An Approach to Biologically Important *S*-Heterocycles, Dithiocarbamyls, and their Relevant Phosphono Derivatives

Maha D. Khidre, Azza A. Kamel and Wafaa M. Abdou

Department of Pesticide Chemistry, National Research Centre, Dokki, Cairo, Egypt

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The feasibility of insertions of carbanions between two sulfur atoms has been reported when 5-(4-chlorophenyl)-4-cyano-1,2-dithiol-3-thione (**1**) and tetramethylthiuram disulfide (**17**) were allowed to react with unsaturated **2a,b** and active phosphonium salts **11a,b**. The reactions afforded, mainly, 1,3-dithiols **4a,b** and **14a,b** together with substituted thiophenes **10a,b** and **16a,b**. Reactions of **1** and **17** with α-alkylthiomethyl phosphonates **24a,b** afforded the phosphonates **25a,b** and **26a,b**, respectively.

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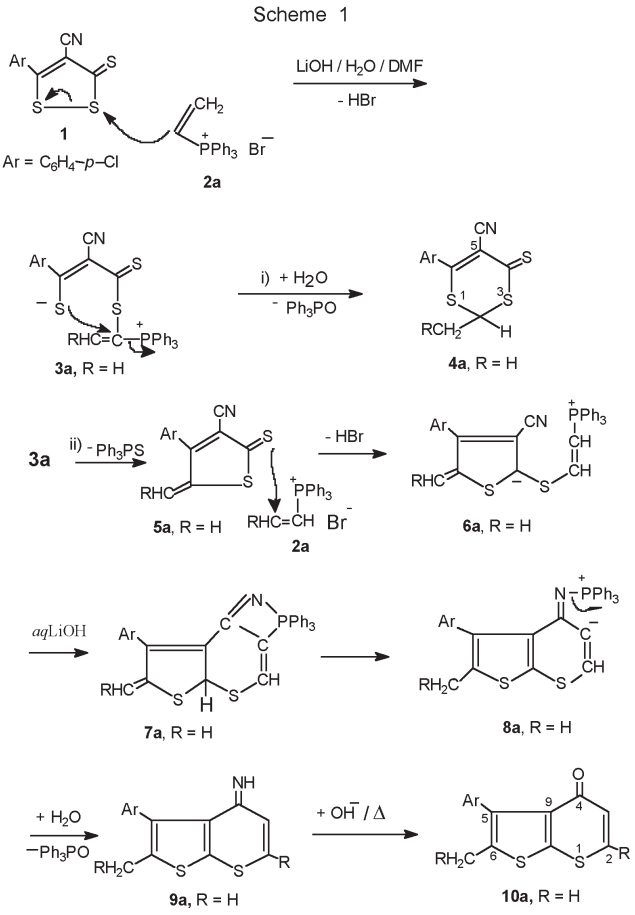
Literature reports the synthesis and utility of many thiol and dithiol derivatives as insecticides, fungicides and seed protectants [1-3] as well as being useful as antioxidants and in volcanization processes [4]. In addition, they are known to possess therapeutic values in controlling diseases, such as pneumonea [5]. For these reasons, the chemistry of the sulfur-sulfur bond continues to be an active area of research from both a mechanistic and a synthetic point of view. The mechanism of nucleophilic attack by carbenoids, carbenes and phosphorus ylides on the S-S linkage in dithiols, followed by substitution reaction at the heteroatomic center (S, N, …*etc*), has been a major point of interest for research in the last three decades [6,7]. For the past few years, one of our research directions has centered on the synthesis of thiols, dithiols and phosphorylated sulfur compounds, derived from the reactions of acyclic and cyclic *cis*-disulfides with P(III) and P(V) reagents [8]. Preliminary results in a screening assay of selected synthesized compounds showed pesticidal and pharmacological activity. The work described in this article involved the reactions of 5-(4-chlorophenyl)-4-cyano-1,2-dithiol-3-thione (**1**) and tetramethylthiuram disulfide (**17**) with unsaturated- **2a,b** and active-**11a,b** phosphonium salts as well as the phosphonate carbanions **24a,b**. The reactions, depicted in Schemes 1- 7, led to the synthesis of the title compounds: new *S*-heterocycles, dithiocarbamyls and their phosphono derivatives, for biological evaluation. The results are compared and discussed, together with other published researchs in this area.

