Conformational dependence of deuterium-induced isotope effects on the olefinic one-bond ^{13}C–^1H and three-bond ^1H–^2H coupling constants in *cis*- and *trans*-stilbene

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Secondary deuterium isotope effects on the olefinic one-bond ^{13}C, ^1H and three-bond ^1H, ^2H spin–spin coupling constant were determined in a series of specifically deuteriated *cis*- and *trans*-stilbene isotopomers. Inverse (^1H detected) heteronuclear multiple quantum correlation (HMQC) NMR pulse sequence was used to measure the coupling constants in these π-conjugated systems of a moderate size. Complete spectral analyses were performed in cases where higher order perturbations took place. All secondary isotope effects on $^1J(^{13}C_\alpha, ^1H)$/Hz are negative, *i.e.* the reduced values from −0.06 to −0.02 were observed. In contrast, the effects on $^3J(^1H_\alpha, ^2H_{\alpha'})$/Hz are all positive from 0.04 to 0.13, thus being on average relatively higher than those on $^1J(^{13}C_\alpha, ^1H)$. Only two primary effects on $^1J(^{13}C_\alpha, ^1H)$ were determined to see whether the same trend holds as for secondary effects. The real values of olefinic coupling constants are given with a high accuracy. In order to relate isotope effects with structural parameters, AM1 semiempirical calculations were performed. Subtle conformational changes due to the deuteriation are discussed in terms of rovibrational averaging and overall geometry.

Introduction

Intrinsic isotope effects received much attention when powerful high-resolution NMR spectrometers became available. Deuterium substitution induces the largest changes in NMR spectral parameters and thus the majority of published data are devoted to deuterium isotope effects. Previous semiempirical calculations[1] and some experiments[2] have shown that effects on spin–spin coupling constants are very small in comparison with those on nuclear shielding[3] or spin–spin and spin–lattice relaxation times.[4] The main problem in determining isotope effects on coupling constants lies in the accuracy of the measurements. Reported isotope effects on $^nJ(^{13}C, ^1H)$ are often within experimental error, hardly enabling any reasonable explanation. Hence, precise measurement is the main prerequisite of successful research. An additional obstacle comes from the complexity of NMR spectra and higher order effects. These are the reasons for the relatively scarce reports dealing with isotope effects on coupling constants.

Previous reports claim that primary and secondary deuterium effects on spin–spin coupling could be both positive and negative,[5–7] depending on hybridization and the presence of lone-pair electrons. Leshcheva *et al.*[7a,b] demonstrated larger secondary than primary effects on the same coupling which contradicted existing theoretical estimates.[1] These predictions were questioned and it was later proved by *ab initio* calculations[8] that primary effects were not necessarily larger than secondary. Though reviewed[5] and treated theoretically,[6,8] isotope effects on coupling constants still attract considerable attention. Further experimental work should throw more light on this phenomenon and also test the quality of *ab initio* calculations of the coupling tensor.

It is our intention to rationalize changes in coupling constants caused by the deuterium substitution in medium sized molecules, such as *cis*- and *trans*-stilbene (Fig. 1). Of special interest is to look for possible conformational and geometrical changes due to the deuteriation. For the sake of clarity the following expressions for the primary eqn. (1) and secondary eqns. (2) and (3) isotope effects on $^1J(^{13}C_\alpha, ^1H)$ and $^3J(^1H_\alpha, ^2H_{\alpha'})$

$$\Delta_p{}^1J(^{13}C_\alpha, ^1H) = (\gamma_H/\gamma_D)\,[|J(^{13}C_\alpha, ^2H)| - |J(^{13}C_\alpha, ^1H)|] \quad (1)$$

$$\Delta_s{}^1J(^{13}C_\alpha, ^1H) = |^1J(^{13}C_\alpha, ^1H)|^* - |^1J(^{13}C_\alpha, ^1H)| \quad (2)$$

$$\Delta_s{}^3J(^1H_\alpha, ^2H_{\alpha'}) = |^3J(^1H_\alpha, ^2H_{\alpha'})|^* - |^3J(^1H_\alpha, ^2H_{\alpha'})| \quad (3)$$

coupling constants are used in this paper,[6a] where γ_H and γ_D are the magnetogyric ratios of hydrogen and deuterium,

