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Molecular structure, experimental and theoretical ^{1}H and ^{13}C NMR chemical shift assignment of cyclic and acyclic α,β-unsaturated esters

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The experimental ^{1}H and ^{13}C NMR spectra of 13 phenyl cinnamates and four 4-methylcoumarins were investigated and their chemical shifts assigned on the basis of the two-dimensional spectra. For the unsubstituted cinnamic acid phenyl ester, optimized molecular structures were calculated at a B3LYP/6-311++G(d,p) level of theory. ^{1}H and ^{13}C NMR chemical shifts were also calculated with the GIAO method at the B3LYP/6-311 + G(2d,p) level of theory. The comparison between experimental and calculated NMR chemical shift suggests that the experimental spectra are formed from the superposition spectra of the two lowest energy conformers of the compound in solution. The most stable s-cis configuration found in our studies is also the conformation adopted for a related phenyl cinnamate in solid state. The experimental results were analyzed in terms of the substituent effects. Copyright © 2013 John Wiley & Sons, Ltd.

Keywords: ^{13}C NMR; ^{1}H NMR; 4-methylcoumarins; conformations; DFT; GIAO; phenyl cinnamates; α,β-unsaturated esters

INTRODUCTION

Cinnamates and coumarins are important compounds widely distributed in the plant kingdom. They have varied bioactivities and applications in cosmetics, pharmaceuticals, food, and agrochemicals.

Compounds with the backbone of cinnamates possess various biological activities such as antioxidant, fungicide, anti-inflammatory, anticancer,[1–3] and antialopecic[4] properties. Some cinnamates are inhibitors of plant growth and in the future could play an important role as agrochemicals against some important pests. Particularly, aryl cinnamates have been used as intermediates for diverse heterocyclic compounds, such as flavanones,[5] chromones,[6] pirazols,[7] dihydrocoumarins,[7,8] and benzofuranones.[9] Additionally, coumarins and their derivatives are widely applied. They are mainly used as active components in the formulation of pesticides and additives in the manufacture of pharmaceuticals, food, and cosmetics.[10]

Structurally, the cinnamate phenyl esters are composed of two rigid phenyl rings connected by a relatively flexible α,β-unsaturated carbonyloxy fragment (−CH = CH–C(O)–O–). In this skeleton, the mobilities around two chemical bonds are important to consider: (i) the C–O– ester linkage, and (ii) the bond between the carbonyl group and the unsaturation = CH–C(O). The conformation of esters of the type –C(O)–O–R (case 1) has been the subject of essential investigation from a very long time, revealing that the Z conformation is favored over the E counterpart[11–15] (**Scheme 1**). One of the reasons is the steric repulsion between the R groups in the E conformation. Also, the large rotational barrier about the C–O ester bond is attributed to resonance delocalization of the lone pair electrons of the ester oxygen.[14,15]

Looking at the C–C bond between the carbonyl and the unsaturation (case 2), the stability of the possible conformations in α,β-unsaturated carbonyl compounds must be considered. The conjugative stabilization favors the s-trans over the s-cis conformer (**Scheme 2**). However, Abraham *et al.*[16] examined the

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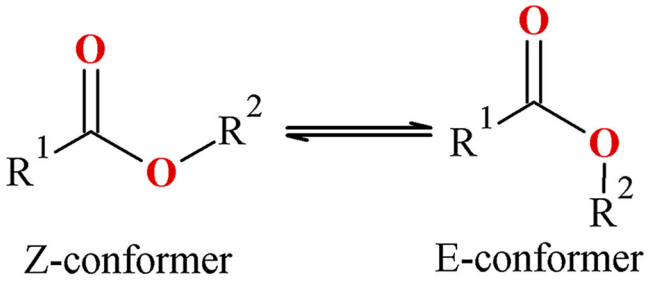
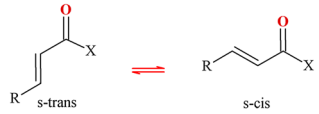


Scheme 1. Conformations in the ester linkage.



Scheme 2. Conformations in α,β-unsaturated carbonyl compounds.

conformational stability of such class of compounds by theoretical calculations and Lanthanide Induced Shift NMR Analysis and concluded that in methyl cinnamate, the s-cis conformation is more stable than the s-trans, the percentage of the latter configuration being only 32%.

