Thiocarbony *versus* Carbonyl Compounds: A Comparison of Intrinsic Reactivities

J.-L. M. Abboud,*,§ O. Mó,† J. L. G. de Paz,† M. Yáñez,† M. Esseffar,‡ W. Bouab,‡,⊥ M. El-Mouhtadi,‡ R. Mokhlisse,‡ E. Ballesteros,§ M. Herreros,§ H. Homan,§ C. Lopez-Mardomingo,§ and R. Notario§

Contribution from the Departamento de Química, C-14, Universidad Autônoma de Madrid, Cantoblanco, E-28049 Madrid, Spain, Departement de Chimie, Université Cadi-Ayyad, Marrakech, Morocco, and Instituto Rocasolano, C.S.I.C., Serrano 119, E-28006 Madrid, Spain

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Abstract: The first systematic comparison of structural effects on the intrinsic reactivities of carbonyl and thiocarbonyl compounds has been carried out. To this end, the gas-phase basicities (GB) of a wide variety of thiocarbonyl compounds XCSY (as well as of some carbonyl derivatives) were determined by means of Fourier transform ion cyclotron resonance spectrometry (FTICR) and SCF and MP2 ab initio calculations at different levels of accuracy were performed on 27 different neutral compounds and their protonated forms. The same set, enlarged by the inclusion of very large systems such as di-*tert*-butyl- and bis-(1-adamantyl)thioketones was also investigated at the AM1 semiempirical level in order to get a more complete view of structural effects. The agreement between the calculated and the experimental changes in thermodynamic state functions is good in all instances. Correlation analysis of the experimental data shows that (i) substituent effects on the gas-phase basicity of thiocarbonyl compounds are linearly related to those of their carbonyl homologs with a slope of 0.80 and (ii) these effects can be quantitatively analyzed in terms of polarizability, field, and resonance effects (Taft–Topsom model). Comparison of the GBs of thiocarbonyl and carbonyl compounds with solution basicities and nucleophilicities sheds light on differential structural and solvation effects. Substituent effects on both neutral and protonated species were explored by means of appropriate isodesmic reactions. These results confirm that all thiocarbonyl compounds investigated are sulfur bases in the gas phase. The features revealed by correlation analysis can be rationalized in terms of the interactions between the MOs of the substituent and the parent compound.

Introduction

Consider a simple process such as the protonation of a base B in the gas phase, reaction (1):

$$B(g) + H^+(g) \rightarrow BH^+(g) \qquad (1)$$

Currently available techniques[1] allow the determination of the intrinsic proton basicity, GB, and the proton affinity, PA, of B, respectively, defined as $GB = -\Delta G_{H^+}(g)$ and $PA = -\Delta H_{H^+}(g)$. The systematic study of gas-phase proton exchange reactions between bases has led to the development of new formalisms describing the quantitative effects of substitution on the GBs of organic compounds.[2] Because of their formal simplicity and general importance, proton-transfer reactions are appealing models for the study of other acid–base reactions, both in the gas-phase and in solution.[3]

Most of the experimental information on structural effects on GBs available nowadays originates in a substantial body of data for N(sp, sp^2 and sp^3) and O(sp^2 and sp^3) n-donor bases and small data sets for S(sp^3) and P(sp^3) compounds.[4] This paper is the first in a series aimed at broadening our knowledge of chemical reactivity through the study of less usual species. In particular, we are interested in unveiling unsuspected properties hidden behind the apparent uniformity of the Periodic Table.

Here we present results of a study on thiocarbonyl compounds, X(CS)Y. These derivatives were chosen for the following reasons: (i) Their structure and reactivity can be varied within very wide limits by appropriate choices of X and Y. (ii) Extremely little is known about their intrinsic (gas-phase) reactivity[5] and the stabilizing or destabilizing role of the different substituents. (iii) Carbonyl compounds (a natural yardstick for comparison) have received a great deal of attention recently.[6] Hence, one of the aims of this paper will be not only to provide as accurate gas-phase basicities as possible for a wide set of thiocarbonyl compounds but also to offer an analysis of substituent effects on their stabilities and the stabilities of their protonated forms and a thorough comparison with carbonyl bases.

Briefly, two main topics are addressed in this work: (i) the influence of the nature of the basic center on the relative basicities of homologous O(sp^2) and S(sp^2) compounds (ii) the analogies

† Universidad Autónoma de Madrid.
‡ Université Cadi-Ayyad.
§ Instituto Rocasolano.
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and differences in the transmission of electronic substituent effects through C=O and C=S groups.

Ab initio quantum mechanical calculations[7] have reached a high level of sophistication, thus allowing us to extract reliable structural information of great value for the understanding of the energetics of ion–molecule reactions such as (1).

Experimental Section

All compounds studied in this work are known. Their structures were confirmed by NMR, IR, and MS. Purity was assessed by GLC and TLC.

The origin of and purification techniques for these materials are as follows: 1,1,3,3-Tetramethyl-2-thiourea (Aldrich) was crystallized from absolute EtOH and vacuum-dried in the presence of phosphorous pentoxide. The highly hygroscopic 1,3-dimethyl-2-thiourea (Aldrich) was dissolved in dry benzene, the solution was stirred for 6 h over finely ground CaH_2 and filtered, and the solvent evaporated. The dry product was sublimed twice under vacuum. 2-Imidazolinethione (Merck), thiourea (Merck), thioacetamide (Merck), and 1,3-dimethyl-2-urea (Aldrich) were twice sublimed under vacuum. *N,N*-Dimethylthioformamide (Aldrich) was vacuum-distilled. *N,N*-Dimethylthioacetamide (±)-thiocamphor and *O*-ethyl thioacetate were synthesized according to Scheeren[8] by treating respectively *N,N*-dimethylacetamide (in MeCN), (±)-camphor (in diglyme), and EtOAc (in MeCN) with P_4S_{10} in the presence of $NaHCO_3$. Residual starting materials were removed by distillation (case of EtOAc) or by treatment with boiling water (DHA and (±)-camphor). *O*-Ethyl thioacetate was purified by GLC. Crude (±)-thiocamphor was crystallized from EtOH–H_2O (1:1) and column chromatographed (silica gel, hexane). Crude *N,N*-dimethylacetamide was crystallized from a 1:1 Et_2O–petroleum ether mixture.

Thiophosgene (Aldrich) and dicyclopropyl ketone (Aldrich) were purified by GLC. *O*-Methyl and *O*-ethyl dimethylthiocarbamates were prepared after Battegay[9] by treating the appropriate sodium alkoxides with dimethylthiocarbamoyl chloride. After removal of the residual alcohols and careful distillation, both compounds were purified by column chromatography (silica gel, 2:1 petroleum ether–CH_2Cl_2).

Dicyclopropyl thioketone was obtained by treating the corresponding ketone with Lawesson's reagent.[10] Purification was achieved by column chromatography (silica gel, hexane). di-*tert*-Butyl thioketone and bis-(1-adamantyl)thioketone were synthesized according to Barton and co-workers[11] from the corresponding ketimines (obtained from pivalonitrile and 1-adamantanecarbonitrile as described by Olah[12]). The latter were first treated with ethereal methyllithium (1:1) in hexane under a dry argon atmosphere, and, when the evolution of methane had ceased, dry CS_2 was added and the mixture was stirred for 3 h. After completion of the reaction, the solvent was evaporated, and the thioketones were obtained by distillation and sublimation, respectively, of the residues. The purification was repeated twice. Bis(1-adamantyl) ketone was obtained by acidic (HCl) hydrolysis of the corresponding ketimine.[12] The ketone was crystallized from MeOH and twice sublimed.

Gas-phase basicities (GB) were determined from equilibrium proton-transfer reactions conducted in a modified Bruker CMS-47 FTICR mass spectrometer.[1] Working conditions were similar to those already described.[13] The average cell temperature is ca. 333 K. These FTICR measurements provide the standard free-energy change, $\delta\Delta G_{H^+}(g)$, for proton-transfer reaction 2 in the gas-phase between a given base B and a reference compound B_{ref}.

$$BH^+(g) + B_{ref}(g) \rightleftarrows B(g) + B_{ref}H^+(g) \qquad K_p, \delta\Delta G_{H^+}(g) \quad (2)$$

The reversibility of reaction 2 was systematically confirmed by means of double resonance experiments.