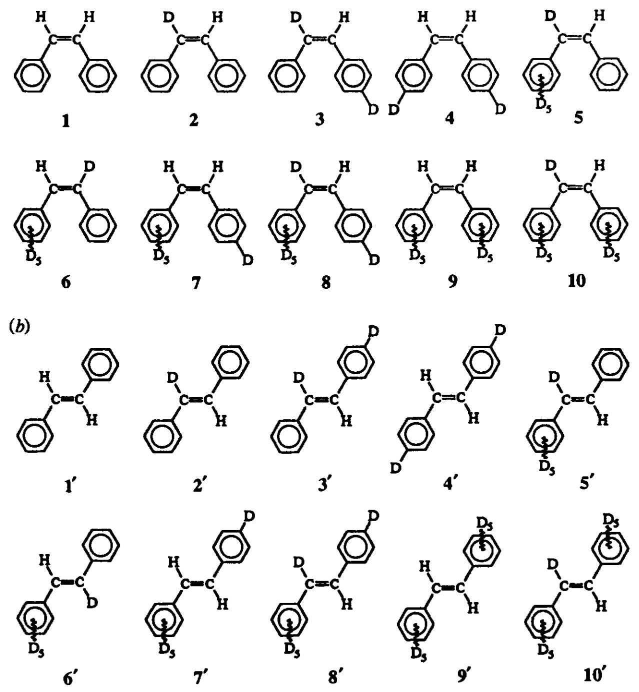

Fig. 1 Isotopomers of (*a*) *cis*- and (*b*) *trans*-stilbene

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respectively, and where the asterisk denotes the deuteriated molecule.

Since the magnitude of a coupling constant depends on magnetogyric ratios, the reduced coupling, *K*, can also be used,[9] but the former notations will be preferred here since they include conventional units of Hz.

A lot of effort has been made to elucidate isotope effects in terms of rovibrational averaging using dynamic and electronic factors.[6a] This vibrational theory applies well to small molecules,[8–10] but it lacks experimental evidence for medium and large molecular systems. Although the Fermi contact term is considered to be the dominant factor,[5b] non-contact contributions to spin–spin coupling, such as orbital and spin–dipolar, should sometimes be taken into account when calculating isotope effects on coupling constants.[8] In spite of advances in computational facilities, calculations at the appropriate *ab initio* level for relatively large π-electron systems such as *cis*- and *trans*-stilbene are unfortunately not yet entirely feasible.

In some reports dealing with isotope effects on coupling constants neither a sufficient number of isotopomers systematically labelled at different sites was used, nor was any conformational and geometrical dependence of these effects discussed in detail. Therefore, we prepared a series of deuteriated *cis*- and *trans*-stilbenes (see Fig. 1) and applied inverse HMQC experiments for measuring the coupling constants in order to determine isotope effects and to establish their possible conformational dependence.

The HMQC experiment[11a] has recently been widely used for structure determinations of various molecules including biomolecules,[11,12] as well as in heteronuclear three-dimensional NMR spectroscopy.[13] Bax and co-workers[13–16] have demonstrated an excellent use of the method for the measurement of coupling constants in proteins. This has encouraged us to use both one- and two-dimensional versions of this inverse experiment for measuring the coupling constants in *cis*- and *trans*-stilbene and their deuteriated isotopomers (Fig. 1).

Experimental

Preparation of isotopomers

The parent compounds were purchased from Aldrich and used after purification. All deuteriated isotopomers were synthesized in our laboratory *via* the Wittig reaction[17] from the corresponding benzyltriphenylphosphonium bromides and benzaldehydes in the presence of sodium ethoxide in ethanol and dimethylformamide. Products of this reaction contain nearly equal amounts of *cis* and *trans* isomer. Specifically deuterated benzyltriphenylphosphonium bromides were obtained from triphenylphosphine and the corresponding benzyl bromides.[18] The latter were prepared by a reaction of specifically deuteriated toluenes with *N*-bromosuccinimide and dibenzoyl peroxide.[19] The same reactions were used for the preparation of deuterium labelled benzaldehydes, where benzyl bromides were allowed to react with hexamethylenetetraamine in a mixture of acetic acid and water. [*p*-^{2}H]benzaldehyde was synthesized from *p*-bromotoluene *via* the Grignard reaction with magnesium activated using 1,2-dibromoethane as entrainer.[20] [$^2H_8$]Toluene, D_2O and [$^2H_5$]benzaldehyde were purchased from Merck, while [α-^{2}H]benzaldehyde was purchased from MSD isotopes.

