# Mechanisms of Acid Decomposition of Dithiocarbamates. 4. Theoretical Calculations on the Water-Catalyzed Reaction

José I. García*,† and Eduardo Humeres‡

*Departamento de Química Orgánica, Instituto de Ciencia de Materiales de Aragón, C.S.I.C.-Universidad de Zaragoza, Pedro Cerbuna 12, E-50009 Zaragoza, Spain; Departamento de Quimica, Universidade Federal de Santa Catarina, 88040-900 Florianópolis, SC, Brazil; and Institute for Fundamental Research in Organic Chemistry, Kyushu University, Hakozaki, Fukuoka, 812-8581 Japan*

*jig@posta.unizar.es*

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A theoretical study of the water-catalyzed dithiocarbamic acid cleavage has been performed using *N*-methyl- (MeDTC) and *N*-phenyldithiocarbamic acid (PhDTC) as model molecules. Calculations have been carried out within the Density Functional Theory (DFT) formalism, using the B3LYP hybrid functional together with medium-sized basis sets, both in gas phase and by considering solvent effects through dielectric continuum methods. According to the results obtained, both in gas phase and in solution, MeDTC decomposes through a proton-transfer step assisted by a water molecule (this being the rate-determining step), leading to a zwitterionic intermediate, followed by a fast N−C bond-breaking process. In the case of PhDTC, the theoretical results point to a one-step mechanism in which the N−C bond breaking takes place in a concerted manner with the proton transfer. The calculated $\Delta\Delta G^{\ddagger}$ of the proton-transfer step for MeDTC and PhDTC is 4.0 kcal mol$^{-1}$, which is similar to the experimental values. For both compounds the water-assisted intramolecular proton transfer occurs with a twisting of the $CS_2$ group that inhibits the resonance of the thiocarbamic group, making the nitrogen more basic and therefore favoring the proton transfer. The difference in the torsional barrier has been calculated to be ca. 5 kcal mol$^{-1}$, and it is therefore concluded that most of the activation barrier of the reaction is due to the torsional barrier of the $CS_2$ group.

## Introduction

The acid decomposition of dithiocarbamates shows different relationships for alkyl- and aryldithiocarbamates, as well as for those derived from cyclic secondary amines.[1] A recent study of the acid cleavage of alkyldithiocarbamates (alkDTC)[2] concluded that the reaction occurs through a zwitterionic intermediate. Depending on the p$K_N$ value, i.e., the acid dissociation constant of the parent amine, the rate-determining step is the N-protonation (p$K_N$ < 9.2) or the C−N bond breakdown (p$K_N$ > 9.2). General acid catalysis was not detected because the basicity of the nitrogen decreases by 14 p$K$ units with respect to the p$K_N$ of the parent amine, and only acids stronger than hydron can efficiently transfer the proton.[3] For parent amines with p$K_N$ > 10, a new mechanism emerges that was proposed to occur by an S to N intramolecular proton transfer in the dithiocarbamic acid, a step that occurs in a concerted manner with the breaking of the N−C bond (Scheme 1).[2]

The acid decomposition of aryldithiocarbamates (arylDTC) in water occurs more than $10^4$ times faster than the corresponding process in alkDTC of similar p$K_N$. The arylic nitrogen has a basicity that is about 5−8 p$K$ units higher than the value expected from the p$K_N$. These higher values were attributed to the inhibition of the delocalization of the electron pair of the nitrogen into the benzene ring due to the strong electron-withdrawing effect of the thiocarbonyl group. According to the proton inventory, there are two protons on flight from a water molecule in a late transition state. It was concluded that water catalyzes the decomposition of the dithiocarbamic acid through an intramolecular S to N proton-transfer concerted with the N−C bond cleavage.[4] The kinetic barrier for this process is similar to the torsional barrier of thioamides,[5] suggesting that the main driving force to reach the transition state is the required torsion of the N−C bond, which in turn inhibits the resonance between the thiocarbonyl group and the aromatic moiety. It has also been observed that for amides the twisting of the N−CO bond involves the pyramidalization of the amino group and possibly the carbonyl carbon atom. In addition, there is a substantial increase in the N−CO bond length, indicating that inhibition of the amide resonance leads to a normal N−C single bond.[6]

In the work described here, we aimed to gain a better understanding of this new mechanism involving water catalysis that produces the dithiocarbamic acid decomposition. We chose methyl- and phenyldithiocarbamates

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† C.S.I.C.-Universidad de Zaragoza.

‡ Universidade Federal de Santa Catarina and Kyushu University.

