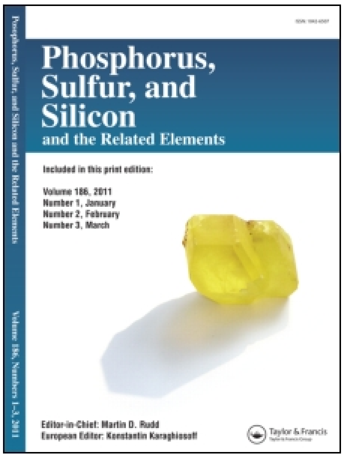


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

EFFICIENCY OF THE MNDO-PM3 METHOD TO DESCRIBE THE GEOMETRIC AND ELECTRONIC STRUCTURE OF 1,2-DITHIOLE-3-THIONES AND 1,2-DITHIOLE-3-ONES

M. Chollet-krugler[a]; A. Botrel[b]; J. J. Charbit[c]; J. Barbe[c]; J. L. Burgot[a]
[a] Laboratoire de Chimie Analytique, Univ. Rennes 1, Fac. Pharmacie, Rennes cedex, France [b] Laboratoire de Physicochimie, Ecole Nationale Supérieure de Chimie de Rennes, Rennes, France [c] GERCTOP-UPRES A CNRS 6009, Univ. Méditerranée, Fac. Pharmacie, Marseille cedex, France

To cite this Article Chollet-krugler, M. , Botrel, A. , Charbit, J. J. , Barbe, J. and Burgot, J. L.(2000) 'EFFICIENCY OF THE MNDO-PM3 METHOD TO DESCRIBE THE GEOMETRIC AND ELECTRONIC STRUCTURE OF 1,2-DITHIOLE-3-THIONES AND 1,2-DITHIOLE-3-ONES', Phosphorus, Sulfur, and Silicon and the Related Elements, 166: 1, 27 — 44

To link to this Article: DOI: 10.1080/10426500008076529

URL: http://dx.doi.org/10.1080/10426500008076529

Phosphorus, Sulfur and Silicon, 2000, Vol. 166, pp. 27-44
Reprints available directly from the publisher
Photocopying permitted by license only

EFFICIENCY OF THE MNDO-PM3 METHOD TO DESCRIBE THE GEOMETRIC AND ELECTRONIC STRUCTURE OF 1,2-DITHIOLE-3-THIONES AND 1,2-DITHIOLE-3-ONES

M. CHOLLET-KRUGLER[a]*, A. BOTREL[b], J.J. CHARBIT[c], J. BARBE[c] and J.L. BURGOT[a]

[a]Laboratoire de Chimie Analytique, Univ. Rennes I, Fac. Pharmacie, 35043 Rennes cedex, France, [b]Laboratoire de Physicochimie, Ecole Nationale Supérieure de Chimie de Rennes, 35700 Rennes, France and [c]GERCTOP-UPRES A CNRS 6009, Univ. Méditerranée, Fac. Pharmacie, 13385 Marseille cedex 5, France

(Received March 21, 2000; In final form May 31, 2000)

In order to validate the PM3 semi-empirical calculation method for the study of electronic and geometric structures of a dithiolethiones and a dithiolones series, we compared:

- the experimental dipole moments of 22 dithiolethiones and 10 dithiolones with those calculated by PM3,
- the experimental bond lengths determined by X-ray of 5 dithiolethiones with the calculated ones.

Finally, we used more elaborate calculation methods such as *ab initio* HF/6–31G* and density functional theory (DFT) B3LYP in order to confirm the net charge distributions calculated by the PM3 method.

Results are satisfactory. PM3 calculations provide a simple, efficient and rapid methodology study of the structure of a large number of molecules belonging to the same series.

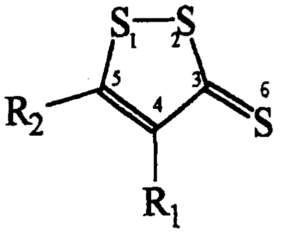
Keywords: 1,2-dithiole-3-thione; dipole moment; electronic structure; PM3; *ab initio*; density functional theory

---

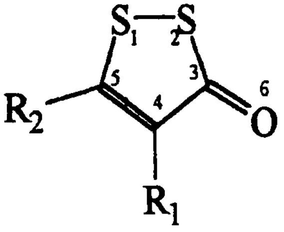
* Corresponding Author.

INTRODUCTION

1,2-dithiole-3-thiones **A** offer considerable promise as cancer chemopreventative drugs.[1,2,3] Some of them are also endowed with interesting non linear optical properties.[4]



A



B

However the relationships between the chemoprotective properties of dithiolethiones and their structure have not been thoroughly studied. Clearly, there is a need to establish Quantitative Structure-Activity Relationships (QSAR) to design new dithiolethiones endowed with enhanced pharmacological activity.[5] Owing to a hypothesis that links the chemopreventive properties of dithiolethiones with their behavior of Michael acceptor[2] and to the fact that these derivatives are aromatic compounds, it is obvious that their electronic properties must be included in QSAR. This is the reason why, as part of our studies devoted to these derivatives,[6,7,8] we are now interested in an accurate description of the electronic and geometric structures of 1,2-dithiole-3-thiones **A** and 1,2-dithiole-3-ones **B** together with a convenient and rapid means to obtain QSAR.