The gas-phase proton basicity GB of B is the negative of $\Delta G_{H^+}(g)$, the standard free-energy change for reaction 3:

$$B(g) + H^+(g) \rightarrow BH^+(g) \qquad \Delta G_{H^+}(g) \quad (3)$$

GB values can be obtained by combining $\delta\Delta G_{H^+}(g)$ data with the GB of the reference bases.

The experimental gas-phase basicities for carbonyl compounds used in the comparison with our measured values for the thiocarbonyl analogues are mostly published values from Taft's laboratory.[5a] These values have been compared to those given in the most recent HPMS determination of GBs and PAs, carried out under extremely careful conditions of temperature monitoring.[14a] The correlation between GBs at 333 K (our nominal working temperature) obtained from ref 14a for 18 bases ranging from water to dimethylamine and Taft's data is exceptionally good: r = 0.9997, sd = 0.34 kcal/mol. The slope is 1.068 ± 0.021 at the 99% level. Taft's values have thus been multiplied by this factor throughout.

Computational Details

Ab initio calculations were carried out with the Gaussian-90 series of computer codes.[15] The geometries of the 27 neutrals and those of their protonated species were optimized at the 6-31G* level[16] using gradient techniques. For most of the species under consideration we have studied not only the protonation at sulfur but also at the other alternative basic sites. For instance, for thioformamide we have investigated both sulfur and nitrogen protonation. In every case sulfur is the most basic atom.

The harmonic vibrational frequencies were determined by analytical second derivatives techniques and used to characterize the stationary points of the potential energy surface and to evaluate zero-point energies, which were scaled by the empirical factor of 0.89.[17] In order to take into account electronic correlation effects, the corresponding protonation energies were obtained in the framework of the Moller–Plesset perturbation theory[18] at second order (MP2) and using a 6-31+G(d,p) basis set,[19] which has been proved to provide reliable protonation energies when used at this level. Hence, protonation energies were calculated as the MP2/6-31+G(d,p)//6-31G* energy difference between protonated and unprotonated species.

This initial set of 27 compounds was enlarged by including three additional systems (**28–30**), which present very large size substituents as *tert*-butyl or adamantyl and for which the corresponding ab initio calculations would become very expensive. Within this enlarged set, both structures and energies were also obtained by employing the AM1 semiempirical method[20] and compared (for the first 27 compounds) with those obtained at the ab initio level. The AM1 calculations have been carried out with the AMPAC package of programs and using the keyword PRECISE. The proton affinities obtained at this semiempirical level were calculated taking for the heat of formation of the proton the experimental value[21] (367.2 kcal/mol).

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Table I. Total Energies (hartrees), Zero Point Energies (ZPE, kcal/mol), and Dipole Moments of Thiocarbonyl Compounds

compd	R_1	R_2	HF/ 6-31G*	ZPE[a]	MP2/ 6-31+G(d,p)// 6-31G*	μ (D)
1	H	H	−436.506 46	16.8	−436.774 19	2.22
1H⁺			−436.807 11	23.9	−437.073 45	
2	CH_3	H	−475.551 75	36.2	−475.967 82	2.96
2H⁺			−475.86845	42.8	−476.28083	
3	NH_2	H	−491.56663	29.8	−492.01122	5.15
3H⁺			−491.90395	36.8	−492.34451	
4	OH	H	−511.38626	21.7	−511.84129	1.90
4H⁺			−511.69362	28.1	−512.14457	
5	F	H	−535.36331	12.8	−535.80548	1.85
5H⁺			−535.64854	19.5	−536.08420	
6	Cl	H	−895.40871	11.7	−895.80511	1.55
6H⁺			−895.70099	18.4	−896.09808	
7	C_2H_5	H	−514.58621	55.6	−515.15151	2.95
7H⁺			−514.90715	62.0	−515.46844	
8	$N(CH_3)_2$	H	−569.62645	67.9	−570.36635	5.86
8H⁺			−569.98182	74.7	−570.71848	(4.74)[b]
9	OCH_3	H	−550.41266	40.7	−551.01038	2.72
9H⁺			−550.73520	46.8	−551.32592	
10	CH_3	CH_3	−514.59400	55.1	−515.16020	3.40
10H⁺			−514.92371	61.4	−515.48439	
11	NH_2	NH_2	−546.61677	41.2	−547.23581	6.11
11H⁺			−546.96797	48.0	−547.58419	
12	OH	OH	−586.26703	25.6	−586.90305	1.05
12H⁺			−586.58121	31.4	−587.21301	
13	F	F	−634.22382	7.9	−634.88211	0.68
13H⁺			−634.49928	14.6	−635.09989	
14	Cl	Cl	−1354.29937	5.6	−1354.23581	0.67
14H⁺			−1354.58797	12.2	−1355.11726	
15	CH_3	NH_2	−530.60912	48.5	−531.20159	5.38
15H⁺			−530.95745	55.4	−531.54543	(4.77)[b]
16	CH_3	OH	−550.43260	40.3	−551.03557	2.34
16H⁺			−550.75387	46.5	−551.35138	
17	CH_3	F	−574.41181	31.5	−575.00113	2.91
17H⁺			−574.71641	37.8	−575.29816	
18	CH_3	Cl	−934.45303	30.4	−934.99801	2.53
18H⁺			−934.76070	36.9	−935.30517	
19	CH_3	$N(CH_3)_2$	−608.66099	86.7	−609.55255	5.85
19H⁺			−609.02490	93.4	−609.91270	(4.74)[b]
20	CH_3	OCH_3	−589.457 55	59.2	−590.203 93	2.87
20H⁺			−589.790 57	65.5	−590.528 23	
21	CH_3	OC_2H_5	−628.497 50	78.2	−629.392 44	3.12
21H⁺			−628.834 84	84.4	−629.722 11	(2.10)[c]
22	C_2H_5	OCH_3	−628.491 67	78.4	−629.387 61	2.57
22H⁺			−628.827 24	84.8	−629.715 60	
23	$NHCH_3$	$NHCH_3$	−624.674 02	79.6	−625.585 85	6.53
23H⁺			−625.036 21	86.5	−625.947 57	
24	$NHCH_2$	$NHCH_2$	−623.517 13	66.3	−624.404 67	6.68
24H⁺			−623.876 30	72.4	−624.758 94	
25	OCH_3	SCH_3	−986.963 48	60.4	−987.838 31	0.98
25H⁺			−987.297 54	66.5	−988.169 18	
26	$N(CH_3)_2$	OCH_3	−683.524 29	90.3	−684.591 06	4.38
26H⁺			−683.87667	96.7	−684.940 76	
27	$N(CH_3)_2$	$N(CH_3)_2$	−702.713 49	117.7	−703.933 54	5.49
27H⁺			−703.108 46	124.7	−704.302 36	

[a] ZPE have been scaled by the empirical factor 0.89. [b] Experimental values taken from ref 34. [c] Experimental values taken from ref 35.

Results and Discussion

1. Structures. The total energies of the species under investigation as well as the scaled ZPE corrections and their dipole moments are summarized in Table I.

The corresponding optimized structures are given as supplementary material. In a great majority of the cases under investigation the potential energy surface presents several minima which correspond to different conformations and which have been also characterized. However, the supplementary material contains only the structure of the global minimum for each neutral and for each sulfur protonated species. Information on the other alternative conformers are available from the authors upon request.

Although a detailed discussion of the geometries of these species is not the aim of this paper, several features should be singled out for comment:

(a) In all compounds C=S bond length varies within very narrow limits (1.60–1.68 Å) independent of the nature of the substituents.

(b) Upon protonation there is, on average, a 0.05 Å elongation of this bond, which indicates that the C=S linkage is difficult to stretch, but which clearly reflects a slight weakening due to the charge transfer toward the incoming proton.

