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Polarization transfer from *para*-hydrogen to heteronuclei: Effect of H/D substitution. The case of AA′X and A₂A₂′X spin systems

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Abstract

Upon hydrogenation from *para*-hydrogen (*p*-H₂), hyperpolarization transfer toward a heteronucleus may be possible even if the two protons are chemically equivalent in the final product (but not magnetically equivalent), provided that *J* couplings with the heteronucleus exist. It is however shown (theoretically and experimentally) that this transfer effectively occurs if the spin system in the hydrogenated molecule is of the type AA′X (A and A′ denoting the two protons originating from *p*-H₂ and X the heteronucleus) but does not occur for a spin system of the A₂A₂′X type. A theory has been worked out for assessing the details of the X spectrum (multiplet patterns) in the case of ALTADENA and PASADENA experiments. Experimental verifications are provided.
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Keywords: Para-hydrogen; Hyperpolarization; Hyperpolarization transfer to heteronuclei; Density operator; Spin systems

1. Introduction

It is now well established that the addition of hydrogen enriched in the *para* spin state (*para*-H₂) to organic or inorganic compounds can lead to strongly enhanced absorptions/emissions in the ¹H NMR spectrum of the hydrogenated substrates [1–6].

This phenomenon occurs provided that the following conditions are satisfied: (a) the spin correlation between the two hydrogen nuclei must be maintained during the hydrogenation, (b) the symmetry of the hydrogen molecule is broken in the reaction product, (c) hydrogenation process is fast enough to prevent the equilibrium population of the spin levels being restored by relaxation in the intermediate states [3,4].

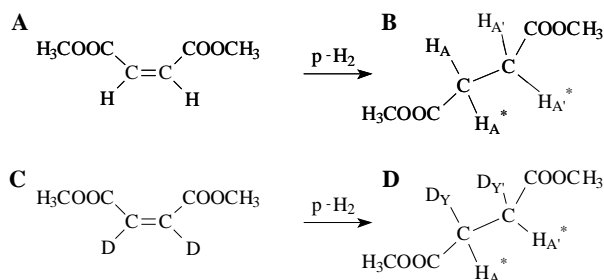The hyperpolarization of the hydrogens set can be transferred to heteroatoms present on the hydrogenated substrates (heteronuclear-*para*-hydrogen induced polariza-tion) by means of scalar coupling with *para*-hydrogen nuclei (polarization transfer through the spin system) or through the nuclear Overhauser effect phenomenon [7–11].

The strongest hyperpolarization effects (up to 2–3 thousand times) are due to scalar coupling (*J* coupling) between heteronuclei and *para*-hydrogen in hydrogenation products. This kind of polarization transfer has been studied from a theoretical point of view and relationships between the intensity of polarization and the strength of J_{H-H} and J_{H-X} (where X is an heteroatom, usually ¹³C) have been proposed [8,10]. This phenomenon has been observed in several *para*-hydrogenated organic molecules, both symmetrical and asymmetrical, especially if the hydrogenation is carried out in a low magnetic field (ALTADENA experiments) [12]. The aim of our work was to explore how different isotopomers may show different heteronuclear *para*-hydrogen Induced Polarization effects as a consequence of the changes in symmetry of the spin states and to account for the details of the heteronucleus spectrum.

To this purpose the *para*-hydrogenation of dimethyl maleate and of its bideuterated analogue (CH₃OOC–CD=CD–COOCH₃) has been considered.

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A

$$H_3COOC \diagdown C=C \diagup COOCH_3$$
$$H \diagup \qquad \diagdown H$$

$$\xrightarrow{p\text{-}H_2}$$

B

(structure of dimethylsuccinate B with labels $H_{A'}$, COOCH₃, H_A, C, C, H_3COOC, H_A^*, $H_{A'}^*$)

C

$$H_3COOC \diagdown C=C \diagup COOCH_3$$
$$D \diagup \qquad \diagdown D$$

$$\xrightarrow{p\text{-}H_2}$$

D

(structure of dimethylsuccinate D with labels D_Y, $D_{Y'}$, COOCH₃, C, C, H_3COOC, $H_{A'}^*$, H_A^*)

2. Experimental results

The *para*-hydrogenation of dimethylmaleate (**A** or **C**) to dimethylsuccinate (**B** or **D**) has been carried out in acetone-d_6 in the presence of [Rh(COD)dppb]$^+$BF$_4^-$ as catalyst (8 mM).

For most experiments, the ALTADENA procedure has been followed, i.e., 0.5 ml of a solution of **A** (150 mM) in a 5-mm NMR tube equipped with a teflon valve is loaded with 4 atm of *para*-hydrogen; after a vigorous shaking the NMR tube is introduced in the magnet and a single scan ^{13}C spectrum is immediately acquired.

In the case of $(\mathbf{A}) \xrightarrow{p\text{-}H_2} (\mathbf{B})$, we do not observe any polarisation in the ^{13}C NMR spectrum: this cannot be explained by considering the J constants between *para*-hydrogen protons ($J_{H^*-H^*}$) and heteronuclei (J_{H^*-C}) but we must take into account the other two protons of the substrate.

The importance of these ^{1}H nuclei on the polarisation transfer to ^{13}C has been demonstrated performing the same experiment on the bideuterated dimethylmaleate

(CH$_3$OOC–CD=CD–COOCH$_3$) (**C**). Compound **C** has been obtained by catalytic deuteration of acetylene dicarboxylate dimethyl ester [Aldrich No. 762-42-5]. The deuteration of the alkyne to the alkene-d_2 has been followed by means of the methyl ^{1}H NMR signal of the alkene product. $(\mathbf{C}) \xrightarrow{p\text{-}H_2} (\mathbf{D})$ was also obtained by means of a PASADENA experiment. For convenience and sensitivity reasons, the hydrogenation reaction was carried out in the fringe of a cryomagnet at relatively high pressure (4 atm).

Contrary to compound **B**, the deuterium containing *para*-hydrogenated dimethylsuccinate **D** displays a detectable polarization in the ^{13}C NMR spectrum. As shown in Fig. 1 (ALTADENA spectrum), **D** shows hyperpolarized ^{13}C signals in the aliphatic region. The multiplet pattern (doublet of triplets) is due to direct scalar coupling constants $^1J_{CH_A}$ and $^1J_{CD}$ and the separation between the absorption and emission peaks is related to the $^2J_{CH_{A'}}$ coupling. The PASADENA spectrum (Fig. 2) exhibits a different pattern in the aliphatic region and presents in addition an enhancement of the carbonyl signal. It is therefore advisable to work out a detailed theoretical investigation of the processes involved in these experiments.

