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Why thiocolchicine does not undergo photochemical isomerization: A theoretical study

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ABSTRACT

The reasons why colchicine undergoes photochemical cyclization to give lumicolchicine, whereas thiocolchicine does not, are investigated by theoretical methods. The relative stability of the reagent and of the products is computed at DFT level of theory and indicates that such a photochemical reaction is energetically possible.

The photochemical reaction path of thiocolchicine is studied within the relaxed energy scan, at MC-SCF level of theory. The results are again rather similar to those of colchicine. Finally, the spin–orbit coupling between S_1 and T_1 has been computed and are two order of magnitude greater than those of colchicine, that makes plausible that spin–orbit is the main reason of the observed reaction quenching.

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1. Introduction

Despite their rather similar molecular structure, colchicine (CC) and thiocolchicine (TCC) (Chart 1) show a very different photochemical behaviour. Indeed CC, when irradiated with photons corresponding at the maximum of the first absorption band, undergoes a rearrangement of the seven-atom ring to form β - and γ -lumicolchicine (LCC), whereas the absorption of photons in TCC does not induce any photochemical reaction and lumithiocolchicine (LTCC) do not form [1]. A similar different behaviour was also observed for colchicine and thiocolchicine [1,2]. The hypothesized mechanism for the photoisomerization of colchicine involves excitation of CC to the first singlet state S_1 , whose decay induces a disrotatory cyclization with a π bond that transforms into a σ bond to form two condensed, not coplanar, rings (see Chart 1). From the very low quantum yield ~ 0.04 measured for the colchicine photoreaction in methanol [3], it may be expected that no straightforward reaction mechanism occurs.

The experiments of transient spectroscopy of CC and TCC [1] irradiated at the wavelength of the maximum of the first absorption band $S_0 \rightarrow S_1$ (360 and 345 nm, respectively), show similar but not identical results. In fact CC and TCC in the populated S_1 state, absorb instantaneously at 510 and, respectively, 650 nm but the former show a longer lifetime, ~ 500 ps. These instantaneous transient absorptions were ascribed to $S_1 \rightarrow S_n$ electronic transitions in the near Franck–Condon region of the $S_0 \rightarrow S_1$ excitation. The most interesting feature is the appearance, after a delay of

300–500 fs, of a new large band at wavelengths around 400 nm, whose lifetime is found to be 20 ps for CC and 500 ps for TCC. On the basis of these very different values and of previous studies [3], this transient band was tentatively assigned to $S_1 \rightarrow S_n$ for CC (with S_1 in a rearranged relaxed geometry) and to $T_1 \rightarrow T_n$ for TCC. The latter assignment implies an efficient $S_1 \rightarrow T_1$ intersystem crossing with formation of long lived triplet states, which was tentatively hypothesized as the most important cause of the reaction quenching in TCC.

A subsequent theoretical study [4] of the photoconversion of CC put in evidence that the energetic of reactant and products is fully consistent with the experimental evidences of formation of β and γ -lumicolchicine. On the basis of the calculation of the relaxed energy scan (RES) of the first two singlet states, a plausible reaction mechanism was proposed. One more result of that work was that the involvement of the methoxylic oxygen (substituted by a sulfur atom in TCC) in the most changing molecular orbitals along the reaction path, does not seem to be relevant, and therefore it is expected that the energetic of CC and TCC are not very different to each other. Nevertheless, calculations are needed, in order to verify whether some differences exist.

In the present paper concerning with the photoreaction of TCC, we want to pursue two main goals. The first involves a series of calculations similar to those previously reported for CC, in order to ascertain possible differences in the energetic, reaction path and geometrical relaxation after $S_0 \rightarrow S_1$ excitation. The second is to verify the presence of an efficient intersystem crossing through the calculation of spin–orbit coupling matrix elements between the relevant singlet and triplet states. All these results will then be used to get new insights about the main problem tackled in the present work: why CC does react and TCC does not.