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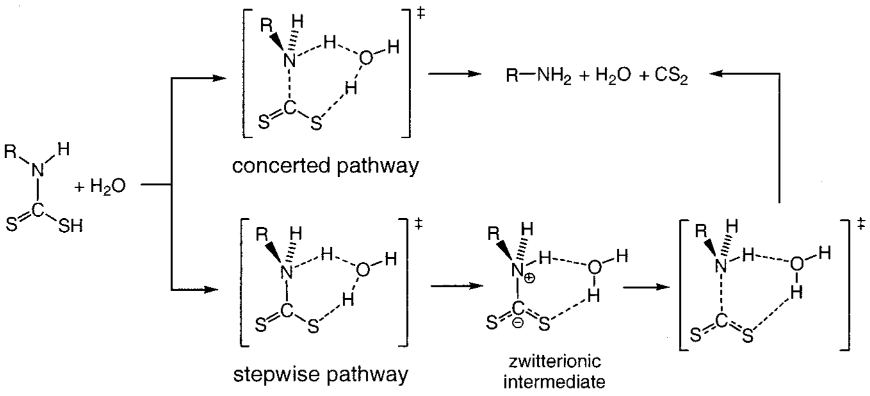
**Scheme 1**



as model compounds on the basis that the former, having a p$K_N$ = 10.7, is in the region of the Brønsted plot where the zwitterionic and intramolecular mechanisms should merge, while the latter should clearly cleave through the intramolecular proton transfer.

## Computational Methods

All calculations were carried out using a Density Functional Theory (DFT) method, based on the three-parameter hybrid correlation functional developed by Becke,[7] plus the Lee–Yang–Parr exchange functional[8] (B3LYP) as implemented in the Gaussian 98 program.[9] Full geometry optimizations using the 6-31G(d) and, in some cases, 6-31+G(d) and 6-31+G(d,p) basis sets were carried out. Solvent effects were taken into account through the use of a continuum dielectric medium with a dielectric permittivity value of 78 (water), by means of the Onsager method,[10] henceforth denoted as Ons/B3LYP/6-31G(d) calculations. Given that the Onsager model only considers spherical cavities and the dipole moment of the solute, more realistic molecular cavity shapes and higher electric moments were accounted for by using the Pisa Continuum Model (PCM),[11] as implemented in the Gaussian 98 program, through single point energy calculations on the geometries calculated with the Onsager model, using the 6-31+G(d) basis set, henceforth denoted as PCM/B3LYP/6-31+G(d) calculations. The PCM model can also account for nonelectrostatic solvation terms such as those due to cavitation and dispersion energies.

Analytical frequencies were calculated at the B3LYP/6-31G(d), B3LYP/6-31+G(d,p), Ons/B3LYP/6-31G(d), and, in some cases, at the Ons/B3LYP/6-31+G(d) levels, the nature of the stationary points being determined in each case according to the appropriate number of negative eigenvalues of the Hessian matrix. Scaled frequencies were not considered since the errors on the calculated thermodynamical properties are almost negligible at this theoretical level.[12]

Unless otherwise stated, only Gibbs free energies (including thermal corrections at 25 °C) were used for the discussion of the relative stabilities of the chemical structures considered.

Hard data on geometries, electronic energies, as well as entropies, enthalpies, and Gibbs free energies (at 25 °C) of all structures considered are available as Supporting Information.

## Results and Discussion

**Gas-Phase Calculations.** Previous theoretical calculations by Abboud and Notario,[13] carried out at the HF/3-21G(d) level, compared the intramolecular with the water-assisted S to N proton transfer for MeDTC and PhDTC molecules. The main conclusion of this study was that the water-assisted mechanism is greatly favored over the direct intramolecular proton transfer by 29.5 kcal mol$^{-1}$ for MeDTC (passing from 49.5 to 20 kcal mol$^{-1}$) and by 13 kcal mol$^{-1}$ for PhDTC (passing from 33 to 20 kcal mol$^{-1}$). The experimental studies also indicate the participation of a water molecule in the S to N proton transfer,[4] i.e., as a reactant, and not merely as a solvation agent. Consequently, in the first stage of our study we examined the possible reaction pathways by considering explicitly the participation of a water molecule in the reaction coordinate without taking into consideration further solvent effects.

Given that water-assisted proton transfer is a key step in the mechanism, as well as the possible existence of zwitterionic intermediates, the choice of a suitable basis set may be of importance to correctly describe the stationary points on the reaction surface. Thus, the results obtained with the standard basis set 6-31G(d) were compared with those obtained with a more extended basis set, which included polarization function on the hydrogen atoms as well as diffuse functions on the heavy atoms [namely 6-31+G(d,p)], in the case of the methyl dithiocarbamate (MeDTC) reaction. Relative energies of the stationary points found using these basis sets in combination with the B3LYP hybrid functional are gathered in Table 1.

Unless otherwise stated, only the B3LYP/6-31G(d) results will be discussed throughout this section.

The starting point of the reaction coordinate for the MeDTC is the reactant with a water molecule coordinated to it. After searching for different arrangements and conformations, the minimum energy structure found (**RMe_v**) is that shown in Figure 1. As can be seen, one water molecule is hydrogen-bonded to the N–H and C=S