The deuterium content determined from the measurements at low ionizing energy using an Extrel FTMS 2001 DD mass spectrometer equipped with a 3T superconducting magnet, was as follows: **2** and **2′** (89% ^{2}H), **3** and **3′** (90% $^2H_2$), **4** and **4′** (88% $^2H_2$), **5** and **5′** (83% $^2H_6$), **6** and **6′** (88% $^2H_6$), **7** and **7′** (94% $^2H_6$), **8** and **8′** (86% $^2H_7$), **9** and **9′** (90% $^2H_{10}$), **10** and **10′** (91% $^2H_{11}$).

All *cis*-stilbene isotopomers were purified by column chromatography and distillation before use in NMR measurements. *trans*-Stilbene isotopomers were recrystallized from acetone.

NMR spectra

HMQC spectra were recorded with a Bruker AM-360 spectrometer from [$^2H_6$]acetone solutions in 5 mm tubes. Care was taken with the concentration and temperature dependence of coupling constants, so that the same concentrations for all samples were used (0.2 mol dm^{-3}) at 294 K. Pulse calibrations prior to NMR experiments were carried out. As part of the heteronuclear multiple quantum pulse sequence a BIRD (bilinear rotation) sequence was used and phase sensitive TPPI (time proportional phase increment) spectra were detected. A pair of dummy scans was used for establishing a steady state magnetization. The number of scans was 100–500.

For the measurements of $^1J(^{13}C_\alpha, {}^1H)$ (all *J* values and ranges given in Hz) we used the spectral width of 200.0–500.0 and appropriate acquisition times which gave the digital resolution in 1D and in f_2 dimension of 2D spectra of 0.010–0.025 per point. For the measurements of $^3J(^1H_\alpha, {}^2H_{\alpha'})$, a spectral width of 100–200 was used. The digital resolution was 0.005–0.013. Prior to the Fourier transformations resolution enhancement functions were used. Spectra were zero filled to 64 K data points.

^{13}C proton decoupled spectra with the Waltz decoupling sequence were recorded on a Varian Gemini 300 and a Bruker AM-360 spectrometer at 294 K. Solvent was [$^2H_6$]acetone and concentration was 0.2 mol dm^{-3}. Spectral width was 500 Hz. Prior to the Fourier transformations resolution enhancement functions were used. Spectra were zero filled to 64 K data points. Digital resolution was 0.020–0.045 Hz. 8000–18 000 scans per spectrum were used.

Accuracy and experimental errors

All coupling constants were measured from six to eight independent experiments to enable the determination of standard deviations. The values of calculated standard deviations (*i.e.* experimental errors) of coupling constants and secondary

Table 1 One-bond, $^1J(^{13}C_\alpha, {}^1H)$, three-bond, $^3J(^1H_\alpha, {}^2H_{\alpha'})$ coupling constants (Hz), and secondary deuterium isotope effects, *Δ* (Hz), in deuterated *cis*-stilbenes[a]

	$^1J(^{13}C_\alpha, {}^1H)$		$^3J(^1H_\alpha, {}^2H_{\alpha'})$	
Isotopomer		*Δ*		*Δ*
1	155.53[a] (0.01)			
2	155.44 (0.01)	−0.06 (0.02)	1.762 (0.006)	
3	155.43 (0.01)	−0.07 (0.02)	1.767 (0.007)	—
4	155.52[a] (0.01)	—		
5	155.35 (0.01)	−0.16 (0.02)	1.802 (0.007)	0.040 (0.013)
6	155.37 (0.01)	−0.15 (0.02)	1.813 (0.006)	0.051 (0.012)
7	155.49[b] (0.01)	−0.04 (0.02)		
8	155.39 (0.02)	−0.14 (0.03)	1.822 (0.013)	0.060 (0.019)
9	155.41[b] (0.02)	−0.12 (0.03)		
10	155.31 (0.03)	−0.20 (0.04)	1.833 (0.019)	0.071 (0.025)

[a] Standard deviations (experimental errors) are given in parentheses. Solvent was [$^2H_6$]acetone. $T = 294$ K. [b] Calculated using PANIC.