These compounds have already been the subject of quantum calculations.[4,9,10,11,12] From the standpoint of performing such calculations easily and rapidly, it is a worth noting that the recent finding [4] with the semi – empirical PM3 method [13] based on the NDDO approximation and used in the framework of the MOPAC 6.0 program[14] leads to a satisfactory prediction of the dipole moment values of 5-phenyl and 5 p- methoxyphenyldithiolethiones and those of the corresponding 1,2-dithiole-3-ones.

This is the reason why it seemed interesting to investigate further the efficiency of this rapid method.

The above finding indicates that it is very likely that both the geometric parameters and electric charges of the ground states of these derivatives are satisfactorily calculated by the PM3 method. It does not however prove that the method is as satisfactory for dithiolethiones other than those substituted by a phenyl group in position 5. To answer this question, we decided on the one hand to compare the calculated dipole moments (with PM3 method) of a lot of variously substituted dithiolethiones and dithiolones with their experimental ones.[15,16,17,18,19] In this work, new experimental dipole moment values were determined in benzene. On the other hand, the experimental bond lengths of some dithiolethiones previously determined by X-ray [20,21,22,23] were compared with their calculated values using PM3. Finally, charge distributions determined by the PM3 method were compared with those determined by *ab initio* HF/6–31G* calculations and by more elaborate methods: DFT B3LYP-6–31Gd and DFT B3LYP-6–31Gdp which take into account the electronic correlation.

Validation of the PM3 calculation method may provide, of course, a wealth of new information concerning the structural features of dithiolethiones.

RESULTS AND DISCUSSION

1) Dipole moments

The results obtained for dithiolethiones and for dithiolones are mentioned respectively in tables I and II.

It appears that the dipole moments determined experimentally in this work are in good agreement with those already obtained in other laboratories for the same dithiolethiones (derivatives **8**, **9**, **13**, **15**) except for the parent product **1**. However, the fact that the experimental conditions which prevailed for the study of this product **1** are unknown must be noted. [18]

Dipole moments, calculated for the minimized-energy conformation by the PM3 method, are quite in agreement with the experimental ones.

TABLE I Determined and calculated (PM3 method) dipole moments of dithiolethiones A

	R_1	R_2	μ_{exp}	μ_{calc}			
				μ_{total}	μ_{π}	$\mu_{(atomic\ dipole)}$	μ_{σ}
1	H	H	3.78 ± 0.07 (4.16)[18]	3.27 (-3.21; 0.63; 0.03)[a]	5.53 (-3.84; –3.98; 0.02)[a]	2.11 (-1.38; 1.60; 0.02)[a]	3.63 (2.20; 3.03;-0.01)[a]
2	CH_3	H	4.25 ± 0.25	3.34 (- 3.17;1.07;0.00)	6.37 (-4.25;-4.75;0.00)	2.09 (-1.39; 1.56; 0.00)	4.90 (2.45;4.23;0.00)
3	H	CH_3	4.17 ± 0.32	3.85 (-3.76;0.86;-0.06)	5.98 (-4.00;-4.44;0.00)	2.00 (-1.29; 4.53; –0.02)	4.05 (1.53;3.75;0.03)
4	CH_3	CH_3	4.52 ± 0.06	3.92 (-3.70;1.29;0.01)	6.48 (-4.34;-4.81;0.00)	2.02 (-1.35; 1.50; 0.00)	5.01 (2.00;4.60;0.00)
5	$-(CH_2)_4-$		4.52 ± 0.03	4.02 (-3.76; 1.43; 0.01)	6.95 (-4.39; –5.38; 0.01)	1.87 (-1.26; 1.38; 0.01)	5.79 (1.88; 5.47; –0.03)
6	$-(CH_2)_3-$		(4.46)[16]	3.97 (-3.76; 1.27; –0.01)	6.84 (-5.13; –4.53; 0.00)	1.95 (-1.30; 1.46; –0.00)	5.11 (2.67; 4.35;-0.01)
7	-CH=CH-C=CH-		(3.83) [15] (3.77)[16]	3.99 (-3.39; 2.12; 0.00)	4.75 (-4.24; –2.14; –2.32)	2.07 (-1.37; 1.55; 0.00)	3.96 (-2.79; 2.81; –0.01)
8	H	C_6H_5	4.76 ± 0.04 (4.93)[15] (4.35) [16] (4.51) [17]	4.70 (-4.56;1.17;-0.01)	6.28 (-5.17;-3.56; 0.00)	1.98 (-1.25; 1.53; 0.00)	4.27 (1.77;3.89;-0.01)
9	H	p $CH_3O-C_6H_4$	5.75 ± 0.03 (5.89)[15] (5.54)[16]	5.73 (-5.72;+0.43;0.04)	7.49 (-7.16;-2 20;-0.03)	1.86 (-1.42; 1.20; –0.01)	3.18 (2.83;1.44;-0.07)