(c) The R_1CR_2 bond angle opens up upon protonation, due to the charge redistributions which take place within the molecule. Protonation causes a considerable polarization of the C=S bonding charge density toward the sulfur atom, which is transmitted to the C–R_1 and C–R_2 bonds. As a consequence, the carbonyl carbon hybrid orbital involved in the C=S linkage increases its *p* character, while those involved in the C–R_1 and C–R_2 bonds, by orthogonality, increase their *s* character. Accordingly, the angle between the latter increases. This increase is particularly important in systems as thioformic acid (**4** and **4H⁺**) or methyl thioformate (**9** and (**H⁺**) because in these cases protonation is accompanied by a significant structural change. While in the neutral species the –OH or the –OMe groups are s-*cis* with respect to the C=S bond, and in the protonated species they are in s-*trans*, in order to favor the interaction between the incoming proton and the electronegative atom of the substituent. In this respect, our topological analysis of their electronic charge densities[22] indicates that there is no bond critical point between both nuclei. Hence, we conclude that in these kinds of systems there is a stabilizing electrostatic interaction between the positive charge of the hydrogen atom bonded to sulfur and the negative charge of the oxygen atom of the substituent but not a typical intramolecular hydrogen bond. A similar effect is not observed when substituents are amino or methylamino groups, perhaps because, in these cases, the nitrogen lone-pair conjugates with the thiocarbonyl π-system.

(d) Unfortunately very few experimental structures have been reported so far: X-ray diffraction studies of thioacetamide[23] and thiourea,[24] the electron diffraction investigation of methylthioformate,[25] and the microwave studies of thioformamide,[26] thioformaldehyde[27] and thioacetaldehyde.[28] For these six cases the agreement between our optimized structural parameters and the experimental ones is good. For the particular cases of thioformaldehyde and its fluorine derivatives (thioacetaldehyde, thioacetone, and thioformic acid) our values are also in good agreement with previously reported theoretical values.[29–32] For the remaining systems we have neither experimental nor theoretical values with which to compare. It must be mentioned however that for 1,3-dimethylthiourea the unequal doublets observed in its NMR spectrum were attributed[33] to the presence of the *cis–cis* and the *cis–trans* isomers in a 3:2 ratio, while our calculations show that the latter is the most stable species in the gas phase. Regarding the dipole moments there is also a reasonably good agreement between our calculated values (if one takes into account that the 6-31G* basis set usually overestimates this magnitude) and published experimental values for *N*-dimethylthioformamide,[34]

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Table II. Experimental Determination of the Gas-Phase Basicities of Selected Thiocarbonyl and Carbonyl Compounds[a]

compd	standard	$\Delta\Delta G_{H^+}$ (std)[b]	$\delta\Delta H_{H^+}$ (g)	$\Delta\Delta G_{H^+}$ (g)	$\Delta\Delta G_{H^+}$ (g) (av)	$T\Delta\Delta S_{H^+}$ (g)	ΔPA[f]
$SC[N(CH_3)_2]$	4-Me pyridine	−22.5	−0.26	−22.76	−22.8 ± 0.1	0.63[c]	−22.2
	4-Et pyridine	−23.3	0.50	−22.80			
$SC(NHCH_3)_2$	n-$C_5H_{11}NH_2$	−17.4	−1.05	−18.45	−18.4 ± 0.1	0.52[c]	−17.9
	t-$C_4H_9NH_2$	−19.0	0.72	−18.28			
$CH_3C(S)N(CH_3)_2$	n-$C_5H_{11}NH_2$	−17.4	−0.60	−18.00	−18.1 ± 0.2	0.78[c]	−17.3
	$(HC{\equiv}C\text{-}CH_2)_3N$	−17.8	−0.21	−18.01			
	C_5H_5N	−18.8	0.47	−18.27			
2-imidazolinethione	$C_3H_7NH_2$	−15.1	−2.09	−17.19	−17.3 ± 0.2	2.96[c]	−14.3
	n-$C_5H_{11}NH_2$	−17.4	0.03	−17.43			
	t-$C_4H_9NH_2$	−19.0	1.71	−17.29			
$(1\text{-}C_{10}H_{15})_2CS$	$H_2C{=}CHCH_2NH_2$	−13.3	−1.76	−15.06	−15.0 ± 0.1	0.90[c]	−14.1
	n-$C_3H_7NH_2$	−15.1	0.26	−14.84			
$C_2H_5OC(S)N(CH_3)_2$	pyridazine	−13.6	−0.70	−14.30	−14.3 ± 0.1	1.02[d]	−13.3
	n-$C_3H_7NH_2$	−15.1	0.82	−14.28			
$HC(S)N(CH_3)_2$	$H_2C{=}CHCH_2NH_2$	−13.3	−0.02	−13.32	−13.3 ± 0.1	0.58[c]	−12.7
	pyridazine	−13.6	0.39	−13.21			
$(c\text{-}C_3H_5)_2CS$	4-Me pyrazol	−12.7	−0.38	−13.08	−13.0 ± 0.2	1.2[c]	−11.8
	3-Me pyrazol	−12.9	−0.01	−12.91			
	$H_2C{=}CHCH_2NH_2$	−13.3	0.15	−13.15			
$CH_3OC(S)N(CH_3)_2$	$(t\text{-}C_4H_9)_2S$	−10.7	−1.30	−12.00	−11.9 ± 0.2	1.47[c]	−10.4
	c-$C_3H_5NH_2$	−12.0	0.25	−11.75			
$SC(NH_2)_2$	$(t\text{-}C_4H_9)_2S$	−10.7	−0.26	−10.96	−10.9 ± 0.1	1.08[c]	−9.8
	c-$C_3H_5NH_2$	−12.0	1.15	−10.85			
$CH_3C(S)NH_2$	2-fluoropyridine	−7.9	−0.41	−8.31	−8.2 ± 0.1	1.94[c]	−6.2
	CH_3NH_2	−10.5	2.48	−8.02			
$(t\text{-}C_4H_9)_2CS$	pyrazine	−6.1	−1.54	−7.64	−7.8 ± 0.2	0.90[e]	−6.9
	2-fluoropyridine	−7.9	0.10	−7.80			
	$HC{\equiv}C\text{-}CH_2NH_2$	−8.5	0.57	−7.93			
thiocamphor	pyrazine	−6.1	−1.03	−7.13	−7.3 ± 0.3	0.90e[e]	−6.4
	$(c\text{-}C_3H_5)_2CO$	−6.1	−1.43	−7.53			
	$(CH_3)_2NCOOCH_3$	−6.8	−0.60	−7.40			
	2-fluoropyridine	−7.9	0.83	−7.07			
$CH_3C(S)OC_2H_5$	$(C_2H_5)_2S$	−1.7	−1.25	−2.95	−2.9 ± 0.3	1.21[c]	−1.7
	$(i\text{-}C_3H_7)_2O$	−2.2	−0.96	−3.16			
	$H_2C(CH_3CO)_2$	−4.0	1.33	−2.67			
$CH_3OC(S)SCH_3$	$(i\text{-}C_3H_7)_2O$	−2.2	−0.53	−2.73	−2.7 ± 0.1	1.02[c]	−1.7
	$H_2C(CH_3CO)_2$	−4.0	1.35	−2.65			
Cl_2CS	c-C_3H_6	21.8	0.14	21.94	22.2 ± 0.2	1.20[c]	23.4
	C_6H_5Cl	21.6	0.77	22.37			
$(c\text{-}C_3H_5)_2CO$	3-cyanopyridine	−6.1	−0.03	−6.13	−6.1 ± 0.1		
	$(i\text{-}C_3H_7)_2S$	−6.7	0.68	−6.02			
$(1\text{-}C_{10}H_{15})_2CO$	2-fluoropyridine	−7.9	−2.38	−10.28	−10.2 ± 0.1		
	$(t\text{-}C_4H_9)_2S$	−10.7	0.50	−10.20			
$OC(HNCH_3)_2$	c-$C_3H_5NH_2$	−12.0	−0.94	−12.94	−13.0 ± 0.1		
	$H_2C{=}CHCH_2NH_2$	−13.3	0.31	−12.99			

[a] All values in kcal/mol. The nominal temperature is 333 K. [b] Values from ref 5a. [c] Theoretical (ab initio) values, see text. [d] Taking the same value as for $CH_3OC(S)N(CH_3)_2$. [e] Estimated using symmetry numbers, see ref 5a. [f] $PA(NH_3)$ = 204.0 kcal/mol taken from ref 14b.

thioacetamide,[34] *N,N*-dimethylthioacetamide,[34] and ethylthioacetate[35] (all of which was obtained in solution).

