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STUDIES ON ORGANOPHOSPHORUS COMPOUNDS—XLI†

FORMATION OF 3-PYRAZOLINE-5-THIONE DISULFIDES FROM 3,5-PYRAZOLIDINEDIONES. C-ALKYLATION OF 3,5-PYRAZOLIDINEDIONES

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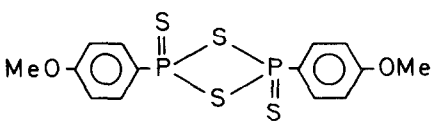
Abstract—4-Substituted-1,2-diphenyl-3,5-pyrazolidinediones (Phenylbutazone analogous) **1a–d** react with 2,4-bi-(4-methoxyphenyl)-1,3,2,4-dithiadiphosphetane 2,4-disulfide (Lawesson Reagent (LR) with formation of the corresponding 3,3'-dithiobis (1,2-dihydro-3**H**-pyrazole-5-thione)'s **2a–d**. When the 4-substituent contains a sulfoxide group this is deoxygenated to the sulfide by LR at room tmeperature. 1-Phthalazinone-4-thione, 1,4-phthalazine-dithione and ethyl aminothioxoacetate have also been prepared from the corresponding carbonyl compounds. Alkylation or acylation of **2a–d** yielded 3H-pyrazole-3-thione derivatives **8** and **9**. Alkylation of 1 with MeI in the presence of Et_3N at room temp. yielded the C-alkylated products **10** exclusively. X-Ray crystallographic investigations of **2b** and **9a** are presented.

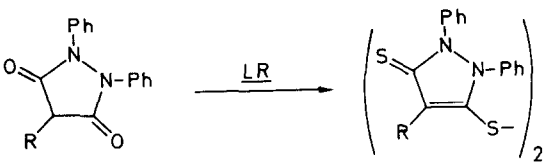
3,5-Pyrazolidinediones are of great interest because of their pharmacological and therapeutic properties (for a review see Ref. 1). To our knowledge 3,5 - pyrazolidine - dithiones are unknown and as it has been shown that LR is one of the most versatile thiation agents[2] commercially available, we felt prompted to continue our studies on reactions between LR and 3,5 - pyrazolidinediones. As a preliminary note we recently published[3] the reaction of 4 - butyl - 1,2 - diphenyl - 3,5 - pyrazolidinedione with LR and we have now investigated other substrates. We have also studied the alkylation and acylation reactions on the products. The preparation of 4-mono and 4,4-disubstituted 3,5-pyrazolidinediones from salts of 3,5-pyrazolidinediones and alkylating agents is well known[4]. We have now found that triethylamine is a convenient reagent for the salt formation as the reaction times are short and the reaction temperature is low. The C-alkylated products are formed in high yields.[22,23]



LR

RESULTS AND DISCUSSIONS

When 4 - substituted - 1,2 - diphenyl - 3,5 - pyrazolidinediones **1a–d** are allowed to react with LR at 80–110° for a few hours the disulfides **2a–d** are formed in reasonable yields.



1 2

a: R = Me
b: R = Bu
c: R = Ph
d: R = CH_2CH_2SPh

The disulfides **2** are yellow solids which are difficult to crystallize (Experimental). The structure of **2b** was determined by X-ray diffraction methods. Details of the analyses are given (Experimental). Fig. 1 is an ORTEP drawing of the molecule showing the atomic numbering. The bond lengths are listed in Table 2.

Compared to other compounds containing the C–S–S–C structure, the C–S bond in **2b** is shorter and the S–S bond is longer, as shown below:

	C–S	S–S
Diphenyldisulfide[6,7]	1.789Å	2.023Å
L-Cystine dihydrochloride[8]	1.865Å	2.044Å
Compound **2b**	1.755Å	2.073Å

A comparison between the S–S bond length and the C–S–S–C torsion angle has been carried out[6,9] which fit our data. The C=S bond lengths are found to be a little shorter (1.663 and 1.686Å, respectively) than the C=S bond in thiourea[10] (1.746Å) and thioacetamide[11] (1.713Å). All other distances are as expected and there are no short intermolecular distances to be taken into account.

†For part XL see S. Scheibye, R. Shabana, S.-O. Lawesson and C. Rõmming, *Tetrahedron* **38**, 993 (1982).

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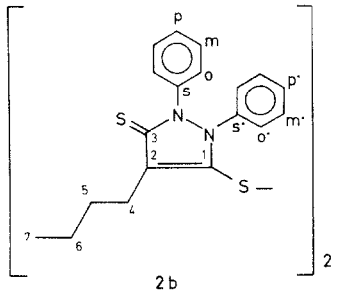
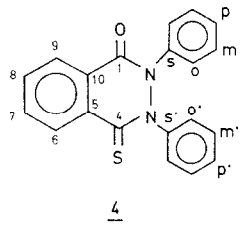
Table 1. ^{13}C NMR data of selected compounds.