The phenyl cinnamates investigated in this study were obtained using some modified methods from phenols and cinnamic acids,[17–19] and 4-methyl coumarins were prepared from *O*-allylation of 7-hydroxy-4-methylcoumarin and subsequent Claisen rearrangement of the products.[20]

Here, we present a detailed ^{1}H and ^{13}C NMR study and signal assignments for 17 cinnamates and 4-methylcoumarins for the first time. In order to try to clarify some questions about structural properties and preferred conformations of the phenyl cinnamate series, we have taken the unsubstituted phenyl cinnamate (1) as a model and used the density functional theory for the conformational searching and the geometry optimization of the most stable conformers. For the most stable conformers, the ^{1}H and ^{13}C chemical shifts were calculated to aid in the assignment of experimental signals. Partial reports of experimental spectra of some related compounds have been published before.[4,19,21–27]

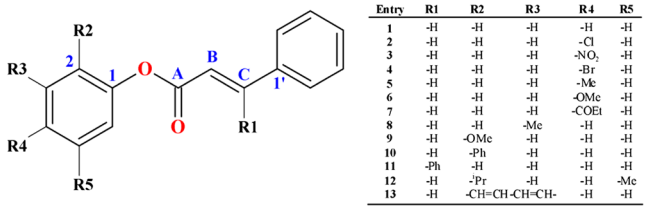
EXPERIMENTAL

NMR measurements

The synthesis of the phenyl cinnamates **1–13** (**Fig. 1**) and 4-methylcoumarins **14–17** (**Fig. 2**) has been described earlier.[20–23] Room temperature ^{1}H (400.1 MHz) and ^{13}C (100.6 MHz) NMR measurements were performed on a Bruker Avance DPX-400 spectrometer. The chemical shift standard was internal tetramethylsilane for ^{1}H and ^{13}C ($\delta = 0$ ppm). Digital resolutions in the 1D NMR spectra were 0.14 Hz/point for ^{1}H, 0.24 Hz/point for ^{13}C, pulse angles were ca. 30°, and sample concentrations were 0.095–0.230 M. Signal assignments were assisted by APT (attached-proton test), DEPT (Distortionless Enhancement by Polarization Transfer), gs-COSY (gradient select COrrelation SpectroscopY), gs-HMQC (gradient select Heteronuclear Multiple Quantum Coherence), and gs-HMBC (gradient select Heteronuclear Multiple Bond Coherence) experiments using standard Bruker software.

Computational details

The density functional theory[28–30] was used to perform the conformational analysis of **1**, in order to determine its more stable conformers.



Entry	R1	R2	R3	R4	R5
1	-H	-H	-H	-H	-H
2	-H	-H	-H	-Cl	-H
3	-H	-H	-H	$-NO_2$	-H
4	-H	-H	-H	-Br	-H
5	-H	-H	-H	-Me	-H
6	-H	-H	-H	-OMe	-H
7	-H	-H	-H	-COEt	-H
8	-H	-H	-Me	-H	-H
9	-H	-OMe	-H	-H	-H
10	-H	-Ph	-H	-H	-H
11	-Ph	-H	-H	-H	-H
12	-H	-^{i}Pr	-H	-H	-Me
13	-H	-CH=CH-	-CH=CH-	-H	-H

Figure 1. Structure, numbering, and identification of phenyl cinnamates **1–13**

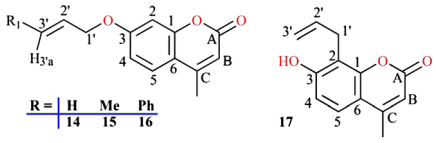


Figure 2. Structure, numbering, and identification of 4-methylcoumarins **14–17**

The calculations were accomplished using Becke's three-parameters hybrid density functional[31] with the gradient-corrected correlation functional due to Lee, Yang, and Parr,[32] a combination that gives rise to the well-known B3LYP method. Potential energy curves of **1** were obtained by performing a relaxed scan around the $C_1 - O$, $O - C_A$ and $C_A - C_B$ bond angles at a B3LYP/6-31g(d) level of theory, see **Fig. 1** for labels.

The geometry of those conformers that became a minimum on the potential energy curves mentioned in the last paragraph was further optimized at a B3LYP/6-311++g(d,p) level of theory. The Hessian matrix of the energy with respect to the nuclear coordinates was constructed and diagonalized for the most stable conformers to confirm whether they are true minima or saddle points on the potential energy surface of the molecule. The eigenvalues of the Hessian matrix of the stable conformers were further utilized in a statistical analysis to obtain Gibbs free energies.

