Mechanisms of Acid Decomposition of Dithiocarbamates. 2. Efficiency of the Intramolecular General Acid Catalysis

Eduardo Humeres,*,† Nito A. Debacher, and M. Marta de S. Sierra

Department of Chemistry, Universidade Federal de Santa Catarina, 88040-900 Florianopolis-SC, Brazil

Received July 15, 1998

The acid decomposition of ethylenebis(dithiocarbamate) (EbisDTC) and glycinedithiocarboxylate (glyDTC) was studied in water at 25 °C in the range of H_o −5 to pH 5. The acid dissociation constants of all species involved were calculated from LFER and from the pH−rate profiles. According to the pK_a of the parent amine of the reactive species, both compounds decompose through the dithiocarbamate anion and a zwitterion intermediate. The intermolecular N-protonation rate constant of the carboxylic conjugate acid of glyDTC anion is 12.6 M^{-1} s^{-1}, slower than the C−N breakdown. This species also cleaves through an intramolecular general acid-catalyzed mechanism where the rate constant for the N-protonation is $(7.1 \pm 4.2) \times 10^3$ s^{-1} and the efficiency of the proton-transfer step as measured by the effective molarity is $(5.6 \pm 3.3) \times 10^2$ M. The acid decomposition of the dithiocarbamic conjugate acid of EbisDTC anion proceeds through a fast N-protonation and a slower C−N breakdown. The intramolecular general acid catalysis rate constant is $(8.2 \pm 2.8) \times 10^6$ s^{-1}, but the efficiency of this fast proton transfer is only (14.3 ± 4.9) M. The intramolecular general acid catalysis of the free acid forms of the carboxylic and dithiocarbamic groups is unfavorable for about 4 kcal mol^{-1} with respect to the protonation of the external hydron, and consequently, no external buffer catalysis is expected to be observed for dithiocarbamates that decompose through a zwitterion intermediate. The difference between the pK_b of the proton acceptor and the pK_a of the donor follows the order of the proton efficiency. Estimation of the strength of the hydrogen bonding in the reagent and product supports the assumption that a thermodynamically favorable change of hydrogen bonding from reagent to product increases the efficiency of proton transfer.

Introduction

Alkyldithiocarbamate anions undergo acid decomposition through a zwitterion intermediate when the pK_a of the parent amine is less than ca. 10.[1] The mechanism explains how the hydron is transferred to the nitrogen and how the transition state adjusts itself to the change of about 14 pK_a units of the nitrogen as the C−N bond is broken.

At pK_a values of the parent amine higher than ca. 10, the alkyldithiocarbamates decompose through another mechanism that has been proposed to occur by a water-catalyzed S to N proton transfer concerted with the C−N bond cleavage.[1] In this mechanism, to reach the transition state, the C−N bond has to twist, inhibiting the resonance of the nitrogen with the thiocarbonyl group, increasing its basicity, and making the transfer of the proton from the thiocarboxylic sulfur to the nitrogen thermodynamically favorable. These two mechanisms, through the zwitterion or by intramolecular proton transfer, agree with those that have been proposed previously[2−7] and show that the basicity of the parent amine is determinant for the change of one to the other.

General acid catalysis is not observed in the acid cleavage of alkyldithiocarbamates,[1,7−9] although some previous publications have reported the presence of general catalysis for this reaction.[3,10] For alkyldithiocarbamates that decompose through the zwitterion, the pK_a of the intermediate is much lower than the solvated proton, making the proton transfer for N-protonation thermodynamically unfavorable, and a general acid catalyst with pK_a higher than the hydron is not expected to be effective, as was confirmed experimentally.[1]

Dithiocarbamates, in particular ethylenebis(dithiocarbamate) metallic salts, are widely used as fungicides. However, their mechanism of action upon fungi is not well understood.[11] The results of a preliminary study of the acid cleavage of ethylenebis(dithiocarbamate) are insufficient for the drawing of any conclusions regarding the mechanisms involved.[12]

---

† Tel.: 55 48 331 9219. Fax: 55 48 331 9711. E-mail: humeres@mbox1.ufsc.br or humeres@qmc.ufsc.br.

(1) Humeres, E.; Debacher, N. A.; Sierra, M. M. de S.; Franco, J. D.; Schutz, A. *J. Org. Chem.* **1998**, *63*, 1598.

(2) Joris, S. J.; Aspila, K. I.; Chakrabarti, C. L. *Anal. Chem.* **1970**, *42*, 647.

(3) De Filippo, D.; Deplano, P.; Devillanova, F.; Trugu, E. F.; Verani, G. *J. Org. Chem.* **1973**, *38*, 560.

(4) Takami, F.; Tokuyama, K.; Wakahara, S.; Maeda, W. *Chem. Pharm. Bull.* **1973**, *21*, 329.

(5) Takami, F.; Tokuyama, K.; Wakahara, W.; Maeda, T. *Chem. Pharm. Bull.* **1973**, *21*, 1311.

(6) Takami, F.; Tokuyama, K.; Wakahara, W.; Maeda, T. *Chem. Pharm. Bull.* **1973**, *21*, 594.

(7) Ewing, S. P.; Lockshon, D.; Jencks, W. P. *J. Am. Chem. Soc.* **1980**, *102*, 3072.

(8) Hallaway, M. *Biochim. Biophys. Acta* **1959**, *36*, 538.

(9) (a) Zahradnik, R.; Zuman, P. *Collect. Czech. Chem. Commun.* **1959**, *24*, 1132. (b) Zahradnik, R. *Collect. Czech. Chem. Commun.* **1958**, *23*, 1435.

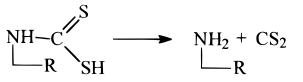
(10) Zahradnik, R. *Collect. Czech. Chem. Commun.* **1956**, *21*, 1111.