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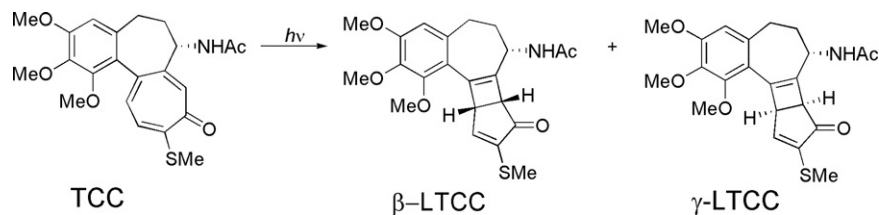


Chart 1. The photochemical reaction of thicolchicine to yield β - and γ -lumithicolchicine, which is expected, but not observed. On the contrary, the corresponding reaction of colchicine (the S atom is substituted by an O atom) is observed.

1.1. Computational details

The geometry of the ground state of colchicine and lumicolchicines was optimized without symmetry constraints, by the density functional theory (DFT) using the hybrid B3LYP functional [5,6] joined with the 6-31G^{*} basis set. In order to include some solvent effects, the calculations were repeated including two methanol molecules in the region of the seven atoms ring. DFT calculations were performed with the GAUSSIAN 03 package [7].

The reaction path was studied within the RES approach, in which an energy curve at the bottom of the valley of the potential energy surface of both S_0 and S_1 was computed at several values of a selected leading coordinate and optimizing the energy with respect to all the remaining internal coordinates. For this reaction, the natural choice of the leading coordinate is the C_4 – C_7 distance (Chart 2) which is the one undergoing the most relevant changes along the photochemical reaction. This leads the non-trivial problem of optimizing the geometry of the first excited state without the possibility of exploiting symmetry facilities, since the molecule has no symmetry irrespectively of the C_4 – C_7 distance.

To save computational time, the calculation of the energy of S_0 and S_1 was computed on a model system (Chart 2) in which the inert aromatic six-member ring trimethoxyphenyl was substituted by a rigid HC=CH group with the C=C bond fixed at the typical aromatic values 1.38 Å, and the amide group was substituted by a hydrogen atom. To verify the effectiveness of this molecular model, which is expected to preserve the original steric features of the reactive molecular region, the geometry of both TCC and LTCC was optimized and then compared with that obtained for the whole molecule. Since the bond lengths of the two calculations

do not differ more than 0.02 Å, the model system was considered adequate for the present study.

The RES of both S_0 and S_1 states was computed by MC-SCF calculations in the restricted active space (RAS) formulation [8,9], considering all the single and double excitations arising from the five higher occupied and the five lowest empty molecular orbitals (MOs). The active orbital space includes all the π and π^* MOs of the TCC model system, as well as the π MOs of the rigid HC=CH group which should mimic the non-reactive aromatic ring. In LTCC there are only four π orbitals and the active orbital space includes even one lone pair orbital on the thiomethyl group, whereas the newly formed C_4 – C_7 bond falls in the inactive space. Therefore, the active space appears to be slightly unbalanced for the reagent and the products. On the other hand, a more accurate description of the formation of the C_4 – C_7 bond would require the inclusion of all the valence orbitals but this is not possible for computational reasons. The first two singlet states were computed using a state averaged two states calculations with equal weights, in order to avoid root flipping problems. Geometry optimization was performed separately for S_0 and S_1 at several C_4 – C_7 distances. The MC-SCF energies along the RES of S_0 and S_1 and the spin–orbit coupling matrix elements [10] were computed with the MOLPRO program [11].

2. Results and discussion

2.1. Energy and geometrical structure of the reagent and products

Chart 3 displays a schematic picture of the four isomers β , γ , *trans*1 and *trans*2 of lumithicolchicine, in the molecular region where they present a different geometrical arrangement. The β and γ isomers differ to each other for the position of the amide group with respect to the five-membered ring: in the former the amide and carbonyl groups are much closer to each other and may form an intra-molecular hydrogen bond. In both the *trans* conformers, the two condensed rings lie roughly in the same plane and no direct interaction with the amide group can occur. Their geometrical difference can be again referred to the amide group: in the *trans*1 conformer, the C_7 –H bond is on the same side as the amide group, whereas in the *trans*2 conformer the C_7 –H bond is on the opposite side.