(e) As mentioned before, for those cases where the substituent contains an alternative basic center (N, O, F, Cl), we have also obtained the structures of the species protonated at the substituent. These structures are available from the authors upon request. In some cases the corresponding protonated system is not stable, as it dissociates in a neutrol and thiocarbonyl cation. A paradigmatic example is offered by FHC=S, where protonation at the fluorine atom leads to a dissociation of the C–F bond, which results in the formation of a FH molecule plus a HCS^+ cation. This phenomenon is due to the strong bond activation of the C–F bond upon protonation, which has been discussed in detail for similar systems elsewhere.[36,37]

(f) In general, the structures obtained at the AM1 level are not very different from those obtained at the HF/6-31G* level, as reflected (as we shall discuss below) by the corresponding relative protonation energies. In general the AM1 bond distances overestimate the ab initio ones by about 0.06–0.1 Å, but the general trends found upon substitution are well reproduced. This semiempirical method overestimates the bond activations mentioned above, predicting not only the dissociation of the FHC=S system upon protonation at the fluorine atom but also the dissociation of thioformic acid (HOCH=S) by protonation at oxygen (while the HF/6-31G* calculations yield a stable cation, although with a long C–O bond).

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2. Gas-Phase Basicities

Table II presents the results of proton-transfer equilibria 2 between the different thiocarbonyl compounds considered and a series of standard reference bases. The values of $\delta\Delta G_{H^+}(g)$ given in Table II are defined as

$$\delta\Delta G_{H^+}(g) = -RT \ln K_p \qquad (4)$$

All GBs are referred to ammonia. Thus, with respect to this reference, $GB(B) = -\Delta\Delta G_{H^+}(g)$ for reaction 5.

$$B(g) + NH_4^+(g) \rightarrow BH^+(g) + NH_3(g) \qquad \Delta\Delta G_{H^+}(g) \quad (5)$$

$\Delta\Delta G_{H^+}(g)$ is the average of the $\Delta\Delta G$ values obtained through eq 6:

$$\Delta\Delta G = \delta\Delta G_{H^+}(g) + \Delta\Delta G_{H^+}(\text{std}) \qquad (6)$$

where $\Delta\Delta G_{H^+}(\text{std})$ pertains to reaction 7:

$$B_{ref}(g) + NH_4^+(g) \rightleftarrows B_{ref}H^+(g) + NH_3(g) \qquad (7)$$

Proton affinities, PA (defined as $PA = -\Delta H^\circ_{H^+}(g)$ for reaction 3) are not determined directly from ICR spectrometry, but entropy

Table III. Structural Effects on the Gas-Phase Basicities of Carbonyl and Thiocarbonyl Compounds X(CO)Y and X(CS)Y[a]

compd		−GB (relative to NH_3)	
X	Y	XC(O)Y	XC(S)Y
$N(CH_3)_2$	$N(CH_3)_2$	−18.9[b]	−22.8[c]
CH_3	$N(CH_3)_2$	−13.7[b]	−18.4[c]
$NHCH_3$	$NHCH_3$	−13.0[b]	−17.9[c]
1-$C_{10}H_{15}$ (1-adamantyl)	1-$C_{10}H_{15}$ (1-adamantyl)	−10.2[b]	−14.1[c]
H	$N(CH_3)_2$	−8.5[b]	−12.7[c]
CH_3O	$N(CH_3)_2$	−6.6[b]	−10.4[c]
c-C_3H_5	*c*-C_3H_5	−6.1[c]	−11.8[c]
t-C_4H_9	*t*-C_4H_9	−3.1[b]	−6.9[c]
camphor	thiocamphor	−2.0[b]	−6.4[c]
CH_3	OC_2H_5	3.9[b]	−1.7[c]
H	H	33.0[b]	18.3[d]
F	F	53.2[b]	36.3[e]

[a] All values in kcal·mol^{-1}. [b] From ref 5a. [c] This work, experimental. [d] Determined by combining the difference between GBs of H_2CO and H_2CS according to ref 5a (14.7 kcal/mol) with the value of GB(H_2CO) from Taft's laboratory corrected as indicated in the text. An uncertainty of ca. 1.3 kcal/mol can be estimated for GB(H_2CS): Jassien, P. G.; Stevens, W. J. *J. Chem. Phys.* **1985**, *83*, 2984. [e] Obtained by using the ab initio PA of F_2CS and correlation equation linking calculated and experimental PAs (see Figure 2). The $T\Delta\Delta S$ term is from the ab initio calculations.

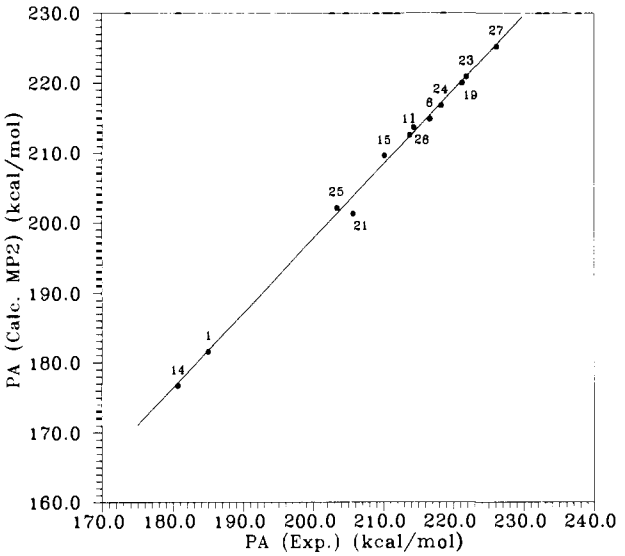

Figure 1. Linear correlation between calculated and experimental proton affinities. The former were obtained at the MP2/6-31+G(d,p)//6-31G* level. The correlation equation is PA(exp) = (0.932 ± 0.037)PA(calc) + (16.1 ± 16.1) kcal/mol, r = 0.996, sd = 0.85 kcal/mol.

terms were instead evaluated in our SCF ab initio calculations. These absolute PA values and those relative to ammonia, ΔPA, are collected in Table III. In the case of large molecules for which ab initio calculated entropies were not available, entropy changes for reaction 7 were estimated using changes in symmetry numbers.[5a] For the purpose of obtaining absolute PAs from our experimental ΔPAs, we have used PA(NH_3) = 204.0 kcal/mol, as it is the best value obtained very recently by Szulesko and McMahon[14a] in a careful HPMS study and agrees remarkably well with the high-level ab initio (G2) result (204.1 kcal/mol) from Smith and Radom.[14b]

Table III also contains the theoretical proton affinities obtained at different levels. There is a linear relationship between the experimental values and the theoretical ones obtained at the MP2/6-31+G(d,p)//6-31G* level after including the corresponding ZPE corrections (see Figure 1). Also significant is the fact that this correlation presents a slope very close to unity and that it covers a wide range (about 50 kcal/mol) of the basicity scale.

