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1,3-DITHIOMESOXALAMIDES : CRYSTAL STRUCTURE AND SYNTHESIS FROM 1,3-DICHLOROACETONE, SULFUR AND SECONDARY AMINES[1,2]

G. Motte-Coppe, F. Dutron-Woitrin, T.G.C. Bird and H.G. Viehe*
Laboratoire de Chimie Organique

J.P. Declercq, G. Germain and M. Van Meerssche
Laboratoire de Chimie Physique et de Cristallographie
Université de Louvain, Place L. Pasteur, 1 B-1348 Louvain-la-Neuve
Belgique

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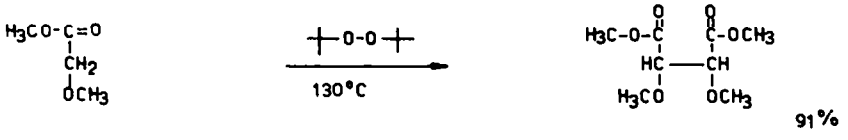
Our postulate[3] that the synergy of acceptor with donor substituents on carbon radicals would increase their thermodynamic stability has become a useful concept for organic synthesis[4].

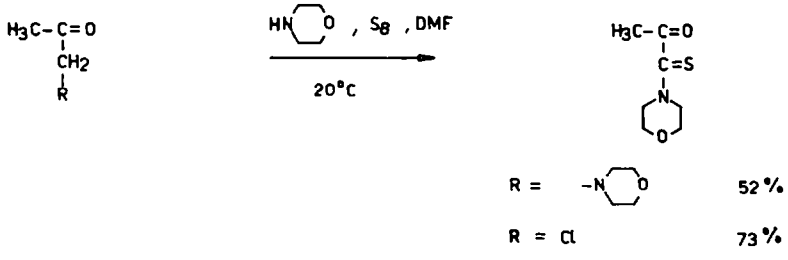
It has also provoked detailed physicochemical analysis[5] and theoretical calculations[6].

Oxidations of compounds containing captodative (cd) methylene groups produce selective dehydrodimerisations[7] on the cd-center in high yield.



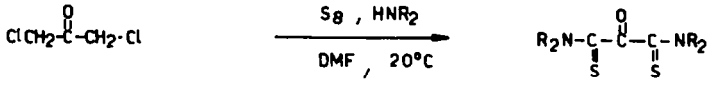
We describe here a part of our work concerning the more general approach aimed at examining elementary sulfur as oxidant on cd-systems.

Under the conditions of the Willgerodt-Kindler reaction sulfuration occurs already at room temperature with donor substituted ketones, amides or nitriles producing thioamides with α-acceptor substituents[8].



Starting with α-chloromethylketones as precursors of cd-compounds furnishes thioamides[8] in high yields. It appeared therefore of particular interest to study the readily available 1,3-dichloroacetone under these conditions. Its treatment with elementary sulfur and with dimethylamine or with morpholine[2] produces the title compounds 1 as so far little known and accessible only by multistep

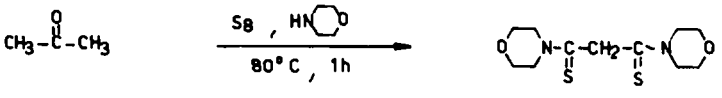
syntheses[9,10,11]



1

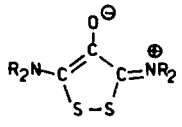
1a : R = – CH_3 65 %
1b : R_2N = morpholino 31 %

It is interesting to note, however, that acetone leads to malondithioamide[2a] under the same conditions.



