SHORT PAPER

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An experimental NMR and semi-empirical theoretical study of the conformation of styrylchromones and styryl alkyl or aryl ketones (benzylidene ketones)†

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The configurations and conformations of styrylchromones and benzylidene ketones were determined by NMR spectroscopy. The cyclisation of the former to xanthones was studied showing clear differences in reactivity. These structural aspects were rationalised with the help of AM1 calculations.

Keywords: styrylchromones, xanthones, benzylidene ketones, NMR, AM1 calculations

In the last years, we have been interested in the structure of 2-styrylchromones **I** and in their cyclisation into xanthones **II**. [1–3] Related to the conformations of styrylchromones is the case of benzylidene ketones **III**.[4,5]

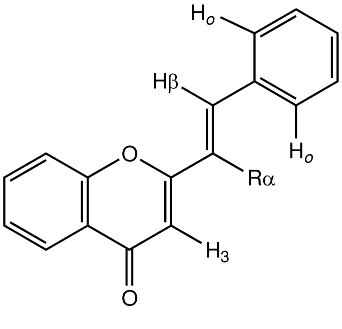
For each case, we will first present the experimental evidence we have gathered on these systems and then describe the results of the AM1 computations.

Styrylchromones **I**: We have studied two systems, R = H **1** and R = CH_3 **2** and represented the four possible conformations in Scheme 1. Since it is a delocalised system, the *sE*/*sZ* conformations about the formal single bond have also to be considered.

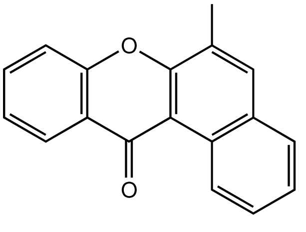
In the first case, the value of the $^3J(H_\alpha H_\beta)$ coupling constant (16 Hz) proves that both hydrogen atoms are in a *trans* disposition (*E*). On the other hand, the observation of a NOE effect between H_α and H_3 and the absence of this effect between H_β and H_3 prove that the compound exists in the *EsZ* conformation (**1a**). There is also a NOE effect between H_α and H_o, but this only allows the exclusion of the *Z* conformers **1c** and **1d**.

In the second case, 2-α-methylstyrylchromone, we have isolated the *E* (**2a** or **2b**) and *Z* (**2c** or **2d**) isomers in 85% and 11% yields, which correspond to an 88:12 ratio. The configurations are based on the value of the allylic coupling constant, $J(Me_\alpha H_\beta)$, with values of 1.3 and 1.5 Hz for *E* and *Z* isomers, respectively. This proves that the barrier across the double bond is high enough to allow the isolation of the isomers. Therefore, in the previous case, the compound is an *E* pure isomer, which is slightly destabilised by the methyl group in the second compound. For the *E* isomer, the observation of NOE effects between the α-methyl group and H_3 demonstrates that the most stable conformer is **2a** (there is also a NOE interaction between α-Me and Ho but it is consistent with both **2a** and **2b**). In the case of the *Z* isomer, we observed NOE's between the α-Me and both H_3 and H_β. The second one is characteristic of the *Z* structure, but the first one corresponds to the *sZ* conformer **2c**. In summary, the most stable conformations are **1a**, **2a** and **2c**, the difference between **2a** and **2c**, at 300 K, being 1.2 kcal/mol. Note that isomers *E* and *Z* do not isomerise on standing in the absence of light. It is important to note that NOE indicates the stable conformation in solution while AM1 calculations refer to the gas phase.

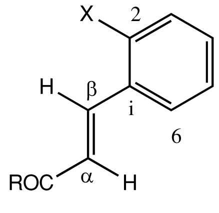
AM1 calculations[6] in the case of compound **1** lead to only three minima: **1a**, $\Delta H_f = 19.2$ kcal/mol, $\mu = 4.08$ D, **1b**, $\Delta H_f = 19.3$ kcal/mol, $\mu = 3.52$ D and **1c**, $\Delta H_f = 23.5$ kcal/mol, $\mu = 3.46$ D. Conformation **1d** is not a minimum of the potential surface and evolves towards the corresponding stable structure **1c** by rotation about the single bond. Note that structures **1a** and **1b** are wholly planar while structure **1c** is distorted. The difference in stability (4.3 kcal/mol with regard to **1c**) and the higher dipole moment should favour structure **1a** in solution, which is in agreement with what was experimentally found. According to the calculations, this compound should exist as a mixture of **1a** and **1b** in rapid equilibrium on the NMR time scale. In mixtures in rapid equilibrium, NOE's should be observed for both conformations. However, there is no NOE between H_β and H_3 and, therefore, conformation **1b** should be in the minority. It appears that AM1 calculations exaggerate the instability of the extended conformation **1b** *EsE*.