2b



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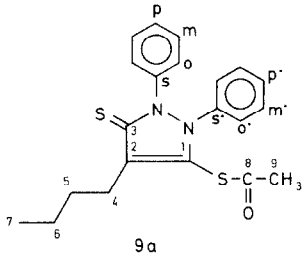
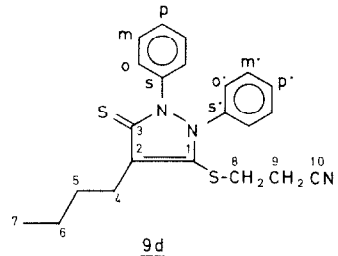
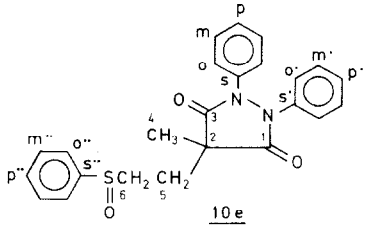


9a



9d



10e

Comp. / C No.	2b	4	9a	9d	10e
1	142.07	158.64	136.00	140.82	172.32
2	133.26	-	132.74	132.72	47.14
3	175.25	-	174.69	175.14	172.32
4	26.01	180.19	25.76	25.77	20.31
5	31.01	133.95	30.36	30.30	27.59
6	22.91	132.89	22.70	22.83	50.61
7	14.01	133.58*	13.95	14.02	-
8	-	134.05*	188.91	30.83	-
9	-	127.46	30.24	18.45	-
10	-	125.30	-	118.00	-
s	136.23	137.29	135.98	136.50	135.31
s'	135.16	141.46	135.54	135.28	135.31
s"	-	-	-	-	142.65
o	128.54	130.27	128.37	129.56	122.45
o'	128.30	129.87	128.57	128.43	122.45
o"	-	-	-	-	124.05
m	129.39	129.30	129.02	129.00	129.02
m'	129.09	129.16	128.91	128.15	129.02
m"	-	-	-	-	129.28
p	129.89	129.11	129.78	129.99	126.99
p'	129.39	129.08	129.24	129.35	126.99
p"	-	-	-	-	131.18

*Assignment not possible.

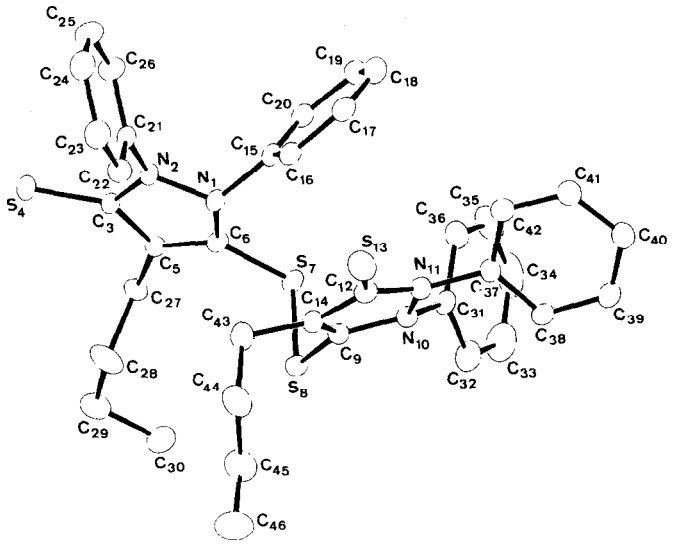


Fig. 1. A perspective view of **2b** with the atom numbering. H atoms are omitted for clarity.

The behaviour of the disulfides in solution is rather unusual. For instance, compound **2b** shows ^{1}H and ^{13}C NMR spectra in $CDCl_3$ solution, which are well compatible with the dimeric structure (Table 1 for ^{13}C data and Ref. 3 for ^{1}H data.) The chemical shift of the thiocarbonyl carbon at 175 ppm is at high field compared to the shifts for thioamides[12,13] but compares well with the shifts in similar compounds (e.g. **4** and **5**). A 3 - pyrazoline - 5 - thione has been reported to have a C=S chemical shift of 170.5 ppm[14]. The spectra in acetone-d_6 or in dimethylsulfoxide-d_6 solution, however, at temperatures around 300 K show evidence for an exchange

Table 2. Bond lengths of **2b** (Å)