(11) (a) Cremlyn, R. J. *Pesticides. Preparation and Mode of Action*; Wiley: Chichester, 1978. (b) Corbett, J. R.; Wright, K.; Baillie, A. C. *The Biochemical Mode of Action of Pesticides*; Academic: London, 1984.

(12) Miller, D. M.; Latimer, R. A. *Can. J. Chem.* **1962**, *40*, 246.

10.1021/jo981382i CCC: $18.00

In this work, we studied the pH−rate profiles of the acid decomposition of ethylenebis(dithiocarbamate), EbisDTC, and glycinedithiocarboxylate, glyDTC, eq 1, to



(1)

R=COOH$_2^+$, COOH, COO$^-$, CH$_2$NH$^+$C(SH)$_2$, CH$_2$NHC(S)SH, CH$_2$NHCS$_2^-$

characterize the mechanisms involved and the possible intramolecular catalysis by the carboxylic and dithiocarbamic groups and their conjugate acids. When properly oriented, catalytic groups become highly efficient in intramolecular reactions.[13]

Experimental Section

Materials. Reagents were all of analytical grade. Ethylenediamine was distilled before use, and dioxane was distilled and filtered through an alumina column. Carbon disulfide was purified over metallic mercury and over phosphorus pentoxide. It was then distilled.

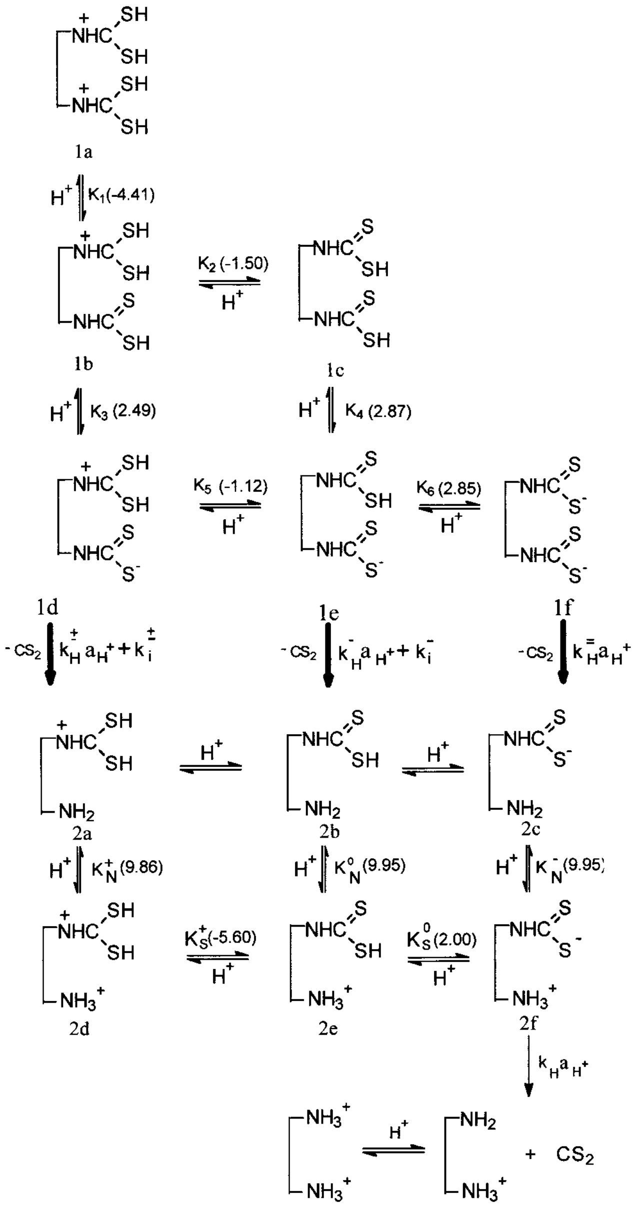
Disodium ethylenebis(dithiocarbamate)[14] was prepared by slowly adding carbon disulfide (61.0 g, 0.8 mol) to a solution of ethylenediamine (31 g, 0.69 mol) in 150 mL of 5.3 M sodium hydroxide (32 g, 0.8 mol) and allowing the mixture to react for 3 h at room temperature. The product was precipitated, recrystallized in acetone, and dried under vacuum: mp > 260 °C (dec);[15] λ_{max} (water) 257 and 284 nm.[16]

A solution of disodium glycine-*N*-dithiocarboxylate[17−19] was prepared from glycine (0.25 g, 3.3 mmol) added to a solution of sodium hydroxide (0.13 g, 3.3 mmol) in water (7 mL), and then stirring the solution until the glycine was dissolved. This solution was treated with carbon disulfide (0.25 g, 3.3 mmol) dissolved in dioxane (7 mL) and was allowed to react with stirring until the glycine was completely consumed as shown by a UV spectrum. The mixture was stripped of half the solvent, under reduced pressure, and 7 mL of ethanol was added. The product was not crystallized, but the solution was kept in the refrigerator until examination, using aliquots of the reaction mixture: λ_{max} (water) 253 and 286 nm.

Acid Dissociation Constants of EbisDTC. Ethylenebis(dithiocarbamic) acids dissociate according to the mechanism shown in Scheme 1, depending on the acidity of the medium.