The isotropic shieldings of ^{1}H and ^{13}C were calculated using the GIAO method[33] at the B3LYP/6-311 + g(2d,p) level of theory[34] for the stable conformers. The isotropic shieldings were turned into chemical shifts by subtracting the corresponding isotropic shieldings of TMS, the reference molecule, which were calculated at the same level of theory.

All the calculations were carried out with the Gaussian 03 package.[35]

RESULTS AND DISCUSSION

We report the assignment of the ^{1}H and ^{13}C NMR spectra for a series of phenyl cinnamates, **1–13**, and 4-methylcoumarins, **14–17**, based on 1D and 2D experiments (APT, DEPT, COSY, HMQC, and HMBC). The results were found to be consistent with the structures in all respects. In addition, the unsubstituted compound **1** was subjected to theoretical calculation to obtain the optimized molecular structures and predict the most stable conformers. Also, gauge-including atomic orbital (GIAO) ^{1}H and ^{13}C NMR chemical shifts were calculated. Structures, numbering, and substitution for the phenyl cinnamates and 4-methylcoumarins are given in **Figs. 1** and **2**, respectively. ^{1}H NMR spectral data are collected in **Tables 1** and **2** for compounds **1–13** and **14–17**, respectively. The ^{13}C NMR chemical shifts of all compounds are listed in **Table 3**. For a better comparison of the NMR data in the tables, we arbitrarily marked atoms by Arabic numerals, prime numbers, and letters (A, B, C). The experimental chemical shifts of compound **1** were compared with those obtained from theoretical calculations, see below, in **Table 4**.

Table 1. ^{1}H NMR chemical shifts and coupling constants *J* (in parentheses) of phenyl cinnamates 1–13[a,b,c]

	H-B	H-C	H2	H3	H4	H5	H6	H2′/6′	H3′/4′/5′
1	6.64, d (16.0)	7.88, d (16.0)	7.16, ddd (8.4, 3.5, 2.5)	7.46–7.40, m	7.26, dt (8.4, 1.1)	7.46 – 7.40, m	7.16, ddd (8.4, 3.5, 2.5)	7.63 – 7.56, m	7.46 – 7.40, m
2	6.61, d (16.0)	7.87, d (16.0)		7.36, ddd (8.6, 5.4, 0.3)	—	7.36, ddd (8.6, 5.4, 0.3)	7.12, ddd (8.6, 2.7, 0.3)	7.62 – 7.54, m	7.45 – 7.40, m
3	6.63, d (16.0)	7.92, d (16.0)	7.37, ddd (8.6, 2.7, 0.3)	8.29, ddd (8.6, 5.4, 0.3)	—	8.29, ddd (8.6, 5.4, 0.3)	7.37, ddd (8.6, 2.7, 0.3)	7.64 – 7.57, m	7.48 – 7.42, m
4	6.61, d (15.9)	7.87, d (15.9)	7.06, ddd (8.6, 2.7, 0.3)	7.51, ddd (8.6, 5.4, 0.3)	—	7.51, ddd (8.6, 5.4, 0.3)	7.06, ddd (8.6, 2.7, 0.3)	7.61 – 7.55, m	7.45 – 7.42, m
5	6.62, d (15.9)	7.86, d (15.9)	7.05, ddd (8.6, 2.7, 0.3)	7.20, ddd (8.6, 5.4, 0.3)	—	7.20, ddd (8.6, 5.4, 0.3)	7.05, ddd (8.6, 2.7, 0.3)	7.62 – 7.54, m	7.42, – 7.38, m
6	6.55, d (15.9)	7.86, d (15.9)	6.92, ddd (8.6, 2.7, 0.3)	7.09, ddd (8.6, 5.4, 0.3)	—	7.09, ddd (8.6, 5.4, 0.3)	6.92, ddd (8.6, 2.7, 0.3)	7.62 – 7.55, m	7.45 – 7.39, m
7	6.61, d (16.0)	7.90, d (16.0)	7.28, ddd (8.6, 2.7, 0.3)	8.04, ddd (8.6, 5.4, 0.3)	—	8.04, ddd (8.6, 5.4, 0.3)	7.28, ddd (8.6, 2.7, 0.3)	7.63 – 7.56, m	7.47 – 7.41, m
8	6.63, d (16.0)	7.86, d (16.0)	6.98, br s	–	7.06, br d (7.6)	7.29, t (7.8)	6.97, br d (8.0)	7.62 – 7.54, m	7.46 – 7.39, m
9	6.67, d (16.0)	7.88, d (16.0)	—	7.12, dd (7.8, 1.4)	6.98, dt (7.1, 1.0)	7.23, dd (7.6, 1.4)	7.01, br d (7.1)	7.63 – 7.55, m	7.46 – 7.37, m
10	6.47, d (16.1)	7.70, d (16.1)	—	7.47–7.22 m	7.47–7.22 m	7.47–7.22 m	7.47–7.22 m	7.54 – 7.48, m	7.45 – 7.41, m
11	—	8.04, s	7.17, ddd (8.3, 2.6, 1.2)	7.34, ddd (9.9, 7.7, 2.2)	7.13, dt (7.2, 1.7)	7.34, ddd (9.9, 7.7, 2.2)	7.17, ddd (8.3, 2.6, 1.2)	7.42 – 7.36, m	7.42 – 7.36, m
12	6.67, d (16.0)	7.88, d (16.0)	—	7.22, d (7.9)	7.05, br d (7.5)	–	6.89, br s	7.64 – 7.57, m	7.46 – 7.40, m
13	6.80, d (15.9)	7.99, d (15.9)	—	—	7.33, br d (8.2)	7.49, dd (8.3, 7.6)	7.76, dd (7.5, 1.0)	7.66 – 7.60, m	7.47 – 7.41, m