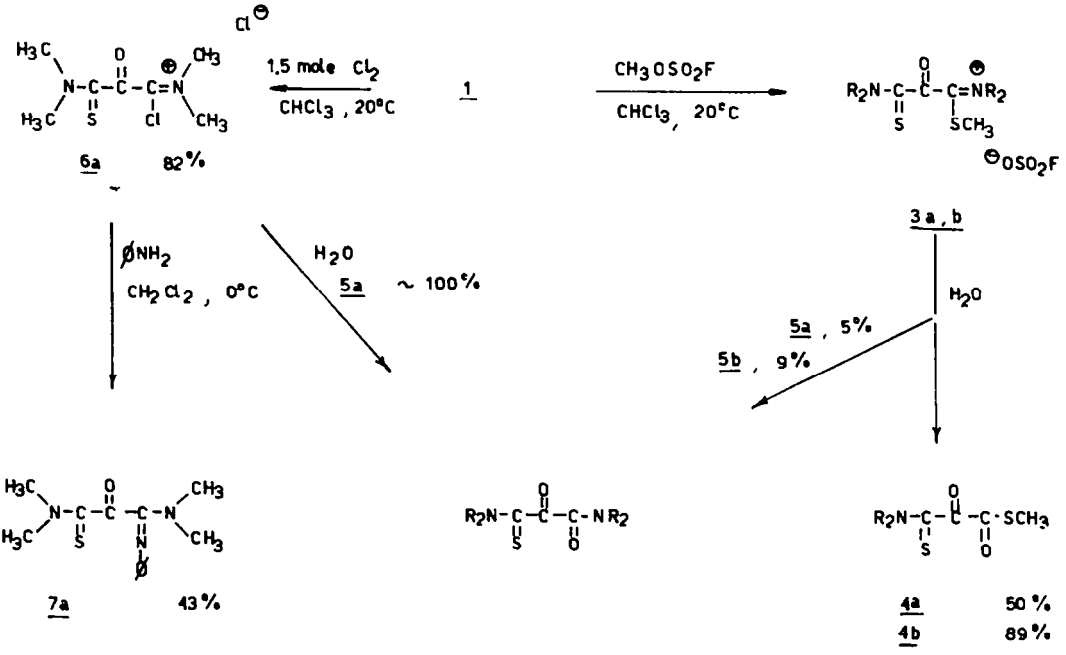
53 %

In contrast to tetramethylmesoxalamide, its dithio analogs 1a[9] and 1b[2b] are surprisingly unreactive towards nucleophiles such as water, alcohols, amines or phenylhydrazine. A mesoionic cyclic structure 2 rather than 1 was proposed[9] in order to explain the lack of reactivity of the central carbonyl group.



2

We present now the X-ray analysis of 1b proving the open structure 1, at least in the crystalline state. Compounds 1a,b are furthermore characterised by some chemical transformations. Thus, monoalkylation of 1 takes place only very slowly with dimethylsulfate but methylfluorosulfonate forms the highly reactive and synthetically promising thioamidium salts 3 already at room temperature.
These oily intermediates were characterised by hydrolysis which leads mainly to monothioesters 4 and monothioamides 5 as minor products. They can be separated by column chromatography.



One and a half equivalent of chlorinedissolved in chloroform transform 1a to the corresponding mono amide chloride 6a which precipitates as crystalline powder. After separation, its suspension in dichloromethane reacts with aniline to furnish the expected amidine 7a. By hydrolysis of 6a the monothioamide 5a[11] is obtained.

X-RAY ANALYSIS

Compound 1b, $C_{11}H_{16}O_3N_2S_2$ crystallized from ethanol as colorless orthorhombic crystals, space group *Pnab* ; a = 7.688 (1), b = 9.047(2), c = 19.770(5)Å ; V = 1375.1 (6)Å^3 ; D_x = 1.39 gcm^{-3} for Z = 4.

926 independent reflections were measured on a Syntex $P2_1$ diffractometer using monochromatized Cu$K\alpha$ radiation (λ = 1.54178 Å) to $2\theta_{max}$ = 114° and with the ω scan technique. 855 of these were considered as observed ($I > 2.5\sigma(I)$) and included in the structure solution. The structure was solved by direct methods using the MULTAN 78[12] computer system and refined with the SHELX 76[13] programme. All the positions of hydrogen atoms were found in a difference Fourier map and refined with an overall isotropic temperature factor (5.46 Å). The final conventional R has the value of 0.045.

Table 1 gives the atomic coordinates following the atom numbering of Fig.1. The molecule possesses a crystallographic twofold axis passing throught the central C=O bond. As far as we know, the present work is the first determination of the central fragment (CS-CO-CS) geometry (Tab.2).

The distance between the two S atoms has the values of 4.27 Å, showing that no bond exists between these atoms. The heterocycle is very similar to the morpholine group observed in N-benzoylmorpholine[15].

Table 1. - *Atomic coordinates (x 10^4 ; for hydrogen x 10^3) with standard deviations in parentheses and equivalent isotropic temperature factors (Å^2) of the compound 1b*

	x	*y*	*z*	B_{eq}
C(1)	10595(6)	2945(6)	4139(2)	4.26
C(2)	11116(7)	4083(6)	3625(2)	5.00
O(3)	11125(4)	3494(4)	2598(1)	5.75
C(4)	9448(7)	2933(6)	2787(2)	5.01
C(5)	8899(6)	1696(5)	3253(2)	3.80
N(6)	8901(4)	2293(3)	3947(1)	3.19
C(7)	7535(5)	2226(4)	4348(2)	2.94
C(8)	7500(0)	3102(6)	5000(0)	2.94
O(9)	7500(0)	4444(4)	5000(0)	3.19
S(10)	5618(2)	1438(1)	4206(1)	4.11
H(C1)	1047(5)	353(5)	460(2)	4.85
H'(C1)	1146(6)	204(5)	415(2)	
H(C2)	1231(6)	447(5)	374(2)	
H'(C2)	1029(6)	493(5)	362(2)	
H(C4)	846(5)	412(5)	280(2)	
H'(C4)	960(6)	257(5)	240(3)	
H(C5)	990(6)	75(5)	324(2)	
H'(C5)	777(6)	115(5)	316(2)	