I



II



III

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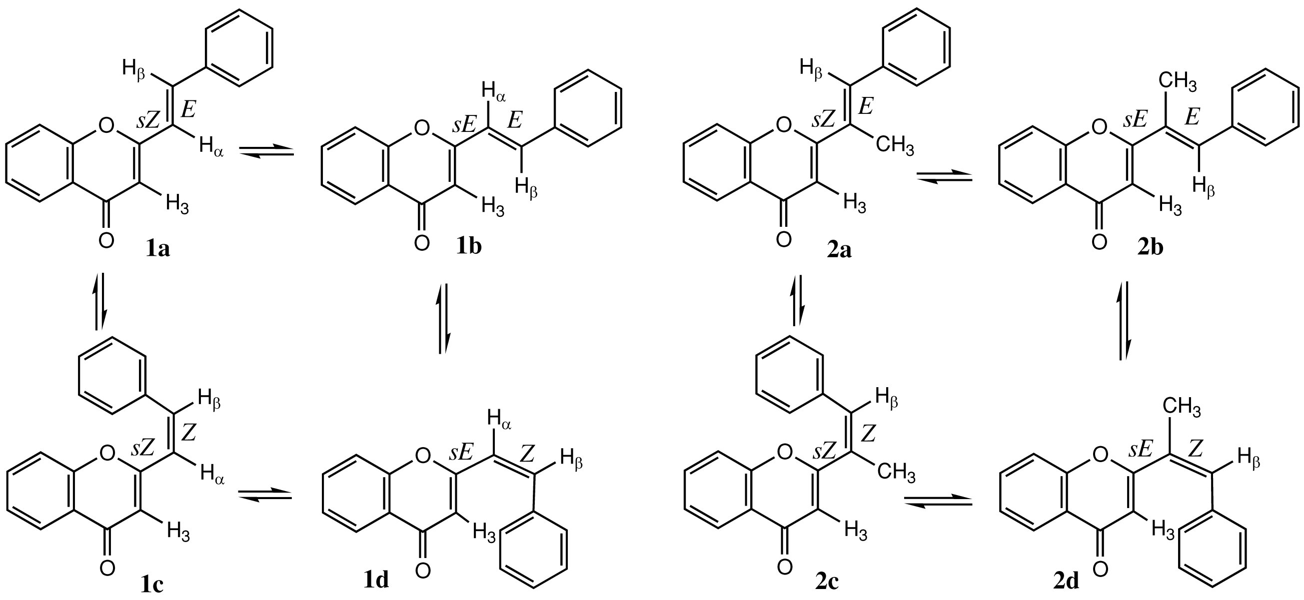
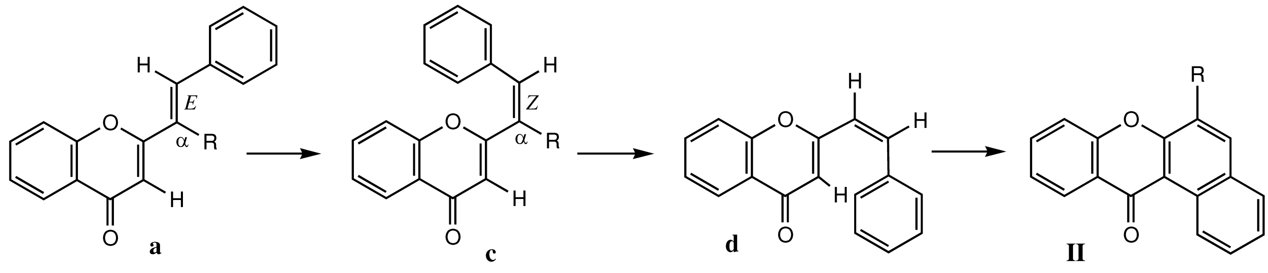
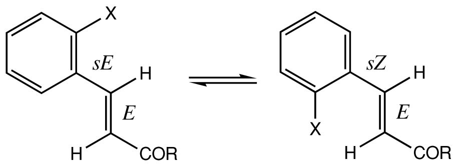
† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M)*.



