

Deuterium Isotope Effects and Their Nonadditivity in ^{13}C -NMR Spectra of Polydeuteriated *trans*-*N*-Benzylideneaniline Isotopomers[†]

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Deuterium-induced isotope effects on ^{13}C -NMR chemical shifts in polydeuteriated isotopomers of *trans*-*N*-benzylideneaniline were measured and analyzed. These effects are influenced by the molecular conformation and lone-pair electrons, which govern their sign, magnitude and extent. The longest observed total isotope effects are those through eight bonds, ${}^{\text{t}(8)}\Delta$, in pentadeuteriated isotopomers **3** and **4**. In general, the trends observed in *trans*-*N*-benzylideneaniline isotopomers investigated here are similar to those found in isoelectronic hydrocarbons and molecules of related type. However, nonadditivity has been found for carbon atoms sensitive to changes in the distribution of rotamer populations caused by the isotopic substitution.

INTRODUCTION

Besides isotope effects in chemical kinetics,¹ stable isotopes play an important role in NMR spectroscopy for at least two main reasons: (i) they are a useful tool in spectral assignment, especially in larger organic molecules and biomolecules, and (ii) they provide information about the overall molecular structure and dynamics in solution. Two distinct types of isotope effects have been investigated in NMR: the intrinsic and equilibrium isotope effects.²

[†] Dedicated to the late Prof. Stanko Borčić (1931–1994).

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A great deal of effort has been made to rationalize changes in NMR spectra caused by isotopic substitution. It is generally accepted that isotope effects are of a rovibrational origin, *i.e.* they arise from different averaged rotational and vibrational geometries of isotopomers.³ Since exact *ab initio* calculations of isotope effects in relatively large molecules are not feasible at present,³ empirical correlations and trends found for isotope effects have usually been rationalized in terms of physical organic concepts.^{2,4}

Among the isotopes studied, deuterium causes the biggest changes in NMR spectral parameters due to the biggest fractional change in mass upon isotopic substitution (²H instead of ¹H causes a 100% change). It is, therefore, not surprising that the main data published so far are devoted to deuterium isotope effects.^{2,3}

We have recently reported on ²H, ¹³C and ¹⁵N intrinsic isotope effects in molecules of the Ph-R and Ph-Z-Ph types (where Ph refers to phenyl, R to a sidechain group and Z to a bridging group) on ¹H and ¹³C chemical shifts,⁴⁻⁸ spin-spin coupling constants⁹ and spin-lattice relaxation times.¹⁰ It has been demonstrated that the sign, magnitude and extent of isotope effects depend on the isotopic position in a molecule,⁵ π -electron delocalization⁶⁻⁸ and the nature of a sidechain (R) or a bridging group (Z).⁴⁻⁸ Furthermore, the transmission of long range isotope effects, *i.e.* those over more than three bonds from the isotopic site, in mono-deuteriated Ph-Z-Ph isotopomers resemble the π -polarization mechanism.^{7,8} Long range deuterium isotope effects have also proved to be a sensitive probe of molecular conformation.⁴

The present study treats the influence of polydeuteriation on the observed trends in isotope effects, especially additivity. Namely, when more deuterium atoms are present in a molecule, the total effect on a particular site should be the sum of individual isotope effects. Additivity was found to hold in the majority of cases,^{2,3} but significant deviations were observed in molecules containing a heteroatom, like oxygen in benzophenone⁸ and benzoic acid.⁸ Therefore, we prepared a series of polydeuteriated *trans-N*-benzylideneaniline isotopomers (Figure 1) and analyzed their ¹³C-NMR spectra. A comparison with closely related polydeuteriated molecules was made as well.

