgó, K. Felföldi, I. Pálinkó*

Department of Organic Chemistry, University of Szeged, Dóm tér 8, Szeged H-6720 Hungary

Received 6 September 2004; revised 11 November 2004; accepted 11 November 2004 Available online 18 January 2005

Abstract

The conformations of E-2-phenyl-3(2'-furyl)propenoic acid and its methyl ester were investigated by NMR spectroscopy. Applying various solvents (methanol, chloroform and dimethyl sulfoxide) the possible conformers in solutions were studied by two-dimensional NOESY measurements. Irrespective to the solvents and whether the investigated moiety was the ester or the acid dimer, no conformational preferences could be identified experimentally.

© 2005 Elsevier B.V. All rights reserved.

Keywords: E-2-phenyl-3(2'-furyl)propenoic acid and its methyl ester; 2D NOESY measurements; Conformers in various solvents (methanol, chloroform or dimethyl sulfoxide).

1. Introduction

Cinnamic acid derivatives are important intermediates in the shikimic acid metabolic pathway of higher plants. They also have interesting structure-forming properties via strong OH···O hydrogen bonds (in acids [1]) in solution and C–H···O close contacts (in acids [1] and also in esters [2]) in the solid state. Upon replacing the phenyl group with heteroatom-containing aromatic ring, like a furyl group in position 3, further possibilities for aggregate formation opens via (aromatic)C–H···(furyl)O intermolecular hydrogen bonds [3].

Theoretically, intramolecular C–H···O bonds may also appear making certain conformers predominant. These interactions in various 2-furyl- and 2-pyridyl-substituted 3-phenyl propenoic acids have already been investigated computationally [4]. In order to make ab initio calculations feasible these systems were simplified: monomeric acids were used instead of the dimers, even though the latter are known to be typical forms of appearance even in the gas phase. This type of simplification seems to be general [5], to our knowledge conformational analysis by computations for dimeric acids has not been performed yet. After studying the potential energy surfaces of these simplified systems [4] one can envisage various conformers. Expectedly, when solvent is present certain conformers may predominate, presumably depending on the properties of the solvent. Thus, it may be of interest to study the effect of solvents on the conformational properties of the molecules. A handy method for such an investigation is NMR spectroscopy.

In this contribution results of 2D NOESY measurements are described. The study aimed at learning about possible conformational preferences of E-2-phenyl-3(2'-furyl)propenoic acid and its methyl ester in various solvents.

2. Experimental

2.1. Materials

The model compounds were E-2-phenyl-3(2'-furyl)propenoic acid (1) and its methyl ester (2) (Fig. 1).

They were prepared by a modified version of the Perkin condensation [6] and esterification. For the synthesis of the acid 2-furylaldehyde (Aldrich) and phenylacetic acid (Aldrich) were applied, esterification was done in dimethyl sulfoxide (DMSO)/KOH/CH₃Cl solution of the acid [7].

^{*} Corresponding author. Tel.: +36 62 544 288; fax: +36 62 544 200. *E-mail address:* palinko@chem.u-szeged.hu (I. Pálinkó).

^{0022-2860/\$ -} see front matter © 2005 Elsevier B.V. All rights reserved. doi:10.1016/j.molstruc.2004.11.052





Fig. 2. The *s*-trans and the *s*-cis conformers of the ester (2) following Ref. [10]

2.2. NOESY measurements

Three different solvents (DMSO- d_6 , chloroform-d and methanol- d_4) were used to study dipolar interactions of

the title molecules. Two-dimensional NOESY experiments were carried out at room temperature on a Bruker DRX 500 instrument in dilute solution to avoid the conformation influencing effects of intermolecular hydrogen bonds between the solute molecules. 0.6 ml of the solution was transferred to a 5 mm diameter Wilmad NMR tube and the standard phase sensitive NOESY pulse sequence (TPPI) was used to obtain the twodimensional maps. As a result of the good ¹H NMR spectral dispersion, only a small fraction of the spectra $(\sim 3.5 \text{ ppm}, 1 \text{ K complex datapoints})$ at the higher chemical shifts was detected with a carrier frequency placed at 6.8 ppm. 64 transients were collected to each of the 256 F_1 increments and 2 s relaxation delay was set between each individual transients, resulting in 14.5 h long experimental time. Squared cosine function was applied as window functions in both detected and incremented dimensions prior to Fourier transformation and a standard baseline correction function was used in both dimensions in order to remove baseline distortions from the two-dimensional map.

For visualisation, HF/3-21G optimised conformers were used, found typical after performing a preliminary conformational search (HyperChem package [8], PM3 semi-empirical code [9]).