Reaction of 1,2-dithiol (**1**) with vinyltriphenylphosphonium bromide (**2a**, 2 molar amounts) in a mixture of 40 ml of dimethylformamide (DMF) and 10 ml of LiOH (0.5 *M*) yielded 6-(4-chlorophenyl)-5-cyano-2-methyl (4*H*)-1,3-dithiacyclohexene-4-thione (**4a**, 43%) and 5-(4-chlorophenyl)-6-methyl-(4*H*)-4-oxothienothiapyran (**10a**, 21%) (Scheme 1). The products **4a** and **10a** were obtained in similar ratio, irrespective of the number of mole equivalents of **2a** that was used.

The formation of **4a** and **10a** could be attributed to initial attack by the carbanion center of **2a** on the cleaved -S-S-linkage, initiated by the alkaline medium [6c,e]. This attack led to the formation of zwitterion **3a**, which, subsequently, could follow two different pathways: i) Intramolecular cyclization and hydrolysis yielding **4a** with concomitant elimination of triphenylphosphine oxide. Similar insertion reaction has been reported previously for the reaction of *cis*-disulfides with active ylides [6b,c], diazomethane [7c], and very recently [8a] for the reaction of **1** with diethyl vinylphosphonate. ii) Extrusion of triphenylphosphine sulfide from **3a** followed by thiophilic addition of a second ylide species **2a** affording the ylide **6a** *via* **5a**. The latter step is presumably invoked by the

Scheme 1

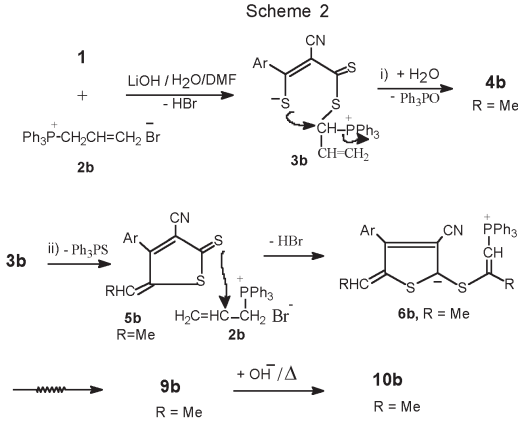


α-electron-withdrawing substituent, CN group [9]. Further attack of the ylide on the carbon-nitrogen triple bond [10] and ring closure afforded dihydroazaphosphete **7a**. The phosphineimine **8a**, which resulted from opening of the four membered ring in **7a** would lead to the formation of the iminothiapyran **9a**. Finally, the product **10a** is regarded as an oxidation form of **9a** through the hydrolysis. An analogous transformation is known for the imino function, in an alkaline solution to the keto-structure [11].

A similar treatment of **1** with 2 equivalents of allyltriphenylphosphonium bromide (**2b**) in a mixture of 40 ml of DMF containing 10 ml of LiOH (0.5 *M*) afforded the analogs **4b** (47%) and **10b** (18%) according to Scheme 2, which followed the same patterns discussed above. Furthermore, the electrophilic attack of thiocarbonyl group in **1** at the central atom of the allyl moiety in **2b** (Scheme 2, pathway ii) has been amply documented [12], and we have evoked it on several occasions to rationalize our experimental findings [13].

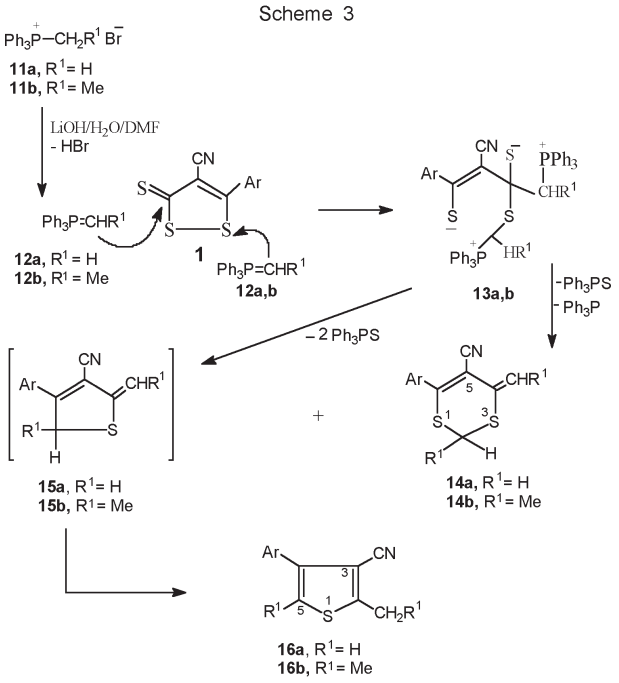
In a systematic study, the reaction of **1** with methylidene-(**12a**) and ethylidenetriphenylphosphoranes (**12b**), prepared *in situ* from the corresponding phosphonium bromide **11a** (or **11b**), proceeded smoothly under the same conditions (with **2a,b**) to give the substituted thiophenes **16a** (16%) and **16b** (17%) in addition to 1,3-dithiols **14a** (52%) and **14b** (50%) as shown in Scheme 3. Structures of the new compounds were delineated from elemental analyses and their spectroscopic properties.