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**Table 1. Relative Energies (in kcal mol$^{-1}$) and Absolute Entropies (in cal mol$^{-1}$ K$^{-1}$) of the Structures Considered in This Work, Calculated in a Vacuum at Several Theoretical Levels**

| | B3LYP/6-31G(d) | | | B3LYP/6-31+G(d,p) | | |
|---|---|---|---|---|---|---|
| structure | $\Delta E$ | $\Delta S$ | $\Delta G$ | $\Delta E$ | $\Delta S$ | $\Delta G$ |
| **RMe_v** | 0.0 | 94.0 | 0.0 | 0.0 | 95.6 | 0.0 |
| **TS1Me_v** | 29.2 | 86.5 | 28.4 | 28.8 | 86.7 | 28.1 |
| **IMe_v** | 13.2 | 92.5 | 15.9 | 13.5 | 93.4 | 16.4 |
| **TS2Me_v** | 18.4 | 97.9 | 17.8 | 18.6 | 101.0 | 17.7 |
| **PMe_v** + **CS$_2$** | 9.1 | 131.0 | −2.5 | 3.5 | 134.8 | −7.9 |
| **RPh_v** | 0.0 | 112.9 | 0.0 | – | – | – |
| **TS1Ph_v** | 31.0 | 103.9 | 31.3 | – | – | – |
| **IPh_v** | –[a] | –[a] | –[a] | – | – | – |
| **TS2Ph_v** | –[a] | –[a] | –[a] | – | – | – |
| **PPh_v** + **CS$_2$** | 2.9 | 150.0 | −8.0 | – | – | – |

[a] Stationary point not located. The initial structure evolves directly to the reaction products.

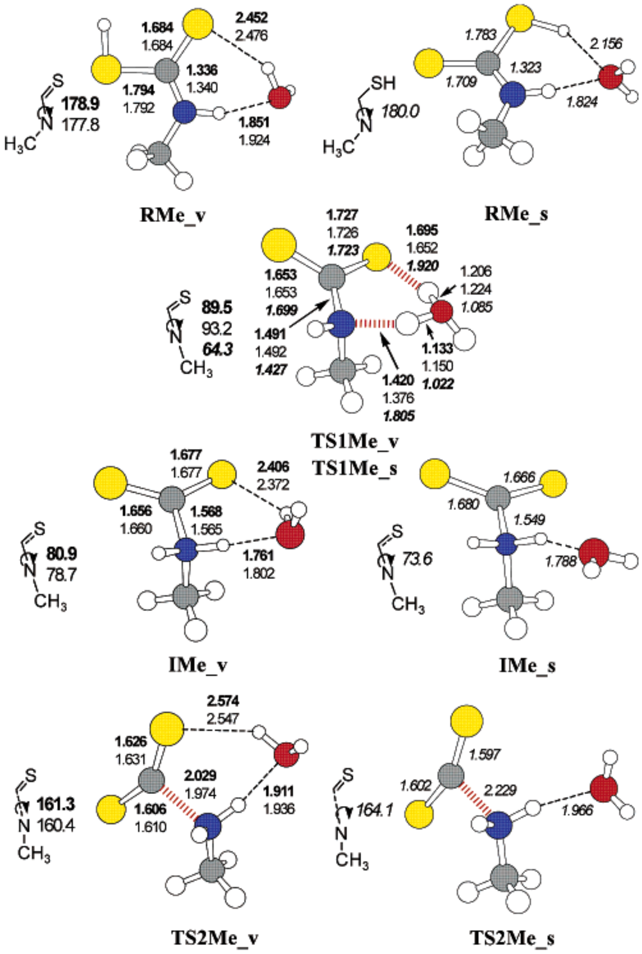

**Figure 1.** Some selected geometrical features of the stationary points of the MeDTC reaction path, calculated at the B3LYP/6-31G(d) (bold typeface), B3LYP/6-31+G(d,p) (normal typeface), and Ons/ B3LYP/6-31G(d) (italic typeface) theoretical levels.

groups, forming a bridge between the two. This arrangement is similar to that recently described for different hydrated forms of thiouracils,[14] whose hydrogen-bond distances (calculated at the B3LYP/6-31+G(d) level) are also close to the values found in the present work. Clearly, this is not a reactive arrangement since, as we will see below, the water molecule assists the S to N proton transfer and, as such, it must be hydrogen bonded to the S−H and N groups in the reaction coordinate. However, as the interconversion between the different conformations and solvates is faster than the subsequent reaction, the Curtin−Hammett principle[15] applies and the minimum energy structure must be taken as the starting point for the reaction coordinate.

The transition structure (TS) of the water-assisted intramolecular proton transfer between the S and the N atoms (**TS1Me_v**) is shown in Figure 1. As can be seen, the structure corresponds to a situation in which the proton from the SH group is being transferred to the water molecule, which, in turn, has already started to transfer a proton to the thiocarbamic nitrogen atom in a concerted way.

It is worth noting that the $CS_2$ group is twisted with regard to the amine moiety (C−N−C−S dihedral angle 89.5°), contrary to the situation in **RMe_v**, which has a planar arrangement. This twisting inhibits the resonance of the thiocarbamic group, making the nitrogen more basic and therefore favoring the proton transfer (see below). This lack of conjugation is evidenced by the lengthening of the N−C bond, which changes from 1.336 Å in **RMe_v** to 1.491 Å in **TS1Me_v**. The completion of the proton transfer leads to a zwitterionic intermediate (**IMe_v**), which has the water molecule hydrogen bonded to the NH and C−S groups. As can be seen, the twisting of the $CS_2$ group is very similar to that calculated for **TS1Me_v** (dihedral angle = 80.9°), and a further weakening of the N−C bond, resulting in bond lengthening to 1.568 Å, is observed.