Table 2 One-bond, $^1J(^{13}C_\alpha, {}^1H)$, three-bond, $^3J(^1H_\alpha, {}^2H_{\alpha'})$ coupling constants (Hz), and secondary deuterium isotope effects, Δ (Hz), in deuteriated *trans*-stilbenes[a]

	$^1J(^{13}C_\alpha, {}^1H)$[b]		$^3J(^1H_\alpha, {}^2H_{\alpha'})$[c]	
Isotopomer		Δ		Δ
1′	152.19[d] (0.12)			
2′			2.210 (0.009)	
3′			2.211 (0.010)	—
4′	152.16[c] (0.01)			
5′			2.300 (0.008)	0.090 (0.017)
6′			2.301 (0.010)	0.091 (0.019)
7′	152.10[d] (0.01)	−0.06 (0.02)		
8′	152.05 (0.02)	−0.11 (0.03)	2.309 (0.015)	0.099 (0.024)
9′	152.03[d] (0.02)	−0.13 (0.03)		
10′	151.98 (0.03)	−0.18 (0.04)	2.340 (0.018)	0.130 (0.027)

[a] Standard deviations (experimental errors) are given in parentheses. $T = 294$ K. [b] Solvent was [$^2H_6$]acetone. [c] Solvent was [^{2}H]chloroform. [d] Calculated using PANIC.

Table 3 The calculated coupling constants (Hz) in the olefinic part of *cis*- and *trans*-stilbene (PANIC)[a]

Isotopomer	$^1J(^{13}C_\alpha, {}^1H)$	$^2J(^{13}C_\alpha, {}^1H)$	$^3J(^1H_\alpha, {}^1H_{\alpha'})$
1	155.53	−1.49	12.32
1′	152.16	−1.65	16.55

[a] Standard deviations are better than 0.016 Hz.

isotope effects are given in Tables 1–3. In the case of secondary isotope effects experimental error is given as the sum of the two individual standard deviations calculated for the coupling constant in deuteriated and undeuteriated molecules, according to the expressions for secondary isotope effects, eqns. (2) and (3). Furthermore, for the two primary effects the experimental error is obtained by multiplying the calculated standard deviation for $^1J(^{13}C_\alpha, {}^2H)$ by the factor γ_H/γ_D plus the standard deviation calculated for $^1J(^{13}C_\alpha, {}^1H)$, according to eqn. (1).

Calculations

Spectral calculations were made using the Aspect 3000 data system and the PANIC program. Structural parameters of both stilbene isomers were obtained using the semiempirical AM1 method (MOPAC, version 6.0) for optimizing molecular geometry.

Results and discussion

Secondary deuterium effects

All isotopomers studied here are shown in Fig. 1. The olefinic parts of the one- and two-dimensional ^1H–^{13}C one-bond HMQC and calculated spectra of *cis*-stilbene **1** are presented in Fig. 2. The numbering of the carbon atoms and conformations of the stilbene isomers are depicted in Fig. 3. Spin–spin coupling constants and secondary deuterium isotope effects are collected in Tables 1 and 2. The effects have been calculated using the expressions (2) and (3). The calculated olefinic coupling constants are given in Table 3.

An additional splitting which can be seen in Fig. 2 stems from the homonuclear $^3J(^1H_\alpha, {}^1H_{\alpha'})$ vicinal coupling retained also in HMQC spectra. The values obtained for these vicinal couplings are consistent with trends observed for similar π-systems, *i.e.* the *trans* coupling is larger than *cis* (see Table 3).

Although the olefinic parts of the spectra in Fig. 2(*a*) and (*b*) appear simple, the splittings do not correspond exactly to the coupling constants, except for $^3J(^1H_\alpha, {}^1H_{\alpha'})$. The two olefinic protons are chemically equivalent but magnetically nonequivalent (anisogamous). Since $^3J(^1H_\alpha, {}^1H_{\alpha'})$ is sufficiently large to provide significant mixing of the spin states, spectra cannot be treated according to the first-order rules.[21] The olefinic part of *cis*-stilbene, **1a**, constitutes a typical ABX nuclear spin system. The exact values of $^1J(^{13}C_\alpha, {}^1H)$ and $^2J(^{13}C_\alpha, {}^1H)$ can only be derived by a complete spectral analysis. Hence, we have performed spectral calculations using the PANIC program and analysed both the AB and X parts of the spectra for isotopomers **1**, **4**, **7** and **9**, where a $C^1H{=}C^1H$ moiety is present. There are fifteen possible transitions between the eight energy levels. The AB part of the spectrum consists of eight observable tran-