[a] δ (^{1}H) in ppm relative to TMS in $CDCl_3$; coupling constants in Hz in parenthesis; letters denote signal multiplicities; s, singlet; d, doublet; t, triplet; q, quartet; spt, septet; m, multiplet; br, broad.

[b] Further ^{1}H chemical shifts of the substituents and other protons: **5** $\delta = 2.35$ ppm, s, 3H, CH_3; **6** $\delta = 3.74$ ppm, s, 3H, OCH_3; **7** $\delta = 3.02$ ppm, q, $J = 7.2$ Hz, 2H, CH_2, 1.24 ppm, t, $J = 7.2$ Hz, 3H, CH_3; **8** $\delta = 2.38$ ppm, s, 3H, CH_3; **9** $\delta = 3.84$ ppm, s, 3H, OCH_3; **10** $\delta = 7.41 - 7.37$ ppm, m, 5H, C_6H_5; **11** $\delta = 7.24$ ppm, br d, 2H, H2″/H6″; 7.20 – 7.14 ppm, m, 2H, H3″/H5″; 7.12 ppm, dt, $J = 7.2$ and 1.7 Hz, 1H, H4″; **12** $\delta = 3.03$ ppm, spt, $J = 6.6$ Hz, 1H, CH, 2.34 ppm, s, 3H, 5–CH_3, 1.21 ppm, d, $J = 6.9$ Hz, 6H, $(CH_3)_2$; **13** (the hydrogen atoms of the second aromatic ring are α and β with respect to the C-2 and C-3 positions) $\delta = 7.52$, dd, $J = 6.3$ and 3.2 Hz, 3H, H2β-H3β, δ 7.88, dd, $J = 5.9$ and 3.6 Hz, 1H, H3α, δ 7.95, dd, $J = 6.2$ and 3.4 Hz, 1H, H2α.

[c] H-2/6 and H-3/5 in compounds **2 – 8** showed an AA′BB′ spin system and coupling constant values were calculated from the spectra (see text).[36]

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Table 2. ^{1}H NMR chemicals shifts and coupling constants *J* (in parentheses) of 4-methylcoumarins 14–17[a,b]

	HB	H2	H4	H5	H1′	H2′	H3′a	H3′b
14	6.12, q (1.3)	6.81, d (2.5)	6.86, dd (8.9, 2.5)	7.49, d (8.8)	4.59, ddd (5.3, 1.6, 1.6)	***6.04, ddt (17.2, 10.6, 5.3)***	5.43, ddt (17.2, 1.6, 1.6)	5.33, ddt, (10.5, 1.6, 1.4)
15	6.10, q (1.2)	6.79, d (2.5)	6.84, dd (8.8, 2.5)	7.47, d (8.8)	4.50, ddq (6.2, 1.2, 1.2)	5.70, dtq (15.4, 6.0, 1.5)	5.88, dqt (15.3, 6.5, 1.2)	—
16	6.13, br d (1.1)	6.87, d (2.5)	6.92, dd (2.4, 8.8)	7.50, d (8.8)	4.75, dd (5.9, 1.3)	6.39, dt (15.9, 5.9)	6.76, br d (15.9)	—
17	6.11, d (1.0)	—	6.87, d (8.7)	7.47, d (8.7)	3.43, br d (6.0)	5.90, ddt (16.6, 10.5, 6.1)	4.93, dt (16.6, 1.7)	4.95, ddd, (10.5, 1.8, 1.3)