N(1) -N(2)	1.407(5)	C(19)-C(20)	1.411(8)
N(1) -C(6)	1.380(6)	C(21)-C(22)	1.374(7)
N(1) -C(15)	1.468(5)	C(21)-C(26)	1.389(7)
N(2) -C(3)	1.369(6)	C(22)-C(23)	1.381(7)
N(2) -C(21)	1.426(6)	C(23)-C(24)	1.395(8)
C(3) -S(4)	1.686(4)	C(24)-C(25)	1.368(8)
C(3) -C(5)	1.424(6)	C(25)-C(26)	1.397(7)
C(5) -C(6)	1.352(6)	C(27)-C(28)	1.546(8)
C(5) -C(27)	1.488(6)	C(28)-C(29)	1.535(9)
C(6) -S(7)	1.752(5)	C(29)-C(30)	1.538(10)
S(7) -S(8)	2.073(3)	C(31)-C(32)	1.380(8)
S(8) -C(9)	1.755(5)	C(31)-C(36)	1.402(7)
C(9) -N(10)	1.385(6)	C(32)-C(33)	1.400(9)
C(9) -C(14)	1.352(7)	C(33)-C(34)	1.385(12)
N(10)-N(11)	1.390(5)	C(34)-C(35)	1.367(11)
N(10)-C(31)	1.421(6)	C(35)-C(36)	1.381(9)
N(11)-C(12)	1.364(6)	C(37)-C(38)	1.397(7)
N(11)-C(37)	1.441(6)	C(37)-C(42)	1.389(7)
C(12)-S(13)	1.663(5)	C(38)-C(39)	1.394(8)
C(12)-C(14)	1.444(7)	C(39)-C(40)	1.379(8)
C(14)-C(43)	1.501(7)	C(40)-C(41)	1.393(8)
C(15)-C(16)	1.388(7)	C(41)-C(42)	1.382(7)
C(15)-C(20)	1.378(7)	C(43)-C(44)	1.534(9)
C(16)-C(17)	1.407(7)	C(44)-C(45)	1.525(9)
C(17)-C(18)	1.360(8)	C(45)-C(46)	1.554(10)
C(18)-C(19)	1.386(8)		

process, which leads to an averaging of the resonances of the phenyl rings. Thus in addition to four signals for aliphatic carbons and a signal for C-4 only 4 signals are observed for the phenyl ring carbons. The signal for the para C shows exchange broadening and becomes sharper on raising the temperature. The signals for C-3 and C-5 (or an averaged signal for these carbons) are not observable, presumably because of excessive exchange broadening. Compound **2a** shows exchange broadening even in $CDCl_3$ solution. We have as yet no explanation for this unusual behaviour. Possibly the disulfide bond is cleaved homolytically and the radicals formed recombine either inter- or intra-molecularly. Attempts to prove the existence of radicals have, however, not yet succeeded, although we have run ESR experiments in various solvents with and without a spintrap (PhN(O)tBu) present.

Mass spectra of the disulfides all show an abundant ion at $((M/2)+1)^+$ but detailed studies of the mass spectra of **2b** showed the presence of M^+ (*m/e* 678, ~0.3%) and $M^+ - S$ (*m/e* 646, ~0.5%) using an inlet temperature of 160°. When the inlet temperature was raised to 250° no peak is seen at *m/e* 678 but M^+-S increases (*m/e* 646, 13%). The base peak corresponds to $((M/2)-S)^+$ (*m/e* 307, 100%) and also $((M/2)+1)^+$ is seen (*m/e* 340, 19%). In general the presence of $((M/2)+1)^+$ and $((M/2)-S)^+$ was considered as support for the structures.

The formation of the disulfides is assumed to proceed via the dithione which can form the enethiol, but it has not been possible, in our hands, to isolate the monomer even when the reaction was run under nitrogen. Other 3,5 - pyrazolidinediones than **1a–d** have been reacted with LR. When R = H and when a benzal group (PhCH=) is attached to C4 only small amounts of a yellow solid could be isolated and in both cases it is believed that a polymer is formed as the products are insoluble in organic solvents. When R = tBu no reaction occurs even at 110° and all the starting material could be recovered.

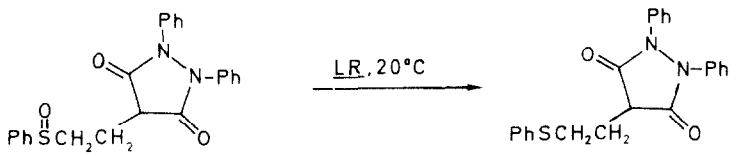
In the case where R contained a sulfoxide group (**1e**) deoxygenation takes place at low temperature[5] and the sulfide **1d** was isolated in a quantitative yield. The product was identified by comparison with an authentic sample.

1,4-Phthalazinedione **3** reacts with LR at 80° and when the molar ratio is 2:1 1 - phthalazine - 4 - thione **4** is formed in a high yield. If the amount of LR is increased to the molar ratio 1:1 1,4 - phthalazinedithione **5** is the only product. Recently also a P_4S_{10}·pyridine complex has been reported[15] to thiate one CO group selectively. The products **4** and **5** were characterized by their m.ps but also the ^1H and ^{13}C NMR spectra supported the structures. In both compounds the >C=S carbon atom absorbed at ~175 ppm as found for the 3H - pyrazole - 5 - thiones. The ^{13}C NMR data of **4** are summarized in Table 1.