Figure 2 illustrates the reasonably good linear relationship between the aforementioned ab initio MP2 values and those

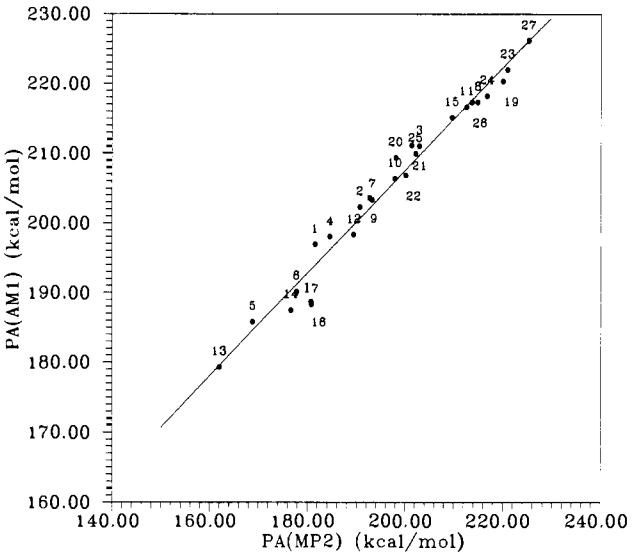

Figure 2. Linear correlation between proton affinities calculated at the AM1 semiempirical level and at the MP2/6-31+G(d,p)//6-31G* level.

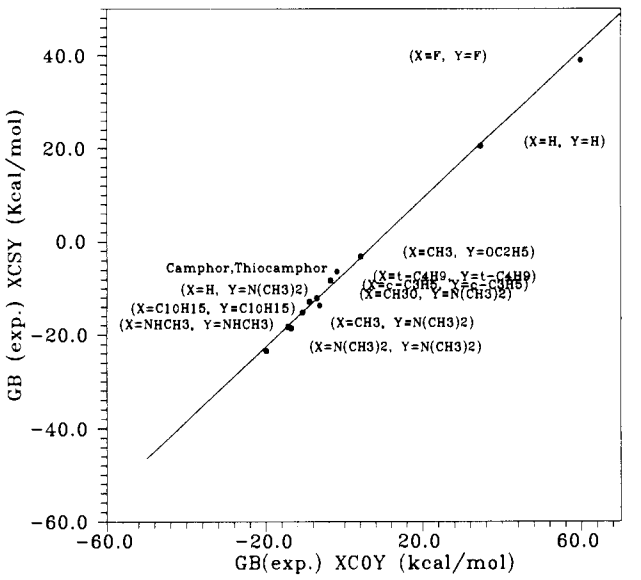

Figure 3. Linear correlation between the experimental gas-phase basicities of carbonyl and thiocarbonyl compounds.

obtained at the AM1 semiempirical level. It must be noticed, however, that in this case the slope of the correlation is greater than unity (1.39), because the absolute AM1 PAs overestimate both the experimental and the ab initio MP2 values. Nevertheless, the goodness of the correlation clearly indicates that relative gas-phase basicities are quite well reproduced. Furthermore, the values predicted for the largest systems (di-*tert*-butyl thioketone (**28**), thiocamphor (**29**), and bis(1-adamantyl) thioketone (**30**)), which were only evaluated at the AM1 level, are also reliable as shown in Table III.

A direct comparison of structural effects on the GBs of carbonyl and thiocarbonyl compounds, as summarized in Table IV, sets the stage for further discussion. Equation 8 embodies the linear correlation existing between both sets of intrinsic basicities (see also Figure 3):

$$\Delta GB(CS) = (0.797 \pm 0.055)\Delta GB(CO) + (6.24 \pm 0.86) \quad (8)$$

in kcal/mol, n = 12 data points, r = 0.9971, and sd = 1.3 kcal/mol. The breadth of structural effects involved (72.1 and 59.1 kcal/mol for carbonyl and thiocarbonyl compounds, respectively)

Table IV. Proton Affinities (kcal/mol) of Thiocarbonyl Compounds

compd	R_1	R_2	PA (ab initio)[a]	PA(AM1)	PA(exp)[b]
1	H	H	181.5	196.9	185.0
2	CH_3	H	190.6	202.3	
3	NH_2	H	202.9	211.0	
4	OH	H	184.6	198.0	
5	F	H	168.9	185.8	
6	Cl	H	177.8	190.1	
7	C_2H_5	H	193.1	203.3	
8	$N(CH_3)_2$	H	214.9	217.3	216.7
9	OCH_3	H	192.6	203.6	
10	CH_3	CH_3	197.8	206.3	
11	NH_2	NH_2	212.6	216.6	213.8
12	OH	OH	189.4	198.3	
13	F	F	162.0	179.3	
14	Cl	Cl	176.7	187.5	180.7
15	CH_3	NH_2	209.6	215.1	210.2
16	CH_3	OH	192.5		
17	CH_3	F	180.8	188.3	
18	CH_3	Cl	180.7	188.7	
19	CH_3	$N(CH_3)_2$	220.0	220.8	221.3
20	CH_3	OCH_3	198.0	209.3	
21	CH_3	OC_2H_5	201.3	211.1	205.7
22	C_2H_5	OCH_3	200.1	206.8	
23	$NHCH_3$	$NHCH_3$	220.9	221.9	221.9
24	$NH(CH_2)$	$NH(CH_2)$	216.8	218.2	218.3
25	OCH_3	SCH_3	202.1	209.9	203.7[c]
26	$N(CH_3)_2$	OCH_3	213.7	217.3	214.4
27	$N(CH_3)_2$	$N(CH_3)_2$	225.2	226.1	226.2
28	$C(CH_3)_3$	$C(CH_3)_3$		214.7	211.1
29	thiocamphor	thiocamphor		213.1	210.4
30	Ad	Ad		218.2	218.1

[a] Obtained at the MP2/6-31+G(d,p)//6-31G* level and including ZPE corrections. [b] PA (NH_3) = 204.0 kcal/mol taken from ref 14a. [c] Taken ref ref 6a.

is possibly the largest ever reported for any linear free-energy relationship[38] (LFER).

We include in Table IV a number of carbonyl compounds XCOY in which X and/or Y are heteroatoms endowed with lone pairs (potential basic sites). It is known[2] that, in the gas phase, these species protonate on the carbonyl oxygen. Equation 8 very strongly suggests[39] that the homologous thiocarbonyl compounds also have a constant basic center, namely, the sulfur atom of the CS group.

The slope in eq 8 reflects the fact that differential substituent effects are 20% smaller in the thiocarbonyl series. This notwithstanding, thiocarbonyl compounds are consistently more basic than their carbonyl homologs over the entire range of reactivity examined in this work. As we show later, this last effect originates in differences in polarizability and electronegativity between oxygen and sulfur.

Experimental evidence indicates that most ketones, esters, amides, and ureas also protonate on the carbonyl oxygen when in acidic solutions[40] and the same holds for the homologous thionocompounds.[41] At variance with the gas-phase results, however, in the few instances in which a direct comparison of the pK_as of the corresponding conjugated acids can be carried out,[42] as in the case of the couples CH_3CONH_2/CH_3CSNH_2, $C_6H_5CONH_2/C_6H_5CSNH_2$, and ϵ-caprolactam/ϵ-thiocaprolactam, one finds that the carbonyl compound is more basic by 1.5–2.0 pK units. This is likely a consequence of two facts: (i) the strong attenuation of polarizability effects in aqueous solution[43] (pK_as are referred to a standard state of pure water) and (ii) the poorer solvation of the protonated thiocarbonyl compounds in aqueous solution. This last point agrees with the hydrogen-bonding acidity of thiols being much smaller than that of alcohols[44] as well as with the experimental solvation parameters[45] (such as Bunnett–Olsen's ϕ[46] or Marziano–Cimino–Passerini's[47] or Cox–Yates'[48,49], m^*). For the latter, it is found that $m^*(CS) > m^*(CO)$. This is of a great importance for, as pointed out by Bagno and Scorrano,[50] when the weaker base (as measured by the pK_a of the conjugated acid) has a larger m^* value (as it is the case here) the basicity gap narrows and eventually leads to a crossover as one moves from pure water to increasingly acidic solutions. This bridges smoothly the gap between the relative basicities of homologous carbonyl and thiocarbonyl compounds in the gas phase and in pure water. For example, for the couple CH_3CONH_2(pK_{BH^+} = –0.73, m^* = 0.55)/CH_3CSNH_2 (pk_{BH^+} = –3.15, m^* = 1.47) in aqueous sulfuric acid one locates the crossover at ca. 50% weight of H_2SO_4.[51]

In order to rationalize the observed substituent effects on the gas-phase basicity of thiocarbonyl derivatives we have resorted in the first place to the Taft–Topsom's model[52] which considers substituent effects classified according to their origin in field (σ_F), resonance (σ_{R^+}), and polarizability (σ_α) effects. The values used for these substituent parameters are those proposed by Taft and Topsom in ref 52. For all the monosubstituted derivatives studied we have found that both experimental and calculated proton affinities follow this model quite well. For the particular case of MP2 PAs, eq 9 is fulfilled by differential substituent effects, δ_xPA, defined as δ_xPA = PA(HCSX) – PA(H_2CS):

$$\delta_x\text{PA} = -(19.0 \pm 1.6)\sigma_\alpha - (46.8 \pm 2.0)\sigma_F - (46.4 \pm 1.6)\sigma_{R^+} \quad (9)$$

with n = 9, r = 0.9978, and sd = 1.1 kcal/mol.