[a]δ(^{1}H) in ppm relative to TMS (upper trace) in $CDCl_3$; coupling constants in Hz in parenthesis (lower trace); letters denote signal multiplicities; s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad.
[b]Further ^{1}H chemical shifts of the substituents and other protons: **14** δ = 2.39 ppm, d, *J* = 1.0 Hz, 4–CH_3; **15** δ = 1.79 ppm, ddt, *J* = 6.4, 1.5 and 1.1 Hz, 3H, 3′–CH_3); **16** δ = 7.30 – 7.24 ppm, m, 1H, H4″; δ = 7.36–7.31 ppm, m, 2H, H2″/H4″; δ = 7.44–7.38 ppm, m, 2H, H1″/H5″; **17** δ = 10.48 ppm, br.s, 1H, OH, 2.35 ppm, d, 1.0 Hz, 3H, 4–CH_3.

^{1}H NMR spectra

Protons H-2 and H-3 in *para* substituted phenyl rings (compounds **2–7**, **Table 1**) show a typical AA′XX′ spin system pattern due to magnetic inequivalence. The corresponding chemical shift values (δ) and coupling constants (*J*) given in **Table 1** were calculated from the experimental spectra.[36] The aromatic protons of the styryl group in compounds **1 – 13** show two multiplets at high frequencies. Protons H3′/4′/5′ are in the area from δ = 7.48 to 7.36 ppm, while the protons H2′/6′ resonate between δ = 7.66 and 7.54 ppm for compounds **1 – 9** and **12** and **13**; δ = 7.54 – 7.48 ppm for compound **10** and δ = 7.42 – 7.36 ppm for compound **11** (see **Table 1**). As is shown in **Scheme 3**, the possible resonance structures in the cinnamyl moiety are responsible for the strong deshielding of the protons in the *ortho*-position. This delocalization is more effective when the carbonyl, the double bond, and the phenyl ring remain coplanar. Probably, the steric effect of the third phenyl ring at C-2 (compound **10**) and C-B (compound **11**) disturbs this coplanarity leading to a protective effect.

With the exception of compounds **10** and **13**, the H-B and H-C protons of the series show resonance signals from δ = 6.67 to 6.55 ppm and from δ = 7.92 to 7.86, respectively. The shielding and deshielding shifts with respect to this media observed in compounds **10** (H-B: δ = 6.47 ppm; H-C: δ = 7.70 ppm) and **13** (H-B: δ = 6.80 ppm; H-C: δ = 7.99 ppm), respectively, were attributed to steric effects of the *ortho*-phenyl group and the naphthyl ring. Hydrogen H-B is also present in the 4-methylcoumarin compounds **14 – 17** (see **Table 2**). Their resonances are between δ = 6.10 and 6.13 ppm and are in concordance with values reported in the literature for other 4-methylcoumarins.[37]

^{13}C NMR spectra

The ^{13}C chemical shifts shown in Table **3** were assigned with the assistance of APT and/or DEPT spectra, the heteronuclear two-dimensional one-bond (HMQC), and long-range (HMBC) correlation. The latter correlation was particularly useful for detecting the insensitive quaternary C-1 and C-1′ atoms in phenyl cinnamates **1–13** and also for distinguishing both phenoxy C-1 and C-3 positions in 4-methylcoumarins **14–17**. The A–B–C carbon chain of the acyclic and cyclic series shows chemical shifts that reflect their differences. The acyclic phenyl cinnamates **1–10** and **13** show chemical shift between δ = 164.3 and 166.5 ppm as well as δ = 116.2 and 117.4 ppm for the nuclei A and B, respectively. The same carbon atoms for the cyclic series have chemical shift in the range δ = 160.3 – 161.7 and 111.8 – 112.0 ppm, respectively. However, for the nucleus C, the range is δ = 146.4 – 148.0 and δ = 153.7 – 155.1 ppm, for the acyclic and cyclic series, respectively. The nucleus C experiences a deshielding of *ca*. 7 ppm, while nuclei A and B are shielded by *ca*. 4 and 5 ppm when going from the acyclic to the cyclic series. A comparison of both structures reveals that the resonance delocalization along the A–B–C chain is favored in the cyclic structure due a fixed planar geometry and to the impossibility of rotation through the A–B bond. This delocalization, which is typical of carbonyl α,β-unsaturated systems,[38] shifts the positive partial charge on nucleus C and the negative partial charge on carbonyl oxygen, causing the observed behavior.