Scheme 2



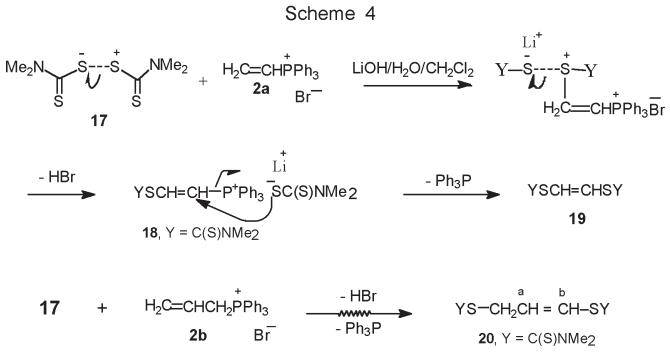
A noteworthy contrast exists between the present behavior of unsaturated and active phosphonium salts **2a**,**b** and **11a,b** with 1,2-dithiol **1** and those reported previously [8c] for the behavior of resonance stabilized ylides toward the same substrate, **1** in toluene. Thus, the results of the former investigation [8c] indicated that ylides of the type (Ph_3P=CHCOR', R'= OMe, OEt, Ph, Me) reacted with **1** mainly at the thiocarbonyl group or further with the nitrile function in the second step whereas compounds derived from an insertion reaction at the -S-S- linkage were the common major products in the present four studied reactions (Schemes 1, 2 and 3).

Scheme 3



When tetramethylthiuram disulfide (**17**) was treated, at room temperature, with an equimolar amount of **2a,b** in a mixture of CH_2Cl_2 and aqueous LiOH (0.5 *M*) (1:4, ratio) α-ω-(bis-dimethyldithiocarbamyl)alkene **19** (or **20**) was obtained in a yield as high as ~ 70%. Rationalization of the reaction of Scheme 4 is that reagent **2** attacks the disulfide bond as an electrophile and that an ylide-like species **18** is produced then rearranges. The ylide intermediate **18** is reminiscent of that reported [7c] in the reaction of aryl disulfides with the Simmons-Smith reagent (ICH_2ZnI).

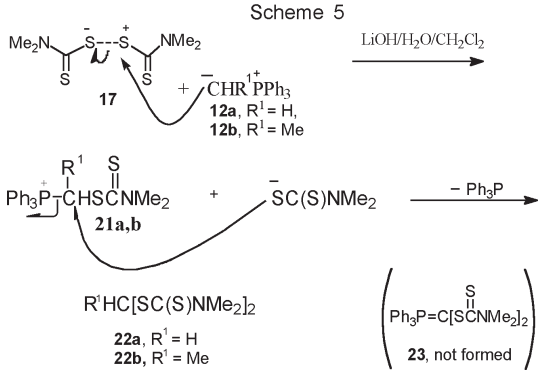
Scheme 4



On the contrary, bis(dimethyldithiocarbamyl)alkanes **22a,b** (~ 62%) - and not the ylides **23 [**6c] -were obtained by treating **17** with alkylidenephosphoranes **12a,b**, prepared *in situ* from the corresponding bromide salt, under the conditions previously mentioned, **17** with **2a,b**. Identification of the insertion products was confirmed by combustion analysis, as well as by mass and NMR spectroscopy. The above result can be fully explained by

assuming that the reaction of **17** with **12a,b** occurs according to Scheme 5. Step A is the expected nucleophilic attack by reagent **12** on the disulfide bond leading to the ylide **21**. Step B is a known reaction of thiocarbamyl anion; since the sulfur anion is the most powerful nucleophile present in the reaction mixture [6c], which undergo a substitution reaction to afford the final products **22a,b**, and does not abstract a hydrogen atom from **21** giving the ylide **23**). Scheme 5 that represent the course of the reactions of **17** with active phosphorus ylides **12a,b**, are in line with what has been previously explored by Field and Banks [6b].