EXPERIMENTAL

¹³C proton decoupled NMR spectra with the Waltz-16 decoupling were obtained with Varian Gemini 300 and Bruker WM 360 spectrometers, operating at 75.4 and 90.6 MHz, respectively. Spectra were recorded from CDCl₃ solutions using 5 mm NMR tubes with sample concentrations of 20–30 mg ml⁻¹ at 294 K. Deuterium from the solvent was used as the lock signal and TMS as the internal standard. Narrow region spectra with spectral widths of 1000–3000 Hz were zero filled to 64 K, thus giving a digital resolution better than 0.05 Hz after Fourier transformations. Stand-

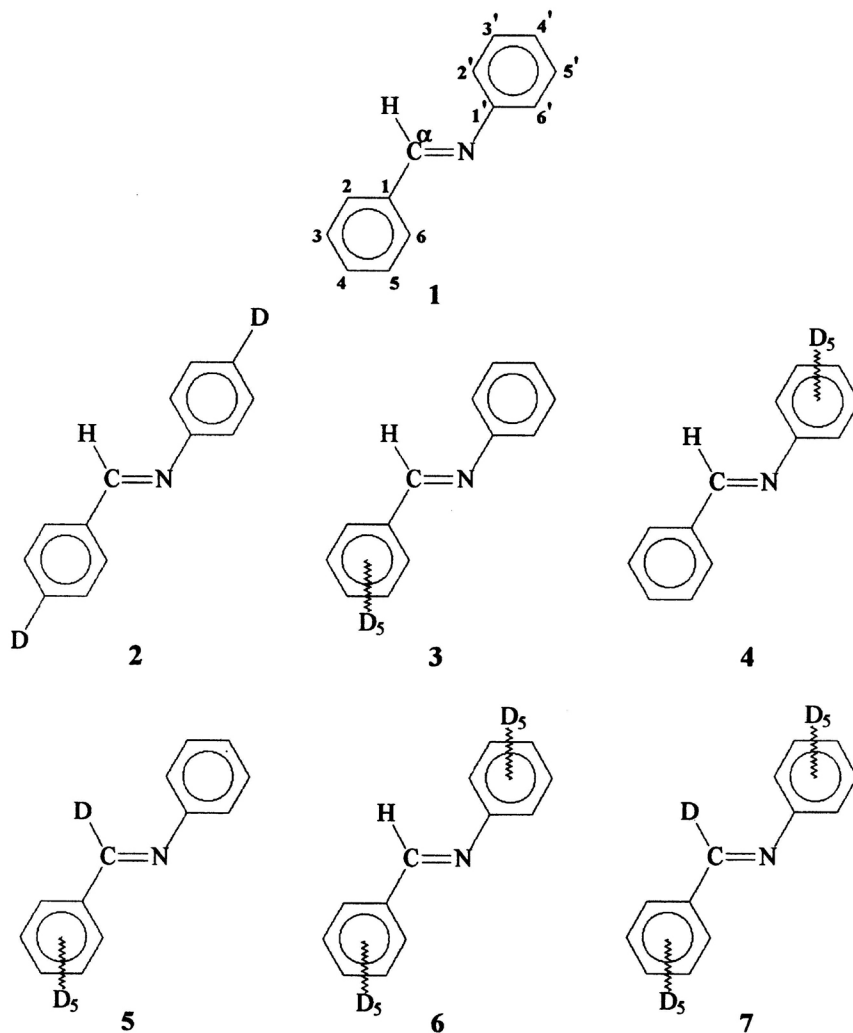


Figure 1. Enumeration of carbon atoms and polydeuteriated isotopomers of *trans*-*N*-benzylideneaniline.

ard errors are given in Table I. In the case of nonadditivity estimations (*i.e.* additivity calculations), total errors were calculated by summing up the individual mean square errors of the respective effects. The deuterium isotope effects on ^{13}C chemical shifts were determined from mixtures of isotopically labelled and unlabelled species, prepared in different ratios.

The isotopomers displayed in Figure 1 were synthesized using the procedure described elsewhere.¹¹

RESULTS AND DISCUSSION

Deuterium isotope effects, $\Delta^{13}\text{C}(^2\text{H})$, on ^{13}C chemical shifts in polydeuteriated *trans-N*-benzylideneaniline isotopomers are listed in Table I. The effects were calculated using the expression

$${}^{t(n)}\Delta^{13}\text{C}(^2\text{H}) = \delta^{13}\text{C}(^1\text{H}) - \delta^{13}\text{C}(^2\text{H}) \quad (1)$$

where ${}^t\Delta$ denotes a total effect and (n) the number of intervening bonds between the carbon under observation and the nearest deuterium atom, while $\delta^{13}\text{C}(^1\text{H})$ and $\delta^{13}\text{C}(^2\text{H})$ are the chemical shifts of the corresponding carbon atoms in the undeuteriated and deuteriated molecules, respectively. A positive sign thus denotes an upfield deuterium-induced chemical shift, *i.e.* a shielding effect. All effects are given in ppb.