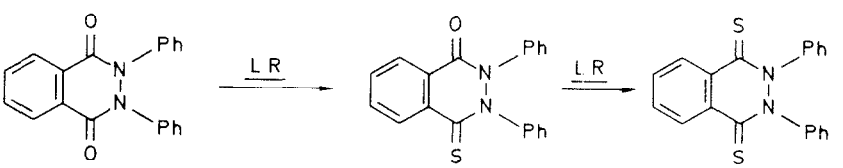
Ethyl aminoxoacetate (ethyloxamate) **6** is easily transformed into the corresponding thioamide **7** after reaction with LR at 80° and the product was characterized by ^1H and ^{13}C NMR spectroscopy and IR. The >C = O stretching frequency was found to 1710 cm^{-1} and in the ^{13}C NMR spectrum the >C=O and >C=S absorbed at δ 159.1 and 187.8, respectively. The formation of **7** is another example of the selectivity of LR in thiation reactions.[16,17]

In order to get a better understanding of the chemistry of the disulfides **2a–d** we have acylated and alkylated a few as shown in Scheme 1. In general the reactions are very smooth, with reaction times below 1 hr and reaction temperatures from 25° to 100°.

The structure of **9a** was determined by an X-ray crystallographic investigation. Details of the analyses are



1e 1d



3 4 5

6 7

Table 3. Bond lengths of **9a** (Å)

N(1) -N(2)	1.398(9)	C(11)-C(16)	1.378(13)
N(1) -C(6)	1.415(11)	C(12)-C(13)	1.400(14)
N(1) -C(11)	1.421(11)	C(13)-C(14)	1.383(15)
N(2) -C(3)	1.350(11)	C(14)-C(15)	1.383(15)
N(2) -C(17)	1.430(10)	C(15)-C(16)	1.411(13)
C(3) -S(4)	1.681(9)	C(17)-C(18)	1.384(12)
C(3) -C(5)	1.446(12)	C(17)-C(22)	1.386(12)
C(5) -C(6)	1.358(12)	C(18)-C(19)	1.412(13)
C(5) -C(23)	1.506(14)	C(19)-C(20)	1.406(14)
C(6) -S(7)	1.751(9)	C(20)-C(21)	1.450(14)
S(7) -C(8)	1.793(12)	C(21)-C(22)	1.417(13)
C(8) -O(9)	1.199(13)	C(23)-C(24)	1.556(16)
C(8) -C(10)	1.498(16)	C(24)-C(25)	1.507(15)
C(11)-C(12)	1.410(13)	C(25)-C(26)	1.524(19)

given (Experimental). Figure 2 shows an ORTEP plot of the molecule with the atomic numbering and in Table 3 bond lengths are listed. The C=S and the C–S bond lengths are both very close to the values found for **2b**.

^{1}H and ^{13}C NMR spectroscopy, IR and MS also comfirm the structure of the compounds **8** and **9**. In the ^{1}H NMR spectra of the S-acetylated products the Me absorbs at ~δ 2.30 and in the S-methylated products at ~δ 2.35. In all products the >C=S absorbs around 175 ppm. The presence of the C(O)S group is proved by an IR absorption between 1685 and 1760 cm^{-1} and also by a peak at ~δ 185 in the ^{13}C NMR spectrum. Table 1 shows the assignment of peaks in the ^{13}C NMR spectra of selected 3H - pyrazole - 5 - thiones.

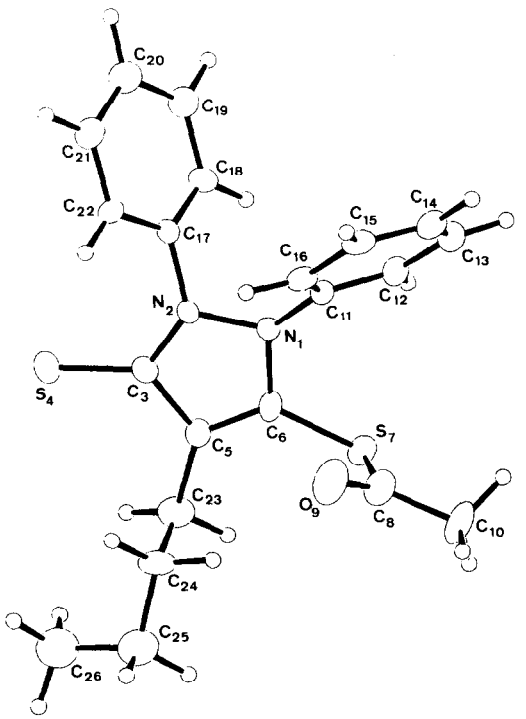


Fig. 2. A perspective view of **9a** showing the numbering of the nonhydrogen atoms.

†The compounds mentioned in this paper were either undistillable oils or not sufficiently stable for satisfactory micro analytical data.

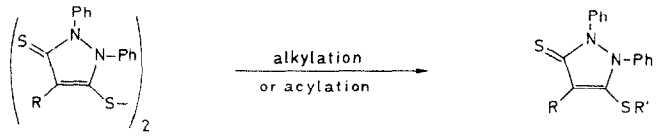
4 - Alkyl - 1,2 - diphenyl - 3,5 - pyrazolidinediones such as **1a**, **1d** and **1e** are easily transformed into the corresponding 4 - methyl - 4 - alkyl compounds by MeI and Et_3N. The reactions are very smooth and the only product isolated is **10** and this is in accord with the HSAB principle[18] as MeI and C4 are both regarded as soft. The structure of **10** is doubtless and no O-alkylation takes place as **10a** shows only seven C absorptions due to the symmetry of the compound and none of the other products show two double bond C atoms as would be expected for the O-alkylated product. In the IR spectra two CO absorptions are seen but in all three ^{13}C NMR spectra only one peak is observed for the two CO carbon atoms.