The TS for the N−C bond breaking (**TS2Me_v**) shows an N−C distance of 2.029 Å and an almost planar arrangement of the $CS_2$ group with regard to the amine moiety (dihedral angle = 161.3°). The loss of the zwitterionic character in **TS2Me_v** with regard to **IMe_v** is reflected in the lengthening of the O···H−N distance, from 1.761 to 1.911 Å, and of the S···H−O distance, from 2.406 to 2.574 Å.

The final products of the reaction, **PMe_v** and $CS_2$, are not shown in Figure 1. **PMe_v** consists of a methylamine molecule with a water molecule hydrogen bonded to it.

The calculated activation energy for the first reaction step (proton transfer) is 29.2 kcal mol$^{-1}$ at the B3LYP/6-31G(d) theoretical level, which decreases to 28.4 kcal mol$^{-1}$ when free energies are considered. The activation energy for the second reaction step (N−C bond breaking) is only 5.2 kcal mol$^{-1}$ at the B3LYP/6-31G(d) level, and this decreases further (to 1.9 kcal mol$^{-1}$) when the free energy of activation is considered. This change indicates a very fast bond breakage once the zwitterionic intermediate is formed. The proton transfer is thus the rate-limiting step in a two-step reaction mechanism.

It should be noted that in the Brønsted plot, in the region of the p$K_N$ of the MeDTC, the zwitterionic intermolecular mechanism occurs with fast *N*-protonation and the rate-determining step is the N−C bond cleavage.[4] Therefore, the water-catalyzed reaction of the MeDTC provides a new path for the zwitterionic mechanism.

As far as the basis set is concerned, neither the geometries nor the energies of the different stationary points suffer from significant changes upon addition of

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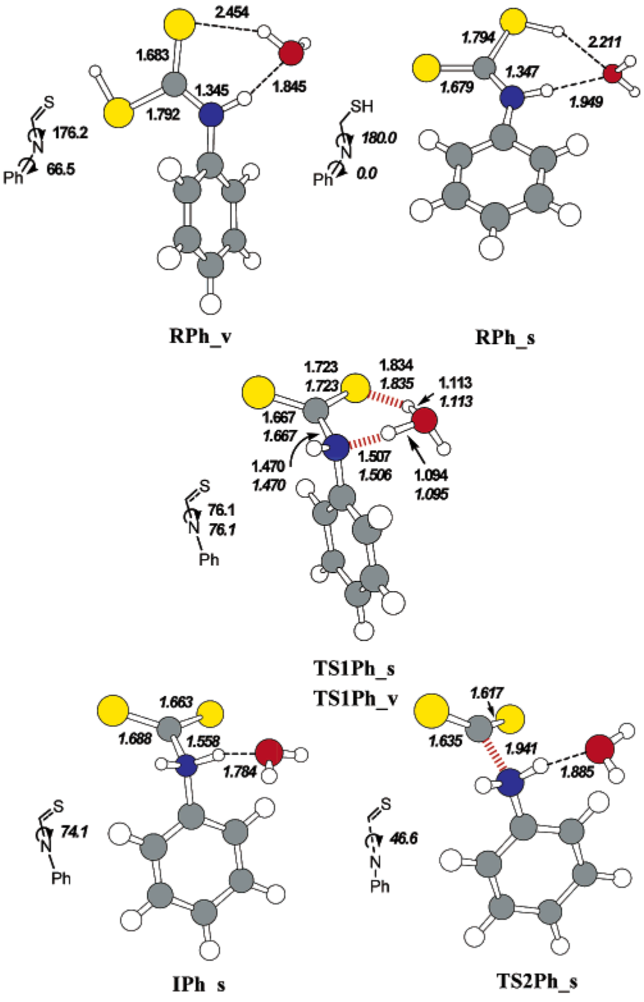

**Figure 2.** Some selected geometrical features of the stationary points of the PhDTC reaction path, calculated at the B3LYP/6-31G(d) (bold typeface) and Ons/B3LYP/6-31G(d) (italic typeface) theoretical levels.

diffuse and polarization functions on the standard 6-31G-(d) basis set, as can be seen by examining Figure 1 and Table 1. Consequently, for the sake of computational efficiency, the 6-31G(d) was used as the reference basis set for the geometry optimizations throughout this work.

In terms of the phenyldithiocarbamate (PhDTC) reaction, from the geometrical point of view, the stationary points found on the potential energy surface for PhDTC are very similar to those found in the case of MeDTC (Figure 2).

Thus, **RPh_v** presents a bridge hydrogen-bonded water molecule and a planar arrangement of the thiocarbamic group (C−N−C−S dihedral angle = 176.2°) that is similar to the one found for **RMe_v**. Unexpectedly, the phenyl group is not coplanar with the thiocarbamic group, presenting a dihedral angle of 66.5°.

**TS1Ph_v** corresponds to a situation similar to that found in the case of **TS1Me_v**, i.e., approximately halfway in the proton transfer between the SH and the N groups. However, there are some differences in the degree of synchronicity of the proton transfer. For example, in **TS1Ph_v** the proton coming from the SH group is transferred to a greater extent to the water molecule than in **TS1Me_v** (longer S···H distance and shorter H···O distance), whereas the proton coming from the water molecule is transferred to a lesser extent to the nitrogen atom (shorter O···H distance and longer H···N distance). The $CS_2$ group is almost perpendicular to the amine moiety (dihedral angle = 76.1°), and this results in a loss of conjugation, lengthening of the N−C bond (from 1.345 Å in **RPh_v** to 1.470 Å in **TS1Ph_v**), and the enhancement of the nitrogen basicity.