Fig. 3. The HF/3-21G optimised typical conformers for the ester: (a) *s-cis* and (b) *s-trans*



Fig. 4. The HF/3-21G optimised typical conformers for the acid dimers: (a) *s-cis–s-cis* and (b) *s-trans–s-cis*

Sable 1
H-NMR chemical shifts (in ppm) of 1 and 2 in three different solvents (CDCl ₃ , methanol-d ₄ (MeOD) and DMSO-d ₆)

#	1			2		
	CDCl ₃	MeOD	DMSO-d ₆	CDCl ₃	MeOD	DMSO-d ₆
=CH	7.81	7.70	7.58	7.73	7.67	7.62
СООН	11.69	-	12.59	_	-	_
COOMe	_	-	-	3.76	3.73	3.69
Ar	7.22-7.46	7.17-7.41	7.20-7.45	7.22-7.45	7.15-7.43	7.20-7.50
3'	5.86	5.80	5.93	5.77	5.81	5.97
4'	6.25	6.27	6.43	6.24	6.29	6.44
5'	7.36	7.42	7.66	7.35	7.45	7.67

3. Results and discussion

3.1. Preliminary considerations

The 2D NOESY measurements were performed in three different solvents, each representing distinct solvent types (DMSO-dipolar, aprotic; methanol-polar, protic; chloro-form-(nearly) apolar) were performed. It was expected that the analysis of these measurements would indicate preferred arrangements from the possible conformers. These possible conformer classes are the *s*-trans and *s*-cis arrangements for the ester and the *s*-trans–*s*-trans, *s*-trans–*s*-cis, and *s*-cis–*s*-cis arrangements for the acid dimers, following the notation of Ref. [10] (i.e. concentrating of the relative positions of the olefinic double bound and the conjugated double bond in the furyl ring) (Fig. 2).

Examples of the ab initio optimised conformers are depicted in Figs. 3 and 4 for the ester and the acid dimer,

respectively. It is to be noted that a preliminary conformational search (see Section 2) could not identify *s*-*trans*-*strans* arrangement for the acid dimer.

3.2. NMR measurements

Three different solvents (DMSO- d_6 , methanol- d_4 and chloroform-d) were selected in order to study the solution structure of the two model compounds (1 and 2). Table 1 shows the ¹H-NMR chemical shift assignment for the two compounds.

Small but significant changes in chemical shifts were observed as the solvent was changed (Fig. 5).

The H-5' proton of the furan ring was the most sensitive to the solvent: approximately 0.3 ppm chemical shift increase was observed in DMSO relative to that was found in chloroform. H-3' and H-4' protons of the furan ring



275



Fig. 6. 2D NOESY spectrum of (a) 1 (in CDCl₃) and (b) 2 (in CDCl₃).

carried an approximate 0.2 ppm chemical shift increase. The chemical shift of the olefinic proton was increased by 0.2 ppm as we went to hydrophilic solvents from chloroform. Less important and significant was the solvent dependent chemical shift change in the methoxy protons.

The solution conformation was monitored by the application of two-dimensional NOESY experiments. The good dispersity of the ¹H-NMR spectrum allowed us to investigate the NOESY interactions of the model compounds in these solvents (Fig. 6).

Since H-3' and H-4' were separated well from the aromatic protons resonating at higher chemical shifts, it was straightforward to analyse the interactions of these hydrogens. The close space proximity results in a strong NOE signal in the spectrum for both compounds regardless of the solvent. The simultaneous appearance of the NOESY cross-peaks of H-3' to H-2", H-6" and =CH indicate that both furyl and phenyl groups have fast rotational freedom in all solutions. Consequently, preferred rotamer populations of the furyl ring based on NOESY interactions between H-3'-=CH and H-3'-H-2'',H-6'' cannot be unambiguously determined. The H-4' proton has only correlations to protons in the furyl ring (H-3' and H-5'). The labile carboxylic OH protons disappear from the methanol-d₄ spectra due to replacement with deuterium, furthermore, the spectra recorded in DMSO-d₄ and CDCl₃ solutions show broad signals as a result of the fast exchange with the solvent residual water, resulting in no NOESY correlations to these protons.

4. Conclusions

Through studying the 2D NOESY spectra of both molecules in various solvents (CDCl₃, methanol- d_4 or DMSO) it has been learnt that both substituents of the propenoic acid retain high rotational freedom, thus, there is no predominating conformer irrespective to the solvent and the two molecules studied.

Acknowledgements

This work was supported by the National Science Fund of Hungary through grant OTKA T034184. The financial help is highly appreciated.

References

- [1] Á. Kukovecz, I. Pálinkó, J. Mol. Struct. 482/483 (1999) 463.
- [2] J.T. Kiss, K. Felföldi, T. Körtvélyesi, I. Pálinkó, Vib. Spect. 22 (2000) 63.
- [3] J.T. Kiss, K. Felföldi, Z. Paksi, I. Pálinkó, J. Mol. Struct. 651–653 (2003) 253.
- [4] T. Körtvélyesi, Á. Kukovecz, S. Lovas, I. Pálinkó, J. Mol. Struct., THEOCHEM 535 (2001) 139.
- [5] Á. Dörnyei, I.G. Csizmadia, J. Mol. Struct., THEOCHEM 666–667 (2003) 135.
- [6] K. Felföldi, M. Sutyinszky, N. Nagy, I. Pálinkó, Synth. Commun. 30 (2000) 1543.
- [7] L. Boros, K. Felföldi, I. Pálinkó, Molecules 9 (2004) 256.
- [8] HyperChem 7.0, Hypecube Inc., Gainesville, FL, USA, (2001).
- [9] J.J.P. Stewart, J. Comput. Chem. 209 (1989) 221.
- [10] S. Fisichella, G. Mineri, G. Scarlata, D. Sciotto, Tetrahedron 31 (1975) 2445.