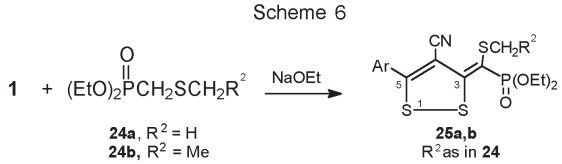
Scheme 5



Next, the reactions of *cis*-disulfides **1** and **17** with α-alkylthiomethyl phosphonates **24a,b** were investigated with regard to the synthesis of new phosphonate derivatives with potential biological activity. The synthesis of phosphono substituted-*S*-compounds should be of great interest as many of them have been reported to possess antibiotic, antineoplastic, antiviral or herbicidal attributes [14]. Treatment of **1** with an equivocal amount of diethyl α-alkylthiomethyl phosphonates **24a,b** in an alcoholic NaOEt at room temperature afforded the phosphonate **25a** (46%) or **25b** (50%), advantageously (Scheme 6). Compound **25** is somewhat compromised as occurring through condensation of the carbanion ion with thioxocarbon-3 in **1** and extrusion of a molecule of H_2S (*Perkin*-type condensation) [8a,15].

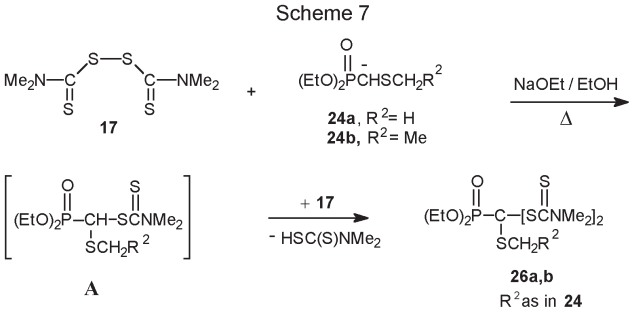
The spectroscopic results demonstrated that in the case of the olefin **25** no isomeric phosphonates arose. Molecular models indicate, in fact, the existence of steric crowding between the nitrile substituent and the phosphorus moiety [P(O)(OEt)$_2$] in the transition state leading stereospecifically to one isomer that has the nitrile and thioalkyl groups in the *cis*-form. Furthermore, the assignment of stereochemistry to compounds **25a,b** was based on ^{1}H NMR, which showed two singlets at δ 2.27 and 2.28 ppm whose peak area integrated to 3 protons, and are assigned to the methyl group (S-CH$_3$). The splitting of the methyl signal is in support with the suggested *cis*-structure of **25**. Finally, the data recorded (deshielded shift) for the splitted signal of the H_3C-S protons in **25a** suggested its *cis*-configuration to the CN group, and could readily eliminate the *trans*-isomer, which would predict a singlet in the range δ 2.23-2.25 for a free H_3C-S [16].

Scheme 6



On the other hand, when the disulfide **17** was allowed to react with the Wittig-Horner reagents **24a,b**, under the same reaction conditions, the phosphonate **26a** (65%) or **26b** (60%) was obtained (Scheme 7). Compounds **26a,b** are considered to proceed through an initial nucleophilic attack by the carbanion center in the phosphoryl carnanion **24a** (or **24b**) on the S-S linkage in **17** leading to an elusive 1:1 intermediate species **A**, which in turn undergoes displacement reaction with a second molecule of **17**, under thiuram-sulfide ion yielding the products **26a,b**.

Scheme 7



Selective examples of the synthesized products: **4a**, **10b**, **14b**, **20**, **22a**, **25a,b** and **26a,b** were screened against bollworms (cotton). The observed activities of the tested pests were compared with the activity of triazophos (Hostathion®) against the pests. Phosphorylated compounds **25a,b** and **26a,b** showed significant activity toward all tested pests. The active products will be subjected to further screening under different factors, and full results will be published together with other results elsewhere.