2.1. Theory of hyperpolarization transfer (general considerations)

As detailed in a previous work [10] and outlined here, the problem can be attacked by relying on the density operator, the initial expression of which is

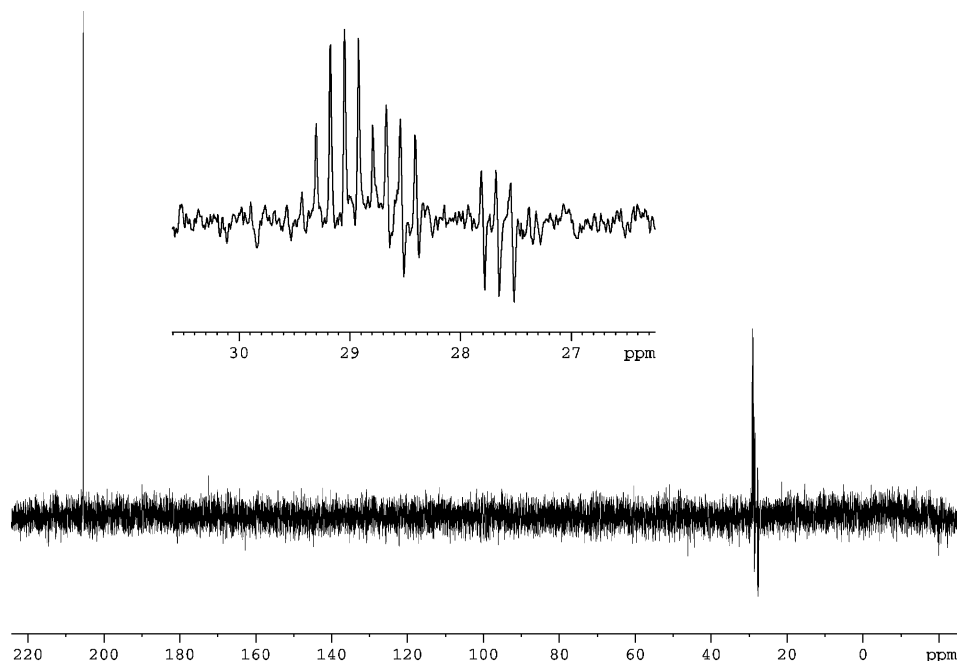$$\sigma(0) = E/4 - I_x^A I_x^{A'} - I_y^A I_y^{A'} - I_z^A I_z^{A'}, \qquad (1)$$

Fig. 1. ^{13}C NMR spectrum (1 scan) of *para*-hydrogenated dimethyl-maleate-d_2, ALTADENA experiment. Only the aliphatic part is enhanced. The multiplet on the left, which partly overlap with the dimethylsuccinate spectrum is due to acetone-d_6.
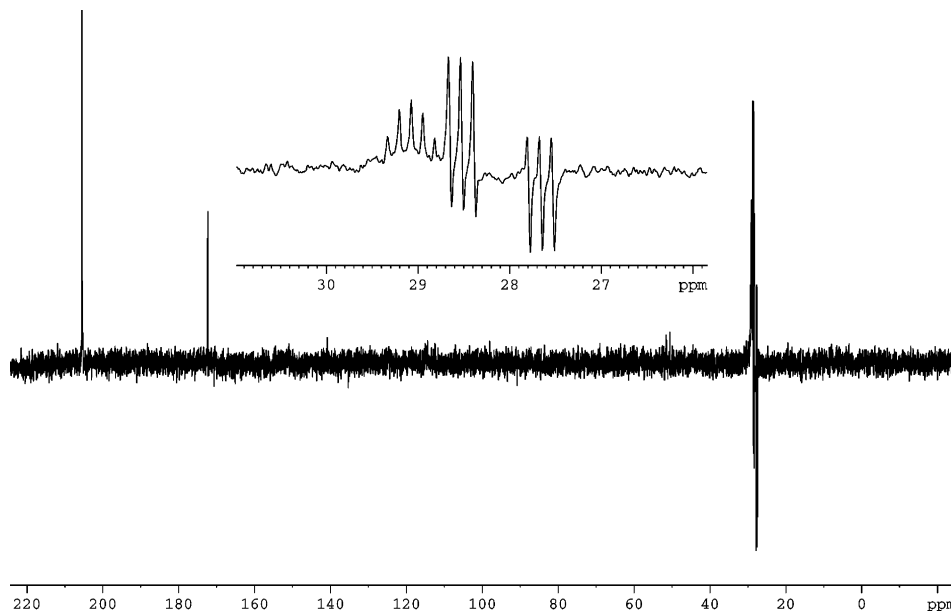
Fig. 2. The PASADENA ^{13}C spectrum of *para*-hydrogenated dimethylmaleate-d$_2$ obtained in experimental conditions described in text. Notice that the aliphatic pattern is different from the one of Fig. 1 and that the carbonyl signal is also enhanced.

where A and A′ denote the two hydrogens in the *para* state. E is the identity operator and I are spin operators.

When hydrogenation process occurs, there is a sudden change of the Hamiltonian governing the spin system and the evolution of the density operator can be deduced from the Liouville–von Neumann equation

$$\frac{d\sigma(t)}{dt} = -i[\mathscr{H}, \sigma(t)]. \tag{2}$$

When the hydrogenation process comes to an end, one reaches a steady state such as $\frac{d\sigma_{st}}{dt} = 0$ which amounts to write

$$[\mathscr{H}, \sigma_{st}] = 0. \tag{3}$$

In other words, the steady state of the spin system is such that the density operator must commute with the Hamiltonian of the new spin system. For an ALTADENA experiment (hydrogenation supposed to take place in zero magnetic field), it is the full J coupling Hamiltonian which can be written as

$$\mathscr{H}_J^{ALT} = \sum_{i<i'} J_{ii'}(I_x^i I_x^{i'} + I_y^i I_y^{i'} + I_z^i I_z^{i'}) \tag{4}$$

for any pair of nuclei (including A and A′) whenever they are not part of a set of magnetically equivalent nuclei. In that case, spin operators related to the whole set of magnetically equivalent nuclei are relevant. We further assume that molecular motions are sufficiently fast to average out dipolar interactions. This is generally the case in the liquid state; this feature arises simply from the fact that the trace of the dipolar tensor is zero and has nothing to do with the strength of the static magnetic field.