The dissociation constant K_1 of the conjugate acid **1a** was determined from a series of measurements of the absorbance at 270 nm, between 4 and 14 M sulfuric acid.[20] The mean value of pK_1 was -4.71 ± 0.07, and the statistically corrected value of -4.41 is used in this text. For the monoanion **1e**, $pK_6 = 3.15 \pm 0.05$ was calculated from the variation of absorbance at 284 nm in the range of pH 1−5 and was also statistically corrected to 2.85. The other pK_a values of EbisDTC were calculated from LFER[1] and adjusted by an iterative program (see below) to the pH−rate profile within a deviation of ±0.04 p*K* unit, taking into consideration the thermodynamic constraint. The pK_a values related to *N*-2-aminoethyldithiocarbamate had been determined previously.[1]

Scheme 1. Values in Parentheses Are the p*K*a Values



Kinetics. The rate of decomposition of the dithiocarbamates in water was followed spectrophotometrically in the region of 270−280 nm at 25 °C in a Cary 219 spectrophotometer. The acidity ranged between H_o −5 to pH 5. The ionic strength of solutions less acid than 1 M HCl was kept equal to unity with KCl. Between pH 2 and 5, the solutions were buffered at least at two buffer concentrations, and no general acid catalysis was observed. For instance, at pH 3.1, when the concentration of formate buffer was increased from 0.2 to 1.0 M, no general catalysis resulted for EbisDTC.

Kinetics were all first order, except for EbisDTC between pH 2.0 and 4.3, where the plot of $\log(A_\infty - A_t)$ vs time was biphasic, corresponding to two consecutive reactions. The rate constant of the first step was calculated by the Guggenheim method.[21] The rate constant of the second step was calculated from the straight line of the second part of the plot. This value was similar to that obtained from the decomposition of the *N*-2-aminoethyldithiocarbamate.[1]

A generalized minimum least-squares program was used to fit the experimental points to the theoretical curve of the pH−rate profiles.

---

[13] (a) Menger, F. M. *Acc. Chem. Res.* **1985**, *18*, 128. (b) Menger, F. M. *Atual. Fis.-Quim. Org.* **1989**, 136.

[14] Klopping, H. L.; Van der Kerk, G. J. M. *Recl. Trav. Chim. Pays-Bas* **1951**, *70*, 949.

[15] Frank, A. W. *Appl. Spectrosc.* **1982**, *36*, 282.

[16] Vandebeek, R. R.; Joris, S. J.; Aspila, K. I.; Chakrabarti, C. L. *Can. J. Chem.* **1970**, *48*, 2201.

[17] Frank, A. W. *Phosphorus, Sulfur Silicon Relat. Elem.***1990**, *54*, 109.

[18] Andreasch, R. *Monatsh.* **1910**, *31*, 785.

[19] Budevsky, O.; Russeva, E.; Mesrob, B. *Talanta* **1966**, *13*, 277.

[20] Albert, A.; Sergeant, E. P. *The determination of Ionization Constants*; Chapman and Hall: London, 1971.

[21] Guggenheim, E. A. *Philos. Mag.* **1926**, *2*, 528.

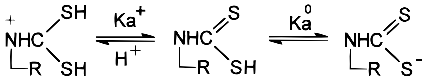
Table 1. Dissociation and Rate Constants Related to the Acid Cleavage of Ethylenebis(dithiocarbamate) and Glycinedithiocarboxylate in Water at 25 °C[a]

no. order	$R-CH_2-NHC(S)SH$, R =	σ_I	pK^+	pK_a	pK_N	10^4k_o, s^{-1}	k_H, M^{-1} s^{-1}
1d	$CH_2NH^+C(SH)_2$	0.05[b]	−4.41	2.49	9.86[c]	20.1 ± 4.8	0.62 ± 0.08[d]
1e	$CH_2NHC(S)SH$	0.04[b]	−1.50	2.87[b]	9.95[c]	4.5 ± 0.6	0.33 ± 0.02[e]
1f	$CH_2NHC(S)S^-$	0.04[b]	−1.12	2.85	9.95[c]	9.3 ± 1.6	0.66 ± 0.05[e,f]
2	$CH_2NH^+{}_3$	0.36[g]	−5.60[d]	2.00[d]	7.52[h]	20.9 ± 0.2[d]	0.21 ± 0.01
3g	$COOH^+{}_2$	0.56	−3.7	−0.07	5.2	352 ± 126	0.03 ± 0.007[d]
3h	COOH	0.34[i]	−3.8	2.1	7.8	22.2 ± 2.8	0.28 ± 0.008[e]
3i	COO^-	−0.17[g]	−1.8	3.3[j]	9.91[j]	1.70 ± 0.22	0.34 ± 0.01[e]

[a] This work unless indicated; pK_N, pK_a of the parent amine. [b] Extrapolated from LFER.[1] [c] Extrapolated from LFER for substituted methylammonium ions.[28] [d] From the pH−rate profile. [e] Extrapolated from Figure 2. [f] Statistically corrected for two basic sites. [g] Reference 28a. [h] Reference 25. [i] Exner, O. In *Advances in Linear Free Energy Relationships*; Chapman, N. B., Shorter, J., Eds.; Plenum: New York, 1972; Chapter 1. [j] Reference 20.

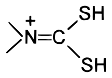
Results and Discussion

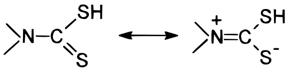
Substituent Constants of the Dithiocarbamic Group. The dithiocarbamic acids dissociate according to eq 2. The values of σ_I for the different forms of the methylenedithiocarbamic group ($R = CH_2NH^+C(SH)_2$, $CH_2NHC(S)SH$, $CH_2NHCS_2{}^-$) were obtained from the LFER of pK_a (or $pK_a{}^+$) vs σ_I[1] (Table 1).

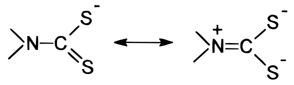


(2)

The substituent constants of the dithiocarbamic groups were calculated from the series $X-CH_2CH_2NHC(S)SH$, ($X = NH_3{}^+$, OMe, OH, H, Et).[1] For $NH^+C(SH)_2$, NHC(S)SH, and $NHC(S)S^-$, σ_I was found to be 0.15, 0.13, and 0.14, respectively. The close similarity of σ_I for the different forms of the dithiocarbamic group, despite the charge on the sulfur atom, suggests that there is little difference of the positive charge on the nitrogen between the conjugate acid (I), the free acid (II and III), and the anion (IV and V) because there extensive delocalization of the nitrogen electron pair to the thiocarbonyl group with predominance of forms III and V. This conclusion is in agreement with results from UV[22] and infrared[23] spectra, i.e., that there is a strong character of double bond between carbon and nitrogen atoms in the dithiocarbamic moiety.