Table 2. - *Principal distances (Å) and angles (°) in the central fragment*

N(6)-C(5)	1.474(4)	C(8)-C(7)-N(6)	120.2(3)
C(7)-N(6)	1.317(5)	S(10)-C(7)-N(6)	128.7(3)
C(8)-C(7)	1.513(4)	S(10)-C(7)-C(8)	110.7(2)
S(10)-C(7)	1.661(4)	C(7)-C(8)-C(7)	116.8(4)
O(9)-C(8)	1.214(6)	O(9)-C(8)-C(7)	121.6(2)

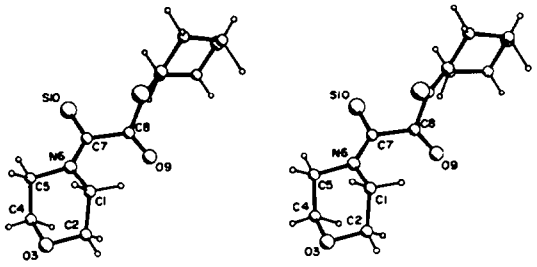


Fig. 1. - *Stereoscopic view of the molecule 1b and atom numbering (Programme PLUTO*[14])

EXPERIMENTAL

^{1}H NMR : Measured in $CDCl_3$ solution at 60 MHz on Varian EM-360.
^{13}C NMR : measured at 20 MHz on Varian CFT-20 spectrometer (Multiplicity due to one-bond couplings : S = singlet, D = doublet, T = triplet, Q = quadruplet, M = multiplet ; multiplicity due to long range coupling : s, d, t, q, ... sept. and m)
IR : Perkin-Elmer 297 infrared spectrometer, measured in $CHCl_3$. Mass : Varian MAT-44S spectrometer.

Preparation of N,N,N',N'-tetramethyl-1,3-dithiomesoxalamide 1a :

Gaseous dimethylamine is passed through a suspension of sulfur (9.6g, 0.3g at.) in DMF (250ml) until complete dissolution of sulfur. The reaction is slightly exothermic. Afterwards, a solution of 1,3-dichloroacetone (6.35g, 0.05 m) in 75 ml of DMF is added dropwise and the mixture is stirred at room temperature for one hour. The thioamide 1a is then precipitated by addition of water to the reaction mixture and is purified by recrystallisation from methanol. Yield 6.63g, 65%, m.p. 121°C. ^{1}H NMR δ = 3.45 (6H,s), 3.55(6H,s). ^{13}C NMR δ = 40.8(Q.q, ^1J 140.5 Hz, ^3J 3 Hz), 43.2 (Q.q, ^1J 140.9 Hz, ^3J 3.1 Hz), 167.9 (S.s), 194.7 (S.sept, ^3J 4.2 Hz). IR 3000, 2950, 1660, 1550, 1405, 1280, 1140, 980 cm^{-1}.

Preparation of dimorpholide of 1,3-dithiomesoxalic acid 1b :

1,3-dichloroacetone (25.4 g, 0.2 m) in 300 ml of DMF is added to a solution of sulfur (38.4 g, 1.2 g.at.) and morpholine (104.4g, 1.2m) in 200 ml of DMF. After one hours' stirring at room temperature, the thioamide 1b is precipitated by addition of water. The crude product is chromatographed on silicagel using pet. ether/ether =2/3 as eluent and recrystallised from ethanol. Yield 17.86g, 31 %, m.p. 151°C. ^{1}H NMR δ = 3.9-4.1 (m). IR : 2980, 2950, 2870, 1660, 1510, 1440, 1280, 1110, 1035, 970 cm^{-1}. SM m/e = 288 (M^+), 203, 130, 86.