Figure 4 illustrates the remarkably good agreement which exists between the values predicted by eq 9 and those obtained in our MP2 calculations. Equation 9 indicates that for thiocarbonyl compounds both the field and the resonance terms are dominant: the first because, as we have shown in Table I, thiocarbonyl derivatives present sizeable dipole moments. Therefore the ion–dipole interactions which take place in the protonation process are significant. On the other hand, as we shall discuss later, electronegative substituents enhance the C^+–S^- polarity of the C=S bond and hence the aforementioned interactions. The large weight of the resonant contribution can be explained in terms of dominant MO interactions between π-type orbitals (see below).

Notice, however, that polarizability contributions are still quite sizeable. Thus, for X = Et, δ_xPA = 11.6 kcal/mol. Out of this value, eq 9 indicates that 9.3 kcal/mol originate in polarizability contributions.

A similar treatment of the CH_3CSX series leads to eq 10, where δ_xPA = PA(CH_3CSX) – PA(CH_3CSH):

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(49) The link between ϕ and m^*, namely $m^* = 1 - \phi$ has been established: Lucchini, V.; Modena, G.; Scorrano, G.; Cox, R. A.; Yates, K. *J. Am. Chem. Soc.* **1982**, *104*, 1958.

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(51) Using data for H_2O–H_2SO_4 mixtures; Johnson, C. D.; Katritzky, A. R.; Shapiro, S. A. *J. Am. Chem. Soc.* **1969**, *91*, 6654.

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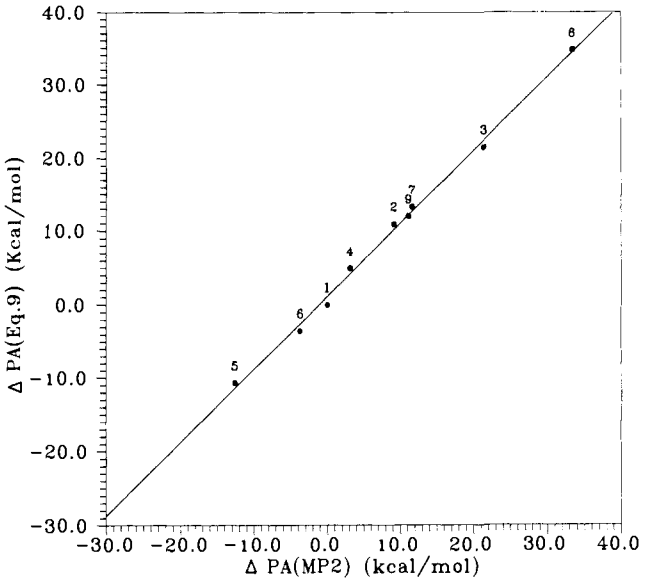
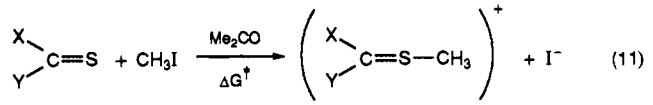


Figure 4. Linear correlation between proton affinities, relative to H_2CS, evaluated using eq 9 and those obtained at the MP2/6-31+G(d,p)//6-31G* level.

$$\delta_x PA = -(10.1 \pm 1.8)\sigma_\alpha - (48.5 \pm 1.8)\sigma_F - (45.6 \pm 1.5)\sigma_{R+} \quad (10)$$

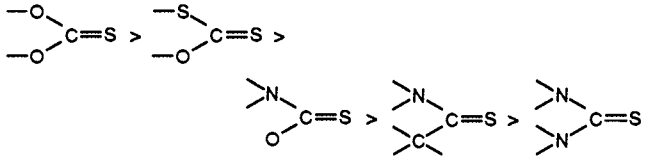
with $n = 9$, $r = 0.9976$, and sd = 1.0 kcal/mol.

This last equation shows that in the thioacetyl series polarizability effects are almost halved with respect to the thioformyl series [eq 9]. This is indicative of "saturation" effects, well documented in the case of carbonyl bases.[1] For the latter, resonance stabilization also displays this effect.[2] Although our data bases (both theoretical and experimental) do not allow an exhaustive investigation of this trend, the excellent statistical quality of eq 8 shows it to be present here, too. Indeed, this equation applies quite precisely to carbonyl compounds in which the saturation of resonance is important (as in the sequence amides–carbamates–ureas) as well as to their thiono homologs. Also, for most of the electron donor (+R) substituents, σ_F and σ_{R+} have opposite signs. Equations 9 and 10 further show that for these substituents, field and resonance effects oppose each other. The resulting pattern of reactivity reflects the balance of these contributions. Arbelot and Chanon[53] have recently reported kinetic data on the alkylation of thiocarbonyl bases, XCSY with MeI in Me_2CO at 25.0 °C (eq 11).



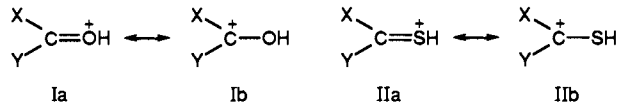
(11)

It is unfortunate that a direct comparison of the activation free energies for these reactions, $\Delta G^{\ddagger}$, is not yet possible, because their data base is mostly built on cyclic compounds. However, the trend of decreasing $\Delta G^{\ddagger}$ with substitution α to the thiocarbonyl, namelyis exactly the same of increasing GB one can deduce from



the data given in Table VI as well as from GBs of thiocarbonyl compounds estimated through eq 8 from values for their carbonyl homologs. It has recently been shown[54] that "extended" Bronsted equations can be obtained that link the GBs of N(sp^2) and N(sp^3) bases with their nucleophilicities toward MeI in MeCN solution at 25.0 °C. The above points at the likelihood of this being also the case for thiocarbonyl compounds.

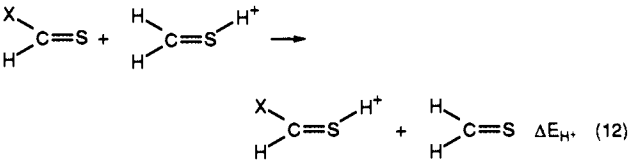
Equation 8 is deceiving in that it indicates a great similarity between carbonyl and thiocarbonyl compounds. Yet, oxygen and sulfur atoms differ in size and electronegativity[55] *inter alia*. One is then led to suspect that this formal analogy originates in canonical structures such as Ib and IIb wherein the positive



Ia Ib IIa IIb

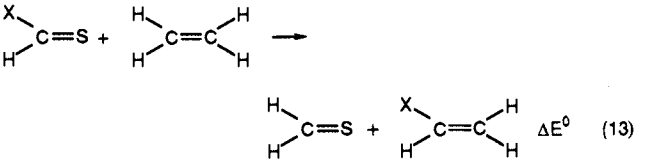
charge of the incoming proton is relayed to the sp^2 carbon through oxygen and sulfur. The quantitative MO study to follow supports this hypothesis.