It was shown [10] that, for a PASADENA experiment, only the J coupling Hamiltonian is again relevant and assuming first order conditions (except of course for A and A′), one has

$$\mathscr{H}_J^{PASA} = J_{AA'}\left(I_z^A I_z^{A'} + I_x^A I_x^{A'} + I_y^A I_y^{A'}\right) + \sum_i (J_{Ai} I_z^A I_z^i$$
$$+ J_{A'i} I_z^{A'} I_z^i) + \sum_{i<j; i,j \neq A,A'} J_{ij} I_z^i I_z^j. \tag{5}$$

The density operator can always be expanded as

$$\sigma = E/4 + \sum_j a_j G_j, \tag{6}$$

where G_j are all possible spin product operators of the form $G_j = \prod_{i=1}^{n} S_i^{(j)}$ where $S_i^{(j)}$ is E^i, I_x^i, I_y^i, or I_z^i and n is the number of spins in the hydrogenated molecule. These operator products are known to be orthogonal, that is

$$\text{Tr}(G_k^+ G_l) = 0 \quad \text{for } k \neq l, \tag{7}$$

where G_k^+ is the adjoint of G_k, i.e., the transposed complex conjugate of G_k.

Owing to the initial state (see (1)), we shall use for convenience the following notations:

$$G_1 = I_x^A I_x^{A'}, \quad G_2 = I_y^A I_y^{A'}, \quad G_3 = I_z^A I_z^{A'}. \tag{8}$$

From Eqs. (2) and (6), the evolution of the spin system can be evaluated by the following equation:

$$\sum_j \frac{da_j}{dt} G_j = -i[\mathscr{H}, \sigma].$$

Resorting to the property expressed by (7) and noting that all operators G_j are hermitian (with the consequence that $G_j^+ = G_j$, we obtain

$$\frac{\mathrm{d}a_j}{\mathrm{d}t} = -\mathrm{i}\,\mathrm{Tr}([\mathscr{H}, \sigma]G_j) = \mathrm{i}\,\mathrm{Tr}([\mathscr{H}, G_j]\sigma). \tag{9}$$

2.2. Invariants

2.2.1. The A_2X and $AA'X$ spin systems

The immediate consequence of (9) is that the quantity G_j does not evolve if the associated operator commutes with the Hamiltonian of the spin system corresponding to the hydrogenated molecule (in that case, $\frac{\mathrm{d}a_j}{\mathrm{d}t} = 0$ and $a_j^{\mathrm{st}} = a_j(0)$). In particular, if $G_1 + G_2 + G_3$ commutes with the Hamiltonian, then $\sigma_{\mathrm{st}} = \sigma(0)$ and no transfer can occur towards any other quantity. This is the case whenever the two hydrogen nuclei remain magnetically equivalent after hydrogenation since the part of the Hamiltonian concerning J coupling between these two nuclei, $J_{AA'}(I_x^A I_x^{A'} + I_y^A I_y^{A'} + I_z^A I_z^{A'})$ (which is, except the factor $J_{AA'}$, nothing else than $G_1 + G_2 + G_3$) is known to commute with the whole Hamiltonian [13]. Thus, no hyperpolarization transfer occurs if the hydrogenated molecule proceeds from an A_2X spin system while transfer toward X becomes possible for an $AA'X$ spin system (the subject of the present study).

2.2.2. The $A_2A_2'X$ spin system

A related situation is when the two hydrogens in the *para* state are embedded, upon hydrogenation, in two different sets of magnetically equivalent nuclei. This is precisely the case for the hydrogenation of dimethylmaleate which results in dimethylsuccinate (see above). For molecules involving a carbon-13 within the initial double bond, we have to deal with a $A_2A_2'X$ spin system, one of the two para hydrogens is A, the other A'. As shown in the next section, hyperpolarization transfer, if it occurs, originates necessarily from $G_1 + G_2 + G_3$ and is mediated by $J_{AA'}$. In other words, only $(I_x^A I_x^{A'} + I_y^A I_y^{A'} + I_z^A I_z^{A'})$ must be multiplied by $J_{AA'}$ in the Hamiltonian of the final spin system. It turns out that such a term no longer exists in the Hamiltonian of a $A_2A_2'X$ spin system. Rather one has (A_1 and A_1' being the two additional protons of the spin system)

$$J_{AA'}(I_x^A I_x^{A'} + I_x^A I_x^{A_1'} + I_x^{A_1} I_x^{A'} + I_x^{A_1} I_x^{A_1'} + I_y^A I_y^{A'} + I_y^A I_y^{A_1'}$$
$$+ I_y^{A_1} I_y^{A'} + I_y^{A_1} I_y^{A_1'} + I_z^A I_z^{A'} + I_z^A I_z^{A_1'} + I_z^{A_1} I_z^{A'} + I_z^{A_1} I_z^{A_1'}).$$

Clearly $G_1 + G_2 + G_3$ vanishes by losing its identity through admixture with the three other terms and by the fact that (A, A_1) on one hand, and (A', A_1') on the other hand, are indistinguishable. *This feature thus precludes any polarization transfer toward X in an $A_2A_2'X$ spin system* and explains the above experimental results. It can, however, be noted that the hyperpolarization originating from p-H$_2$ cannot be lost and remains amid the proton spin system (observed experimental results not shown). Albeit not transferred to X, it actually appears as enhanced ^{13}C satellites in the proton spectrum since the presence of a carbon-13 is necessary for breaking the symmetry, thus unraveling the existence of hyperpolarization.

2.3. Polarization transfers

In other situations, where $G_1 + G_2 + G_3$ is still present in the Hamiltonian without commuting with it, we can expect transfers toward other quantities through equations derived from $[\mathscr{H}, \sigma_{\mathrm{st}}] = 0$. These transfers will be assessed by the coefficients a_j^{st} involved in the expansion in the steady state density operator (see (6)) $\sigma_{\mathrm{st}} = \sum_j a_j^{\mathrm{st}} G_j$ whereas the effective part of the Hamiltonian can be expanded as $\mathscr{H} = \sum_i J_i G_i$ where J_i is the J coupling between two spins and G_i the two-spin product operator corresponding to this coupling. Resorting to $[H, \sigma_{\mathrm{st}}] = 0$ leads to equations of the type

$$\sum_{i,j} J_i[G_i, G_j]a_j^{\mathrm{st}} = 0. \tag{10}$$

The commutator in (10) is non-zero provided that the two-spin product operators G_i and G_j share one spin and that $[G_i, G_j] = F_k$, where F_k is a three-spin product operator involving the three *different* spins which appear in G_i and G_j. An equation is obtained for all pairs (G_i, G_j) leading to the *same* F_k. This means that, if we start from an hyperpolarized state (the source, say $G_1 = I_x^A I_x^{A'}$), there will be a coupling (thus transfer) with another state (target) represented by G_j, provided that the commutator $[G_1, G_j]$ on the one hand, and the coupling constants J_1 and J_j on the other hand, are non-zero. This leads at least to the following equation:

$$\pm J_1 a_j^{\mathrm{st}} \mp J_j a_1^{\mathrm{st}} = 0. \tag{11}$$

Additional terms may be involved if other commutators lead to the same F_k as $[G_1, G_j]$.