The relative energy of thicolchicine and of the four isomers of lumithicolchicine at the optimized geometries obtained by DFT calculations on the whole molecules, with and without two methanol molecules, are reported in Table 1, together with some structural parameters.

The calculations on the isolated molecules indicate clearly that both the *trans* forms of LTCC are much higher in energy than the β and γ conformers. The reason is found in the steric tension of the seven-atom ring in the *trans*-LTCC's, where the *trans* position of the hydrogen atoms bonded to the C_4 and C_7 atoms generates a large distortion from planarity in both the two condensed rings, as indicated by the high RMS values of the least squares planes, reported in Table 1. Conversely, in the *cis*-LTCC's (both β and γ) the two condensed rings are nearly planar and form an angle of about

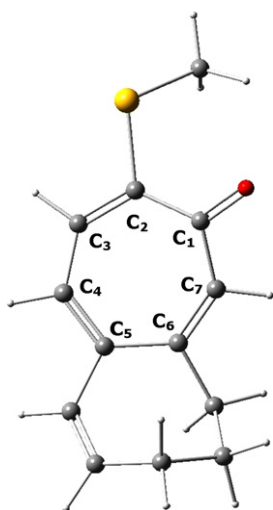


Chart 2. Model system of thicolchicine adopted for the relaxed energy scan MC-SCF calculations for the S_0 and S_1 states. The atom numbering in the reactive seven atoms ring is reported and will be considered in Table 1.

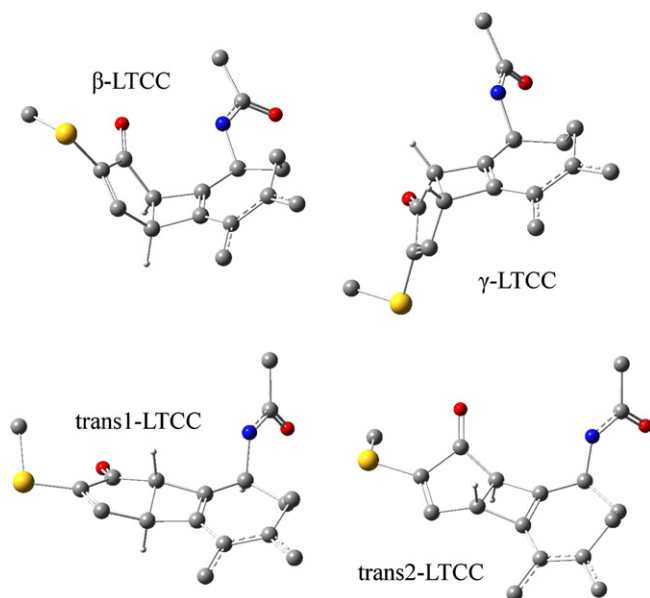


Chart 3. The reactive molecular region of the four isomers of lumithioicolchicine (LTCC). The colors of the atoms indicate: red O, blue N, yellow S, grey C, grey small H. Only the hydrogen atoms bonded to C₄ and C₇ are shown. The four atoms linked by full + dashed lines belong to the aromatic six-member ring. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Table 1

Relative energy (kcal mol⁻¹) and some relevant internal coordinates (Å or °) of thioicolchicine and lumithioicolchicines at their equilibrium geometry, obtained by B3LYP/6-31G^{*} calculations

	TCC	β-LTCC	γ-LTCC	trans1-LTCC	trans2-LTCC
Energy	0.00 ^a	9.77	14.03	58.26	57.88
Energy + 2MeOH	0.00	8.15	7.48	59.51	59.08
C ₄ –C ₇	3.06	1.55	1.56	1.54	1.54
C ₁ –C ₂	1.48	1.50	1.49	1.56	1.55
C ₂ –C ₃	1.37	1.35	1.35	1.35	1.35
C ₃ –C ₄	1.42	1.49	1.50	1.51	1.51
C ₄ –C ₅	1.37	1.54	1.55	1.54	1.55
C ₅ –C ₆	1.45	1.36	1.36	1.37	1.37
C ₆ –C ₇	1.37	1.53	1.52	1.54	1.54
C ₇ –C ₁	1.46	1.53	1.52	1.52	1.52
θ ^b	3.3	63.0	62.2	13.8	14.5
RMS (C ₄ –C ₅ –C ₆ –C ₇)	0.002	0.003	0.000	0.046	0.039
RMS (C ₁ –C ₂ –C ₃ –C ₄ –C ₇)	0.028	0.007	0.001	0.205	0.213
C=O...H–N ^c	4.70	2.15	4.50	4.82	3.82

^a Absolute energy is –1682.39688389H.