Another important question related with substituent effects on gas-phase basicities of thiocarbonyl compounds is whether these substituent effects arise from interactions within the neutral or within the protonated species, or both. To answer this question it is useful to define the relative proton affinities along the monosubstituted series of compounds by means of the isodesmic process:

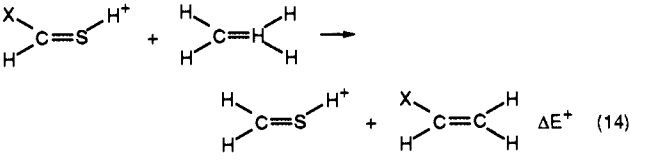


(12)

This isodesmic process may be decomposed into two reactions, accounting, respectively, for substituent effects on the neutral (13) and on the protonated species (14): It is obvious that the



(13)



(14)

isodesmic process 12 is obtained by adding to reaction 13 the reverse of reaction 14. This analysis has been carried out for $-CH_3$, $-NH_2$, $-OH$, $-F$, and $-Cl$ monosubstituted derivatives. This implies that the total energies of the corresponding monosubstituted derivatives of ethylene should be obtained at the same level of accuracy, and they have been included, as a footnote, in Table V. The values of ΔE_{H^+} and those of their components ΔE^0 and ΔE^+ have been summarized in the same table. The first conspicuous fact is that process 13 is always endothermic. This indicates that all substituents lead to a stabilization of the thiocarbonyl group, which prefers to be substituted by electronegative groups, although this stabilization is not significantly different for amino or hydroxy groups. Quite

(53) (a) Arbelot, M.; Chanon, M. *J. Chim. Phys.* **1992**, *89*, 1667. (b) Arbelot, M.; Samat, A.; Rajzmann, M.; Meyer, M.; Gastand, M.; Chanon, M. In *Sulfur-Centered Reactive Intermediates in Chemistry and Biology*; Chatjilialoglu, C., Asmus, K.-D., Eds., Plenum Press: New York, 1990; pp 19–30.

(54) (a) Abboud, J.-L. M.; Notario, R.; Bertrán, J.; Solá, M., *Prog. Phys. Org. Chem.* **1993**, *19*, 1. (b) Abboud, J.-L. M.; Notario, R.; Bertrán, J.; Taft, R. W. *J. Am. Chem. Soc.* **1991**, *113*, 4738. (c) Abboud, J.-L. M.; Notario, R. *J. Chim. Phys.* **1992**, *89*, 1531.

(55) Schaumann, E. In *The Chemistry of Double-bonded Functional Groups*; Patai, S., Ed.; John Wiley: New York, 1989; Chapter 17, pp 1269–1367.

Table V. SCF-6-31G* Energies (kcal/mol) Corresponding to the Isodesmic Reactions 12–14[a]

		ΔE^0		ΔE^+		ΔE_{H^+}	
R_1	R_2	C=S	C=O	C=S	C=O	C=S	C=O
CH_3	H	+3.5	+6.2	+13.5	+18.8	−10.0	−12.6
NH_2	H	+18.9	+21.5	+42.0	+50.3	−23.1	−28.8
OH	H	+16.4	+26.5	+20.6	+32.3	−4.2	−5.8
F	H	+4.1	+19.6	−5.5	+6.4	+9.6	+13.1
Cl	H	+0.2	+8.3	−5.1	−0.7	+5.3	+9.0
CH_3	CH_3	+1.6	+10.2	+9.7	+19.3	−8.1	−9.1
NH_2	CH_3	+17.2		+37.0		−19.8	
OH	CH_3	+17.0		+19.9		−2.9	
F	CH_3	+6.2		−1.4		+7.6	
Cl	CH_3	−0.4		−6.1		+5.7	
NH_2	NH_2	+12.6		+21.3		−8.7	
OH	OH	+17.0		+21.3		−4.3	
F	F	+6.4		+0.3		+6.1	
Cl	Cl	−7.1		−9.4		+2.3	

[a] The total energies of the 6-31G* optimized structures of ethylene and their CH_3, NH_2, OH, F, and Cl derivatives are (in hartrees) −78.031 72; −117.071 47; −133.061 70; −152.885 39; −176.881 95; −536.933 69.

importantly, a similar finding has been reported very recently by Wiberg et al.[7d] for a wide set of carbonyl compounds. This may be interpreted as a significant analogy between thiocarbonyl and carbonyl derivatives when considering the stabilizing effects of the different substituents, which, as we have discussed above, is well reflected in the linear correlation (eq 8) and Figure 3 and which indicates that similar effects must be responsible for the variations observed in their intrinsic basicities upon substitution.

It must be noticed, however, that Wiberg et al.[7d] have used ethane, rather than ethylene, as the reference system in their isodesmic processes. For our purposes, we have considered it more suitable to employ ethylene, so that the substituted carbon always maintains a sp^2 hybridization. For the sake of comparison we have considered it of interest to include in our analysis the corresponding monosubstituted carbonyl derivatives (see Table V).

Significantly, Table V also indicates that process 14 is also strongly endothermic with the exception of fluorine and chlorine derivatives. Hence, we conclude that, similarly to what we have previously found when investigating the gas-phase basicity of substituted pyridines and azoles.[13,56] the substituent effects are dominant in the protonated species. It is the extra stabilization of the protonated molecule by the methyl, amino, and hydroxy substituents that is responsible for the enhanced basicity of these species with respect to the parent compound. It is also apparent that this stabilizing effect is maximum for the amino derivative and much smaller for the hydroxy compound, while, when the electronegativity of the substituent increases further (as in fluorine), the effect becomes destabilizing, yielding systems of quite low intrinsic basicity.

These effects have been also analyzed for the corresponding disubstituted systems in two cases: (a) when one of the substituents is always a methyl group and (b) when both substituents are identical. The corresponding values, which in case (a) and refer to thioacetaldehyde and in case (b) to the monosubstituted compound, are also included in Table V. For the first set only slight changes are observed with respect to the monosubstituted derivatives, manifested by an attenuation of the stabilization provided by the second substituent. This seems to indicate that the presence of a methyl group makes the system less demanding of electronic charge. The same qualitative behavior can be observed in the (b) series of compounds. However, from a quantitative point of view, the attenuation is dramatic for the diamino derivative, for which reaction 14 is endothermic only by 21.3 kcal/mol, half the value obtained for the monosubstituted compound. Similarly, for the difluoride system, reaction 14 becomes slightly endothermic, while for the monosubstituted compound it was clearly exothermic. These findings seem to indicate, as is the case also in carbonyl compounds,[7d] that the greater the electronic depopulation at the thiocarbonyl carbon atom the greater is the interaction with the substituent lone pairs. The presence of a first substituent renders the thiocarbonyl system electronically less demanding, and a considerable attenuation of the stabilizing effect associated to the second substituent is observed. The same arguments may explain why fluorine substitution slightly stabilizes the neutral form but destabilizes the protonated one. In the protonated species, where a considerable amount of charge has been transferred to the incoming proton, the electronic demand of the thiocarbonyl systems increases quite significantly. Only if the substituents can be further polarized toward the thiocarbonyl carbon the system will be stabilized. This is the case for NH_2 and, to a lesser degree, for OH. When the substituent is highly electronegative as fluorine, this polarization is not likely to occur and the protonated species destabilizes.

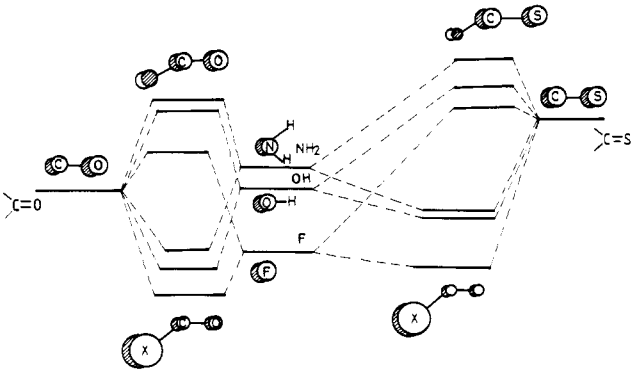


Figure 5. Diagram illustrating the interactions between the π-MO of C=O and C=S and the adequate orbitals of NH_2, OH, and F substituents.

The energetic information contained in Table V poses several questions: What is the origin of the stabilization of the neutral carbonyl compounds upon amino, hydroxy, fluorine, etc. substitution? Why are these effects very similar in carbonyl and thiocarbonyl compounds? Why are they significantly greater for the protonated species?