Total deuterium isotope effects in 4,4'-dideuteriated isotopomer **2** are spread between -4.5 and 296.0 ppb. The only negative (deshielding) value of -4.5 ppb was observed at C-1', whereas no effect was observed at C-1, C-2,6 and C- α . The absence of isotope effects at C-1 and C-2,6 is due to the action of lone pair electrons. However, the effect at C- α (otherwise found in related monodeuteriated molecules) is cancelled out due to the opposite signs and similar magnitudes of ${}^5\Delta$ and ${}^6\Delta$, acting from the 4- and the 4'-positions, respectively.⁶ The magnitude and sign of all effects are consistent with those observed previously.⁴⁻⁸

In pentadeuterio (${}^2\text{H}_5$) isotopomers **3** and **4**, having the perdeuteriated benzylidene (Ph-C) and aniline (Ph-N) ring, respectively, all effects are positive except for those observed at C-1' in **3** and C-1 in **4** (Table I). Within the deuteriated rings, similar values of the total effects at C-4,4' and C-3,5,3',5' were measured (*ca.* 500 ppb) whereas only 423.0 ppb at C-2,6 and 396.0 ppb at C-2' were detected. These lower values are simply due to the lack of one of the ${}^2\Delta$ contributions, since one of the carbons next to C-2,6 and C-2',6' is the quarternary carbon, C-1 or C-1' (Figure 1). On average, the total effects in deuteriated ring of **4** are smaller than those of **3**, due to the closer proximity of the nitrogen lone pair to the aniline ring, which inductively diminishes the magnitude of the effect. The effect at C- α in **3** is reduced by *ca.* 30% from the values obtained in *cis*-stilbene⁷ and *trans*-stilbene,¹² both being hydrocarbons, also as a consequence of the inductive effect of the lone pair. In the corresponding isotopomers of *trans*-azobenzene and benzophenone,⁸ where two lone pairs exist, even smaller values than those in **3** were observed at the same site. Contrary to positive values at C- α in pentadeuteriated isotopomers of *cis*-stilbene, *trans*-stilbene, *trans*-azobenzene, benzophenone and **3**, isotope effects are negative at C-1'. In the undeuteriated phenyl ring (Ph-N) of isotopomer **3**, no total effect at C-2',6' and C-3',5' was observed, while an effect of 4.0 ppb was determined at C-2,6 of isotopomer **4**. The effects at C-4' in **3** and at C-4 in **4**, both having the same value of

TABLE I

Deuterium isotope effects, $t^{(n)}\Delta/\text{ppb}$,* in ^{13}C -NMR spectra of polydeuterated *trans*-*N*-benzylideneaniline isotopomers