Preparation and hydrolysis of thioamidium salts 3a and 3b : methyl fluorosulfonate (0.015m) is added rapidly to a concentrated solution of 1,3-dithiomesoxalamide (0.005m) in dry $CHCl_3$. After two days' stirring at room temperature the solvent is evaporated and the oily residue is hydrolysed by adding 10 ml of $CHCl_3$ and 10 ml of water. Stirring is maintained during twenty minutes. The organic phase is dried and concentrated to give a mixture of 4 and 5. They are separated by column chromatography (silicagel ; pet.ether/ether = 2/3). 4a : 0.48g, 50 % ^{1}H NMR J = 2.4 (3H, s,SCH_3), 3.2 (3H,s), 3.4(3H,s). IR : 3000, 2980, 2940, 1690, 1660, 1540, 1400, 910 cm^{-1}. SM m/e = 191 (M^+), 163, 88, 70, 47, 42. 5a : 0.047g, 5 %, m.p. 80°C, ^{1}H NMR δ = 3.0(3H,s) ; 3.2(3H,s), 3.42 (6H,s, $CSN(CH_3)_2$. ^{13}C NMR δ = 34.8 (Q.q, ^1J 139.3 Hz, ^3J 3.6 Hz), 37.8 (Q.q, ^1J 139.4 Hz, ^3J 3.1 Hz), 40.7 (Q.q, ^1J 140.7 Hz, ^3J 3.0 Hz), 42.9 (Q.q, ^1J 140.8 Hz, ^3J 2.1 Hz), 166.8 (S.sept., ^3J 3.2 Hz), 175.2 (S.s) 195.6 (S. sept. ^3J 3.2 Hz), 175.2 (S.s), 195.6 (S. sept. ^3J 4 Hz). IR : 3000, 2970, 2950, 1690, 1650, 1550, 1400 cm^{-1}. SM m/e = 188 (M^+), 88, 72.
4b : 1.04 g, 89 %. ^{1}H NMR δ = 2.4 (3H,s,SCH_3), 3.63 (2H,m), 3.7 (2H,m), 3.88 (2H,m),

4.1 (2H,m). ^{13}C NMR δ = 11.6(Q.s, ^{1}J 142.7Hz), 47.2(T,m, ^{1}J 143 Hz), 52.3 5.m, ^{1}J 142 Hz), 66.0 (T.m, ^{1}J 145-147 Hz), 66.4 (T.m, ^{1}J 145-147 Hz), 173.7 (S.s), 191.6 (S.m), 191.7 (S.m). IR : 3020, 2980, 2950, 2870, 1690, 1660, 1510, 1440, 1280, 1265, 1115, 1060, 1030, 910 cm^{-1}. SM m/e = 233 (M^+), 163, 130, 83, 47, 32. 5b : 0.12g, 9%, m.p. 122°C (acetone-hexane). ^{1}H NMR δ = 3.65-3.75 (8H,m), 3.83 (4H,s), 3.85 (2H,m). 4.1 (2H,m). IR : 3020, 2980, 2950, 2870, 1690, 1645, 1510, 1440, 1280, 1115, 980 cm^{-1}. SM m/e = 272 (M^+), 130, 114, 86, 70, 42.

Preparation and aminolysis of amide chloride 6a : 0.75g (0.021 g.at.) of chlorine dissolved in 15 ml of dry $CHCl_3$ are added dropwise to a $CHCl_3$ (10 ml) solution of dithiomesoxalamide 1a (1.43g, 0.007 m) at 20°C. Amide chloride 6a which precipitates immediately is collected under argon and washed several times with $CHCl_3$ and Et_2O. The orange powder is dried under vacuum (1.39g, 82%). 0.697g (0.0075 m) of aniline are added dropwise at 0°C to a suspension of amide chloride 6a (0.607g, 0.0025 m) in dry CH_2Cl_2 (10 ml). The stirring is continued for about 5 hrs and then the hydrochloride of aniline is removed by filtration. The CH_2Cl_2 solution is concentrated, the residue is washed with water and extracted with CH_2Cl_2. The solution is dried over $MgSO_4$ and concentrated to give the amidine 7a which is purified on silicagel (CH_2Cl_2) and recrystallised in methanol (0.28g, 43%), m.p. 1110°C. ^{1}H NMR δ = 28.0(Q.q), 40.7 (Q.q), 41.7(Q.q), 122.4 (D,t), 122.8 (D.s), 128.6 (D.t), 148.5 (S.t), 156.8 (S.m), 179.7 (S.s), 192.9 (S.m). IR : 3000, 2950, 1670, 1610, 1590, 1540, 1400 cm^{-1}. SM m/e = 263 (M^+), 147, 132, 88, 70, 43, 42.

Hydrolysis of amide chloride 6a : an aqueous solution of $NaHCO_3$ is added to a suspension of amide chloride (1.215 g, 0.005m) in $CHCl_3$ (10 ml). Stirring is maintained during twenty minutes. The aqueous solution is extracted with $CHCl_3$. The combined extracts are dried over $MgSO_4$. Evaporation of solvent leaves yellow crystals of monothiomesoxalamide 5a (0.93 g, ± 100%).

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