It can be noticed that the right hand-side member of all equations derived from relation (10) is zero. These equations need therefore to be appended by an equation, the right hand-side member of which is non-zero. This can be provided by a conservation equation based on the norm of the density operator. In a very general way, the norm of an hermitian operator (as the density operator) is equal to the trace of its square. The norm of the density operator must be kept constant provided that it describes a steady state (a state devoid of time evolution, i.e., a state for which no precession occurs). This is because the square of the density operator represents the "populations" (contributions) of the various spin operators upon which it is expanded. This is true for $\sigma(0)$ and σ_{st}. One has thus

$$\mathrm{Tr}(\sigma_{\mathrm{st}}^2) = \mathrm{Tr}(\sigma^2(0)). \tag{12}$$

This can be written as

$$\sum_j |a_j^{\mathrm{st}}|^2 = |a_1(0)|^2 + |a_2(0)|^2 + |a_3(0)|^2 = 3|a_1(0)|^2. \tag{13}$$

It can be noticed that the rightmost member of (13) is not of paramount importance as it represents merely a scaling factor associated with the rate of hyperpolarization (which may depend on a lot of experimental factors).

Additional relations can possibly be obtained by looking at linear combinations of G_j which commute with the Hamiltonian. In that case, the linear combination is invariant

thus leading to a relation between the relevant coefficients a_j^{st} and $a_j(0)$. Such a linear combination which is *always* valid can be found by remembering that $F_z = \sum_i I_z^i$ commutes with the Hamiltonian. This is also true for $F_z^2 = \sum_i (I_z^i)^2 + 2\sum_{i<i'} I_z^i I_z^{i'}$. As $(I_z^i)^2 = 1/4$, it follows that $\sum_{i<i'} I_z^i I_z^{i'}$ commutes with the Hamiltonian for *all* pairs (i, i') of nuclei implied in the J coupling network. Let j the numbering of spin pairs with $j = 1$ for the pair (A, A'); G_{3j} will therefore represent the operator product $I_z^i I_z^{i'}$ if j corresponds to the pair (i, i'). As a consequence of the commutation property discussed above, we have always

$$\sum_j a_{3j}^{st} = \sum_j a_{3j}(0) = a_3(0). \tag{14}$$

This relation is very important because G_{3j} are generally the only relevant product operators in a PASADENA experiment, besides, of course, G_1 and G_2 (see (5)) and other similar terms when first order conditions do not prevail. Concerning these two latter operators, as z is the only specified direction, one has $a_1^{stat} = a_2^{stat}$. On the other hand, as the ALTADENA Hamiltonian is isotropic (see (4)), the coefficients of $I_x^i I_x^{i'}$, $I_y^i I_y^{i'}$, $I_z^i I_z^{i'}$ are identical and it suffices to consider again the coefficients a_{3j}. From the summation in the left hand-side of (14), we can of course remove the coefficients a_{3j}^{st} corresponding to combinations of product operators, which turn out to commute with the Hamiltonian. Such combinations remain constant and thus do not benefit from polarization transfer.

2.4. Application to the AA'X system

Although compound D involves two deuterium nuclei and represents therefore a more complex spin system, it is deemed useful to determine how ^{13}C hyperpolarization arises in a symmetric molecule [6] described as an AA'X spin system.

2.4.1. Product operators and commutators

As explained in the previous section, we have to consider the following product operators (in addition to $G_1 = I_x^A I_x^{A'}$, $G_2 = I_y^A I_y^{A'}$, $G_3 = I_z^A I_z^{A'}$): $G_4 = I_x^A I_x^X$, $G_5 = I_y^A I_y^X$, $G_6 = I_z^A I_z^X$; $G_7 = I_x^{A'} I_x^X$, $G_8 = I_y^{A'} I_y^X$, $G_9 = I_z^{A'} I_z^X$.

We give below the non-zero commutators necessary for the application of Eq. (10).

$$[G_1, G_5] = iI_z^A I_x^{A'} I_y^X, \quad [G_1, G_6] = -iI_y^A I_x^{A'} I_z^X,$$
$$[G_1, G_8] = iI_x^A I_z^{A'} I_y^X, \quad [G_1, G_9] = -iI_x^A I_y^{A'} I_z^X,$$
$$[G_2, G_4] = -iI_z^A I_y^{A'} I_x^X, \quad [G_2, G_6] = iI_x^A I_y^{A'} I_z^X,$$
$$[G_2, G_7] = -iI_y^A I_z^{A'} I_x^X, \quad [G_2, G_9] = iI_y^A I_x^{A'} I_z^X,$$
$$[G_3, G_4] = iI_y^A I_z^{A'} I_x^X, \quad [G_3, G_5] = -iI_x^A I_z^{A'} I_y^X,$$
$$[G_3, G_7] = iI_z^A I_y^{A'} I_x^X, \quad [G_3, G_8] = -iI_z^A I_x^{A'} I_y^X$$
$$[G_4, G_8] = iI_x^A I_y^{A'} I_z^X, \quad [G_4, G_9] = -iI_x^A I_z^{A'} I_y^X$$
$$[G_5, G_7] = -iI_y^A I_x^{A'} I_z^X, \quad [G_5, G_9] = iI_y^A I_z^{A'} I_x^X$$
$$[G_6, G_7] = iI_z^A I_x^{A'} I_y^X, \quad [G_6, G_8] = -iI_z^A I_y^{A'} I_x^X$$

2.5. The steady state density operator in PASADENA experiments

From (5), we can write the relevant Hamiltonian as

$$\mathscr{H}_J^{PASA} = J_{AA'}\left(I_z^A I_z^{A'} + I_x^A I_x^{A'} + I_y^A I_y^{A'}\right) + J_{AX} I_z^A I_z^X + J_{A'X} I_z^{A'} I_z^X$$