EXPERIMENTAL

Melting points are uncorrected. The IR spectra were recorded on Perkin Elmer 317 Grating IR spectrophotometer, using KBr disc. The ^{1}H and ^{13}C NMR spectra were measured on a Jeol-270 MHz instrument using $SiMe_4$ as an internal reference. The ^{31}P NMR spectra were recorded relative to external H_3PO_4 (85%) with a Varian CFT-20 instrument. The mass spectra were performed at 70 eV on a Shimadzu GCS-QP 1000 EX spectrophotometer provided with a data system. The appropriate precautions in handling moisture-sensitive compounds were observed.

Solvents were dried by standard techniques. Light petroleum refers to the fraction 40-60 °C.

General Procedure for the Reaction of 1,2-Dithiols **1** and **17** with Phosphonium Bromides **2a**, **2b**, **11a** and **11b**.

To a stirred solution of two mol equiv of the appropriate salt **2a, 2b, 11a** or **11b** and one molar equivalent of **1** [17] in 40 ml DMF, freshly prepared 10 ml (0.5 *M*) of LiOH was added in one portion to the mixture. The two-phase system was stirred at r.t. up to the consumption of the starting dithiol (~12 h for salts **2a** and **11a** and for ~24 h for **2b** and **11b**). The mixture was then extracted with $CHCl_3$ (2 X 100 ml). The combined organic extracts were backwashed with 30 ml H_2O, dried, and the solvent was evaporated in the presence 7 g (Kieselgel 60, particle size 0.2- 0.5 mm; E. Merk, Darmstadt) and packed with light petroleum.

Reaction of **1** with Vinyltriphenylphosphonium Bromide (**2a**).

According to the general procedure: A mixture of 0.8 g (2.97 mmoles) of **1** and 2.19 g (5.94 mmoles) of **2a** in 40 ml DMF containing 10 ml (0.5 *M*) of LiOH was refluxed for 12 h. After the usual workup, the residue was applied to column chromatography, which was developed with light petroleum containing increasing amounts of ethyl acetate. The fraction (9.5:5, v/v) yielded colorless needles of triphenylphosphine sulfide (ca 68%), mp 162 °C.

5-(4-Chlorophenyl)-6-methyl-(4*H*)-4-oxothienothiapyran (**10a**).

Compound **10a** was obtained (9:1, v/v) as colorless crystals (182 mg, 21%), mp 168-170 °C (MeCN); IR 1654 cm^{-1} (CO); ^1H NMR ($CDCl_3$): δ 1.54 (s, 3H, CH_3), 6.41 (d, J = 4.4 Hz, 1H, 3-H), 7.44, 7.47 (2d, J = 8.1 Hz, 2H, 3'-H, 5'-H), 7.57 (d, J = 4.4 Hz, 1H, 2-H), 7.75, 7.78 (2d, J = 8.1 Hz, 2H, 2'-H, 6'-H); ^{13}C NMR ($CDCl_3$): δ 14.8 (CH_3), 126.7 (1'-C), 129.3, 129.8 (2'-C, 3'-C, 5'-C, 6'-C), 139.8 (4'-C), 113.4 (3-C), 124.9 (2-C), 127.6 (9-C), 139.3 (6-C), 141.3 (5-C), 151.2 (8-C), 171.6 (C=O); ms: m/z (EI) (%) 293 (16), 292 (M^+, 29), 277 (18), 223 (37), 181 [(M^+- $^+ClC_6H_4$), 100], 111 (33), 75 (20).

Anal. Calcd. For $C_{14}H_9ClOS_2$ (292.8): C, 57.43; H, 3.1; Cl, 12.11; S, 21.9. Found: C, 57.49; H, 3.15; Cl, 12.07; S, 21.83%.

6-(4-Chlorophenyl)-5-cyano-2-methyl-(4H)-1,3-dithiacyclohexene-4-thione (**4a**).