EXPERIMENTAL†

^{1}H NMR spectra were recorded on a Varian EM-360 operating at 60 MHz or in certain cases on a Bruker HX-360 at 360 MHz. ^{13}C NMR spectra were obtained at 90.52 MHz on the Bruker HX-360 or at 20.12 MHz on a Varian CFT 20 instrument. If nothing else is stated, $CDCl_3$ was used as solvent and TMS as internal reference standard. All chemical shifts are expressed as δ-values and coupling constants are given as |J| (Hz). Mass spectra were recorded on a Micromass 7070 F spectrometer operating at 70 eV using a direct inlet. IR spectra were recorded on a Beckmann IR 18 A spectrophotometer. Silicagel 60 (Merck) was used for column chromatography. M.Ps and b.ps are uncorrected.

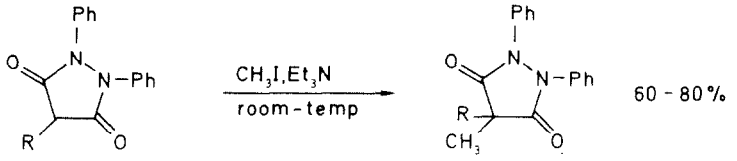
Starting materials were prepared by known methods[19,20] or were placed at our disposal by Ciba-Geigy, Basel, Switzerland (**1b**, **1d**, **1e**) or by Hoechst AG, Frankfurt, FRG (**3**). Compound **6** is commercially available. LR was prepared as earlier described[16] (also commercially available from Fluka AG, Merck-Schuchardt AG, Hoechst AG, or from Aldrich Chemical Co.).

Scheme 1. Alkylation- and acylation-reactions of 3,3' - dithiobis (1,2 - dihydro - 3H - pyrazole - 5 - thione)'s



2 8,9

Compound	R	R'	Agent
8a	Me	Ac	AcCl , Et_3N
8b	Me	Bz	BzCl , Et_3N
8c	Me	Me	MeI , N◯
9a	Bu	Ac	AcCl or Ac_2O, Et_3N
9b	Bu	Bz	BzCl ,Et_3N
9c	Bu	Me	MeI , Et_3N
9d	Bu	CH_2CH_2CN	CH_2=CH-CN



a : R = Me
d : R = CH_2CH_2SPh
e : R = $CH_2CH_2S(O)Ph$

General procedure for the reactions of **1a–d** *with* LR. The appropriate pyrazolidinedione (0.01 mol) and 4.04 g (0.01 mol) of LR were heated to reflux temp. with stirring using benzene or toluene as solvent. When no more of the starting material could be detected (tlc), the mixture was allowed to cool to room temp. and it was then evaporated on silica gel under reduced pressure. Column chromatography over silica gel yielded the corresponding disulfide **2**. The disulfides are generally yellow oils which are difficult to crystallize and they often show a tail on a tlc plate. Crystallization of the oil is performed in one of the following ways:

(1) Dissolve the disulfide in MeOH and cool to −78° for 6–8 hr, then filter of the solid (most of the disulfide is still in the mother liquid and evaporation yields the oil).

(2) Dissolve the oil in CH_2Cl_2/AcOEt 3:1 v/v and add 10–20% (vol) ligroin. After standing for some days a yellow solid can be filtered off. The residue is evaporated to the oil.

(3) The viscous oil obtained from the column is allowed to stand for some weeks and then a ppt forms. The solvent used in the reactions and the reaction times are given below.

Compound **2a**. 3,3' - Dithiobis (1,2 - diphenyl - 4 - methyl - 3 - pyrazoline - 5 - thione). Solvent: toluene. Time: 4 hr. Yield: 2.54 g (85%). M.p. 215°. MS [*m/e*(%, rel. int.)]: M^+(*m/e* 594) not observed, 298(100) (M/2) + 1, 266(31), 265(60), 268(38), 233(66). ^{1}H NMR ($CDCl_3$): δ 2.24 (6H, s) CH_3, 7.27 (20H, s) Ph. ^{13}C NMR: (DMSO-d_6, 320 K): δ 135.1 (quaternary C–N), 129.4 (*p*-C), 128.9, 128.5 (*o*-, *m*-C), 126.3 (C-4), 11.0 (Me). C3 and C5 not observed due to broadening.

Compound **2b**. 3,3' - Dithiobis (4 - butyl - 1,2 - diphenyl - 3 - pyrazoline - 5 - thione). Solvent: toluene. Time: 1.5 hr. Yield: 3.03 g (89%). M.p. 142°. MS: see text. ^{1}H NMR: given earlier[3]. ^{13}C NMR: see Table 1.