^b Angle between the two least squares planes given by the C₄–C₅–C₆–C₇ and C₁–C₂–C₃–C₄–C₇ atoms. The root mean square (RMS) value (in Å) of the two least squares planes is reported in the lines below.

^c O...H distance.

60° (sixth column of Table 1) and all the angles and dihedrals take values similar to those expected for stable molecules. The different stability of the β and γ conformers can be probably ascribed to an intra-molecular hydrogen bond between the carbonyl group and the H atom of the amide group, which occurs for β-LTCC. This is clearly indicated by the O–N distance reported in the last column of Table 1: 2.1 Å for β-LTCC versus 4.5 Å for γ-LTCC.

The bond lengths reported in Table 2 for LTCC are very similar for the four isomers and take the typical values of single and double C–C bond indicating that small aromaticity is present. On the contrary, from the C–C bond lengths of TCC it seems that the seven atoms ring has a certain degree of aromaticity: the double C–C bonds show the typical double bond length (1.34 Å) but the single

Table 2

Some relevant bond distances (Å) for thioicolchicine and lumithioicolchicines for the S₀ and S₁ states, obtained by MC-SCF calculations

	C ₄ –C ₅	C ₅ –C ₆	C ₆ –C ₇
Geometry optimized for S ₀ TCC	1.35	1.47	1.35
Geometry optimized for S ₁ TCC ^a	1.45	1.39	1.42
Geometry optimized for S ₀ LTCC	1.54	1.37	1.54

^a The geometry was optimized for S₁ with the constraint C₄–C₇ = 3.055 Å.

C–C bonds (C₁–C₂, C₃–C₄, C₅–C₆, C₁–C₇) are shorter than the typical value of 1.54 Å.

Since the photochemical experiments were carried out in methanol, a better insight of the energetic of the reagents and products can be obtained by taking into account the solvent effect. For this reason, we have performed a further calculation in which two methanol molecules have been added to the molecular systems. As mentioned in the previous section, the geometry optimization was started by placing the two solvent molecules at large distance from the reactive molecular region, in order not to bias between the different possibilities of forming solute–solvent partial bonds. The main effect of the two methanol molecules concerns with the β-LTCC isomer, whose intra-molecular hydrogen bond C=O...H–N, occurring in the isolated molecule, is destroyed by one methanol molecule which interposes between the carbonylic and the amidic groups. For TCC and the other LTCC conformers, the methanol molecules form hydrogen bonds with the ether, carbonyl or amide groups. The smaller solvation energy of β-LTCC with respect to γ-LTCC can be probably ascribed to the destruction of the already discussed intra-molecular hydrogen bond between the carbonyl and the amide groups. The relative energies from these new calculations show however that the fraction of solvation energy accounted for two solvent molecules does not change appreciably the relative stability of the conformers, with respect to the gas phase calculations.

From energetic considerations, the absorption of a photon of wavelength 360 nm (~80 kcal mol⁻¹) in TCC [1] could lead to the formation of LTCC, with the *trans* isomers that appear less favoured than the *cis*. The relative energies of the considered molecules are rather similar to those of the colchicine and lumicolchicine [4], so that the reasons of the different photochemical behaviour of CC and TCC can not be found in the energetic of the reagents and products.