Table 3. ^{13}C NMR chemical shift of phenyl cinnamates 1–11 and 13 and 4-methylcoumarins 14–17[a]

	A	B	C	1	2	3	4	5	6	1′	2′	3′	4′
							Phenyl cinnamates						
1	165.4	117.4	146.6	150.9	121.6	129.4	125.8	129.4	121.6	134.2	128.3	129.0	130.7
2	165.1	116.9	147.0	149.3	123.0	129.5	131.1	129.5	123.0	134.1	128.3	129.0	130.8
3	164.3	116.2	148.0	155.6	122.5	125.2	145.5	125.2	122.5	133.8	128.5	129.1	131.2
4	165.0	116.9	147.0	149.8	123.4	132.5	118.8	132.5	123.4	134.0	128.3	129.0	130.8
5	165.6	117.4	146.4	148.6	121.3	129.9	135.4	129.9	121.3	134.3	128.3	129.0	130.6
6	165.8	117.4	146.4	144.3	122.4	114.5	157.3	114.5	122.4	134.2	128.3	129.0	130.6
7	164.8	116.8	147.3	154.4	121.8	129.6	134.5*	129.6	121.8	134.0*	128.4	129.1	130.9
8	165.5	117.4	146.4	150.8	122.2	139.6	126.6	129.2	118.6	134.2	128.3	129.0	130.7
9	164.9	117.1	146.5	139.9	151.3	112.5	126.9	120.8	122.9	134.3	128.3	128.9	130.6
10	165.3	117.1	146.5	147.8	134.9	128.2*	126.3	127.4*	123.0	134.2	128.3	128.9	130.6
11	166.4	132.0	141.9	151.2	121.6	129.4	125.7	129.4	121.6	134.5	128.3	128.9	129.4
13	165.4	117.1	147.0	146.7	134.7	127.0	126.0	125.5	118.1	134,2	128.4	129.0	130.8
							4-methylcoumarins			**1′**	**2′**	**3′**	**Me**
14	161.5	112.0	155.1	152.5	101.7	161.3	112.7	125.5	113.6	69.2	132.1	118.5	18.4
15	161.7	111.8	155.1	152.6	101.6	161.3	112.8	125.4	113.4	69.1	131.6	124.9	18.6
16	161.3	112.0	155.1	152.5	101.7	161.2	112.8	125.5	113.7	69.1	133.9	123.8	18.6
17	160.3	111.9	153.7	152.9	109.9	158.7	115.0	123.9	112.6	26.5	135.3	112.0	18.1

[a]δ(^1H and ^{13}C) in ppm relative to TMS in $CDCl_3$.
[b]Further ^{13}C chemical shifts of the substituents and other carbons: **5** $\delta = 20.9$ ppm (CH_3); **6** $\delta = 55.6$ ppm (CH_3O); **7** $\delta = 199.6$ (CO), 31.8 (CH_2) and 8.3 ppm (CH_3); **8** $\delta = 21.3$ ppm (CH_3); **9** $\delta = 55.9$ ppm (CH_3O); **10** $\delta = 137.6$ (1″), 128.9 (3″), 128.5 (4″) and 128.3 ppm (2″); **11** $\delta = 135.5$ (1″), 130.8* (3″), 129.9* (2″) and 128.0 ppm (4″); **13** (the carbon atoms of the second aromatic ring are α and β with respect to the C-2 and C-3 positions) $\delta = 128.0$ (3α), 126.4 (2β and 3β) and 121.3 ppm (2α).
*Interchangeable.