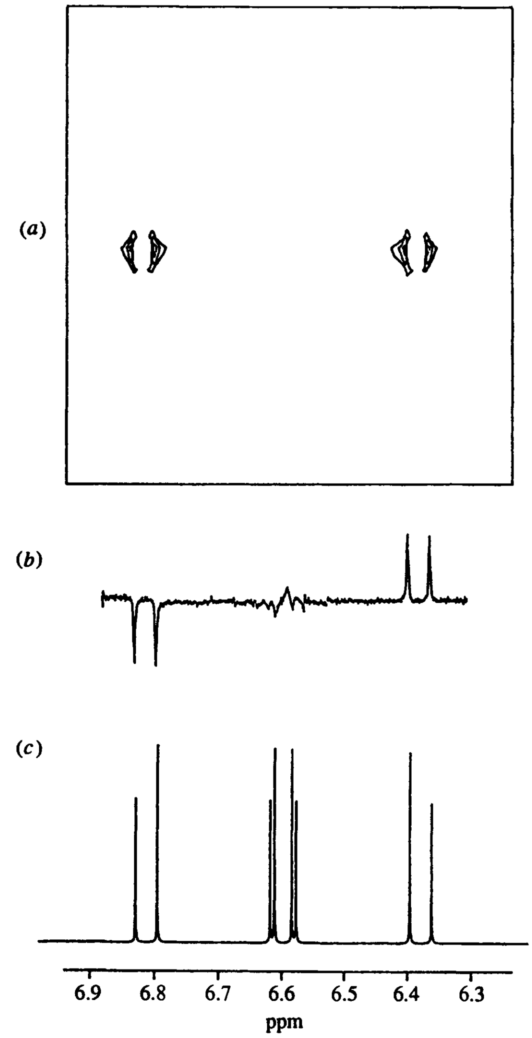
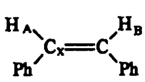


Fig. 2 The HMQC spectra of *cis*-stilbene **1**: (*a*) 2D, (*b*) 1D, (*c*) AB-part of the calculated spectrum (PANIC). The HMQC out of phase spectra were recorded at 360 MHz, with a delay set to optimize the $^1J(^{13}C_\alpha, {}^1H)$ coupling.



1a

sitions, the X part of six, while one transition has zero intensity. Two of the allowed transitions in the X region are combinations which were obtained only in the calculated spectra (Fig. 2), while their experimental intensities are very low. The real values of the coupling constants of *cis*- and *trans*-stilbene are given in Table 3. On the contrary, all isotopomers containing one deuterium atom at the α-position, *i.e.* **2**, **3**, **5**, **6**, **8** and **10**, constitute an AMX spin system which can be treated as a first-order spectrum and the splittings observed in the HMQC spectra represent the true coupling constant values.

In spite of their very small values, isotope effects are measured very accurately for all deuteriated isotopomers (Table 1). The secondary effect on ${}^{1}J({}^{13}\mathrm{C}_\alpha, {}^{1}\mathrm{H})$ in α-deuteriated isotopomer **2** amounts to −0.06, in hexadeuteriated (${}^{2}\mathrm{H}_6$) isotopomer **5** it amounts to −0.16, while that in undecadeuteriated (${}^{2}\mathrm{H}_{11}$) isotopomer **10** has the value of −0.20. The additivity rule seems to hold (within experimental error) for deuterium effects on one-bond coupling, as was also found for the effects on ${}^{13}\mathrm{C}$ chemical shifts.[22] For the two ${}^{2}\mathrm{H}_6$ isotopomers, **5** and **6**, very similar values of −0.16 and −0.15, respectively, have been determined. These two isotopomers differ only with respect to whether the olefinic deuterium atom is placed at the α- or α′-position (see Fig. 1). The same holds for the isotopomer **8** (${}^{2}\mathrm{H}_7$) if the contribution of *para*-deuterium is neglected. The change due to the deuterium effect in monodeuteriated **2** is 0.04% and in perdeuteriated **10** it is 0.13% of the original coupling constant value. In the majority of reports on ${}^{n}J({}^{13}\mathrm{C},{}^{1}\mathrm{H})$ coupling constants, secondary isotope effects are negative and do not exceed 0.10% of the magnitude.[5,6]