We have thus to consider $G_1 = I_x^A I_x^{A'}$, $G_2 = I_y^A I_y^{A'}$, $G_3 = I_z^A I_z^{A'}$, $G_6 = I_z^A I_z^X$ and $G_9 = I_z^{A'} I_z^X$. As G_3 commutes with the Hamiltonian, $a_3^{st} = a_3(0)$. Moreover, from (14), we can write $a_3^{st} + a_6^{st} + a_9^{st} = a_3(0)$ (because $a_6(0) = a_9(0) = 0$). It follows immediately that $a_6^{st} = -a_9^{st}$. Now, applying the strategy described by Eqs. (10) and (11), we obtain (noticing that $a_1^{st} = a_2^{st}$)

$$a_6^{st} = \frac{J_{AX} - J_{A'X}}{2J_{AA'}} a_1^{st}.$$

Defining the initial hyperpolarization as $K = -a_1(0)$ and using (13), we obtain the steady state density operator

$$\sigma_{st}^{PAS}(AA'X) = E/4 + K\left[\frac{2J_{AA'}}{\sqrt{4J_{AA'}^2(J_{AX} - J_{A'X})^2}}(I_x^A I_x^{A'} + I_y^A I_y^{A'})\right.$$
$$\left. + I_z^A I_z^{A'} - \frac{J_{AX} - J_{A'X}}{\sqrt{4J_{AA'}^2(J_{AX} - J_{A'X})^2}}(I_z^A I_z^X - I_z^{A'} I_z^X)\right]. \tag{15}$$

From (15), it can be seen that transfer towards X occurs provided that $J_{AX} \neq J_{A'X}$, consistently with the conclusions of the previous section. Moreover, if one excepts $I_z^A I_z^{A'}$ which is not affected by the hydrogenation process, the balance between the hyperpolarization which remains at (A, A') and the one gained by X is given by the ratio $2J_{AA'}/(J_{AX} - J_{A'X})$. It can also be realized that the two longitudinal orders $I_z^A I_z^X$ and $I_z^{A'} I_z^X$ benefit from the same polarization transfer (with opposite signs) irrespective of the *individual* values of J_{AX} and $J_{A'X}$.

2.5.1. The steady state density operator in ALTADENA experiments

As already mentioned, the Hamiltonian is fully isotropic

$$\mathscr{H}_J^{ALT} = J_{AA'}(I_x^A I_x^{A'} + I_y^A I_y^{A'} + I_z^A I_z^{A'}) + J_{AX}(I_z^A I_z^X + I_y^A I_y^X + I_x^A I_x^X) + J_{A'X}(I_z^{A'} I_z^X + I_y^{A'} I_y^X + I_x^{A'} I_x^X)$$

and consequently one has the following equalities:

$$a_1^{st} = a_2^{st} = a_3^{st}; \quad a_4^{st} = a_5^{st} = a_6^{st}; \quad a_7^{st} = a_8^{st} = a_9^{st}.$$

Therefore, we have to deal with three unknowns; we shall choose a_3^{st}, a_6^{st}, and a_9^{st} just because the two latter correspond to longitudinal spin orders which can be readily converted into observable quantities. Defining again K as the initial hyperpolarization factor and referring to Eqs. (13) and (14), we easily obtain two equations:

$$|a_3^{st}|^2 + |a_6^{st}|^2 + |a_9^{st}|^2 = K^2,$$

$$a_3^{st} + a_6^{st} + a_9^{st} = a_3(0) = -K.$$

The missing equation is provided by resorting on relations such as (10) and (11) along with the above commutators

$$(J_{AX} - J_{A'X})a_3^{st} + (J_{A'X} - J_{AA'})a_6^{st} + (J_{AA'} - J_{AX})a_9^{st} = 0.$$

From the two latter equations, we can derive a relation which can be very useful in view of the interpretation of carbon-13 spectra

$$\frac{a_6^{st}}{a_9^{st}} = \frac{(J_{AX} - J_{AA'}) - (2J_{AX} - J_{A'X} - J_{AA'})(a_3^{st}/a_3(0))}{(J_{A'X} - J_{AA'}) - (-J_{AX} + 2J_{A'X} - J_{AA'})(a_3^{st}/a_3(0))}. \tag{16}$$

This relation tells us that a_6^{st} may become negligibly small if J_{AX} is the dominant coupling and if the ratio $a_3^{st}/a_3(0)$ is ca. 0.5. Such a situation may well be encountered and this explains (see below) why the longitudinal order $I_z^A I_z^X$ does not (surprisingly) benefit from any polarization transfer in spite of the large value of J_{AX}.

The full solution can be obtained by using the whole set of the three equations. If we define x as $x = a_3^{st}/a_3(0)$, we obtain:

$$a_6^{st} = a_3(0)\frac{(J_{AX} - J_{AA'}) - (2J_{AX} - J_{A'X} - J_{AA'})x}{J_{AX} + J_{A'X} - 2J_{AA'}},$$

$$a_9^{st} = a_3(0)\frac{(J_{A'X} - J_{AA'}) - (-J_{AX} + 2J_{A'X} - J_{AA'})x}{J_{AX} + J_{A'X} - 2J_{AA'}}, \tag{17}$$

while x is a root of the following equation:

$$3x^2 - 2x$$
$$+ \frac{-J_{AA'}^2 - J_{AX}J_{A'X} + J_{AA'}(J_{AX} + J_{A'X})}{J_{AX}^2 + J_{A'X}^2 + J_{AA'}^2 - J_{AX}J_{A'X} - J_{AA'}(J_{AX} + J_{A'X})}$$
$$= 0. \tag{18}$$

It can be again noticed that, if J_{AX} is the dominant coupling, then the third term is very small leading to a value of 2/3 for x.

2.6. Carbon-13 spectra

The next step is to delineate hyperpolarization effects on NMR spectra and, more especially here, on carbon-13 spectra. These effects are usually considered as arising from the fact that the wavefunction of nuclear spins in *para*-hydrogen $(\psi_p = \frac{1}{\sqrt{2}}|\alpha_A\beta_{A'} - \beta_A\alpha_{A'}\rangle)$ is overlapped only with some of the spin states of the product molecule. For example, if the *para*-hydrogen nuclei form an AX spin system, only the $\alpha\beta$ and $\beta\alpha$ states become equally hyperpopulated while the population of $\alpha\alpha$ and $\beta\beta$ states equal these of the corresponding triplet state of the hydrogen molecule [2].