2.2. Study of the reaction path

The MC-SCF energies of the ground state S₀ and of the first singlet excited state S₁ as arising from RES calculations which connect TCC and the γ-LTCC isomer are displayed in Fig. 1. The calculations refer to the model molecule shown in Chart 2, in which the leading coordinate C₄–C₇ distance is kept fixed and all the remaining internal coordinates are optimized. The analogous results for the β-LTCC are practically indistinguishable from the reported ones. This is because the differences between γ-LTCC and β-LTCC isomers, due to an intra-molecular hydrogen bond, are cancelled in the adopted model molecule, in which the amide group has been substituted by a hydrogen atom. The four curves refer to the energy of the S₀ and S₁ states computed along the S₀-RES and S₁-RES (the state whose energy is minimized is indicated by the label in parentheses). For instance the S₁(0) curve in Fig. 1, denotes the S₁ energy computed at the geometries optimized for S₀. Thus S₁(0)–S₀(0) represents the vertical excitation energy at the geometry optimized for S₀, whereas S₁(0)–S₁(1) is the relaxation energy of the excited state due the change of internal coordinates other than the fixed C₄–C₇ distance. The angle between the five- and the four-member plains is reported for both states.

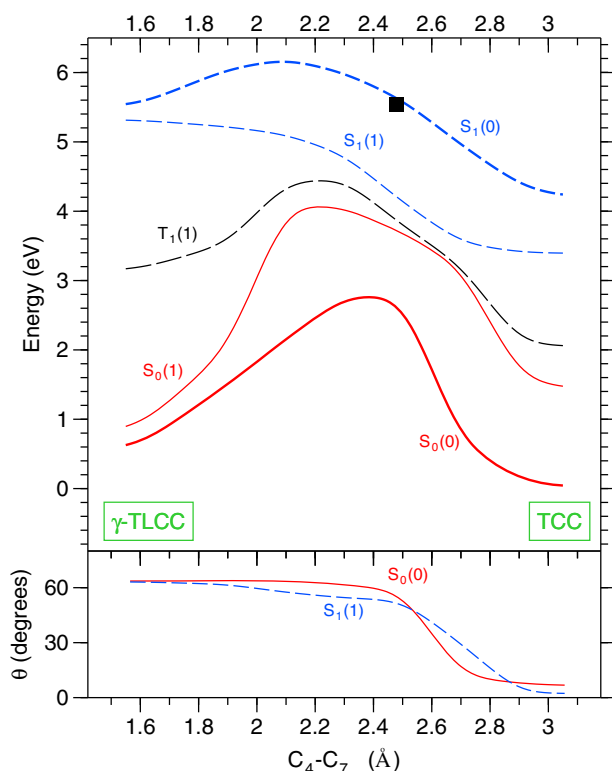


Fig. 1. The energy of the S_0 (full red lines) and of the S_1 (dashed blue lines) states along their own relaxed energy path connecting thiocolchicine with γ -lumithiocolchicine. The 0 in parentheses indicates the S_0 -RES (heavy lines); the 1 indicates the S_1 -RES (light lines). The RES profile of the first triplet state T_1 (dashed black line) is also reported. In the lower panel the change of the inter-plane rings is reported along the S_0 and S_1 RES curves. The black square represents a point of the S_1/S_0 conical intersection. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

The analysis of the CI expansion coefficients of the MC-SCF calculations indicate that for all the C_4 – C_7 values, S_0 corresponds to a closed-shell configuration whereas S_1 corresponds to a HOMO \rightarrow LUMO single excitation. An inspection of the involved molecular orbitals (MOs) reveals that the dynamics of the HOMO and LUMO along the two RES curves is similar to that of colchicine [4]. The main feature concerns with the geometrical relaxation of S_1 in TCC: the HOMO along the $S_0(0)$ curve is a typical π bonding orbital of conjugate systems, with relevant contributions to the order of several C–C bonds, whereas in the relaxed geometry (i.e. on going from $S_1(0)$ to $S_1(1)$ at C_4 – $C_7 = 3.05$ Å) the HOMO is almost completely localized on the carbonylic oxygen, with a consequent general weakening of the seven-atom ring. The main effects of this charge migration are summarized in Table 2, where the change some C–C distances in the geometry relaxation of S_1 in TCC is reported, together with the some bond lengths in LTCC.

It is apparent that on going from S_0 to S_1 a remarkable increase of the C_4 – C_5 and C_6 – C_7 distances occurs, together with a decrease of the C_5 – C_6 bond length. Both changes are directed from the C_4 – C_5 – C_6 – C_7 sequence of TCC towards the C_4 – C_5 – C_6 – C_7 sequence occurring in LTCC. This geometrical relaxation of S_1 was already observed for CC and was interpreted as a feature consistent the observed photochemical reaction of colchicine.