Table 4. Theoretical and experimental chemical shifts for the two lowest conformers of **1**[a]

Atom	Conformer I (78 %)[b]	Conformer II (22 %)[b]	Weighted average	Experimental	Δ[c]
A	170.8	169.5	170.5	165.4	−5.1
B	119.1	122.4	119.8	117.4	−2.4
C	154.1	152.0	153.7	146.6	−7.1
1	159.1	158.9	159.1	150.9	−8.2
2	128.2	125.3	127.6		
6	124.8	128.7	125.6		
2/6	126.5	127.0	126.6	121.6	−5.0
3	133.2	133.4	133.2		
5	133.2	133.1	133.2		
3/5	133.2	133.3	133.2	129.4	−3.8
4	129.3	129.3	129.3	125.8	−4.3
1′	140.6	140.7	140.6	134.2	−6.4
2′	138.4	138.1	138.3		
6′	129.8	129.9	129.8		
2′/6′	134.1	134.0	134.1	128.3	−5.8
3′	133.8	133.7	133.8		
5′	133.3	133.5	133.3		
3′/5′	133.5	133.6	133.5	129.0	−4.5
4′	136.0	135.8	136.0	130.7	−5.3
H-B	6.97	6.79	6.93	6.64	−0.29
H-C	8.12	8.13	8.12	7.88	−0.24
H-2	7.31	7.42	7.33		
H-6	7.63	7.28	7.56		

(*Continues*)

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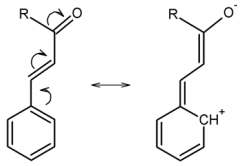
Table 4. *(Continued)*

Atom	Conformer I (78 %)[b]	Conformer II (22 %)[b]	Weighted average	Experimental	Δ[c]
H/2–6	7.47	7.35	7.44	7.16	−0.28
H-3	7.58	7.62	7.58		
H-5	7.53	7.62	7.55		
H/3–5	7.55	7.62	7.56	7.40–7.46	
H-4	7.40	7.42	7.40	7.26	−0.14
H-2′	7.63	7.62	7.63		
H-6′	8.25	8.21	8.24		
H/2′–6′	7.94	7.91	7.93	7.63–7.56	
H-3′	7.55	7.62	7.56		
H-5′	7.69	7.62	7.67		
H/3′–5′	7.62	7.62	7.62	7.40–7.46	
H-4′	7.61	7.62	7.61	7.40–7.46	

[a]$\delta(^{13}C)$ in ppm relative to TMS in $CDCl_3$.
[b]Percent population based on Gibbs free energies and Maxwell–Boltzmann statistics.
[c]$\Delta = \delta_{exp} - \delta_{calc}$.



Scheme 3. Charge delocalization in the cinnamyl moiety.

Theoretical calculations

Looking at the structure of compound **1**, both rigid phenyl rings are connected by the C_1–O–C_A(O)–C_BH=C_CH– chain with a certain degree of flexibility. The potential energy surface around the three single bonds C_1 – O, O – C_A and C_A – C_B was studied. The potential energy curve around the C_1 – O bond delivered two conformers of similar energy values at 30° and 150°. The latter conformer is only 0.024 kcal/mol more stable than the former. These conformations are shown in **Fig. 3**, where the phenyl ring plane is deviated ±30° off the selected dihedral angle.

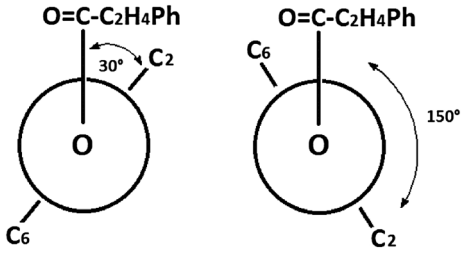


Figure 3. Stable conformations around the C1–O bond

The O – C_A bond refers to the preferred conformation around the C(O)–O–R ester function. As described above, the Z conformations of esters are expected to be more stable than the E conformations[11–13] (**Scheme 1**). In accordance with these results, our theoretical calculations reveal that the Z conformation is 4.91 kcal/mol more stable than its E counterpart.