Concerning an AA'X spin system, it is not obvious, owing to the number of spin states, that the interpretation will be as straightforward. In order to proceed, we must first diagonalize the matrix associated with the Hamiltonian operator

$$\mathscr{H} = -(I_z^A + I_z^{A'})\nu_A - I_z^X \nu_X$$
$$+ J_{AA'}\left[I_z^A I_z^{A'} + \frac{1}{2}(I_+^A I_-^{A'} + I_-^A I_+^{A'})\right] + J_{AX}I_z^A I_z^X$$
$$+ J_{A'X}I_z^{A'} I_z^X \tag{19}$$

we obtain the eight spin states (eigenvectors):

$$\psi_1 = \alpha_A\alpha_{A'}\alpha_X$$
$$\psi_2 = \alpha_A\alpha_{A'}\beta_X$$
$$\psi_3 = c_1(1/\sqrt{2})(\alpha_A\beta_{A'} - \beta_A\alpha_{A'})\alpha_X + c_2(1/\sqrt{2})(\alpha_A\beta_{A'} + \beta_A\alpha_{A'})\alpha_X$$
$$\psi_4 = d_1(1/\sqrt{2})(\alpha_A\beta_{A'} - \beta_A\alpha_{A'})\alpha_X - d_2(1/\sqrt{2})(\alpha_A\beta_{A'} + \beta_A\alpha_{A'})\alpha_X$$
$$\psi_5 = c_1(1/\sqrt{2})(\alpha_A\beta_{A'} - \beta_A\alpha_{A'})\beta_X - c_2(1/\sqrt{2})(\alpha_A\beta_{A'} + \beta_A\alpha_{A'})\beta_X$$
$$\psi_6 = d_1(1/\sqrt{2})(\alpha_A\beta_{A'} - \beta_A\alpha_{A'})\beta_X + d_2(1/\sqrt{2})(\alpha_A\beta_{A'} + \beta_A\alpha_{A'})\beta_X$$
$$\psi_7 = \beta_A\beta_{A'}\alpha_X$$
$$\psi_8 = \beta_A\beta_{A'}\beta_X \tag{20}$$

where we have introduced the two orthonormalized functions $\psi_p = \frac{1}{\sqrt{2}}|\alpha_A\beta_{A'} - \beta_A\alpha_{A'}\rangle$ and $\psi_o = \frac{1}{\sqrt{2}}|\alpha_A\beta_{A'} + \beta_A\alpha_{A'}\rangle$ which characterize the hydrogen *para* and *ortho* states, respectively. The coefficients c_1, c_2, d_1, and d_2 are eigenvector components and are given below.

With

$$r = \frac{J_{AX} - J_{A'X}}{2J_{AA'}} \tag{21}$$

the corresponding eigenvalues are as follows:

$$E_1 = -\nu_A - \nu_X/2 + (J_{AA'} + J_{AX} + J_{A'X})/4,$$
$$E_2 = -\nu_A + \nu_X/2 + (J_{AA'} - J_{AX} - J_{A'X})/4,$$
$$E_{3,4} = -\frac{\nu_X}{2} - \frac{J_{AA'}}{4} \pm \frac{J_{AA'}}{2}\sqrt{1 + r^2},$$
$$E_{5,6} = \frac{\nu_X}{2} - \frac{J_{AA'}}{4} \pm \frac{J_{AA'}}{2}\sqrt{1 + r^2}, \tag{22}$$
$$E_7 = \nu_A - \nu_X/2 + (J_{AA'} - J_{AX} - J_{A'X})/4,$$
$$E_8 = \nu_A + \nu_X/2 + (J_{AA'} + J_{AX} + J_{A'X})/4.$$

These results are obtained by constructing the Hamiltonian matrix on an appropriate basis essentially made of simple spin product functions (however, because we are dealing with *para*- and *ortho*-hydrogen, we have inserted, when necessary, the hydrogen the *para* and *ortho* functions ψ_p and ψ_o, see above): $\phi_1 = \alpha_A\alpha_{A'}\alpha_X$, $\phi_2 = \alpha_A\alpha_{A'}\beta_X$, $\phi_3 = (1/\sqrt{2})(\alpha_A\beta_{A'} - \beta_A\alpha_{A'})\alpha_X$, $\phi_4 = (1/\sqrt{2})(\alpha_A\beta_{A'} + \beta_A\alpha_{A'})\alpha_X$, $\phi_5 = (1/\sqrt{2})(\alpha_A\beta_{A'} - \beta_A\alpha_{A'})\beta_X$, $\phi_6 = (1/\sqrt{2})(\alpha_A\beta_{A'} + \beta_A\alpha_{A'})\beta_X$, $\phi_7 = \beta_A\beta_{A'}\alpha_X$, $\phi_8 = \beta_A\beta_{A'}\beta_X$. It turns out that the Hamiltonian matrix is diagonal except for the two subspaces (ϕ_3, ϕ_4) and (ϕ_5, ϕ_6). For instance, the sub-matrix associated with (ϕ_3, ϕ_4) is of the form

$$H = \begin{pmatrix} -\frac{\nu_X}{2} - \frac{3J_{AA'}}{4} & \frac{J_{AX} - J_{A'X}}{4} \\ \frac{J_{AX} - J_{A'X}}{4} & -\frac{\nu_X}{2} + \frac{J_{AA'}}{4} \end{pmatrix}.$$

The eigenvalues of this matrix correspond to the energies: $E_{3,4} = -\frac{\nu_X}{2} - \frac{J_{AA'}}{4} \pm \frac{J_{AA'}}{2}\sqrt{1 + r^2}$ and the coefficients c_1, c_2, d_1 and d_2 are the eigenvectors components:

$$E_3 \rightarrow \begin{cases} c_1 = \dfrac{r}{\sqrt{2}\sqrt{1+r^2+\sqrt{1+r^2}}} \\ c_2 = \dfrac{\sqrt{1+r^2}+1}{\sqrt{2}\sqrt{1+r^2+\sqrt{1+r^2}}} \end{cases}$$

$$E_4 \rightarrow \begin{cases} d_1 = \dfrac{r}{\sqrt{2}\sqrt{1+r^2-\sqrt{1+r^2}}} \\ -d_2 = -\dfrac{\sqrt{1+r^2}-1}{\sqrt{2}\sqrt{1+r^2-\sqrt{1+r^2}}} \end{cases} \tag{23}$$

When J_{AX} is much larger than the other couplings, c_1, c_2, d_1, and d_2 are close to $1/\sqrt{2}$. This approximation will be used in the forthcoming applications.