Compound **2c**. 3,3' - Dithiobis (1,2,4 - triphenyl - 3 - pyrazoline - 5 - thione). Solvent: benzene. Time: 2 hr. Yield: 2.8 g (78%). M.p. 282°. MS [*m/e*(%, rel. int.)]: M^+(*m/e* 718) not observed, 360(100) (M/2) + 1, 328(44), 327(88), 295(56). ^{1}H NMR ($CDCl_3$): δ 7.3 (s) Ph.

Compound **2d**. 3,3' - Dithiobis (4 - (2 - phenylthio) ethyl - 1,2 - diphenyl - 3 - pyrazoline - 5 - thione). Solvent: toluene. Time: 0.5 hr. Yield: 3.1 g (74%). M.p. 198°. MS [*m/e*(%, rel. int.)]: M^+ (*m/e* 838) not observed, 420(100) (M/2) + 1, 388(40), 387(81).

X-ray data on compound **2b**. Crystals of the disulfide were obtained from a mixture of EtOH and n-hexane. The specimen used for the X-ray experiments had dimensions 0.6 × 0.2 × 0.15 mm and was orange and transparent. Data were collected on a Philips single crystal diffractometer PW 1100 using graphite monochromated CuKα radiation (λ = 1.5418 Å). Intensity data were recorded using the $\theta - 2\theta$ scanning mode in the range of 2θ:6°–110°. Out of the 4844 reflections recorded 3810 with $I > 2\sigma(I)$ were retained for the structure analysis.

Crystal data of compound **2b**. 3,3' - Dithiobis (4 - butyl - 1,2 - diphenyl - 3 - pyrazoline - 5 - thione). $C_{38}H_{40}N_4S_4$, monoclinic. a = 13.471 Å; b = 12.543 Å; c = 22.124 Å; β = 106.55°. V = 3583 Å^3; M = 681.03; Z = 4; D_x = 1.262 g cm^{-3}. Space group $P2_1/c$ (no. 14).

Structure determination. The structure was determined by

direct methods (MULTAN 77). Block Diagonal Least Squares refinements with anisotropic temperature factors for the 46 non-H-atoms (isotropic for hydrogen atoms) converged to R = 0.055.

Deoxygenation of **1e**. 4.04 g (0.01 mol) of **1e** was dissolved in anhyd benzene and 4.04 g (0.005 mol) of LR was added. After stirring for 0.5 hr. at room temp. the solvent was stripped off under reduced pressure and column chromatography yielded 3.8 g (95%) of **1d**, m.p. and mixed m.p. 112°.

Compound **4**. 1 - Phthalazinone - 4 - thione. As the general procedure above. Solvent: toluene. Reaction temp.: 80°. Time 2 hr. Yield: 2.94 g (85%). M.p. 192°. Lit.[15] m.p. 199°. MS [*m/e*(%, rel. int.)]: 330(M^+, 100), 314(84), 298(28), 297(52), 269(21), 238(20). ^{13}C NMR: Table 1.

Compound **5**. 1,4 - Phthalazinedithione. As above. Reaction temp.: 100°. Time: 4 hr. Yield: 3.15 g (91%). M.p. 226°. Lit.[15] m.p. 229°. MS [*m/e*(%, rel. int.)]: 346(M^+, 55), 345(88), 314(100), 313(88), 237(85). ^{13}C NMR ($CDCl_3$): δ 182.9 (C1), 141.8 (s), 133.9 (C6), 129.4 (C9), 130.3, 129.3 (o, m), 129.4 (p), 132.3 (C5). For the numbering see Table 1.

Compound **7**. Ethyl aminothioxoacetate. As above. Solvent: toluene. Temp.: 80°. Time: 1 hr. Yield: 1.16 g (87%). M.p. 64°. Lit.[21] m.p. 58–60°. MS [*m/e*(%, rel. int.)]: 133(M^+, 55), 89(14), 60(100). ^1H NMR ($CDCl_3$): δ 1.35 (3H, t) Me, 4.31 (2H, q) CH_2, 8.0 (2H, br.s) NH_2. ^{13}C NMR ($CDCl_3$): δ 187.8 (C=S), 159.1 (C=O), 64.2 (CH_2), 13.9 (Me).

General procedure for the reactions of the disulfides **2a,b** *with alkylating/acylating agents*

The appropriate disulfide (0.5 mmol) was dissolved in 10 ml of anhyd CH_2Cl_2 or benzene and 0.51 g (0.51 mmol) of Et_3N was added. Then 0.5 mmol MeI or acyl halide or acyl anhydride (see below) was added drop by drop to the stirred soln. After reflux for the times given below the mixture was evaporated on silica gel and applied to a column using ether/ligroin 3:1 v/v as eluent.