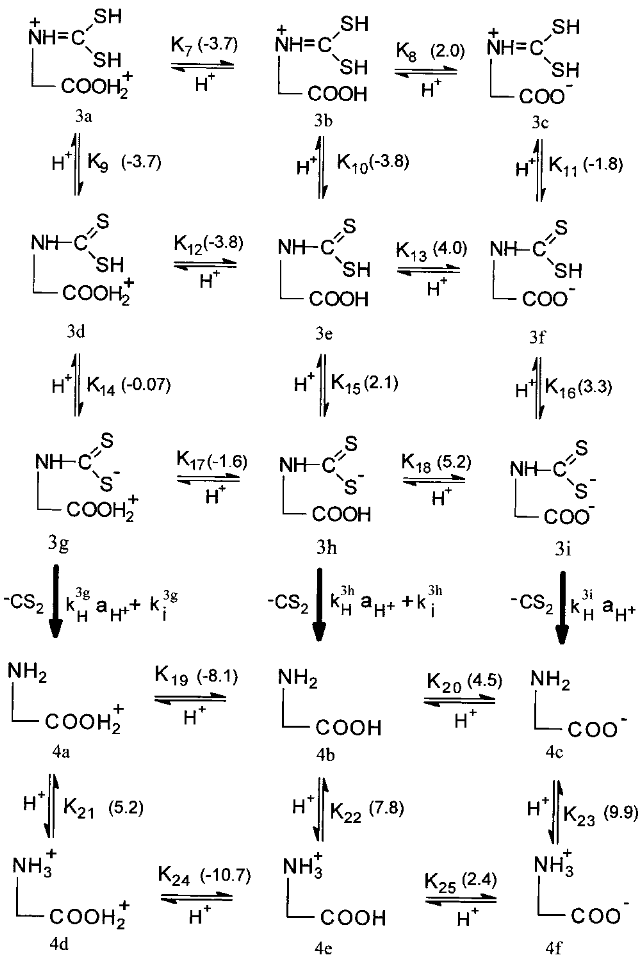

I


II III


IV V

The large decrease of about 14 units in the pK_a calculated for the protonation of nitrogen as a consequence of the dithiocarboxylate group in alkyldithiocarbamates has been ascribed to this strong electron withdrawing effect of the thiocarbonyl group.[1]

Scheme 2. Values in Parentheses Are the pK_a Values



Acid Dissociation Constants of Glycinedithiocarboxylate. The microscopic pK_a values of glycine (Scheme 2) were obtained assuming that pK_{22} is equal to that of the methyl ester,[24] and taking into account the values of the experimental macroscopic constants $pK_A = 2.36 = pK_{25}$ and $pK_B = 9.91 = pK_{23}$. [20,25–27] The thermodynamic constraint permitted the calculation of pK_{20}. The correlation for the pK_N of substituted methylammonium ions[28]

---

(22) (a) Jansen, M. J. *Recl. Trav. Chim. Pays-Bas* **1960**, *79*, 454. (b) Jansen, M. J. *Recl. Trav. Chim. Pays-Bas* **1960**, *79*, 464. (c) Jansen, M. J. *Recl. Trav. Chim. Pays-Bas* **1960**, *79*, 1068.

(23) (a) Thorn, G. D.; Ludwig, R. A. *Can. J. Chem.* **1954**, *32*, 872. (b) Thorn, G. D. *Can. J. Chem.* **1960**, *38*, 1439. (c) Chatt, J.; Duncanson, L. A.; Venanzi, L. M. *Suom. Kemistil.* **1956**, *B29*, 75. (d) Chatt, J.; Duncanson, L. A.; Venanzi, L. M. *Nature* **1956**, *177*, 1042. (e) Wahlberg, A. *Acta Chem. Scand., Ser. A* **1976**, *30*, 433. (f) Cox, B. G.; de Maria, P. *J. Chem. Soc., Perkins Trans. 2* **1977**, 1385.

(24) Sober, H. A., Hart, R. A., Eds. *Handbook of Biochemistry*; CRC Press: Cleveland, 1968.

(25) Kortum, G., Vogel, W., Andrussow, K., Eds. *Dissociation Constants of Organic Acids in Aqueous Solution*; IUPAC−Butterworth: London, 1961.

(26) Adams, E. Q. *J. Am. Chem. Soc.* **1916**, *38*, 1503.

(27) Fleck, G. M. *Equilibria in Solution*; Holt, Rinehart, Winston: New York, 1966; Chapter 5.