Scheme 1

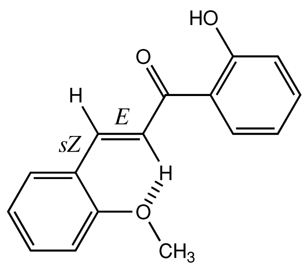


Scheme 2



R = CH_3, X = Cl	**3a**	**3b**
X = Br	**4a**	**4b**
X = OCH_3	**5a**	**5b**
R = 2-(OH)C_6H_4, X = Cl	**6a**	**6b**
X = Br	**7a**	**7b**
X = CH_3	**8a**	**8b**
X = OCH_3	**9a**	**9b**

Scheme 3



9b

For compound **2**, only two minima were found; they correspond to **2a**, ΔH_f = 38.8 kcal/mol, µ = 3.77 D and **2d**, ΔH_f = 16.4 kcal/mol, µ = 3.17 D (the geometry of **2d** is highly distorted). In this case, the discrepancy is double: **2d** is the minimum and not **2c** and **2a** is much less stable than **2d**. However, the possibility remains that the yield of **2a** (88%) and **2c** (12%) results from the reaction rates (kinetic composition) and not from the thermodynamic differences in stability.

Cyclisation of styrylchromones **I** *to xanthones* **II**. Under solar light or UV irradiation, the cyclisation **I** → **II** took place. It implies an *E* to *Z* isomerisation followed by an electrocyclisation and an oxidation (Scheme 2).[3] The order isomerisation/rotation, **acd** or **adc**, is arbitrary.

Compounds with a substituent in an α position, like **2**, cyclise faster than the parent compound **1**: 25–30 days for **2** and about 50 days for **1**. AM1 calculations (see preceding section) have shown that *E* isomers are more stable than *Z* ones for R = H **1** while the contrary happens for R = CH_3 **2**. This provides a possible explanation for the experimental results.

Benzylidene ketones **III**: In the course of structural characterisation of benzylidene ketones **III** by NMR we have found that the vinylic system of these compounds has an *E* configuration [^3J(HαHβ) = 15–16 Hz]. Due to the deshielding mesomeric effect of the carbonyl group the H-β resonances of these compounds appear at higher frequency values than those corresponding to H-α. However, these H-β signals appear at

Table 1 Heats of formation, dipole moments relative stabilities (the most stable conformation in bold), and some torsion angles of benzylidene ketones **3a–9b**

Compound	ΔH_f/kcal/mol	μ/D	$\Delta\Delta H_f$/kcal/mol	Torsions angles/°
3a	–6.50	3.87	**0.00**	Planar
3b	–6.00	2.80	0.50	Hβ-Cβ-Ci-Co = 47.6
4a	6.12	3.96	**0.00**	Planar
4b	6.19	2.84	0.07	Hβ-Cβ-Ci-Co = -62.8
5a	–38.42	3.51	**0.00**	Planar (save 2 H of the Me)
5b	–37.35	4.32	1.07	Planar (save 2 H of the Me)
6a	–18.89	4.32	**0.00**	Hβ-Cβ-Ci-Co = 29.1, Cα-Cβ-Ci-Co = 30.6
6b	–17.52	3.78	1.37	Hβ-Cβ-Ci-Co = -46.4, Cα-Cβ-Ci-Co = –49.6
7a	–6.31	4.02	**0.00**	Hβ-Cβ-Ci-Co = 40.5, Cα-Cβ-Ci-Co = 41.4
7b	–6.20	3.91	0.11	Hβ-Cβ-Ci-Co = -51.1; Cα-Cβ-Ci-Co = –51.2
8a	–19.85	3.18	**0.00**	Hβ-Cβ-Ci-Co = 28.2, Cα-Cβ-Ci-Co = 29.1
8b	–18.49	3.42	1.36	Hβ-Cβ-Ci-Co = 40.9, Cα-Cβ-Ci-Co = 43.3
9a	–50.27	4.50	**0.00**	Hβ-Cβ-Ci-Co = 19.5, Cα-Cβ-Ci-Co = 21.4
9b	–49.15	4.97	1.08	Hβ-Cβ-Ci-Co = 0.45, Cα-Cβ-Ci-Co = 0.2

higher frequency values (+ 0.3 to + 0.4 ppm) than those of the corresponding unsubstituted derivatives (X = H). This effect can be explained by the steric interactions between H-β and the X substituent (Cl, Br, CH$_3$, OCH$_3$),[7] and was proved by NOE experiments; there was a NOE effect between H-6 and H-α, while no effects were observed upon irradiation of the H-β resonance. In the case of compound **8** a close proximity between 2-CH$_3$ and H-β was also found. All these NMR data prove that the benzylidene ketones **III** exist in the *sE* conformation (Scheme 3).

The AM1 calculations of the seven pairs of benzylidene ketones **III** (Scheme 3) are reported in Table 1. The only conformation of benzylidene ketones **III**, R = 2-(OH)C$_6$H$_4$, which is almost planar (excepting the hydrogen atoms of the methyl groups) is **9b** with a torsion angle of 0.2°. We tentatively assign this fact to the existence of an intramolecular C-H···O=C hydrogen bond (HB). This kind of HB is not very common but Desiraju and Steiner have described some related examples.[8]

In all cases **a** conformers are more stable than the **b** ones, although the differences are in some cases very small. The dipole moments favour the **a** structures in condensed phases save in the cases of compounds **5b**, **8b** and **9b**, but in these cases, the differences in stability are large enough to prevent a reversal of the situation calculated for the gas phase.