	R_1	R_2	μ_{exp}	μ_{calc}			
				μ_{total}	μ_{π}	$\mu_{(atomic\ dipole)}$	μ_{σ}
10	H	p CH_3-C_6H_4	$(5.28)^{16}$	5.19 (-5.00; 1.38; 0.01)	6.25 (-4.73; –4.08; 0.00)	1.98 (-1.24; 1.54; 0.00)	4.06 (0.94; 3.95; –0.00)
11	H	p Cl-C_6H_4	$(3.30)^{16}$	3.84 (-3.76; 0.79; –0.01)	6.37 (-5.37; –3.42; 0.00)	1.50 (-0.76; 1.29; 0.00)	3.65 (2.49; 2.67; 0.00)
12	H	p Br-C_6H_4	$(3.32)^{16}$	3.31 (-3.41; 0.65; 0.00)	6.07 (-4.89; –3.59; –0.24)	1.88 (-1.16; 1.49; 0.00)	4.28 (2.29; 3.58; –0.49)
13	C_6H_5	H	3.91 ± 0.01 $(3.70)^{16}$ $(3.20)^{17}$	3.41 (-3.11; 1.41;-0.04)	3.63 (-3.02; 2.01; 0.00)	2.02 (-1.34; 1.51; 0.01)	2,78 (1.34;-2.84;-0.97)
14	p $CH_3C_6H_4$	H	$(3.95)^{16}$	3.59 (-3.13; 1.76; –0.04)	4.09 (-3.92; 1.18; –0.01)	2.02 (-1.34; 1.51; –0.02)	1.97 (1.22; –1.55; –0.01)
15	C_6H_5	C_6H_5	4.52 ± 0.02 $(4.37)^{16}$ $(4.40)^{17}$	4.31 (-3.91;1.74;-0.06)	8.10 (-6.04;5.37; –0.07)	1.86 (-1.21; 1.41; 0.00)	5,99 (3.32; –4.18; 0.10)
16	CH_3	C_6H_5	4.86 ± 0.06	4.24 (-3.98;1.46;-0.06)	7.51 (-7.37;-1.40; –0.07)	1.93 (-1.28; 1.44; –0.05)	4.28 (4.28; 0.03; 0.19)
17	H	CHO	1.72 ± 0.26	1.79 (-1.05; 1.45; 0.09)	3.83 (-1.81; –3.37; 0.07)	1.85 (-0.87; 1.64; –0.01)	3.60 (1.64; 3.21; –0.02)
18	H	CO CH_3	2.60 ± 0.02	2.56 (-1.37; 1.49; –1.56)	5.01 (-1.25; –4.69; –1.23)	1.87 (-0.94; 1.61; –0.16)	4.69 (0.84; 4.62; –0.11)
19	COOH	H	4.83 ± 0,24	4.80 (-3.81; –1.94; –2.18)	7.36 (-4.42; 5.85; 0.55)	1.97 (-1.71; 0.97; –0.17)	9.35 (2.39; –8.68;- 2.54)

	R_1	R_2	μ_{exp}	μ_{calc}[a]			
				μ_{total}	μ_{π}	$\mu_{(atomic\ dipole)}$	μ_{σ}
20	COOH	CH_3	5.02 ± 0.03	4.93 (-3.89; 0.12; 1.01)	4,93 (-3,40; 10,44; 0,13)	1.69 (-1.42; 0.9; 0.25)	4.93 (-0.32; −13.4; 2.15)
21	CN	CH_3	5.40 ± 0.29	4.17 (-3.57; −2.16; 0.04)	6.55 (-4.06; −5.14; 0.00)	1.41 (-1.26; 0.63; 0.02)	2.92 (1.75; 2.34; 0.02)
22	$COCH_3$	CH_3	3.74 ± 0.07	4.15 (-3.53; −0.18; −2.18)	12,06 (-5.26;-10.63;-2.18)	1.76 (-1.25; 1 22; −0.19)	9.34 (1.98;9.13;0.08)

a. Components on the x, y, z axis

TABLE II Experimental and calculated (PM3 method) total dipole moments of some 1,2-dithiole-3-ones **B**

R_1	R_2	μ *exp*	μ *total (PM3)*
C_6H_5	C_6H_5	3.96[16]	3.96
H	C_6H_5	4.29[16] 4.30 [15]	4.19
H	pCH_3-C_6H_4	4.30[16]	4.63
H	pCH_3O-C_6H_4	4.91[16] 5.14 [15] 5.29 [19]	4.93
H	pCl-C_6H_4	2.82 [16]	3.31
H	pBr-C_6H_4	3.11[16]	2.97
pCH_3-C_6H_4	H	3.63 [16]	3.45
C_6H_5	H	3.22 [16]	3.20
-$(CH_2)_3$-		3.92 [16]	3.53
-CH=CH-C=CH-		3.36[15] 3.22[16]	3.89