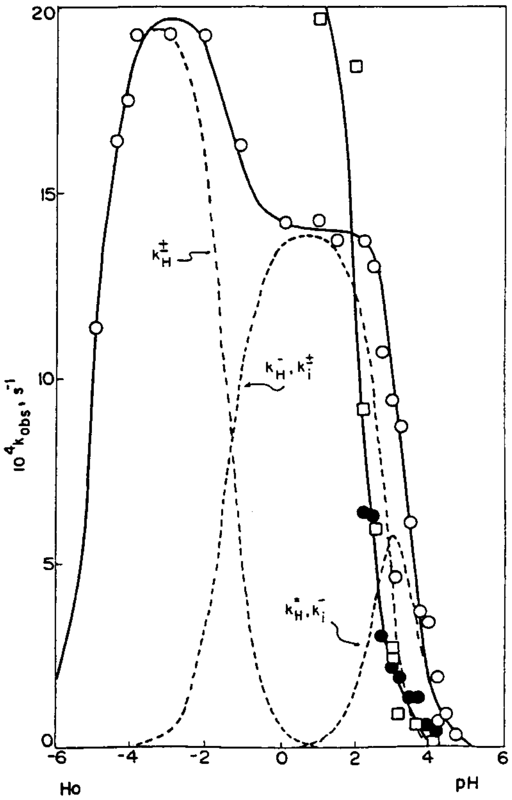


Figure 1. pH−rate profile of the acid decomposition of ethylenebis(dithiocarbamate) in water at 25 °C: ○, cleavage of the first group; ●, cleavage of the second group; □, *N*-2-aminoethyldithiocarbamate; —, calculated rate constant; ---, contribution of the kinetic terms.

was used to calculate pK_{21}, assuming that the substituent constant of the $COOH_2^+$ group is similar to that of the NH_3^+ group. The pK_a values of the substituted conjugate acetic acids were estimated from eq 3[29,30] adjusted for the

$$pK_a^{\ +} = -7.5\sigma_I - 6.8\ (n = 3, r = 0.710) \qquad (3)$$

thermodynamic constraint with a standard deviation of ±0.5 p*K* unit.

The set of equilibrium constants of glyDTC (Scheme 2) was obtained as a first approximation from LFER[1] and eq 3. The pK_a's of the substituted acetic acids were calculated from eq 4.[28]

$$pK_a = -3.95\sigma_I + 4.71\ (n = 13, r = 0.996) \qquad (4)$$

Then, the set of values was optimized and adjusted by the iterative method and the thermodynamic cycle to the pH−rate profile of the acid decomposition, with a deviation of ±0.04 p*K* unit. The values of pK_{13}, pK_{15}, pK_{16}, and pK_{18} coincided with those calculated from LFER. The pK_a values of the dithiocarbamic and carboxylic conjugate acids were higher than those calculated from LFER, possibly due to intramolecular hydrogen bonding.

pH−Rate Profile of Ethylenebis(dithiocarbamate). The pH−rate profile of the acid cleavage of the first dithiocarbamic group of EbisDTC is shown in Figure 1.

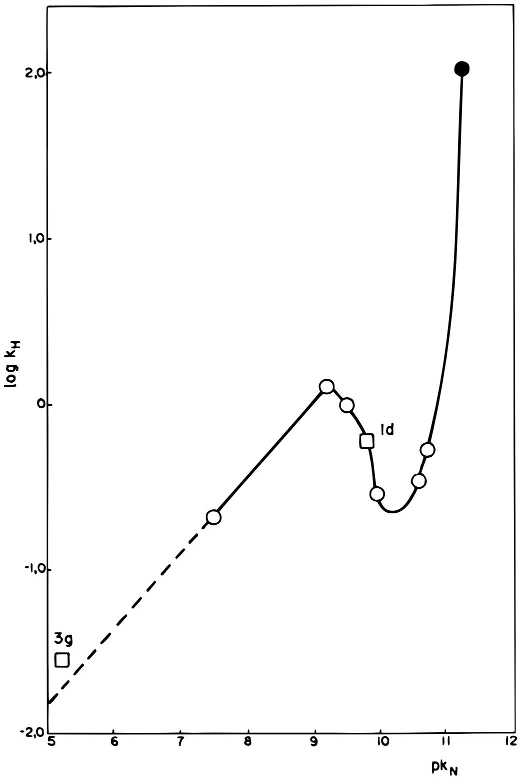


Figure 2. Brønsted plot of the specific acid catalysis rate constants and the pK_N of the leaving amine for the acid decomposition of substituted methyldithiocarbamates in water at 25 °C: ○, ref 1; ●, ref 7; □, this work.

The pK_N values of the parent amine of species **1b**,**d**, **1c**,**e**, and **1f** are 9.86, 9.95, and 9.95, respectively (Table 1, Scheme 1). Therefore, the decomposition should occur through the dithiocarbamate anion and the zwitterion species with specific acid catalysis on **1d**, **1e**, and **1f** and rate constants $k_H^{\pm}$, k_H^-, and $k_H^=$ respectively,[1] plus the possible intramolecular general acid catalysis on **ld** and **1e** by the acid forms of the other dithiocarbamic moiety, with rate constants $k_i^{\pm}$ and k_i^- as shown in eq 5a, where $X_{\mathbf{1d}}$, $X_{\mathbf{1e}}$, and $X_{\mathbf{1f}}$ are the corresponding molar fractions. Equation 5a is kinetically equivalent to eq 5b.

$$k_{obs} = [k_H^{\ \pm} a_{H^+} + k_i^{\ \pm}]X_{\mathbf{1d}} + [k_H^{\ -} a_{H^+} + k_i^{\ -}]X_{\mathbf{1e}} + k_H^{\ =} a_{H^+} X_{\mathbf{1f}} \qquad (5a)$$

$$k_{obs} = \left[k_0^{\ \mathbf{1b}} + k_0^{\ \mathbf{1c}}\frac{K_2}{a_{H^+}} + k_0^{\ \mathbf{1e}}\frac{K_2K_4}{(a_{H^+})^2}\right]X_{\mathbf{1b}} \qquad (5b)$$

where

$$k_0^{\ \mathbf{1b}} = k_H^{\ \pm}K_3;\ k_0^{\ \mathbf{1c}} = k_H^{\ -}K_4 + k_i^{\ \pm}\frac{K_4}{K_5};$$
$$k_0^{\ \mathbf{1e}} = k_H^{\ =}K_6 + k_i^{\ -}$$

The curve of the pH−rate profile in Figure 1 was obtained for $k_0^{\mathbf{1b}} = (2.01 \pm 0.04) \times 10^{-3}$ s^{-1}, $k_0^{\mathbf{1c}} = (1.40 \pm 0.03) \times 10^{-3}$ s^{-1}, and $k_0^{\mathbf{1e}} = (1.42 \pm 0.17) \times 10^{-3}$ s^{-1}. The specific acid catalysis rate constant $k_H^{\pm}$ of the decomposition of species **1d** (Scheme 1) is equal to $k_0^{\mathbf{1b}}/K_3 = (0.62 \pm 0.08)$ M^{-1} s^{-1} and is the expected value from the Brønsted plot (Figure 2) considering that from Table

---

(28) (a) Charton, M. *J. Org. Chem.* **1964,** *29*, 1222. (b) Charton, M. *Prog. Phys. Org. Chem.* **1981**, *13*, 119.