Very precise measurements of ${}^{3}J({}^{1}\mathrm{H}_\alpha,{}^{2}\mathrm{H}_{\alpha'})$ have enabled us to determine deuterium effects on three-bond proton–deuterium couplings for the first time. Contrary to effects on ${}^{1}J({}^{13}\mathrm{C}_\alpha,{}^{1}\mathrm{H})$, all effects on ${}^{3}J({}^{1}\mathrm{H}_\alpha,{}^{1}\mathrm{H}_{\alpha'})$ are positive. Again the effect is larger when more deuterium atoms are involved. The effect in [${}^{2}\mathrm{H}_{11}$]-*cis*-stilbene **10** is 0.07, which is a 4.0% change in the coupling constant magnitude.

In *trans*-stilbene an accurate measurement of the ${}^{1}J({}^{13}\mathrm{C}_\alpha, {}^{1}\mathrm{H})$ coupling constant in the HMQC spectra was hindered due to the overlapping of the α- and *para*-proton resonances. This obstacle is overcome in those isotopomers which bear the deuterium at both *para*-positions, such as **4′**, **7′**, **8′**, **9′** and **10′**. Assuming no deuterium effect on ${}^{1}J({}^{13}\mathrm{C}_\alpha, {}^{1}\mathrm{H})$ in isotopomer **4′**, where both deuterium atoms are placed five bonds away from the coupled nuclei, the measured value is taken as the reference. The olefinic part of isotopomers **1′**, **4′**, **7′** and **9′** constitute an ABX spin system and spectral calculations were performed in order to obtain the real coupling constant values. The secondary effects are similar to those revealed for *cis*-isomer as can be seen in Table 2.

A reduction of one-bond coupling constant is greater when more deuterium atoms are involved. The cumulative effect seems to hold for these isotopomers too. The largest effect is found in the [${}^{2}\mathrm{H}_{11}$]-*trans*-stilbene **10′**, amounting to −0.18, which is a reduction by 0.12%.

The secondary effects on ${}^{3}J({}^{1}\mathrm{H}_\alpha, {}^{2}\mathrm{H}_{\alpha'})$ are all positive as in *cis*-isotopomers, but range from 0.09 in **5′** and **6′** to 0.13 in **10′**. The latter change in the coupling constant value is 5.9% and thus significantly larger than that in the corresponding *cis*-isotopomer **10** (4.0%). To the best of our knowledge this is the biggest change in coupling constant value originating from a secondary deuterium effect.

Primary deuterium effects

Primary deuterium effects on the one-bond ${}^{13}\mathrm{C}_\alpha$–${}^{1}\mathrm{H}$ coupling constant could be determined less precisely. In some cases error in measured ${}^{13}\mathrm{C}$, ${}^{2}\mathrm{H}$ coupling constants is larger than in ${}^{13}\mathrm{C}$, ${}^{1}\mathrm{H}$ due to the contributions of quadrupolar relaxation of ${}^{2}\mathrm{H}$.[9] Deuterium relaxation influences the relaxation mechanisms of all neighbouring nuclei and usually broadens the lines in proton decoupled ${}^{13}\mathrm{C}$ spectra. In his review on isotope effects on coupling constants, Sergeyev[5a] discussed in detail the contribution of quadrupolar relaxation to the linewidths. In cases where, due to quadrupolar effects, an appreciable line broadening occurs, a decoupling of the deuterium or a lineshape analysis are required to obtain an appropriate accuracy. Furthermore, the experimental error is unavoidably increased by a factor of $\gamma_\mathrm{H}/\gamma_\mathrm{D}$ when calculating ${}^{1}J({}^{13}\mathrm{C}_\alpha, {}^{1}\mathrm{H})$ using eqn. (1). A much longer time is necessary to gain a good signal-to-noise (S/N) ratio in ${}^{13}\mathrm{C}$ NMR spectra. The accompanying temperature gradients even if composite pulse decoupling sequences (like Waltz) are used, usually lead to additional broadening of the lines, and thus less accurate determination of coupling constants. Bearing in mind the points stated above, we have measured ${}^{1}J({}^{13}\mathrm{C}_\alpha, {}^{2}\mathrm{H})$ coupling constants for both monodeuteriated stilbene isomers, **2** and **2′**, only to see if the trend found for secondary effects are also preserved for primary effects. The values of 23.808 (standard deviation is 0.055) for **2** and 23.266 (standard deviation is 0.075) for **2′** have been determined. In order to obtain more accurate values the mentioned lineshape procedure is required. According to the eqn. (1) the primary effects on ${}^{1}J({}^{13}\mathrm{C}_\alpha, {}^{1}\mathrm{H})$ are calculated to be −0.44 (standard deviation is 0.37) and −0.60 (standard deviation is 0.49) for **2** and **2′**, respectively.