Isotopomer	$4,4'\text{-}^2\text{H}_2\text{-tBA}$ (2)	$^2\text{H}_5$ (B)-tBA (3) [#]	$^2\text{H}_5$ (A)-tBA (4) [#]	$^2\text{H}_6$ (B)-tBA (5) [#]	$^2\text{H}_{10}$ -tBA (6)	$^2\text{H}_{11}$ -tBA (7)
Carbon	$t^{(n)}\Delta/\text{ppb}$					
C- α		$t^{(3)}\Delta = 31.5$	$t^{(4)}\Delta = 8.0$	$t^{(1)}\Delta = 291.0$	$t^{(3)}\Delta = 28.0$	$t^{(1)}\Delta = 287.0$
C-1'	$t^{(4)}\Delta = -4.5$	$t^{(5)}\Delta = -11.5$	$t^{(2)}\Delta = 121.5$	$t^{(3)}\Delta = -17.0$	$t^{(2)}\Delta = 123.0$	$t^{(2)}\Delta = 128.0$
C-1		$t^{(2)}\Delta = 153.0$	$t^{(5)}\Delta = -6.5$	$t^{(2)}\Delta \approx 225.0$	$t^{(2)}\Delta = 146.0$	$t^{(2)}\Delta = 223.0$
C-4	$t^{(1)}\Delta = 296.0$	$t^{(1)}\Delta = 513.5$	$t^{(8)}\Delta = 6.0$		$t^{(1)}\Delta = 513.0$	$t^{(1)}\Delta = 508.0$
C-3',5'	$t^{(2)}\Delta = 111.0$		$t^{(1)}\Delta = 504.0$		$t^{(1)}\Delta = 507.0$	$t^{(1)}\Delta = 500.0$
C-2,6		$t^{(1)}\Delta = 423.0$	$t^{(6)}\Delta = 4.0$	$t^{(1)}\Delta = 448.0$	$t^{(1)}\Delta = 416.0$	$t^{(1)}\Delta = 458.0$
C-3,5	$t^{(2)}\Delta = 110.0$	$t^{(1)}\Delta = 513.5$		$t^{(1)}\Delta = 513.5$	$t^{(1)}\Delta = 506.0$	$t^{(1)}\Delta = 511.0$
C-4'	$t^{(1)}\Delta = 287.0$	$t^{(8)}\Delta = 6.0$	$t^{(1)}\Delta = 506.0$	$t^{(6)}\Delta = 13.0$	$t^{(1)}\Delta = 488.0$	$t^{(1)}\Delta = 501.0$
C-2',6'	$t^{(3)}\Delta = 7.0$		$t^{(1)}\Delta = 396.0$	$t^{(4)}\Delta = -8.0$	$t^{(1)}\Delta = 390.0$	$t^{(1)}\Delta = 394.0$

* $t^i\Delta$ denotes a total effect and (n) the number of intervening bonds between the carbon under observation and the nearest deuterium atom; standard deviations are better than 1.0 ppb for the effects in **2** and better than 2.0 ppb for the other effects.

[#] (A) denotes aniline (PhN) and (B) benzylidene (PhC) ring.

only 6.0 ppb (Table I), are conformationally dependent. Namely, they depend on the dihedral Ph-C and Ph-N angles, since the corresponding effects in almost planar *trans*-stilbene and *trans*-azobenzene are as high as 11.3¹² and 11.1 ppb,¹³ respectively. In distorted *cis*-stilbene, as well as in **3** and **4**, where dihedral angles are about 50°, these effects are much smaller. A similar conformational dependence was found also for ⁶Δ in 4-deuteriated and ³Δ in α-deuteriated Ph-Z-Ph compounds.^{4,7,13}

In hexadeuterio isotopomer **5**, having in comparison with **3** an additional deuterium atom at the α-position, two negative effects were found in the undeuteriated ring, *i.e.* at C-1' and C-2',6' (Table I). The relatively smaller ^{t(1)}Δ at C-α (291.0 ppb) in **5** than that in *cis*-stilbene (383.6 ppb) and *trans*-stilbene (349.8 ppb) is consistent with the established dependence of ¹Δ in α-deuteriated Ph-Z-Ph isotopomers¹³ on C-atom hybridization.¹⁴

Total effects in the decadeuteriated isotopomer **6** are all positive, which is in agreement with the observed trends. Since the contributions of ¹Δ and ²Δ to the total effects at the ring carbons are always large and positive, they exceed small negative long range contributions giving rise to the overall positive values. The effect at C-α is much smaller in **6** and decadeuteriated benzophenone,⁸ both having a heteroatom with lone pairs, than in the corresponding *cis*-stilbene⁷ and *trans*-stilbene.¹²

In the perdeuteriated isotopomer **7** (²H₁₁) similar trends to those in **6** were observed. The effect at C-α is smaller by as much as 43% and 30% than the corresponding values in *cis*-stilbene⁷ and *trans*-stilbene,¹² respectively. A significantly smaller value was observed also at the C-1' position.