One would expect some enhancement for transitions which involve eigenfunctions possessing a contribution of the *para* wave function $\psi_p = \frac{1}{\sqrt{2}}|\alpha_A\beta_{A'} - \beta_A\alpha_{A'}\rangle$. Proceeding that way would however lead (with some ambiguity) to conclusions contrary to experimental observations. It is thus mandatory to rely on the rigorous procedure described thereafter.

The intensity of ^{13}C transitions can be calculated on the basis of the difference in the populations of spin levels by applying the usual formula $|\langle\Psi_i|I_+^X|\Psi_j\rangle|^2(P_i - P_j)$, where I_+^X is the X raising operator while P_i is the population of the ith energy level to be calculated from possible polarization transfers originating from *para*-hydrogen. This population is simply deduced from the scalar product $\langle\psi_i|\sigma|\psi_i\rangle$, where σ is the density operator. The expression of the density operator has been established in the previous section and are rewritten below in a more compact way:

$$\sigma^{PAS} = C_{AA'}^{PAS}[(I_+^A I_-^{A'} + I_-^A I_+^{A'})/2] + D_{AA'}^{PAS} I_z^A I_z^{A'} + C_{AX}^{PAS}(I_z^A I_z^X - I_z^{A'} I_z^X), \tag{24}$$

$$\sigma^{ALT} = C_{AA'}^{ALT}[I_z^A I_z^{A'} + (I_+^A I_-^{A'} + I_-^A I_+^{A'})/2] + C_{AX}^{ALT}[I_z^A I_z^X + (I_+^A I_-^X + I_-^A I_+^X)/2] + C_{A'X}^{ALT}[I_z^{A'} I_z^X + (I_+^{A'} I_-^X + I_-^{A'} I_+^X)/2], \tag{25}$$

where the coefficients $C_{AA'}$, $D_{AA'}$, C_{AX}, and $C_{A'X}$ represent the part of *para*-hydrogen hyperpolarization which has been transferred to the AA'X spin system (as calculated in the previous sub-section: see Eq. (15) for the PASADENA experiment while $C_{AA'}^{ALT}$, C_{AX}^{ALT} and $C_{A'X}^{ALT}$ can be identified to a_3^{st}, a_6^{st} and a_9^{st}, respectively and thus deduced from Eq. (17)).

2.6.1. The PASADENA spectrum

We obtain for the energy level populations:

$$P_1 = P_2 = P_7 = P_8 = D_{AA'}^{PAS}/4,$$
$$P_3 = P_5 = -(c_1^2 + c_2^2)D_{AA'}^{PAS}/4 + (c_2^2 - c_1^2)C_{AA'}^{PAS}/2 + (c_1 c_2)(C_{AX}^{PAS}),$$
$$P_4 = P_6 = -(d_1^2 + d_2^2)D_{AA'}^{PAS}/4 + (d_2^2 - d_1^2)C_{AA'}^{PAS}/2 - (d_1 d_2)(C_{AX}^{PAS}). \tag{26}$$

Transition intensities, for carbon-13 transitions, can then be calculated according to $|\langle\Psi_i|I_+^X|\Psi_j\rangle|^2(P_i - P_j)$, as explained before. The results given below are obtained under the hypothesis that no mixing effect occurs due to a non equilibrium state [14]. In a general way, this corresponds to spectra obtained under small flip angle conditions or, as this is here the case in practice, to first order spectra (see Table 1).

The enhanced spectrum is thus made of an antiphase doublet which corresponds in fact to the outer lines of the doublet of doublets (see Fig. 3, middle) if one assumes that J_{AX} and $J_{A'X}$ are of opposite signs. This latter hypothesis is certainly true in the case of dimethylsuccinate and is consistent with the experimental observations of Fig. 2. Of course, further splitting due to coupling with the deuterium nucleus (in the form of a 1:1:1 triplet) has to be taken into account. We can also notice a small residual pattern of the same type as the one observed in ALTADENA experiments (see below) which is presumably due to imperfect experimental conditions.

2.6.2. The ALTADENA spectrum

We obtain for the energy level populations:

$$P_1 = P_8 = (C_{AA'}^{ALT} + C_{AX}^{ALT} + C_{A'X}^{ALT})/4,$$
$$P_2 = P_7 = (C_{AA'}^{ALT} - C_{AX}^{ALT} - C_{A'X}^{ALT})/4,$$
$$P_3 = P_5 = (-3c_1^2 + c_2^2)C_{AA'}^{ALT}/4 + (c_1 c_2/2)(C_{AX}^{ALT} - C_{A'X}^{ALT}),$$
$$P_4 = P_6 = (-3d_1^2 + d_2^2)C_{AA'}^{ALT}/4 - (d_1 d_2/2)(C_{AX}^{ALT} - C_{A'X}^{ALT}). \tag{27}$$

The carbon-13 characteristics are gathered in Table 2.

From the last column of the above table it can be seen that the observed spectrum will depend on the relative values of C_{AX}^{ALT} and $C_{A'X}^{ALT}$ (see Fig. 3, bottom) or on their ratio as calculated in the previous section (see formula (16) with $\frac{a_6^{st}}{a_9^{st}} = \frac{C_{AX}^{ALT}}{C_{A'X}^{ALT}}$). In particular, if C_{AX}^{ALT} becomes negligibly small (due to the values of the various couplings and to the fact

Table 1

Transition	Frequency	Intensity	Approximate intensity[a]
$\psi_1 \rightarrow \psi_2$	$\nu_X - (J_{AX} + J_{A'X})/2$	$P_1 - P_2 = 0$	0
$\psi_3 \rightarrow \psi_6$	$\nu_X - (J_{AX} - J_{A'X})/2$	$(c_1 d_1 + c_2 d_2)^2[(-c_1^2 - c_2^2 + d_1^2 + d_2^2)D_{AA'}^{PAS}/4 + (-c_1^2 + c_2^2 + d_1^2 - d_2^2)C_{AA'}^{PAS}/4 + (c_1 c_2 + d_1 d_2)C_{AX}^{PAS}]$	C_{AX}^{PAS}
$\psi_3 \rightarrow \psi_5$	ν_X	$(c_1^2 - c_2^2)(P_3 - P_5) = 0$	0
$\psi_4 \rightarrow \psi_6$	ν_X	$(d_1^2 - d_2^2)(P_4 - P_6) = 0$	0
$\psi_4 \rightarrow \psi_5$	$\nu_X + (J_{AX} - J_{A'X})/2$	$(c_1 d_1 + c_2 d_2)^2[(c_1^2 + c_2^2 - d_1^2 - d_2^2)D_{AA'}^{PAS}/4 + (c_1^2 - c_2^2 - d_1^2 + d_2^2)C_{AA'}^{PAS}/4 - (c_1 c_2 + d_1 d_2)C_{AX}^{PAS}]$	$-C_{AX}^{PAS}$
$\psi_7 \rightarrow \psi_8$	$\nu_X + (J_{AX} + J_{A'X})/2$	$P_7 - P_8 = 0$	0

[a] With $c_1 = c_2 = d_1 = d_2 \approx 1/\sqrt{2}$.