The profile of inter-plane angle θ of Fig. 1 along the two RES profiles indicates that the most relevant geometrical changes occur in a small range of the C_4 – C_7 distance, namely in the 2.6–2.7 Å, where the seven-membered ring bends towards an angle of about 60°. This geometrical change is more sharp for S_0 than for S_1 . In both cases, the θ change is accompanied by changes in the bond lengths, corresponding to shift from single to double bond or vice versa.

Turning to the energy curves of Fig. 1, we could consider for TCC the same reaction mechanism already proposed for CC [4]. The reaction starts with a sudden photoexcitation of S_1 in TCC, followed by its geometrical relaxation with a weakening of the bonds in the reactive seven-atom ring. The next step is a non-adiabatic transition $S_1(1) \rightarrow S_0(1)$, which could be enhanced by the quasi degeneracy of the $S_0(1)$ and $S_1(1)$ curves in the 2.2–2.6 Å range of the C_4 – C_7 distance. Finally, the geometrical relaxation of $S_0(1)$ may lead to the γ -LTCC product.

The energy curves of Fig. 1 are very similar to those of colchicine and therefore in principle it seems reasonable to hypothesize the same mechanism for the photochemical reaction of CC and TCC. Unfortunately the two molecules behave in a different way. At this point, it may be useful to consider the proposed mechanism in the light of the experimental data available for colchicine.

The proposed mechanism for the photoconversion of colchicine appears as the most probable, taking into account the experimental evidence that triplet states play no role in reaction, since the presence of oxygen in the reaction site does not quench the photo-product formation [3,12]. The slope of the $S_0(1)$ curve around the supposed non-adiabatic transition left open the possibility that the geometrical relaxation of the $S_0(1)$ state gives rise to the reactant. This feature is consistent with the very low quantum yield ~ 0.04 [3] observed for the colchicine photoreaction in methanol. Therefore, the proposed reactive path is not the most probable event following photoexcitation of CC or TCC, since most decays lead to the reactant after fluorescence and non-radiative processes. In this context, we have looked for the presence of minimum energy crossing point between the S_0 and S_1 states at the geometry where presumably the non-adiabatic transition occurs in the reactive trajectories. For this calculation, we have used the penalty function method of Ciminelli et al. [13] which does not require the calculation of the non-adiabatic transition matrix elements. The results are again very similar for CC and TCC (displayed in Fig. 1) and shows clearly that, the conical intersection is too high in energy (~ 5.5 eV) to play a significant role in the reaction mechanism. This finding is in agreement with the experimental data for CC, since the presence of an efficient crossing point would be inconsistent with the observed very low quantum yield. In summary, the different photochemical behaviour of CC and TCC is accounted for neither the energetic of the reagent and products nor in the differences in the approximate reaction path given by the RES approach.

At this point, we consider the possibility that the quenching of the photochemical reaction of TCC is due to an intersystem crossing from the S_1 state to low-lying triplet states, whose geometrical relaxation could lead to the reagent. In previous calculations on colchicine we found that T_1 has always a lower energy than S_1 and that the pure electronic spin–orbit (SO) coupling between these two states does not exceed 0.5 cm^{-1} . From that results, we deduced that the coupling is inefficient in populating triplet states, in accords with an experimental study in which, in presence of several triplet acceptors, no reaction quenching was observed [12] in the quantum yield of LCC. For TCC, we consider the possibility that the dulfur atom can induce a heavy atom effect with the result of enhancing the spin–orbit matrix elements between S_1 and T_n with an increased efficiency of the intersystem crossing. In order to verify whether this supposition is realistic, we have computed the T_1 and T_2 states along the S_1 RES curve and the spin–orbit coupling matrix elements with the S_1 state. To be effective, the coupling has to occur in the early stages of the photochemical reaction, during the geometrical relaxation of S_1 which immediately follows the excitation. The question is whether the spin–orbit transition to T_1 or T_2 is favoured with respect to non-adiabatic transition to S_0 .