The answers to these questions are directly related to the MO redistribution which take place upon substitution. For the sake of simplicity we shall start our analysis with the carbonyl compounds. The highest occupied MO (HOMO), ψ_8, of formaldehyde is essentially an oxygen lone-pair, while the next one, ψ_7, is a C–O π-bonding orbital. Upon substitution there are two dominant interactions, those involving the ψ_7 π-MO and those affecting the lower σ-MOs. The ψ_7 MO interacts with the appropriate MO of the substituent (NH_2, OH, F) leading to a stabilized π-MO (in phase combination) and to a destabilized π-MO (out of phase combination). These interactions are quantitatively different depending on the substituent. For the amino and hydroxyl groups they are quite strong because the interacting MOs are close in energy, while they are very weak for fluorine whose π-type orbital is much lower in energy than ψ_7 (see Figure 5). Consequently, for the fluorine derivative the in-phase and out-of-phase combinations have strong contributions from the fluorine orbitals and from the C=O subunit orbitals, respectively, while for amino and hydroxy substituents these weights are more evenly balanced. From the energetic point of view this implies that the out-of-phase combination will be much higher in energy when the substituents are NH_2 or OH than when the substituent is fluorine. A quantitative calculation shows that in the first two cases this orbital becomes the HOMO of the system (see Figure 5). In other words, while in the fluorine derivative the HOMO is the same as in the parent compound (basically an oxygen lone-pair), in formamide and formic acid

(56) Catalán, J.; de Paz, J. L. G.; Yáñez, M.; Claramunt, R. M.; López, C.; Elguero, J.; Anvia, F.; Quian, J. H.; Taagepera, M.; Taft, R. W. *J. Am. Chem. Soc.* **1990**, *112*, 1303.

this orbital lies below the aforementioned π-MO. Scheme of Figure 5 also illustrates that these π-type interactions are slightly more favorable for OH than for NH_2 substituents, since for the former both interacting MOs are almost degenerate. This fact is also reflected in the values of ΔE^0 in Table V.

There is a second interaction which affects the lower energy σ-orbitals of C=O. These interactions become more effective as the electronegativity of the substituent increases. In contrast to π-orbitals, the σ-MOs of the parent compound contain a contribution from the hydrogen atom orbitals. when hydrogen is replaced by a more electronegative system the contribution of the substituent orbitals to the corresponding σ-MO increases considerably. This implies that the larger the electronegativity of the substituent the lower should be the participation of the carbon orbitals to the corresponding MO. This perturbation should be reflected in a greater C^+–O^- polarity of the carboxylic bond and hence in stabilization of the system.

In summary, one may conclude that the stabilization of the neutral carbonyl systems upon substitution has a double origin. On one hand, it is due to an effective π-conjugation between the C=O π-system with the appropriate orbitals of the substituent, which follow the sequence $OH \geq NH_2 \gg F$. On the other hand, to σ-type interactions which lead to a greater polarity of the C=O bond and which follow the trend $NH_2 < OH < F$. These conclusions are in agreement with those found by Wiberg et al.[7d] through an analysis of electron populations, bond orders, and atom energies of different carbonyl systems.[57] Furthermore, the values of ΔE^0 reported in Table V for carbonyl compounds are linearly correlated with the resonance energies reported by Pilcher[58] for the same set of compounds, which were obtained from the corresponding experimental heats of formation and bond enthalpies. This agreement could be initially interpreted as an evidence that substituent stabilization arises exclusively from π-conjugation; however, the definition of the resonance energy used in ref 58 cannot separate the two effects discussed above. Therefore one should take the reported resonance energy as a measure of the stabilization energy induced by the substituent, which explains the good correlation with our ΔE^0 values.

For the thiocarbonyl series the situation is qualitatively similar but quantitatively different from carbonyl systems. The MOs of the parent compound (thioformaldehyde) are analogous to those of formaldehyde and in the same energetic order. However, the π-interactions mentioned above are now less favorable because the π-MO of the C=S subunit lies higher in energy than that C=O compounds. As a consequence, the energy gap with respect to the substituent orbitals increases (see Figure 5). This is reflected in the fact that, while formamide presents the two HOMOs in a reversed order with respect to formaldehyde, in thioformamide the order is the same as in thioformaldehyde. The diagram of Figure 5 also illustrates that the interaction is now more favorable with the orbitals of the NH_2 group than with those of the OH. This is in good agreement with the results of Table V, which show that while the carbonyl system is more stabilized by hydroxy than for amino substitution, the reverse situation is found in the case of thiocarbonyl compounds.

Upon protonation the π-interactions mentioned above should be enhanced, since the carbonyl carbon (which in the neutral species is already an electron-deficient center) becomes electronically depopulated. The possible charge transfer from the substituent to the electron deficient carbon is less favorable the greater is the electronegativity of the substituent, as is also revealed by the ΔE^+ values presented in Table V. Hence, for the protonated species they follow the sequence $NH_2 > OH > F$. In conclusion, one should expect substituent effects on the gas-phase basicities of carbonyl and thiocarbonyl compounds to be similar, although slightly greater for the former, in agreement with the experimental evidence. These interactions lead to sizeable redistributions of the electronic charge densities, which will be investigated by means of an analysis of the Laplacian of the electron density[22] in a separate paper. We can anticipate that this analysis shows that the C=S bond is not affected in a significant way by protonation because the charge transferred to the proton produces a polarization and, in some cases, a depopulation of the bonds in which the thiocarbonyl carbon atom participates.

(57) Analyses of halogen substituent effects on the stability of carbocations can be found: (a) Stams, D. A.; Thomas, T. D.; MacLaren, D. C.; Ji, D.; Morton, T. H. *J. Am. Chem. Soc.* **1990**, *112*, 1427. (b) Reynolds, C. H. *J. Am. Chem. Soc.* **1992**, *114*, 8676.

(58) Pilcher, G. In *The Chemistry of Acid Derivatives*; Patai, S., Ed.; John Wiley & Sons: New York, 1992; Supplement B, Part 2.

Conclusions

From our study we can conclude that thiocarbonyl compounds are sulfur bases in the gas phase. Even for those derivatives which present quite basic alternative centers, as *N,N*-dimethyl thiourea, the protonation at the other basic centers is not competitive with protonation at sulfur. In general thiocarbonyl derivatives are more basic than their carbonyl counterparts, although the latter are slightly more sensitive to substituent effects than the former. This is so because the parent compound of the former series (thioformaldehyde) is much more basic than formaldehyde, since, on one hand, sulfur is less electronegative than oxygen and, on the other hand, is much more polarizable. However, the two mechanisms involved in the basicity enhancement upon substitution are more effective in carbonyl than in thiocarbonyl compounds. These two mechanisms are related to the π-conjugation of the lone-pairs of the substituent and the π-system of the carbonyl or the thiocarbonyl subunits, on one hand, and to the electronegativity of the substituent, on the other hand. The former mechanism is less favorable for thiocarbonyl derivatives because, in general, the C=S π-orbital is much higher in energy than the π-orbital of C=O and hence further away from the substituent orbitals. The latter effect, which produces an increase of the C^+–O^- or C^+–S^- polarities, is also slightly greater for carbonyl derivatives, because in the unsubstituted compound the carbonyl carbon is already electronically deficient, while this is not the case in thioformaldehyde. These findings are also mirrored in the large weights that the field and resonant terms have when the gas-phase basicity of these systems is analyzed in the light of Taft–Topsom's model. One may then conclude that substituent effects in both series of compounds have the same origin, and they are only slightly different from the quantitative point of view, which explains the very good linear correlation observed between both basicity scales.

An analysis of the basicity trends for a given series of substituents based on isodesmic processes reveals that substituent effects are dominant in the protonated species, similarly to what has been previously reported for the particular case of pyridines and azoles.[13,56] However, while for pyridines and azoles, substituent effects were found to be quite small for the corresponding neutrals, for carbonyl and thiocarbonyl compounds they are significant.

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Supplementary Material Available: Structures giving bond distances and angles (5 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.