(29) Arnett, E. M. *Prog. Phys. Org. Chem.* **1963**, *1*, 223.

(30) Goldfarb, A. R.; Mele, A.; Gutstein, N. *J. Am. Chem. Soc.* **1955**, *77*, 6194.

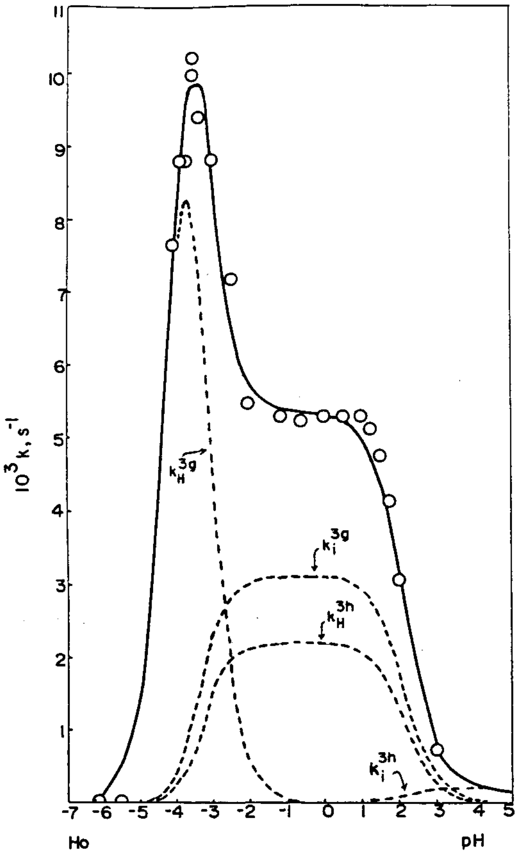


Figure 3. pH−rate profile of the acid decomposition of glycinedithiocarboxylate in water at 25 °C: ○, observed rate constants; —, calculated rate constant; ---, contribution of the kinetic terms.

1, $pK_N = 9.86$ for species **1d**. This provides strong evidence that eq 5b correctly describes the reaction.

The rate constant k_0^{1c} contains the specific acid catalysis rate constant k_H^- of the cleavage of species **1e** (Scheme 1) with $pK_N = 9.95$ (Table 1). The extrapolated value of k_H^- is 0.33 ± 0.02 M^{-1} s^{-1}. Since $pK_4 = 2.87 \pm 0.03$ (Scheme 1), the term $k_H^- K_4 = (0.45 \pm 0.06) \times 10^{-3}$ s^{-1} is too small compared to k_0^{1c}, and consequently $k_i^{\pm} K_4/K_5$ must be different from zero with an intramolecular rate constant $k_i^{\pm}$ equal to 9.3 ± 2.1 s^{-1}. It is not possible to obtain the pH−rate profile curve without considering this intramolecular catalytic term.

Following the same reasoning, the specific acid rate constant $k_H^{=}$ of the decomposition of **1f** (statistically corrected for the two dithiocarbamate groups) is 0.66 ± 0.05 M^{-1} s^{-1}, since $pK_N = 9.95$ (Table 1). Considering the value of $pK_6 = 2.85 \pm 0.04$, the intramolecular catalytic term k_i^- is $(4.9 \pm 3.3) \times 10^{-4}$ s^{-1}. Consequently, species **1d** and **1e** in Scheme 1 decompose through specific acid catalysis and also through an intramolecular general acid-catalyzed mechanism.

pH−Rate Profile of Glycinedithiocarboxylate. Glycinedithiocarboxylic acids provide the opportunity to study the effect of a neighboring carboxylic group as intramolecular general acid catalyst on the rate of acid cleavage in the carboxylic free acid form or as the conjugate acid $COOH_2^+$. The pH−rate profile of the acid decomposition of glycinedithiocarboxylate is shown in Figure 3. It was considered that it cleaves through species **3g**, **3h**, and **3i** (Scheme 2) because the pK_N of the corresponding parent amines of species **3d**,**g**, **3e**,**h**, and **3f**,**i** are 5.2, 7.8, and 9.9, respectively.[1] The total experimental first-order rate constant is given by eq 6a, where k_H^{3g}, k_H^{3h}, and k_H^{3i} are the specific acid-catalyzed rate constants

$$k_{obs} = [k_H^{3g} a_{H^+} + k_i^{3g}]X_{3g} + [k_H^{3h} a_{H^+} + k_i^{3h}]X_{3h} + k_H^{3i} a_{H^+} X_{3i} \qquad (6a)$$

$$k_{obs} = \left(k_0' + k_0'' a_{H^+} + \frac{k_0'''}{a_{H^+}}\right) X_{3e} \qquad (6b)$$

where

$$k_0' = \frac{k_i^{3g} K_{14}}{K_{12}} + k_H^{3h} K_{15}$$

$$k_0'' = \frac{k_H^{3g} K_{14}}{K_{12}}$$

$$k_0''' = k_i^{3h} K_{15} + k_H^{3i} K_{16} K_1$$

of the species with molar fractions X_{3g}, X_{3h}, and X_{3i}, respectively. Species **3g** and **3h** can also undergo intramolecular general acid-catalyzed cleavage, with first-order rate constants k_i^{3g} and k_i^{3h}. The molar fractions can be related to X_{3e}, and eq 6a becomes kinetically equivalent to eq 6b.