**Table 2. Relative Energies (in kcal mol$^{-1}$) and Absolute Entropies (in cal mol$^{-1}$ K$^{-1}$) of the Structures Considered in This Work, Calculated in Solution at Several Theoretical Levels**

| | Ons/B3LYP/6-31G(d) | | | PCM/B3LYP/6-31+G(d)[a] | |
|---|---|---|---|---|---|
| structure | Δ*E* | Δ*S* | Δ*G* | Δ*E* | Δ*G*[b] |
| **RMe_s** | 0.0 | 94.2 | 0.0 | 0.0 | 0.0 |
| **TS1Me_s** | 30.9 | 86.7 | 32.1 | 26.8 | 28.0 |
| **IMe_s** | 7.3 | 99.3 | 8.0 | 7.7 | 8.4 |
| **TS2Me_s** | 17.6 | 106.9 | 14.0 | 18.1 | 14.5 |
| **PMe_s** + **CS$_2$** | 6.9 | 136.2 | −5.5 | 2.2 | −10.2 |
| **RPh_s** | 0.0 | 113.4 | 0.0 | 0.0 | 0.0 |
| **TS1Ph_s** | 27.4 | 104.0 | 27.8 | 23.6 | 24.0 |
| **IPh_s** | 4.8 | 114.8 | 15.4 | 10.9 | 21.5 |
| **TS2Ph_s** | 14.6 | 119.0 | 13.4 | 12.1 | 12.1 |
| **PPh_s** + **CS$_2$** | 4.4 | 148.5 | −6.7 | −3.3 | −14.4 |

[a] Single point energy calculation on Ons/B3LYP/6-31G(d) geometries. [b] Using Ons/B3LYP/6-31G(d) ZPE and thermal corrections.

In contrast to the situation for MeDTC, a zwitterionic intermediate, **IPh**, could not be located on the potential energy surface. All attempts to optimize such a structure resulted in the N−C bond breaking and formation of the reaction products. This result is not unexpected, taking into account the low free energy of activation calculated for the second reaction step in the case of MeDTC and the greater reactivity expected for PhDTC.

The calculated activation energy for the proton transfer is 31.0 kcal mol$^{-1}$ at the B3LYP/6-31G(d) theoretical level, and this remains almost unchanged (31.3 kcal mol$^{-1}$) when free energies are considered. These values are somewhat higher than those corresponding to the MeDTC reaction.

**Solvent Effects.** As discussed above, the existence of zwitterionic intermediates, and the activation barrier for the decomposition of these intermediates, must be clearly influenced by electrostatic solvation effects. Consequently, we decided to carry out a search for the stationary points on the potential energy surface taking into account these effects by means of a continuum dielectric method, namely the Onsager method.[10] In this model, the solute is considered to occupy the center of a spherical cavity, and this is surrounded by an infinite dielectric medium, characterized by its dielectric permittivity, with which it interacts only through its dipolar moment. In all cases, the dielectric permittivity of water (78.0) was used. The Onsager method, as implemented in Gaussian 98, allows geometry optimizations and analytical frequency calculations to be carried out. This allows the nature of the stationary points to be properly checked and the zero point energies (ZPE) and thermodynamical properties to be calculated.

The corresponding relative energies for all the stationary points found (reactants, intermediates, transition structures, and products) are given in Table 2. Some structural parameters of the stationary points found are shown in Figures 1 (MeDTC) and 2 (PhDTC).

After searching for different arrangements and conformations, the minimum energy structure found for the reactant in the case of the MeDTC reaction (**RMe_s**) is that shown in Figure 1. As can be seen, one water molecule is hydrogen-bonded to the N−H and C−SH groups, forming a bridge between the two. In this case, and in contrast to the situation found in the absence of a solvent, this structure represents the real starting point for the reaction coordinate.

The transition structure (TS) of the water-assisted intramolecular proton transfer between the S and the N atoms (**TS1Me_s**) is shown in Figure 1. It corresponds to a situation where the proton from the SH group has been almost completely transferred to the water molecule, which, in turn, has not started to transfer a proton to the thiocarbamic nitrogen atom. This arrangement looks very similar to a hydronium molecule coordinated to the methyl dithiocarbamate anion, but the frequency analysis confirms that it is indeed a genuine TS. It can then be concluded that solvent effects strongly influence the position of the proton-transfer TS in the reaction coordinate.

As happened in the calculations corresponding to a vacuum, the CS$_2$ group is twisted with regard to the amine moiety (C−N−C−S dihedral angle = 64.3°). The loss of conjugation is again evidenced by the lengthening of the N−C bond, which changes from 1.323 Å in **RMe_s** to 1.427 Å in **TS1Me_s**. On the other hand, the N−C bond length in **TS1Me_s** is shorter than that calculated in **TS1Me_v**, a situation that corresponds to a less developed proton transfer to the nitrogen atom in solution.