Compound **8a**. 3 - Acetylthio - 4 - methyl - 3 - pyrazoline - 5 - thione. Acetylating agent: acetyl chloride. Solvent: benzene. Temp.: 25°. Time: 0.25 hr. Yield: 0.24 g (71%). M.p. 160–1°. MS [*m/e*(%, rel. int.)]: 340 (100, M^+), 298(38), 297(50) M–$COCH_3$, 265(75) M–$SCOCH_3$, 233(44). ^1H NMR ($CDCl_3$): δ 2.22 (3H, s) CH_3, 2.30 (3H, s) CH_3, 7.30 (10H, m) Ph. ^{13}C NMR ($CDCl_3$): δ 188.3 (C=O), 174.8 (C=S), 136.4, 135.9, 135.4, 129.9, 129.3, 129.1, 129.0, 128.4, 30.3 ($\underline{C}H_3CO$), 11.4 ($\underline{C}H_3$–C=C). IR(KBr) cm^{-1}: 1730 (C=O).

Compound **8b**. 3 - Benzoylthio - 4 - methyl - 3 - pyrazoline - 5 - thione. Acetylating agent: benzoyl chloride. Solvent: benzene. Temp.: 25°. Time: 1.5 hr. Yield: 0.31 g (77%). M.p. 172–4°. MS [*m/e*(%, rel. int.)]: 402 (100, M^+), 297(51) M^+–COPh, 265(94) M^+–SCOPh. Exact mass measurement on M^+: 402.077. Calc. for $C_{23}H_{18}N_2OS_2$: 402.086. ^1H NMR ($CDCl_3$): δ 2.28 (3H, s) CH_3, 7.3 (13H, m), 7.8 (2H, dd, J 8 Hz, J 1.5 Hz) o-protons. ^{13}C NMR ($CDCl_3$): δ 184.4 (C=O), 174.3 (C=S), 135.8 – 127.5 14 absorptions, 11.1 (CH_3). IR(KBr) cm^{-1}: 1690 (C=O).

Compound **8c**. 4 - Methyl - 3 - methylthio - 3 - pyrazoline - 5 - thione. Alkylating agent: MeI. Solvent: benzene. Temp.: 25°. Time: 1 hr. Yield: 0.24 g (77%). M.p. 164°. MS [*m/e*(%, rel. int.)]: 312 (4, M^+), 265(4) M^+–SCH_3, 220(25), 205(100). ^1H NMR ($CDCl_3$): δ 2.30 (3H, s) CH_3, 2.36 (3H, s) CH_3, 7.4 (10H, m) Ph.

Compound **9a**. 3 - Acetylthio - 4 - butyl - 3 - pyrazoline - 5 - thions. Acetylating agent: acetic anhydride, or acetyl chloride. Solvent: CH_2Cl_2. Temp.: 40°. Time: 1 hr. Yield 0.18 g (46%) using AcCl, 0.23 g (60%) using Ac_2O. App. 30% of the starting material recovered. M.p. 139–41°. Analysis correct for $C_{21}H_{22}N_2OS_2$ (C, H, N, S). MS [*m/e*(%, rel. int.)]: 382 (58, M^+), 339(100) M^+–$COCH_3$, 307(71) M^+–$SCOCH_3$. ^1H NMR ($CDCl_3$): δ 0.95 (3H, t) δ–CH_3, 1.41 (2H, m) γ–CH_2, 1.68 (2H, m) β–CH_2, 2.30 (3H, s) CH_3CO, 2.68 (2H, t) α–CH_2, 7.07–7.40 (10H, m) Ph. ^{13}C NMR: Table 1. IR($CHCl_3$) cm^{-1}: 2940(s), 1740(s) C=O, 1600(m). UV(EtOH) [nm(log ε)]: 228(5.64), 350(5.46).

Compound **9b**. 3 - Benzoylthio - 4 - butyl - 3 - pyrazoline - 5 - thione. Acylating agent: benzoyl chloride. Solvent: benzene. Temp.: 50°. Time: 1 hr. Yield: 0.30 g (67%). 0.9 g (30%) of the starting material was recovered, m.p. 130–2°. MS [*m/e*(%, rel. int.)]: 444(53, M^+), 339(100) M^+–COPh, 307(75) M^+–SCOPh. Exact mass measurement on M^+: 444.1328. Calc. for $C_{26}H_{24}N_2OS_2$: 444.1330. ^1H NMR ($CDCl_3$): δ 0.95 (3H, t) CH_3, 1.1–2.0 (4H, m) β–CH_2, γ–CH_2, 2.72 (2H, t) α–CH_2, 7.27 (13H, m) Ph, 7.78 (2H, dd) o-protons. ^{13}C NMR ($CDCl_3$): δ 184.8 (C=O), 173.8 (C=S), 135.4–127.2 (12 arom. C and C=C), 29.8 (α–CH_2), 24.2 (β–CH_2), 22.1 (γ–CH_2), 13.4 (CH_3). IR(KBr) cm^{-1}: 1700 (C=O).

Compound **9c**. 4 - Butyl - 3 - methylthio - 3 - pyrazoline - 5 - thione. Alkylating agent: methyl iodide. Solvent: benzene. Temp.: 80°. Time 1 hr. Yield: 0.30 g (84%). Oil. ^1H NMR ($CDCl_3$): δ 1.00 (3H, t) CH_3, 1.3–2.0 (4H, m) β–CH_2, γ–CH_2, 2.30 (3H, s) SCH_3, 2.91 (2H, t) α–CH_2, 7.45 (10H, m) Ph.