In summary, very simple and accessible computations provide a base for the rationalisation of a series of related experimental observations. We do not pretend that semi-empirical calculations using Dewar's AM1 method are the solution for most chemical problems. In the case of compound **2** the results of the calculations are not entirely satisfactory. Moreover, the ground state properties of these fully conjugated systems are well adapted to this type of calculation.

Experimental

2-Styrylchromones **I** (**1** and **2**) and xanthones **II**, obtained by daylight photo-oxidative cyclisation of **I**, were prepared and fully characterised as previously reported.[2] Benzylidene ketones **III** (**3–9**) have been prepared, from the base-catalysed aldol reaction of the appropriate ketones and benzaldehydes, and fully characterised as previously reported.[4,5]

^{1}H and ^{13}C NMR spectra were recorded in CDCl$_3$ solutions, on a Bruker AMX 300 spectrometer, at 300.13 and 75.47 MHz, respectively; the chemical shifts are expressed in δ (ppm) values relative to TMS as internal reference. ^{1}H assignments were made by using 2D COSY and NOESY (mixing time of 800 ms) experiments, while ^{13}C assignments were made using HETCOR and HMBC (delays for long-range *J* C/H couplings were optimised for 7 Hz) experiments. Homonuclear NOE difference experiments were performed by using 2 s for the irradiation time and 4 s for the relaxation delay.

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References

1 A.M.S. Silva, D.C.G.A. Pinto and J.A.S. Cavaleiro, *Tetrahedron Lett.*, 1994, **35**, 5899; D.C.G.A. Pinto, A.M.S. Silva and J.A.S. Cavaleiro, *Tetrahedron Lett.*, 1994, **35**, 9459; D.C.G.A. Pinto, A.M.S. Silva and J.A.S. Cavaleiro, *J. Heterocycl. Chem.*, 1996, **33**, 1887; A.M.S. Silva, A.M.G. Silva, A.C. Tomé and J.A.S. Cavaleiro, *Eur. J. Org. Chem.*, 1999, 135; D.C.G.A. Pinto, A.M.S. Silva and J.A.S. Cavaleiro, *New J. Chem.*, 2000, **24**, 85.

2 J.A.S. Cavaleiro, J. Elguero, M.L. Jimeno and A.M.S. Silva, *Chem. Lett.*, 1991, 445; A.M.S. Silva, J.A.S. Cavaleiro and J. Elguero, *Liebig's Ann. Chem.*, 1997, 2065; A.M.S. Silva, J.S. Vieira, J.A.S. Cavaleiro, T. Patonay, A. Lévai and J. Elguero, *Heterocycles*, 1999, **51**, 481; D.C.G.A. Pinto, A.M.S. Silva, J.A.S. Cavaleiro, C. Foces-Foces, A.L. Llamas-Saiz, N. Jagerovic and J. Elguero, *Tetrahedron*, 1999, **55**, 10187.

3 A.M.S. Silva, D.C.G.A. Pinto, H.R. Tavares, J.A.S. Cavaleiro, M. L. Jimeno and J. Elguero, *Eur. J. Org. Chem.*, 1998, 2031; A.M.S. Silva, H.R. Tavares and J.A.S. Cavaleiro, *Heterocycl. Commun.*, 1996, **3**, 251.

4 A.M.S. Silva, H.R. Tavares, A.I.N.R.A. Barros and J.A.S. Cavaleiro, *Spectrosc. Lett.*, 1997, **30**, 1655; A.M.S. Silva, J.A.S. Cavaleiro, G. Tarrago and C. Marzin, *New J. Chem.*, 1999, 329.

5\. A.M.S. Silva, PhD Thesis, University of Aveiro, Portugal, 1993. A.M.S. Silva, D.C.G.A. Pinto and J.A.S. Cavaleiro, to be published.

6 M.J.S. Dewar, E.G. Zoebisch, E.F. Healy and J.J.P. Stewart, *J. Am. Chem. Soc.*, 1985, **107**, 3902.

7 D.M. Grant and B.V. Cheney, *J. Amer. Chem. Soc.*, 1967, **89**, 5315. E. Breitmaier and W. Voelter, *Carbon-13 NMR Spectroscopy*, 3rd Edition, VCH, Weinheim, 1989, pp. 115–116.

8 G.R. Desiraju and T. Steiner, *The Weak Hydrogen Bond*, International Union of Crystallography, Oxford Science Publications, Oxford University Press, 1999, p. 93.