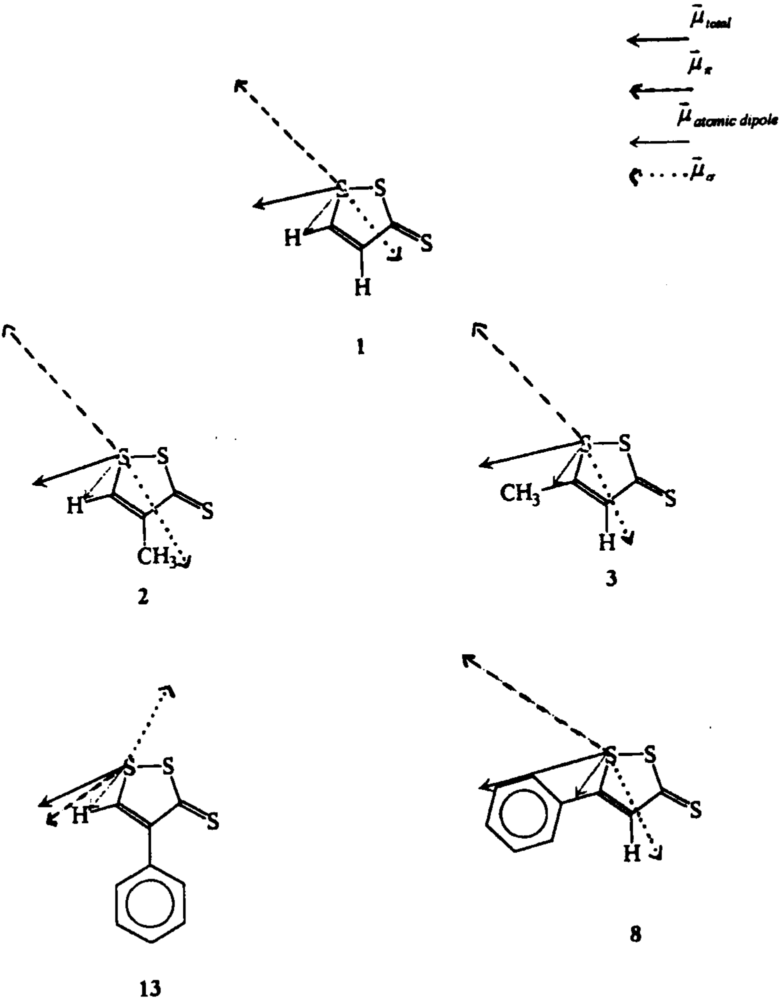
Results found using the PM3 method indicate that the hybridization moments due to the occurrence of atomic dipoles represent an important part of the total dipole moment. This is in agreement with the well known fact that atomic dipole moments are large.[24] The weakness of μ_z component values for all dithiolethiones except for the functionalized ones (Table I) is the result of geometry optimization which gives a nearly planar structure. [25,26] Directions of the total, π, σ and atomic dipole moments in the x,y plane calculated by the PM3 method for compound **1**, some alkyl and phenyldithiolethiones are given in scheme 1.

2) Geometric structure

Calculated and experimental (determined by X-ray) bond length values of dithiolethiones **1**[20], **2**[21], **8**[22], **9**[23] and **13**[22] are mentioned in scheme 2.

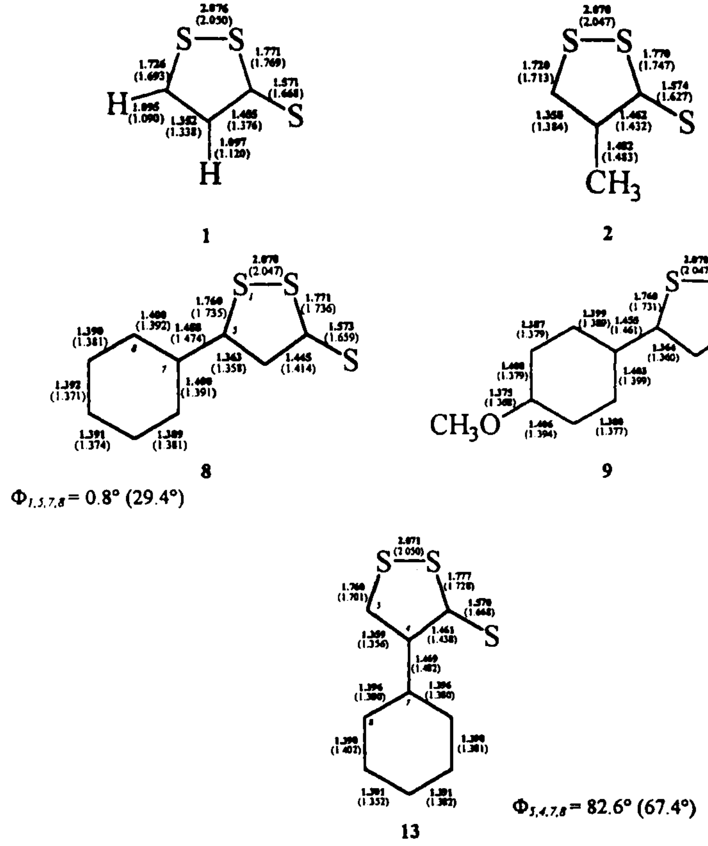
As shown in this scheme there is good coherence between experimental and calculated PM3 values except for the C_3-S_6 bond for which we have systematically a difference of about 0.1 Å (see below). For compound **13**, the value of the calculated PM3 dihedral angle $\Phi_{5,4,7,8} \cong 80°$ between the two planes is confirmed by the experimental one ($\Phi_{5,4,7,8} \cong 70°$).

Likewise, the PM3 calculation gives a nearly planar conformation for **8** ($\Phi_{1,4,7,8} \cong 1°$) when the X-ray measurements show a weak twisting



SCHEME 1 Direction of total, π, σ and atomic dipole moments of some 1,2-dithiole-3-thiones (PM3 method)

(≅ 30°). Therefore we can consider that the aryl rest and dithiole nucleus are roughly in the same plane for compound **8** and anticoplanar for compound **13**. The lack of conjugation between the dithiole and the phenyl groups for compound **13** and, hence, the existence of a dihedral angle of

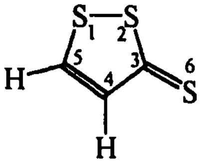


SCHEME 2 Comparison of the calculated PM3 bond lengths (Å) of dithiolethione **1**, **2**, **8**, **9** and **13** with experimental data in parenthesis

the order of 90° between them had been indirectly evidenced previously after measurements of water/n-octanol partition coefficients of dithiolethiones. [7,27] Partition coefficients can indeed be predicted with some accuracy by addition of the partition coefficient values of the fragments of the molecule under consideration. When there are supplementary physical or chemical effects, the additivity rule can no longer be applied. This is an indirect way to detect such effects. In the 4-phenyl dithiolethione **13**, it was found that the additivity rule was respected and, hence, that conjugation between the two nuclei was not effective.