Compound **9d**. 4-Butyl-3-(2-cyanoethylthio)-3-pyrazoline-5 - thione. Alkylating agent: acrylonitrile. 5.0 mmol was used in order to increase the yield of **9d**. Solvent: p-dioxane. Temp.: 100°. Time: 3 hr. Yield: 0.33 g (84%). M.p. 180–3°. MS [*m/e*(%, rel. int.)]: 393(50, M^+), 339(75) M^+–CH_2CH_2CN, 307(100) M^+–SCH_2CH_2CN. Exact mass measurement on M^+: 393.1333. Calc. for $C_{22}H_{23}N_3S_2$: 393.1333. ^1H NMR ($CDCl_3$): δ 1.01 (3H, t) CH_3, 1.1–2.0 (4H, m) β–CH_2, γ–CH_2, 2.25–2.90 (6H, m) α–CH_2 and CH_2CH_2CN. ^{13}C NMR: Table 1.

X-ray data on compound **9a**. Crystals were obtained from diisopropylether by evaporation at room temp. The crystal used for the experiments had dimensions 0.39 × 0.33 × 0.05 mm and was yellow and transparent. Data were collected as mentioned for **2b**. Out of the 2887 reflections collected, 2104 with $I > 2\sigma(I)$ were retained for the analysis.

Crystal data of compound **9a**. 3 - Acetylthio - 4 - butyl - 3 - pyrazoline - 5 - thione. $C_{21}H_{22}ON_2S_2$, monoclinic, a = 10.231 Å; b = 9.498 Å; c = 21.761 Å; β = 100.84°. V = 2078 Å^3; M = 382.56; Z = 4; D_x = 1.223 g cm^{-3}. Space group $P\,2_1/c$ (no. 14).

Structure determination. As mentioned for **2b**. Block Diagonal Least Squares refinements with anisotropic temperature factors for the 25 non-H-atoms (isotropic for H atoms) converged to R = 0.072.

General procedure for the alkylation of 3,5 - *pyrazolidinediones* **1a**, **1d** *and* **1e**

0.005 mol of **1** and 0.5 g (0.005 mol) of Et_3N in 2 ml anhydr benzene or CH_2Cl_2 was stirred and then 0.71 g (0.005 mol) of MeI was added drop by drop at room temp. After stirring for the times given below the soln was filtered and the residue was evaporated to yield the product **10**.

Compound **10a**. 4,4 - Dimethyl - 1,2 - diphenyl - 3,5 - pyrazolidinedione. Solvent: benzene. Time: 10 hr. Yield: 0.84 g (60%). M.p. 132–4°. MS [*m/e*(%, rel. int.)]: 280(M^+, 100), 266(10), 183(19), 182(35). Exact mass measurement on M^+: 280.1222. Calc. for $C_{17}H_{16}N_2O_2$: 280.1212. ^1H NMR ($CDCl_3$): δ 1.48 (6H, s) CH_3, 7.3 (10H, s) Ph. ^{13}C NMR ($CHCl_3$): δ 174.1 (C=O), 135.9 (quart. C), 128.8, 122.2 (o, m–C), 126.5 (p–C), 44.2 ($C(CH_3)_2$), 21.6 (CH_3). IR(KBr) cm^{-1}: 1750(s), 1720(s) (C=O).

Compound **10d**. 4 - (2 - Phenylthioethyl) - 4 - methyl - 1,2 - diphenyl - 3,5 - pyrazolidinedione. Solvent: CH_2Cl_2. Time: 0.5 hr. Yield: 1.5 g (74%). M.p. 94°. MS [*m/e*(%, rel. int.)]: 402(M^+, 13), 266(100) M^+–CH_2CH_2SPh. Exact mass measurement on M^+: 402.1358. Calc. for $C_{24}H_{22}N_2O_2S$: 402.1402. ^1H NMR ($CDCl_3$): δ 1.35 (3H, s) CH_3, 2.18 (2H, m) α–CH_2, 2.85 (2H, m) β–CH_2, 7.15 (15H, m) Ph. ^{13}C NMR ($CDCl_3$): δ 172.9 (C=O), 135.7–122.4 8 C's, 48.4 (quart. C), 35.3 (SCH_2), 28.6 (CCH_2), 21.5 (CH_3). IR (KBr) cm^{-1}: 1750(s), 1715(s) (C=O).

Compound **10e**. 4 - (2 - Phenylthienylethyl) - 4 - methyl - 1,2 - diphenyl - 3,5 - pyrazolidinedione. Solvent: benzene. Time: 0.7 hr. Yield 2.9 g (70%). M.p. 130°. MS [*m/e*(%, rel. int.)]: 418(M^+, 100) all others <5%. ^1H NMR ($CDCl_3$): δ 1.40 (3H, s) CH_3, 2.12 (2H, m) CCH_2, 2.85 (2H, m) SCH_2, 7.1–7.4 (15H, m) Ph. ^{13}C NMR ($CDCl_3$): Table 1. IR(KBr) cm^{-1}: 1740(s), 1700(s) (C=O).

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