The completion of the proton transfer leads to a zwitterionic intermediate (**IMe_s**), which has the water molecule hydrogen bonded only to the NH group. Clearly, the solvation of the zwitterionic intermediate by the dielectric results in a structural change in **IMe**, which loses the bridging hydrogen bond observed in the gas phase. As can be seen, the twisting of the CS$_2$ group is only slightly greater than that calculated for **TS1Me_s** (dihedral angle = 73.6°), and a further weakening of the N−C bond, resulting in bond lengthening to 1.549 Å, is observed.

The TS for the N−C bond breaking (**TS2Me_s**) shows an N−C distance of 2.229 Å and an almost planar arrangement of the CS$_2$ group with regard to the amine moiety (dihedral angle = 164.1°). The loss of the zwitterionic character in **TS2Me_s** in comparison to **IMe_s** is reflected in the lengthening of the O···H−N distance, from 1.788 to 1.966 Å. With regard to the gas-phase calculations, the N−C distance is longer, indicating a later TS in solution. As happened in the case of **IMe**, the solvation of **TS2Me** results in a loss of the bridging hydrogen bond and, in this case, the water molecule remains linked to the N−H group.

The potential and free energy reaction profiles are shown in Figure 3. It must be pointed out that the energy in solution is really composed of an intrinsic term (internal energy), plus a solvation free energy, coming from the reaction field. The free energy values correspond to single point energy calculations, carried out at the PCM/B3LYP/6-31G(d)//Ons/B3LYP/6-31G(d) theoretical level, to which thermal corrections, calculated at the Ons/B3LYP/6-31G(d) level, have been added.

The calculated activation energy for the first reaction step (proton transfer) is 30.9 kcal mol$^{-1}$ at the Ons/B3LYP/6-31G(d) theoretical level, and this increases to 32.1 kcal mol$^{-1}$ when free energies are considered. On considering a more realistic solvation model, which involves single point PCM/B3LYP/6-31+G(d) calculations, the activation barrier decreases to 26.8 kcal mol$^{-1}$. On using the ZPE and thermal corrections calculated at the Ons/B3LYP/6-31G(d) level, a free energy of activation of 28.0 kcal mol$^{-1}$ can be estimated for this step.

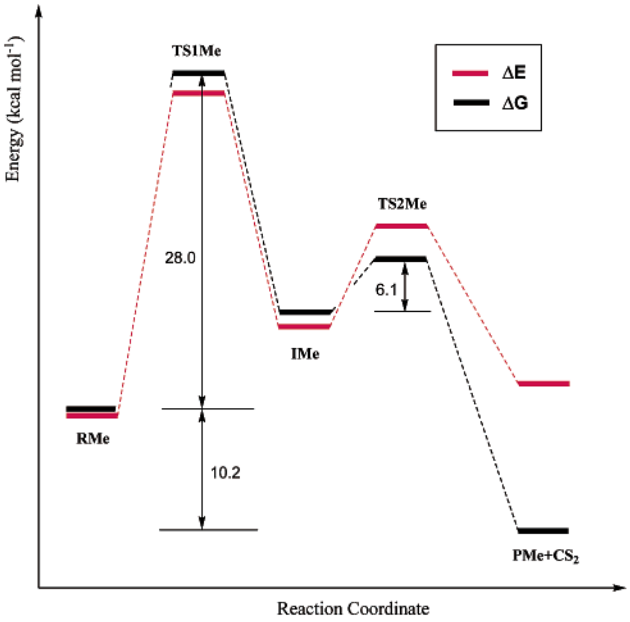

**Figure 3.** Potential and free energy reaction profiles of the reaction of MeDTC, calculated at the PCM/B3LYP/6-31G(d)//Ons/B3LYP/6-31G(d) theoretical level.

The activation energy for the second reaction step (N−C bond breaking) is 10.3 kcal mol$^{-1}$ at the Ons/B3LYP/6-31G(d) level and this changes to 10.4 kcal mol$^{-1}$ when the PCM/B3LYP/6-31+G(d) energies are considered, i.e., in this case the solvation model does not have such a marked influence, as one would expect for a unimolecular bond breaking reaction. The calculated free energy of activation (Figure 3) is as low as 6.1 kcal mol$^{-1}$, indicating a very fast bond breaking once the zwitterionic intermediate is formed. The proton transfer is thus the rate-limiting step in a two-step reaction mechanism. The activation barrier for the reaction is then 28.0 kcal mol$^{-1}$, which is somewhat higher than the experimental value (ca. 22 kcal mol$^{-1}$).[2]

The calculated activation entropy for this step is −7.5 cal mol$^{-1}$ K$^{-1}$. The overall process is exergonic, with a reaction energy of −10.2 kcal mol$^{-1}$.

It is worth noting that the activation barrier for the rate-determining step is almost the same as that obtained in the gas-phase results, which indicates a modest solvent effect in this part of the reaction. As expected, as the charge separation appears along the reaction coordinate, solvent effects become more important and, therefore, the activation barrier for the second step is higher in solution due to the differential solvation of the zwitterionic intermediate **IMe**.