The efficiency of the PM3 method may be scrutinized by comparison with the results J. Fabian and K. Herzog obtained by more elaborate calculations such as DFT (B3LYP/6–31G(d)) and *ab initio* (MP2/6–31G*).[12] Our results concerning bond length values for 1,2-dithiole-3-thione **1** calculated by the PM3 method and *ab initio* (HF/6–31G*)[28] together with those calculated by J. Fabian and K. Herzog are mentioned in Table III. We can note a good correlation between the PM3 calculation values and those performed with the help of the other theoretical methods for all the bond lengths except for the C_3-S_6 bond for which a discrepancy exists [1.57 Å (PM3), 1.63 Å – 1.65 Å (*ab initio* and DFT methods) and 1.67 Å (experimental)] Maybe there is some lack of reliability of the PM3 method there.

TABLE III Comparison of calculated DFT (B3LYP), *ab initio* MP2 (6–31G*) and *ab initio* HF (6–31G*) bond lengths of 1,2-dithiole-3-thione **1** with calculated PM3 values



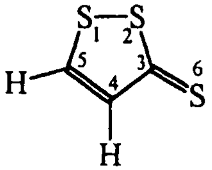
	PM3[a]	*6–31G* (HF)*[a]	*6–31G* (MP2)*[b]	*DFT (B3LYP)*[b]
S_1-S_2	2.076	2.070	2.075	2.112
S_2-C_3	1.771	1.753	1.763	1.778
C_3-C_4	1.455	1.450	1.437	1.441
C_4-C_5	1.352	1.332	1.357	1.355
C_5-S_1	1.726	1.735	1.721	1.739
C_3-S_6	1.571	1.634	1.645	1.655

a. our results
b. J. Fabian and K. Herzog calculation results[12]

3) Charge distributions

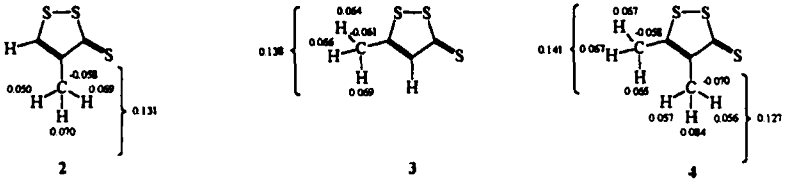
Charge densities calculated by the PM3 method provided a very surprising result: contrary to what has often been stressed in the literature the total electronic charges of carbons 3 and 5 of dithiolethiones were not more positive than those of carbon 4. They were even found to be more negative. This is in contradiction with the well known fact that nucleophilic reactions performed upon dithiolethiones result from an attack on carbon atoms 5 or 3.[25,26] This contradiction was also evidenced and even amplified by an *ab initio* calculation performed with a 6–31 G* basis and by "higher-level" DFT (B3LYP/6–31Gd and B3LYP/6–31Gdp) calculations as well.[28] Table IV gives the results obtained with the parent dithiolethione **1**.

TABLE IV Net charge distributions and dipole moments of 1,2-dithiole-3-thione 1 calculated by PM3, *ab initio* HF (6–31G*), DFT (B3LYP/6–31Gd) and DFT (B3LYP/6–31Gdp) methods



	PM3	*6–31G*(HF)*	*B3LYP/6–31Gd*	*B3LYP/6–31Gdp*
S_1	0.141	0.156	0.150	0.149
S_2	0.105	0.215	0.183	0.184
C_3	-0.176	-0.245	-0.233	-0.240
C_4	-0.161	-0.131	-0.033	0.016
C_5	-0.212	-0.366	-0.330	-0.284
S_6	-0.01	-0.157	-0.143	-0.142
μ (D)	3.27	4.42	4.12	4.12

Gonbeau et al [29] had already found such a surprising result with the parent dithiolethione **1** after an spd CNDO/2 calculation. However, this result was only found in the framework of the spd approximation. With sp and spd* ones, calculations gave total electronic charges on carbon 3,4 and 5 in agreement with the reactivity of dithiolethiones. Any way, all these results concerning the charges of carbon 3 and 5 deserve further studies in the field of the mechanisms of nucleophilic attack of dithiolethiones. Still concerning the calculated charges, it is worth noting that the methyl groups in position 4 and 5 in dithiolethiones **2**, **3** and **4** exhibited nearly the same global charges (Scheme 3):



SCHEME 3 Charges of the methyl groups in 5 and 4 methyl dithiolethiones (PM3 calculation)

However, it is known that only methyl and methylene groups in position 5 of dithiolethiones exhibit a pseudo acidic character.[30] Character, which hence cannot originate from the positive charges of the hydrogen atoms of the methyl groups. This explanation has already been given for some derivatives of other heterocycles series exhibiting activated methyl groups.[31] Likewise, the two juxtanuclear methylene groups of dithiolethiones **5** and **6** have similar positive charges while only that in position 5 is activated. The difference of acidity between 5 or 4 methylene or methyl groups of dithiolethiones may be ascribed to a particular stability of the corresponding conjugated carbanions.