Additivity

We have recently demonstrated that the additivity rule holds for deuteriated isotopomers of *cis*-stilbene.⁷ However, this is not true of all the isotopomers of *trans*-*N*-benzylideneaniline (Table II), being isoelectronic with *cis*-stilbene, but containing a heteroatom with a lone-pair and a considerably different conformation. The largest deviation from the additivity is found at C-α in isotopomer **6** (Table II), where the calculated value is on average (depending on which isotopomers are taken into account) by 45% lower than the measured one. The deviation is 11.5 ± 4.0 ppb if the corresponding values of isotopomers **4** and **5** are summed up, but as high as 13.5 ± 5.0 ppb if contributions of the effects in monodeuteriated isotopomers are taken into account.⁶ For the same carbon, a similar deviation is detected also in isotopomer **7**, but being much smaller, *i.e.* about 4.5% different from the measured value in **7**. However, if the effects in decadeuterio **6** and α-²H-*trans*-*N*-benzylideneaniline⁶ are summed up, no deviation is found. The aforesaid deviations are all negative, *i.e.* larger calculated than measured values are obtained (Table II). Small, but significant deviations are also observed at C-1', C-2,6 and C-4' (Table II). It is interesting to note that the deviations are positive at C-1' and C-2,6 but negative at C-α and C-4'.

TABLE II
 Observed and calculated isotope effects and their difference (all in ppb) in some polydeuteriated
trans-N-benzylideneaniline isotopomers

Atom	C- α			C-1'			C-2,6			C-4'		
	obs. §	calc.	diff.	obs.	calc.	diff.	obs.	calc.	diff.	obs.	calc.	diff.
3 + 4 (\approx 6)	28.0	39.5	-11.5	123.0	109.9	13.1	416.0	427.0	11	488.0	512.0	-24
3 + 4 + α^* (\approx 7)	287.0	299.5	-12.5	128.0	104.9	23.1	458.0	448.5	9.5	501.0	518.5	-17.5
6 + α (\approx 7)	287.0	288.0	-1.0	128.0	118.0	10.0	458.0	437.5	20.5	501.0	494.5	6.5
4 + 5 (\approx 7)	287.0	299.0	-12.0	128.0	104.4	23.6	458.0	452.0	6.0	501.0	519.0	-18.0

§ obs. = observed, calc. = calculated, diff. = difference (obs. - calc.).

* α = α - ^2H -*trans-N*-benzylideneaniline.

The nonadditivity of deuterium effects in polydeuterated isotopomers of *trans-N*-benzylideneaniline are attributed to redistribution of rotamer populations upon deuteration. It was found in deuterated biphenyls¹⁵ that the perdeuterated phenyl ring has a slightly different rotational barrier than an undeuterated one. The deviations in **6** and **7** are due to a shorter C-²H than C-¹H bond, which releases the strain between *ortho*-positions and lone electron pair, thus affecting rotations about Ph-C and Ph-N axes. This brings about differences in the distribution of rotamer populations between deuterated and undeuterated molecules, whereby chemical shifts are changed. The same perturbation on perdeuteration was also observed in polydeuterated benzophenone isotopomers.⁸ Deviations from the additivity discussed here, as well as differences in values of individual deuterium effects, such as ²Δ and ³Δ in *ortho*- and *meta*-deuterated benzene derivatives,⁵⁻⁸ will be completely understood after thorough normal coordinate analyses have been accomplished.

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SAŽETAK

Deuterijski izotopni efekti na ^{13}C -NMR kemijske pomake polideuteriranih izotopomera *trans-N*-benzilidenanilina i njihova neaditivnost

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Određeni su i analizirani deuterijski izotopni efekti na ^{13}C -NMR kemijske pomake polideuteriranih izotopomera *trans-N*-benzilidenanilina. Efekti ovise o konformaciji molekule, te o utjecaju slobodnoga elektronskog para, što određuje predznak, iznos i doseg izotopnih efekata. Najdalji opaženi ukupni efekti su oni kroz osam veza, ${}^{t(8)}\Delta$, u pentadeuteriranim izotopomerima **3** i **4**. Općenito, trendovi opaženi u istraživanim izotopomerima *trans-N*-benzilidenanilina slični su onima u izoelektronskim ugljikovodicima i drugima strukturno srodnim molekulama. Međutim, opažena je neaditivnost izotopnih efekata za one atome ugljika koji su osjetljivi na promjene u raspodjeli rotamera izazvane zamjenom izotopa.