From the geometrical point of view, the stationary points found on the potential energy surface for PhDTC keep a close similarity with those found in the case of MeDTC (Figure 2). Thus, **RPh_s** contains a bridge hydrogen-bonded water molecule and a planar arrangement of the thiocarbamic group (C−N−C−S dihedral angle = 180.0°) similar to that found for **RMe_s**. Unlike the gas-phase structure, the phenyl group is coplanar to the thiocarbamic group, thus favoring conjugation. It is worth noting that the N−C distance in **RPh_s** (1.347 Å) is somewhat longer than that calculated for **RMe_s** (1.323 Å), indicating a smaller double bond character in the former case. This effect could be due to the conjugation of the phenyl group and may have a significant effect on the relative reactivity of **RPh_s** and **RMe_s**.

**TS1Ph_s** corresponds to a situation similar to that found in the case of **TS1Me_s**, i.e., approximately halfway into the proton transfer between the SH and the N groups. As happened in the gas-phase calculations, there are some differences in the degree of synchronicity in the proton transfer, but in this case these differences are in the reverse direction. In **TS1Ph_s** the proton coming from the SH group is transferred to a lesser extent to the water molecule than in **TS1Me_s** (shorter S···H distance and longer H···O distance), whereas the proton coming from the water molecule is transferred to a greater extent to the nitrogen atom (longer O···H distance and shorter H···N distance). The $CS_2$ group is almost perpendicular to the amine moiety (dihedral angle = 76.1°), and this is associated with a consequent loss of conjugation, lengthening of the N−C bond (from 1.347 Å in **RPh** to 1.470 Å in **TS1Ph**), and the enhancement of the nitrogen basicity. It is worth noting that the geometries of **TS1Ph_v** and **TS1Ph_s** are almost identical, which indicates a modest solvent effect on the position of this TS on the reaction coordinate, a situation in contrast to that found in the case of **TS1Me**.

A zwitterionic intermediate, **IPh_s**, was located on the solvated potential energy surface, whose main features are similar to those found for **IMe_s**; namely the twisting of the $CS_2$ group with regard to the amine moiety (dihedral angle = 74.1°) and the lengthening of the N−C bond to 1.558 Å. Clearly, in this case the differential stabilization of the zwitterion in solution is in the origin of the existence of this reaction intermediate.

The N−C bond breaking process takes place through **TS2Ph_s**. With regard to **TS2Me_s**, this TS is earlier (N···C distance 1.941 Å for **TS2Ph_s** and 2.229 Å for **TS2Me_s**) and the $CS_2$ group is still slightly twisted with regard to the amine moiety (dihedral angle = 46.6°). These characteristics are also in agreement with a closer resemblance between this TS and the corresponding intermediate. Similarly, the water molecule is also closer to the N−H group (1.885 Å for **TS2Ph_s** versus 1.966 Å for **TS2Me_s**).

The potential and free energy reaction profiles are shown in Figure 4. The calculated activation energy for the first reaction step (proton transfer) is 27.4 kcal $mol^{-1}$ at the Ons/B3LYP/6-31G(d) theoretical level, and this increases to 27.8 kcal $mol^{-1}$ when free energies are considered. These values are lower, by a reasonable amount, than those corresponding to the MeDTC reaction. On considering a more realistic solvation model, obtained using single point PCM/B3LYP/6-31+G(d) calculations, the activation barrier diminishes to 23.6 kcal $mol^{-1}$. Upon adding the ZPE and thermal corrections calculated at the Ons/B3LYP/6-31+G(d) level, a free energy of activation of 24.0 kcal $mol^{-1}$ can be estimated for this step (Figure 4).

The activation energy for the second reaction step (N−C bond breaking) is as low as 2.4 kcal $mol^{-1}$ at the Ons/B3LYP/6-31G(d) level. This value is smaller than 5*k*T at room temperature, and therefore the validity of the classical Transition Structure Theory for locating this TS can be questioned.[16] In fact, when the free energy reaction path is considered, it can be seen that **TS2Ph_s** lies 9.4 kcal $mol^{-1}$ *below* **IPh_s**; it can be speculated, therefore, that this TS does not exist in the free energy reaction surface. Under these conditions the reaction mechanism turns out to be a one-step process, as found in the gas-phase calculations, with the N−C bond breakage taking place after the proton transfer and without an activation barrier. This result is also consistent with that of the proton inventory, which suggested a transition state close to a zwitterionic structure.[4]

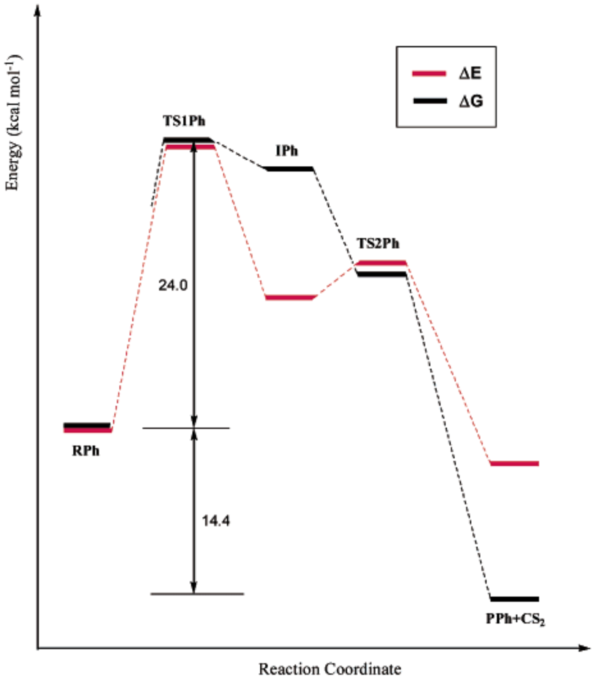

**Figure 4.** Potential and free energy reaction profiles of the reaction of PhDTC, calculated at the PCM/B3LYP/6-31G(d)//Ons/B3LYP/6-31G(d) theoretical level.