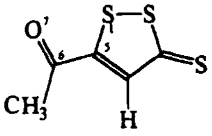
4) Functionalized dithiolethiones

The fairly good results using the PM3 method allowed us to use it to calculate electronic and geometric parameters.

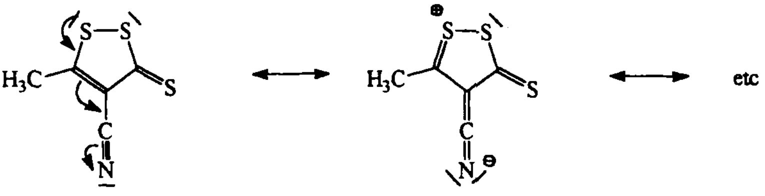
Concerning the 5-acetyldithiolethione **18**, the calculated dipole moment (PM3 method) was studied in detail by varying the $\Phi_{1,5,6,7}$ dihedral angle between the thione and acetyl groups (Table V).

We note a very low energy difference between the four studied conformations. The calculated dipole moment ($\mu = 2.56$ D) is close to the experimental one only when the dihedral angle is equal to 40°. Hence, we can conclude that component **18** in benzene solution takes part in the conformation in which the thione and carbonyl groups are antiparallel and slightly out of the dithiole plane.

TABLE V Calculated dipole moments $\mu_{total\ calc}$ and Final Heat of Formation HF_f after study of the acetyl group rotation versus the dithiolethione plane

struture	$\Phi_{1,5,6,7}$ (°)	HF_f (kcal.mol^{-1})	$\mu_{total\ calc}$ (D)
 **18**	0 (C=O trans)	32.65	2.35
	40	31.41	2.56
	90	30.44	3.17
	180 (C=O cis)	30.89	3.14

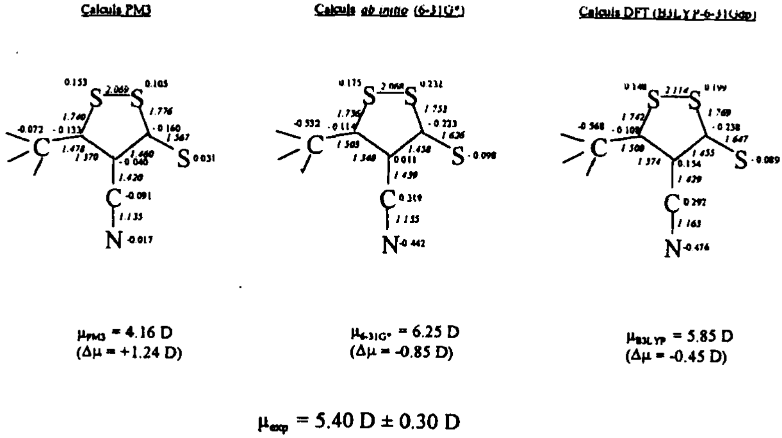
The calculated and experimental dipole moment values of 4-cyano-5-methyldithiolethione **21** greatly differ. A supplementary polarisation dipole moment may occur in this molecule. It would originate probably from a resonance effect accounted for by the following scheme: involving a donor effect from the dithiole nucleus toward the electroattractivre group in position 4.



21

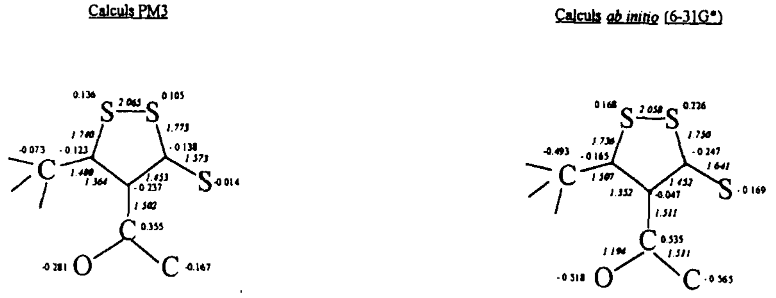
This "Push-pull" effect has already been pointed out. It is even more striking in the first excitated state of these derivatives. This has been evidenced previously by CNDO/S-CI calculations performed for 5-phenyl dithiolethiones and dithiolones.[4] Hence, it appears that the PM3 method does not account enough for this effect. It is also interesting to note that *ab initio* (6–31 G^*) and DFT (B3LYP-6–31Gdp) calculations confirm this analysis and underscore the "Push-pull" effect in compound **21** (scheme IV). *Ab initio* (6–31 G^*) and DFT (B3LYP-6–31Gdp) calculations give respectively a dipole moment value of 6.25 D and 5.85 D which exceed the experimental one (5.40 D).