The potential energy curve around the C_A – C_B bond takes into account the stability of conformations in α,β-unsaturated carbonyl compounds. Although the conjugative stabilization favors the s-trans over the s-cis conformer (**Scheme 2**), the relaxed scan around the C_A – C_B bond shows that the s-cis conformation is ca. 1 kcal/mol more stable than the s-trans, in agreement with the result found by Abraham *et al.*[16]

After the conformational searching, two energy minima were found for each of the three bonds investigated (C_1 – O: 30° and 150°, O – C_A: 0° and 180°, and C_A – C_B: 0° and 180°). According to these results, eight conformations are taken as starting point for further optimization at the B3LYP/6-311++G (d,p) level of theory. After optimization, only the two lowest energy conformers (designed as conformer **I** and conformer **II**) were considered since the others are about 6 kcal/mol higher in Gibbs free energy and consequently are undetectable at room temperature. The optimized conformations of both conformers are depicted in **Fig. 4**, while relative Gibbs free energies and geometrical parameters are presented in **Table 5**. The conformer **I** was predicted to be the most stable form (**Fig. 4**). It exhibits a φ(O=C_A–C_B–C_C) torsion angle of −0.53° (s-cis conformation) and the O=C–O–Ar ester moiety in Z conformation with φ(O=C_A–O–C_1)=−0.55°. The conformer **II** differs from **I** in the arrangement of the α,β-unsaturated carbonyl moiety

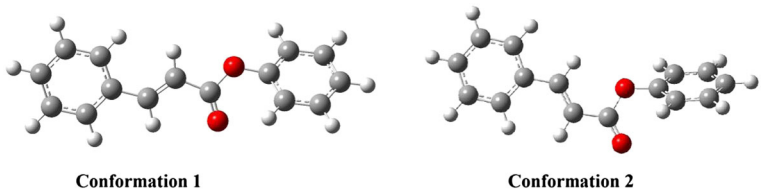


Figure 4. Optimized structures of the two lowest energy conformations, **I** and **II**, of phenyl cinnamate **1**

Table 5. Selected structural parameters of **1** and its two lowest energy conformers.[a] Relative Gibbs free energies, percent populations, and dipole moments are also given for conformers **I** and **II**

	Conf. I	Conf. II	Exp.[b]
Structural parameters: dihedral angles (degrees)			
$C_2C_1OC_A$	127.6 (30.0)	121.2 (150.0)	69.5
$C_1OC_A=O$	−0.5 (0.0)	−1.3 (0.0)	−3.9
$O=C_AC_BC_C$	−0.5 (0.0)	178.5 (180.0)	−2.3
Structural parameters: angles (degrees) and bond lengths (Å)			
C_1OC_A	120.3	119.6	119.6
OC_AC_B	109.4	112.4	110.3
$C_A=O$	1.205	1.206	1.198
C_A–O	1.376	1.374	1.351
C_A–C_B	1.473	1.471	1.461
Relative Gibbs free energies (kcal/mol), percent population and dipole moment (debye)			
ΔG	0.0000	0.7486	
Pop.[c]	78	22	
Dipole moment	2.4943	3.1809	

[a]Calculated at the B3LYP/6-311++G(d,p) level of theory.
[b]From single-crystal X-ray data taken from ref.[39]
[c]Percent population based on Gibbs free energies and Maxwell–Boltzmann statistics.

with $\varphi(O=C_A–C_B–C_C)$ =178.47° (s-trans conformation) and $\varphi(O=C_A–O–C_1)$ = −1.31°. Moreover, data of the crystal structure of p-cresyl cinnamate[39] confirm that the most stable conformation predicted by theoretical calculations is also the conformation adopted by phenyl cinnamates in the solid state (see **Table 5**).

Conclusions

In this work, we established the ^{1}H and ^{13}C NMR chemical shift assignment of a series of phenyl cinnamates and 4-methylcoumarins employing 1D and 2D methodologies. The studied molecules are examples of naturally occurring compounds that also exhibit many biological properties, so that this first systematic NMR assignment is of interest. The experimental chemical shifts were compared with those arising from theoretical calculations for the unsubstituted phenyl cinnamate. The result shows that the GIAO method is appropriate to predict chemical shifts for these classes of compounds with a maximal deviation of 8 ppm and 0.3 ppm for ^{13}C and ^{1}H NMR, respectively. The structural study reveals that the rather flexible chain between the phenyl rings in the phenyl cinnamates has two important contributions: the conformation around the ester function and the α,β-unsaturated carbonyl moiety. The results show that phenyl cinnamate **1** can exist as a mixture of two conformers, both having the ester function in Z-conformation, but the most stable has the α,β-unsaturated carbonyl moiety in s-cis configuration, while its counterpart in s-trans is 0.75 kcal/mol higher in energy. The most stable s-cis configuration found in our studies is also the conformation adopted for a related phenyl cinnamate in solid state.

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