Table 2

| Transition	Frequency	Intensity	Approximate intensity[a]
$\psi_1 \rightarrow \psi_2$	$\nu_X - (J_{AX} + J_{A'X})/2$	$C_{AX}^{ALT} + C_{A'X}^{ALT}$	$C_{AX}^{ALT} + C_{A'X}^{ALT}$
$\psi_3 \rightarrow \psi_6$	$\nu_X - (J_{AX} - J_{A'X})/2$	$(c_1 d_1 + c_2 d_2)^2 [(-3c_1^2 + c_2^2 + 3d_1^2 - d_2^2)C_{AA'}^{ALT}/4 + (c_1 c_2 + d_1 d_2)(C_{AX}^{ALT} - C_{A'X}^{ALT})]$	$C_{AX}^{ALT} - C_{A'X}^{ALT}$
$\psi_3 \rightarrow \psi_5$	ν_X	$(c_1^2 - c_2^2)(P_3 - P_5) = 0$	0
$\psi_4 \rightarrow \psi_6$	ν_X	$(d_1^2 - d_2^2)(P_4 - P_6) = 0$	0
$\psi_4 \rightarrow \psi_5$	$\nu_X + (J_{AX} - J_{A'X})/2$	$(c_1 d_1 + c_2 d_2)^2 [(3c_1^2 - c_2^2 - 3d_1^2 + d_2^2)C_{AA'}^{ALT}/4 - (c_1 c_2 + d_1 d_2)(C_{AX}^{ALT} - C_{A'X}^{ALT})]$	$-(C_{AX}^{ALT} - C_{A'X}^{ALT})$
$\psi_7 \rightarrow \psi_8$	$\nu_X + (J_{AX} + J_{A'X})/2$	$-(C_{AX}^{ALT} + C_{A'X}^{ALT})$	$-(C_{AX}^{ALT} + C_{A'X}^{ALT})$

[a] With $c_1 = c_2 = d_1 = d_2 \approx 1/\sqrt{2}$.
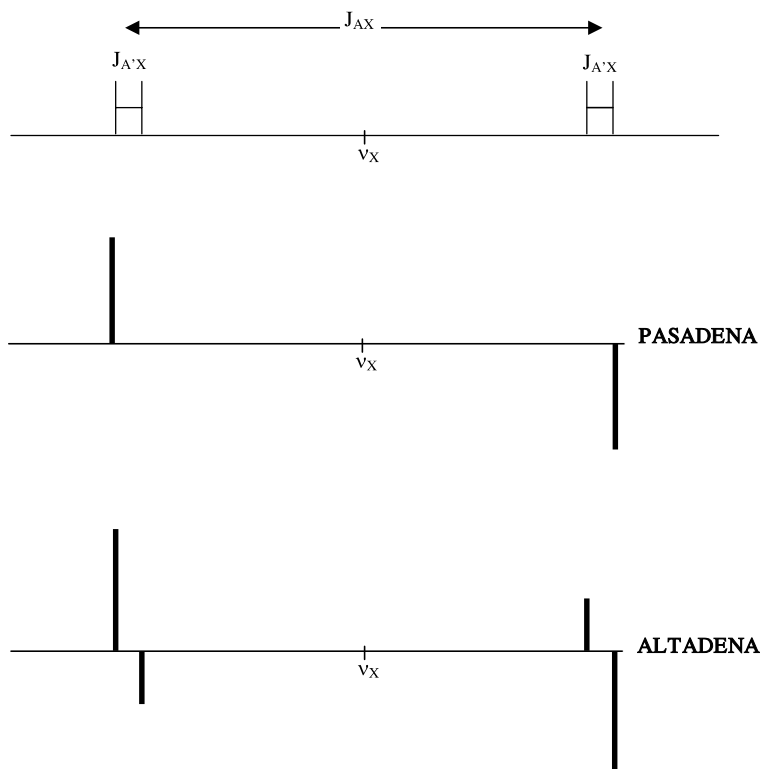
Fig. 3. Schematic spectra of a carbon-13 coupled to two chemically equivalent protons (AA'X spin system). From top to bottom: conventional, PASADENA and ALTADENA spectra. For the PASADENA spectrum, the signs of J_{AX} and $J_{A'X}$ are assumed to be opposite whereas the sketch of the ALTADENA spectrum corresponds to a situation for which $C_{A'X}^{ALT}$ is larger than C_{AX}^{ALT} (see text).

that, in (16), further transfers toward deuterium [10] and mediated by the carbon-13 nucleus have not been accounted for), one would observe two *identical* antiphase doublets (of splitting $J_{A'X}$) and separated by J_{AX}. The agreement between theory and experiment appears quite reasonable if one considers the additional splitting in the form of a 1:1:1 triplet due to coupling with the deuterium nucleus (see Fig. 1).

3. Conclusion

This study has demonstrated the importance of a proper theoretical treatment for understanding (and predicting) the detailed features of the spectra obtained after *para*-hydrogen polarization transfer. Line intensities are seen to depend critically not only on the J values but also on the type of experiment (ALTADENA or PASADENA). Important differences in the spectra of Figs. 1 and 2 illustrate this property which arises from quite different combinations of J couplings in the expressions relevant to these two experiments. Another important result of the present work is the absence of transfer toward X when the two *para*-hydrogen spins are, in the product obtained after hydrogenation, part of an $A_2A'_2X$ spin system. This lack of transfer can be easily explained by the nature and the symmetry of the spin system. This feature has been confirmed with other molecules (else than the one considered here), especially in the case of ethylene as obtained by *para*-hydrogenation of acetylene.

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