Since the S_1 – T_2 matrix elements were found to be rather small, we discuss only the first triplet state. The T_1 curve along the RES

curve of S_1 (computed in the same MC-SCF active space) is reported in Fig. 1. As found for colchicine, the T_1 energy is always lower than the S_1 energy and the two states are quasi degenerate for C_4 – C_7 in the 2.2–2.6 Å range. The calculated spin–orbit matrix elements $|\langle T_1 | SO | S_1 \rangle|$ along the S_1 RES curve are 8.2, 11.7 and 15.6 cm^{-1} at C_4 – C_7 values of 3.05 (TCC), 2.90 and 2.70, respectively. These values are almost two order of magnitude greater than the corresponding values of colchicine, and, recalling that the square of the matrix element enters the transition rate, with may expect a SO transition in TCC four order of magnitude higher than for colchicine. Although a more extended portion of the S_1 potential energy surface should be explored in order to make firm assertions, it seems that a non-radiative spin–orbit transition to T_1 is a realistic possibility.

By applying the Fermi golden rule (ignoring the vibrational degrees of freedom) the $S_1 \rightarrow T_1$ transition velocity is about 10^{-4} fs^{-1} . This may gives a qualitative explanation of the transient spectroscopy experiments for TCC [1] in which the band at 400 nm with very long lifetime was tentatively assigned to a triplet state. The interesting data is that this transient band appears with a delay of about 500 fs from the pump excitation. According to our calculations, the T_1 population after 500 fs is about 0.06, a value which can be considered capable to give rise to detectable $T_1 \rightarrow T_n$ electronic transitions.

3. Conclusions

From the computed energies of thiocolchicine and of the four possible isomers of lumithiocolchine, it is apparent that the β and γ conformers are strongly favoured as possible products of the intra-molecular photocyclization reaction. The energy profiles of the ground and of the first singlet excited states allow tracing a possible reaction path, using the distance of the two carbon atoms forming the new σ bond, as the leading coordinate. All these

results are rather similar to those previously obtained for colchicine and are therefore unable to explain the reason for their different photochemical behaviour. On the contrary, the spin–orbit matrix elements with the first triplet state in much more pronounced for thiocolchicine and the computed approximate rise time of the first triplet state is of the same order of that experimentally observed. Therefore, these results reinforce the previously formulated conjecture that the spin–orbit coupling is responsible of the photochemical inactivity of thiocolchicine.

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References

- [1] L. Bussotti, I. Cacelli, M. D'Auria, P. Foggi, G. Lesma, A. Silvani, V. Villani, *J. Phys. Chem. A* 107 (2003) 9079.
- [2] L. Bussotti, M. D'Auria, P. Foggi, G. Lesma, R. Righini, A. Silvani, *Photochem. Photobiol.* 71 (2000) 29.
- [3] A.L.P. Nery, et al., *Photochem. Photobiol.* 73 (2001) 213.
- [4] I. Cacelli, M. D'Auria, V. Villani, *J. Chem. Theory Comput.* 3 (2007) 649.
- [5] A.D. Becke, *J. Chem. Phys.* 98 (1993) 5648.
- [6] C. Lee, W. Yang, R.G. Parr, *Phys. Rev. B* 37 (1988) 785.
- [7] M.J. Frisch, et al., GAUSSIAN 03, Gaussian Inc., Pittsburgh, PA, 2003.
- [8] J. Olsen, B.O. Roos, P. Jørgensen, H.J.A. Jensen, *J. Chem. Phys.* 89 (1988) 2185.
- [9] P.Å. Malmqvist, B.O. Roos, B. Schimmelpfennig, *Chem. Phys. Lett.* 357 (2002) 230.
- [10] A. Berning, M. Schweizer, H.-J. Werner, P.J. Knowles, P. Palmieri, *Mol. Phys.* 98 (2000) 1823.
- [11] H.J. Werner, MOLPRO, 2002, A Package of Ab-initio Programs Designed by H.-J. Werner and P.J. Knowles.
- [12] R. Croteau, R. Leblanc, *Photochem. Photobiol.* 28 (1978) 33.
- [13] C. Ciminelli, G. Granucci, M. Persico, *Chem. Eur. J.* 10 (2004) 2372.