Geometrical considerations

Isotope effects on coupling constants could also be understood in terms of the usual physicochemical concepts. The C–${}^{2}\mathrm{H}$ stretching mode makes the greatest contribution to the change in rovibrational averaging. It has been shown by microwave and Raman spectroscopies,[23] electron and neutron diffraction,[24] as well as by calculations[25] that the C–${}^{2}\mathrm{H}$ bond is shorter than the original C–${}^{1}\mathrm{H}$ bond and has a smaller amplitude of vibration. Changes in neighbouring bond lengths, as well as possible angle deformations on deuteriation can sometimes be significant too.[10] Since both ${}^{1}J({}^{13}\mathrm{C}, {}^{1}\mathrm{H})$ and ${}^{3}J({}^{1}\mathrm{H}, {}^{1}\mathrm{H})$ depend on hybridization and bond or dihedral angles,[26] *i.e.* conformation, any change in these parameters should effect the coupling. It has been shown that ${}^{3}J({}^{1}\mathrm{H}, {}^{1}\mathrm{H})$ increases, while ${}^{1}J({}^{13}\mathrm{C}, {}^{1}\mathrm{H})$ decreases with decreasing CCH angle.[27] In this respect it is worth checking whether deuteriation influences bond or dihedral angles in the stilbene molecules and whether that would affect the olefinic coupling constants.

The conformations of *cis*- and *trans*-stilbene determined experimentally[28] and theoretically[29] are a consequence of steric repulsions between *ortho*- and α-protons (Fig. 3) and competitive π-conjugation, leading to a nonplanar arrangement in both isomers. In order to relate deuterium isotope effects to structural parameters and conformation, we have performed quantum mechanical calculations using the semiempirical AM1 method (MOPAC, version 6.0). Some of the structural parameters obtained in this way are presented in Table 4. The *ortho*–α (H-6, H-α) nonbonding proton distance in *cis*-stilbene is shorter than the *ortho*–*ortho′* (H-2, H-2′) distance; however, both are longer than the corresponding *ortho*–α (H-6, H-α) and *ortho*–α′ (H-2, H-α′) proton distances in the *trans*-isomer. The repulsion between neighbouring *ortho*-protons (H-2, H-2′) in *cis*-stilbene is the main cause of a rather large Ph–C=C dihedral angle found in this molecule. The only significant interactions in the *trans*-isomer are those between *ortho* (H-2) and α′-protons (Fig. 3) leading to a slight deviation from planarity. Therefore, shorter C_α–${}^{2}\mathrm{H}$ and C_{ortho}–${}^{2}\mathrm{H}$ bonds in comparison with C_α–${}^{1}\mathrm{H}$ and C_{ortho}–${}^{1}\mathrm{H}$ release the strain between olefinic and phenyl moieties in both *cis*- and *trans*-stilbene isotopomers and thus could slightly increase the p-character of the remaining C–${}^{1}\mathrm{H}$ olefinic bond. The increase of ${}^{3}J({}^{1}\mathrm{H}, {}^{2}\mathrm{H})$ and the decrease of ${}^{1}J({}^{13}\mathrm{C}, {}^{1}\mathrm{H})$ (Tables 1 and 2)

Table 4 Some nonbonding proton distances (Å), and Ph–C=C dihedral angles (°), in *cis*- and *trans*-stilbene as calculated using the AM1 method