Such a supplementary polarisation dipole moment may also exist in the two carboxylic acids **19** and **20** but considering the experimental dipole moment values it is appreciably less marked than in the cyano derivative. This is in agreement with the intensities of the withdrawing effects of cyano and carboxylic groups. It is interesting to note that PM3 calculations give a minimum of energy for acids **19** and **20** for conformations in which the carboxylic groups and the dithiole nucleus are not coplanar. For derivative **19** the dihedral angle C_3C_4CO is −56° and for compound **20** +73°. This explains why the calculated μ_z components are respectively −2.18 D and 1.01 D (table I). Incidentally, it may be remarked that there exists no significant difference of dipole moment values between these two derivatives although we evidenced a significant difference of their p$K_a$value in water, derivative **20** being the more acidic.[32]



SCHEME 4 Total electronic charges and bond lengths (in itallic) of the dithiolethione **21** computed with PM3, *ab initio* (6–31 G* basis) and DFT (B3LYP-6–31Gdp) methods

Finally, the behaviour of 4-acetyl-5-methyldithiolethione **22** is abnormal since it exhibits a measured dipole moment value weaker than the one calculated by the PM3 method. The calculated value (4.04 D) obtained by the 6–31G* *ab initio* method is also greater than the experimental one. Scheme V mentions the bond lengths and the total electronic charges of dithiolethione **22** calculated by the PM3 and the *ab initio* 6–31G* methods. This result is obtained despite the presence of a strong attractive group in position 4. It can be inferred from it that unlike in the preceding 4-cyano-5-methyldithiolethione there is some lack of conjugation between the carbonyl and the dithiole groups. PM3 and *ab initio* 6–31G* calcultions support this view since at the minimum of energy the dihedral angles C_3C_4CO exhibited the values –98° and 40°. Besides, dithiolethione **22** is endowed with a μ_z component of –2.18 D. Interestingly, to support further this view, 5-methyldithiolethione **3** and 4-acetyl-5-methyldithiolethione **22** exhibited nearly the same dipole moment value.



$\mu_{PM3} = 4.15$ D
($\Delta\mu = -0.41$ D)

$\mu_{6\text{-}31G^*} = 4.04$ D
($\Delta\mu = -0.30$ D)

$\mu_{exp} = 3.74$ D ± 0.07 D

SCHEME 5 Total electronic charges and bond lengths (in itallic) of the dithiolethione 22 computed with PM3 and *ab initio* (6–31 G* basis) methods

EXPERIMENTAL

• Materials

All dithiolethiones, but one, had been described in the literature. They were synthetized in the laboratory according to standard procedures.[25,26] Their purity was checked by T.L. chromatography and by a careful melting point determination.

4-acetyl-5-methyl-1,2-dithiole-3-thione 22

This derivative was obtained by sulfuration of ethyl 2-acetylacetoacetate with phosphorus pentasulfide according to a standard procedure,[33] Orange crystals; mp 89–90°C (hexan); ν_{max}/cm^{-1} 1684 (C=O); m/z (EI): 189.959 (calc. for $C_6H_6OS_3$: 189.958).

• Dipole moment measurements

Dipole moments of compounds as solutes were measured in anhydrous benzene at 25.00 ± 0.05°C. Permittivity and refractive index of solutions were extrapolated to infinite dilution according to Guggenheim [34] and Smith.[35] Permittivity was measured using a WTW DM01 dipolemeter with a DFL1 cell while refractivity was measured using a OPL Abbe-type refractometer.

The quantity $(\varepsilon_{12} - n_{12}^2) - (\varepsilon_1 - n_1^2)$ was plotted versus the molar concentration, C, of the solute. The slope of the curve at C = 0, was used to calculate the dipole moment, μ, by:

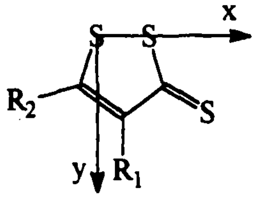
$$\mu^2 = \frac{9kT}{4\pi N} \times \frac{3}{(\varepsilon_1 + 2) - (n_1^2 + 2)} \times \frac{(\varepsilon_{12} - n_{12}^2) - (\varepsilon_1 - n_1^2)}{C}$$

where k is the Boltzmann constant, N is Avogadro's number, T is the absolute temperature, ε_1 and n_i are the permittivity and refractivity indexes, respectively of the solutes (index 1) and of the solutions (index 12).

• Theoretical calculations

- The PM3 method was used for geometry optimizations and ground state properties: magnitudes of total moment dipoles together with their μ_x, μ_y, μ_z components were given directly by the PM3 method within the framework of MOPAC program. The method did not take into account the d orbitals of sulfur atoms. Hybridization moments were also given directly by the program. Magnitudes of π, σ moment dipoles were calculated by an original program starting from the charge values given in the density matrix and from the optimized geometric parameters given also by PM3 calculation. Reference axes were chosen as represented below:
- *Ab initio* calculations were performed with a basis 6–31 G*.

The 6–31 G* basis set (with d functions added to heavy atoms) is becoming very common for calculations in which up to the medium-sized systems are involved. This basis set is particularly efficient for the calculation of interatomic distances.[27]



- DFT (B3LYP)

The calculations were carried out with the Gaussian 98 program[28] using the B3LYP [36] gradient corrected density functional with the 6–31Gd and 6–31Gdp basis sets. The introduction of gradient corrected density functional allows to significantly improve the accuracy of numerical results.