The curve of the pH−rate profile shown in Figure 3 was obtained for $k_0' = (5.35 \pm 0.16) \times 10^{-3}$, $k_0'' = (5.56 \pm 0.17) \times 10^{-6}$, and $k_0''' = (1.61 \pm 0.05) \times 10^{-6}$. The calculated value of $k_H^{3g} = k_0'' K_{12}/K_{14} = (3.0 \pm 0.7) \times 10^{-2}$ M^{-1} s^{-1} is close to the expected value for the decomposition of species **3g** as can be observed in Figure 2, and it is another piece of evidence that eq 6 properly describes the mechanism. From the Brønsted plot (Figure 2), the extrapolated values of the specific acid catalysis rate constants for **3h** and **3i** are $k_H^{3h} = 0.28$ and $k_H^{3i} = 0.34$ M^{-1} s^{-1}, respectively, and like EbisDTC, the intramolecular catalytic rate constants must be different from zero to obtain the pH−rate profile curve, with values of $k_i^{3g} = (16.8 \pm 5.4)$ s^{-1} and $k_i^{3h} = (2{,}0 \pm 0.3) \times 10^{-4}$ s^{-1}, calculated from eq 6b.

Intramolecular General Acid Catalysis. Proton transfer between electronegative centers are intrinsically rapid, and they can become rate determining in reactions involving high energy intermediates. However, intramolecular proton transfer in general acid catalysis is typically inefficient as measured by the effective molarity.[31] Although the rate of an intramolecular reaction depends on a critical distance between the reacting groups,[13] for intramolecular proton transfer reactions this is not the only parameter involved, and it has been proposed that the efficiency of the proton transfer increases when the transferred proton ends up in a thermodynamically favored intramolecular hydrogen bond in the reaction product.[32] In Table 2 are shown the main features of the intramolecular acid catalysis of some of the reactive species of EbisDTC and glyDTC according to Scheme 3. We note that the calculation of the effective molarity is not strictly correct because the intermolecular reaction is between the reactant and the hydron. Nonetheless the

---

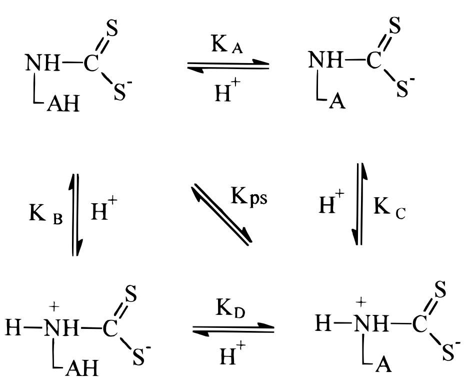
(31) Kirby, A. J. *Adv. Phys. Org. Chem.* **1980**, *17*, 183.
(32) Kirby, A. J. *Acc. Chem. Res.* **1997**, *30*, 290.

Table 2. Intramolecular General Acid Catalysis of the Acid Cleavage of Ethylenebis(dithiocarbamate) and Glycinedithiocarboxylate in Water at 25 °C[a]

AH	species	EM[b]	k_{2i}, s^{-1}	pK_A[c]	pK_B[d]	pK_C[d]	pK_D	pK_{ps}
$CH_2NH^+C(SH)_2$	**1d**	14.3 ± 4.9	$(8.2 \pm 2.8) \times 10^6$	−1.12	−4.24	−4.15	−1.21	3.03
$CH_2NHC(S)SH$	**1e**	$(1.5 \pm 1.1) \times 10^{-3}$	$(1.1 \pm 0.8) \times 10^3$	2.85	−4.15	−4.15	2.85	7.00
$COOH_2^+$	**3g**	$(5.6 \pm 3.3) \times 10^2$	$(7.1 \pm 4.2) \times 10^3$	−1.6	−8.90	−6.30	−4.20	4.70
COOH	**3h**	$(7.1 \pm 1.1) \times 10^{-4}$	3.6 ± 0.6	5.2	−6.30	−4.20	3.10	9.40

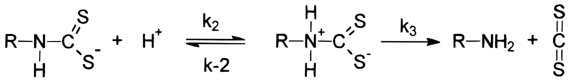
[a] From Scheme 3. [b] Effective molarity. [c] From Schemes 1 and 2. [d] From ref 1.

Scheme 3



pK_a values of the conjugated acids (dithiocarbamic and carboxylic) are quite close to that of the hydron. It can be observed that the rate constant for the intramolecular proton transfer k_{2i} does not determine the efficiency. The intramolecular proton switch constant K_{ps} is thermodynamically unfavorable, and for the same type of general acid, the efficiency increases when pK_{ps} decreases for the same pair of electronegative centers. There is also an apparent relationship between the difference the pK_b of the proton acceptor and the pK_a of the donor that follows the order 24.5 > 19.4 > 15.3 > 15.1 for **3g**, **1d**, **1e**, and **3h**, respectively, the same as the proton efficiency.