The free energy of activation for this reaction is thus 24.0 kcal $mol^{-1}$, a value significantly lower than that calculated for MeDTC. This indicates a greater reactivity of PhDTC, which agrees well with the experimental findings. However, as happened in the case of PhDTC, the calculated barrier is higher than the experimental value for the free energy of activation for this reaction (16.8 kcal $mol^{-1}$).[4]

The difference between the calculated activation barriers of MeDTC and PhDTC of 4 kcal $mol^{-1}$ is, however, practically the same as the experimental values, suggesting that the higher values for each of them might be due to a difference in the free energy of the initial state.

The calculated activation entropy for this step is −9.4 cal $mol^{-1}$ $K^{-1}$, which is in reasonable agreement with the experimental value of −5.6 cal $mol^{-1}$ $K^{-1}$,[4] taking into account that cooperative hydrogen bonding between different solvent molecules is not explicitly considered by our simple model. The overall process is exergonic, with a reaction energy of −14.4 kcal $mol^{-1}$.

**Torsional Effects on the Relative Reactivity.** As we have already seen, the TS for the intramolecular proton transfer in both MeDTC and PhDTC demands a twisting of the thiocarbamic group. It seems logical to conclude that at least part of the activation barrier of

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(16) Williams, I. H. *Chem. Soc. Rev.* **1993**, 277−283, and references therein.

**Table 3. Relative Energies (in kcal mol$^{-1}$) and Absolute Entropies for the Torsion of the Thiocarbamic Group in MeDTC and PhDTC, Calculated at Several Theoretical Levels**

| | Ons/B3LYP/ 6-31+G(d) | | | IPCM/B3LYP/ 6-31+G(d)[a] | |
|---|---|---|---|---|---|
| structure | $\Delta E$ | $\Delta S$ | $\Delta G$ | $\Delta E$ | $\Delta G$[b] |
| **MeDTC** | 0.0 | 81.4 | 0.0 | 0.0 | 0.0 |
| **TSrot_MeDTC** | 19.6 | 76.3 | 20.1 | 18.6 | 19.1 |
| **PhDTC** | 0.0 | 99.9 | 0.0 | 0.0 | 0.0 |
| **TSrot_PhDTC** | 14.7 | 94.4 | 15.1 | 13.8 | 14.2 |

[a] Single point energy calculation on Ons/B3LYP/6-31+G(d) geometries. [b] Using Ons/B3LYP/6-31+G(d) ZPE and thermal corrections.

this process will come from the decrease in the resonance energy arising from the loss of conjugation resulting from this twisting.

It has been speculated that the phenyl group can influence the twisting energy barrier by partial delocalization of the nitrogen lone pair. As already mentioned, this effect can be detected by monitoring the N−C bond distance, which is longer for PhDTC than for MeDTC.

To test this hypothesis, the torsional barriers for the twisting of the thiocarbamic group were calculated for isolated MeDTC and PhDTC molecules at the Ons/B3LYP/6-31+G(d) theoretical level. Single point energy calculations were performed at the IPCM/B3LYP/6-31G-(d) level. The corresponding relative energies are given in Table 3.

As can be seen, the torsional barrier for PhDTC is ca. 5 kcal mol$^{-1}$ lower than that calculated for MeDTC. The calculated energy difference between the activation barriers of the two reactions is 4 kcal mol$^{-1}$ (Table 1), whereas the experimental value for this difference is ca. 5.2 kcal mol$^{-1}$.[4] Therefore, this result strongly suggests that most of this energy difference comes from the different torsional barrier found for the reactants.

## Conclusion

The theoretical results obtained in this work lead us to conclude that the water-assisted S to N proton transfer constitutes the key step in the decomposition of alkyldithiocarbamates from strongly basic amines and aryldithiocarbamates. In the former case, the mechanism of the decomposition is stepwise and takes place through a zwitterionic intermediate. In the latter case, the decomposition is a one-step process in which the proton transfer is concerted with the N−C bond breakage.

A study of the torsional barrier of the thiocarbamic group suggests that most of the energy difference between the activation barriers in the decomposition of those alkyl- and aryldithiocarbamates comes from the difference in the rotational barrier of this group in both kinds of compounds.

The inclusion of solvent effects in the calculations, through continuum models, was revealed to be of importance in order to obtain a realistic picture of the reaction mechanisms involved.

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**Supporting Information Available:** Tables of electronic energies, as well as enthalpies, entropies, Gibbs free energies (the last three data series at 25 °C), and Cartesian coordinates for the different structures described in this work. This material is available via the Internet at http://pubs.acs.org.

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