	Distance				Ph–C=C angle
Isotopomer	*ortho–ortho*	*ortho*–α	*ortho*–α′	α,α′	
1	(H-2, H-2′) 2.933	(H-6, H-α) 2.514 (H-2, H-α) 3.675	(H-6, H-α′) 4.539 (H-2, H-α′) 3.908	(H-α, H-α′) 2.384	40.4
1′	(H-2, H-2′) 4.485 (H-6, H-6′) 4.485	(H-6, H-α) 2.402 (H-2, H-α) 4.586	(H-6, H-α′) 4.586 (H-2, H-α′) 2.163	(H-α, H-α′) 3.116	22.2

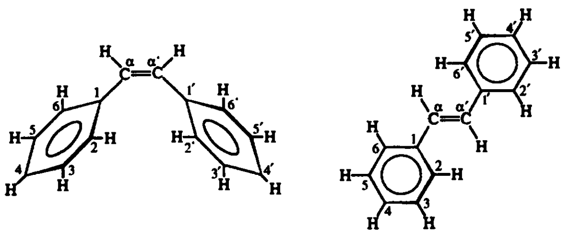


Fig. 3 Conformations of *cis*- (left) and *trans*-stilbene (right) as calculated by the AM1 semiempirical method

reflect a subtle conformational change due to deuteriation. Larger effects on $^3J(^1H, ^2H)$ than on $^1J(^{13}C, ^1H)$ indicate a higher sensitivity of the former to this change. As evidenced from our experimental results and AM1 calculations, the conformations of both α-deuteriostilbenes undergo changes due to a smaller steric requirement of the respective $C–^2H$ bonds and therefore less pronounced *ortho*–α repulsions, giving somewhat smaller valence C=C–H and probably also dihedral Ph–C=C angles. When more deuterium atoms are present at the α- and *ortho*-positions (isotopomers **8**, **8′**, **9**, **9′**, **10** and **10′**) the strain is even more released. These results are in agreement with those reported for *p*-fluoro-α-deuterio-*trans*-stilbene by Mitchell and Philips.[30] Although the authors concluded from ^{19}F NMR spectra that the deuteriated molecule becomes more coplanar than the undeuteriated one, the contribution of the π-system to the shielding or coupling tensor was not established. The question still remains, how does the isotopic substitution affect conjugational properties of the molecule, if it does at all? However, in explaining the observed isotope effects it is not necessary to invoke conjugation effects. Changes in relative rotamer populations associated with different dihedral angles and bonds and vibrational averaging over these should account for the measured isotope effects on coupling constants.

As shown by the AM1 calculations the *ortho*–α′ (H-2, H-α′) distance in the *trans* isomer is the shortest of all nonbonding proton–proton distances (only 2.163 Å) and therefore the strongest interactions exist. Hence, one should expect larger secondary effects on $^3J(^1H_\alpha, ^2H_{\alpha'})$ in α-deuteriated *trans*- than in the corresponding *cis*-isotopomers (Fig. 1), which was confirmed in our experiments (see Tables 1 and 2). It is therefore most likely that the aforementioned interactions account for the differences between the secondary effects on $^1J(^{13}C_\alpha, ^1H)$ and $^3J(^1H_\alpha, ^2H_{\alpha'})$ in *trans*- and *cis*-stilbene isotopomers. A comparison of the secondary with the primary effects could not be made quantitatively because of the relatively large standard deviations calculated for the latter. Primary effects are also found to be slightly larger in the α-deuterio-*trans*-stilbene than in the corresponding *cis*-isotopomer, owing to the same steric origin.

The present results demonstrate larger negative primary than secondary deuterium isotope effects on $^1J(^{13}C_\alpha, ^1H)$ in both stilbene isomers. On the other hand, the secondary effects on $^3J(^1H_\alpha, ^2H_{\alpha'})$ are all positive, but significantly larger in *trans*- than in *cis*-stilbene isotopomers. This is attributed to a greater relative change in conformation for the former, stemming from a higher steric release due to the deuteriation. These secondary effects are larger than those so far reported in the literature.[5,6]

In α-deuteriated-*cis*- and *trans*-stilbenes[22] we have recently measured a reduced deuterium effect (*ca.* 50%) over two bonds on ^{13}C chemical shifts in comparison with other structurally related hydrocarbons. It gives further support to a steric and conformational origin of the respective isotope effects, since again the effect was larger for the *trans*- than for the *cis*-isomer.

Experimental and theoretical work on isotope effects also including other isotopes like ^{13}C and ^{15}N, are being carried out in our laboratory[31] for a series of labelled benzene derivatives.

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