The acid decomposition of alkyldithiocarbamates from parent amines with pK_N < 10 occurs through the dithiocarbamate anion and a zwitterion intermediate (eq 7).[1]



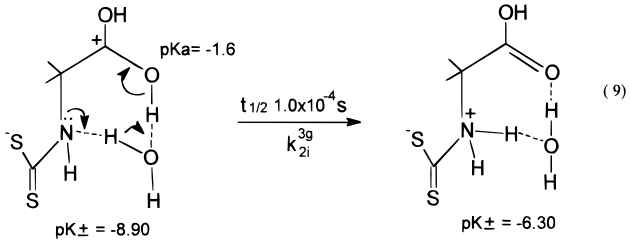
$$R-NH-C(=S)S^- + H^+ \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} R-NH_2^+-C(=S)S^- \xrightarrow{k_3} R-NH_2 + S=C=S \qquad (7)$$

The specific acid catalysis rate constant is given by eq 8, where K_a is the acid dissociation constant of the dithiocarbamic acid.

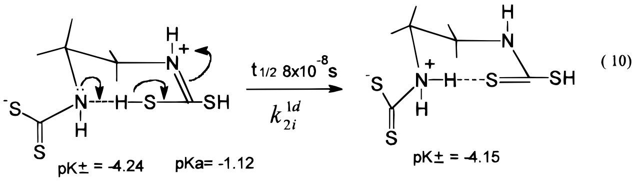
$$k_H = \frac{k_2 k_3 K_a}{k_3 + k_{-2}} \qquad (8)$$

The intermolecular N-protonation of species **3g** is slower than the C−N breakdown and $k_2^{3g} = 12.6$ M^{-1} s^{-1}.[1] For the intramolecular general acid-catalyzed cleavage, the effective molarity (EM) = (5.6 ± 3.3) × 10^2 M represents the efficiency of the N-protonation step, because according to eq 8, $k_i^{3g}/k_H^{3g} = k_{2i}^{3g}/k_2^{3g}$ and consequently $k_{2i}^{3g} = (7.1 \pm 4.2) \times 10^3$ s^{-1}. In eq 9 it is assumed that the O to N proton transfer occurs through a water molecule, which does not change the type of the hydrogen bonds but improves the position of the heavy atoms involved for the proton transfer. The acid dissociation constant of the zwitterion (p$K_\pm$) increases 2.6 pK units upon the proton transfer because the donor and acceptor groups are not electronically independent.

The acid decomposition of species **1d** proceeds through a fast N-protonation and a slower C−N breakdown (eq 10).[1] The intramolecular general acid catalysis rate constant k_{2i}^{1d} is (8.2 ± 2.8) × 10^6 s^{-1}, but the efficiency of this fast S to N proton transfer is low (EM = 14.3 ± 4.9 M). The value of p$K_\pm$ does not change after the proton transfer, and the thiocarbonyl sulfur is known to be a poor hydrogen bond acceptor.



3g



1d

The negligible EM for both the dithiocarbamic and carboxylic free acid groups indicates that the intramolecular catalysis is about 4 kcal mol^{-1} unfavorable regarding the protonation by the external hydron. This result might be a consequence of the fact that high values of pK_a increase the strength of the hydrogen bonding in the reagent. Also, it indicates that intermolecular general acid catalysis by acids with higher pK_a values must be negligible for dithiocarbamates that decompose through a zwitterion intermediate, as was found experimentally.[1]

It is difficult to evaluate the strength of the hydrogen bonding in the reagent and product, but a rough estimation can be made considering the difference between the calculated pK_a from the pH−rate profile and that from LFER. As mentioned above, in some cases a difference of 2−3 pK units was observed and was attributed to intramolecular hydrogen bonding. For the reagent species **2a**, **2b**, **4a**, and **4b**, the ΔpK value due to N···H bonding is low, in the range of −1.2 to 0.3. For the dithiocarbamic species (**1d**, **1e**, **3g**, and **3h**), the difference is much higher, suggesting that the dithiocarbamic group is part of the main group involved in the hydrogen bonding. The weak N···H bond estimated for the amino species must be much weaker for the dithiocarbamic species because of the strong electron-withdrawing effect of the dithiocarboxylate group.

The hydrogen bonding strength in the product can be estimated from the difference in the p$K_\pm$ values, those for **1e**, **1f**, **3h**, and **3i** species are 1.1, −2.8, 0.6, and −7.2, respectively. Therefore, for the conjugate acid group pair there is an increase in the hydrogen bonding strength from reagent to product of $\Delta\Delta pK$ 2.3 and 1.0 for **1d** and **3g**, while for the free acid group pair, **1e** and **3h**, there is a decrease of −2.1 and −7.5, respectively. These results support the assumption that a thermodynamically favorable change of hydrogen bonding from reagent to product would increase the efficiency of proton transfer.

Conclusions

The acid decomposition of ethylenebis(dithiocarbamate) and glycinedithiocarboxylate anions is intramolecularly general acid catalyzed by the neighbor conjugate acid group. For the carboxylic group, the effective molarity is $(5.6 \pm 3.3) \times 10^2$ M, and for the dithiocarbamic group it is 14.3 ± 4.9 M. For both the dithiocarbamic and carboxylic free acid groups, the intramolecular catalysis is about 4 kcal mol^{-1} unfavorable with respect to the protonation by the external hydron. Accordingly, intermolecular general acid catalysis by acids with higher pK_a values must be negligible for alkyldithiocarbamates that decompose through a zitterion intermediate, as was found experimentally.

The rate constant for the intramolecular proton transfer does not determine the efficiency. The intramolecular proton switch constant K_{ps} is thermodynamically unfavorable, and for the same type of general acid, the efficiency increases when pK_{ps} decreases for the same pair of electronegative centers. The difference between the pK_b of the proton acceptor and the pK_a of the donor follows the order of the proton's efficiency. Estimation of the strength of the hydrogen bonding in the reagent and product supports the assumption that a thermodynamically favorable change of hydrogen bonding from reagent to product increases the efficiency of proton transfer.

Acknowledgment. This paper was written in part during the stay of E.H. at the Chemistry Department of the University College London, as an Academic Visitor. We thank CNPq for the travel grant and Professor Brian Capon for his comments.

JO981382I