References

1. P.A. Egner, T.W. Kensler, T. Prestera, P. Talalay, A. H. Libby, H. Howard Joyner and T. Curphey, *Carcinogenesis*, **15** (**2**), 177, (1994).
2. P. Talalay, M.J. De Long and H.J. Prochaska, *Proc. Natl. Acad. Sci.* USA, **85**, 8261, (1998).
3. Y.Y. Maxuitenko, A.H. Libby, H.H. Joyner, T.J. Curphey, D.L. Mac Millan, T.W. Kensler and B.D. Roebuck, *Carcinogenesis*, **19(9)**, 1609, (1998).
4. A. Botrel, B. Ilien, P. Rajczy, I. Ledoux and J. Zyss, *Theor. Chim acta*, **87**, 175, (1993).
5. G. Burgot, M. Bona, M.O. Christen and J.L. Burgot, *Int. J. Pharmaceutics*, **129**, 295, (1996).
6. M. Abazid, H.O. Bertrand, M.O. Christen and J.L. Burgot, *Phosphorus Sulfur*, **88**, 195, (1994).
7. P. Boudeville, M. Bona and J.L. Burgot, *J. Pharm. Sci*, **85(9)**, 990, (1996).
8. M. Chollet, B. Legouin and J.L. Burgot, *J. Chem. Soc., Perkin Trans. 2*, 2227, (1998).
9. J. Fabian, A. Melhorn, J. Bormann and R. Mayer, *Wiss Z. Techn. Univers. Dresden*, **14(2)**, 285, (1995).
10. R.A.W. Johnstone and S.D. Ward, *Tetrahedron*, **25**, 5485, (1969).
11. D. Gonbeau, C. Guimou, J. Deschamps and G. Pfister-Guillouzo, *J. Electron Spectrosc*, **6**, 99, (1975).
12. J. Fabian and K. Herzog, *Vibrational Spectroscopy*, **16**, 77, (1998).
13. J.J.P. Stewart, *J. Comp. Chem*, **10**, 209., (1989).
14. Quantum chemistry program exchange, 1990, Indiana University, n° 455.
15. A. Lüttringhaus and J. Grohmaun, *Z. Naturforsch*, **10b**, 365, (1955).
16. H.F. Eicke, F. Boberg and J. Knoop, *Z. Naturforsch.*, **23b**, 413, (1968).
17. H.F. Eicke and H. Christen, *Helv. Chim. Acta*, **55**, 213, (1972).
18. A. Mehlorn, *Chem. Listy*, **61**, 32, (1967).
19. F. Boberg, *Liebigs Ann. Chem.*, **693**, 212, (1966).
20. C.H. Wei, *Acta Cryst.*, **C41**, 1768, (1985).
21. G.A. Jeffrey and R. Shiono, *Acta Cryst.*, **12**, 447, (1959).
22. C.H. Wei, *Acta Cryst.*, **C42**, 1836, (1986).
23. B.Y. Wang, H.C. Lin and C.H. Wei, *Acta Cryst.*, **C41**, 1242, (1985).

24. V.I. Minkin, O.A. Osipov and Y.A. Zhadanox, in *Dipole Moments in Organic Chemistry*, Ed. Plenum press, New York, 45, (1970).
25. C.Th. Pedersen, in *Advances in Heterocyclic Chemistry*, Academic Press, New York, **31**, 63, (1982).
26. C. Th. Pedersen, *Sulfur Reports*, **16**, 173, (1995).
27. M. Bona, P. Boudeville and J.L. Burgot, *J. Pharm. Sci.*, **84(9)**, 1107, (1995).
28. Gaussian 98, Revision A.5, M.J. Frisch, G.W. Trucks, H.B. Schlegel, G.E. Scuseria, M.A. Robb, J.R. Cheeseman, V.G. Zakrzewski, J.A. Montgomery, Jr. R.E. Stratmann, J.C. Burant, S. Dapprich, J.M. Millam, A.D. Daniels, K.N. Kudin, M.C. Strain, O. Farkas, J. Tomasi, V. Barone, M. Cossi, R. Cammi, B. Mennucci, C. Pomelli, C. Adamo, S. Clifford, J. Ochterski, G.A. Petersson, P.Y. Ayala, Q. Cui, K. Morokuma, D.K. Malick, A.D. Rabuck, K. Raghavachari, J.B. Foresman, J. Cioslowski, J.V. Ortiz, B.B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R. Gomperts, R.L. Martin, D.J. Fox, T. Keith, M.A. Al-Laham, C.Y. Peng, A. Nanayakkara, C. Gonzalez, M. Challacombe, P.M.W. Gill, B. Johnson, W. Chen, M.W. Wong, J.L. Andres, C. Gonzalez, M. Head-Gordon, E.S. Replogle, and J.A. Pople, Gaussian, Inc., Pittsburgh PA, (1998).
29. D. Gonbeau, C. Guimon and G. Pfister-Guillouzo, *Tetrahedron*, **29**, 3599, (1973).
30. H. Quiniou and N. Lozac'h, *Bull. Soc. Chim.*, 517, (1958).
31. J. Metzger and A. Pullman, *Comptes-rendus Acad. Sci.*, 1613, (1948).
32. M. Chollet and J.L. Burgot, *J. Chem. Soc., Perkin Trans. 2*, 387, (1998).
33. S. Gargadennec and J.L. Burgot, private communication, University of Rennes I, (1998).
34. E.A. Guggenheim, *Trans. Faraday Soc.*, **45**, 174, (1949).
35. J.W. Smith, *Trans. Faraday Soc.*, **46**, 394, (1950).
36. A.D. Becke "Density functional thermochemistry. III The role of exact exchange", *J. Chem. Phys*, **98**, 5648, (1993).