Compound **4a** was obtained (7:3, v/v) as straw yellow crystals (380 mg, 43%), mp 126-128 °C (CH_2Cl_2); IR 2218 (CN), 1488 cm^{-1} (C=S); ^1H NMR ($CDCl_3$): δ 1.46 (d, J = 8.4 Hz, 3H, CH_3), 4.55 (q, J = 8.4 Hz, 1H, 2-H), 7.45, 7.47 (2d, J = 8.1 Hz, 2H, 3'-H, 5'-H), 7.59, 7.66 (2d, J = 8.1 Hz, 2H, 2'-H, 6'-H); ^{13}C NMR ($CDCl_3$): δ 13.5 (CH_3), 30.3 (2-C), 108.2 (5-C), 117.3 (CN), 126.3 (1'-C), 129.1, 129.7 (2'-C, 3'-C, 5'-C, 6'-C), 139.5 (4'-C), 141.6 (6-C), 192.4 (C=S); ms: m/z (EI) (%) 298 (29), 297 (M^+, 53), 271 (18), 155 ($ClC_6H_4CS^+$, 100), 111 (30), 75 (16). The fraction 6:4, v/v gave triphenylphosphine oxide (54%), mp 156 °C.

Anal. Calcd. for $C_{12}H_8ClNS_3$ (297.8): C, 48.39; H, 2.71; Cl, 11.90; N, 4.70; S, 32.30. Found: C, 48.44; H, 2.75; Cl, 11.82; N, 4.66; S, 32.36%.

Reaction of **1** with Allyltriphenylphosphonium Bromide (**2b**).

According to the general procedure: A mixture of 0.8 g (2.97 mmoles) of **1** and 2.28 g (5.94 mmoles) of **2b** in 40 ml DMF containing 10 ml (0.5 *M*) of LiOH was refluxed for 30 h. After the usual workup, the residue was applied to a column chromatography, which was developed with light petroleum containing increasing amounts of ethyl acetate. Pure light petroleum eluted colorless crystals of triphenylphosphine (TLC), mp 77-80 °C. The fraction (9.5:5, v/v) yielded colorless needles of triphenylphosphine sulfide (ca 50%), mp 162 °C.

5-(4-Chlorophenyl)-6-ethyl-2-methyl-(4H)-4-oxothienothiapyran (**10b**).

Compound **10b** was obtained (9:1, v/v) as colorless crystals (170 mg, 18%), mp 191-193 °C (acetone); IR 1670 cm^{-1} (CO), ^1H NMR ($CDCl_3$): δ 1.15 (t, J = 7.6 Hz, 3H, $6CCH_3$), 1.42 (s, 3H, $2\text{-}CH_3$), 2.73 (q, J = 7.6 Hz, 2H, CH_2), 6.28 (s, 1H, 3-H), 7.45, 7.47 (2d, J = 8.1 Hz, 2H, 3'-H, 5'-H), 7.78, 8.0 (2d, J = 8.1 Hz, 2H, 2'-H, 6'-H); ^{13}C NMR ($CDCl_3$): δ 13.3, 14.7 (2 x CH_3), 28.4 ($6\text{-}CH_2$), 125.6 (1'-C), 128.8, 129.2 (2'-C, 3'-C, 5'-C, 6'-C), 138.6 (4'-C), 114.8 (3-C), 139.4 (2-C), 137.7 (6-C), 141.6 (5-C), 175.4 (CO); ms: m/z (EI) (%) 321 (14), 320 (M^+, 23), 305 (9), 290 (12), 237 (44), 209 [(M^+- $^+ClC_6H_4$), 100], 111 (33), 75 ($C_6H_3^+$, 18).

Anal. Calcd. for $C_{16}H_{13}ClOS_2$ (320.8): C, 59.89; H, 4.08; Cl, 11.05; S, 19.99. Found: C, 59.8; H, 4.03; Cl, 11.11; S, 19.88%.

6-(4-Chlorophenyl)-5-cyano-2-ethyl-(4*H*)-1,3-dithiacyclohexene-4-thione (**4b**).

Compound **4b** was obtained (7:3, v/v) as straw yellow crystals (435 mg, 47 %), mp 142-144 °C (EtOH); IR 2220 (CN), 1485 cm^{-1} (C=S); ^1H NMR ($CDCl_3$): δ 0.92 (t, J = 6.8 Hz, 3H, CH_3), 3.21-3.26 (m, 2H, CH_2), 4.62 (t, J = 8.1 Hz, 1H, 2-H), 7.45, 7.47 (2d, J = 8.1 Hz, 2H, 3'-H, 5'-H), 7.72, 7.75 (2d, J = 8.1 Hz, 2H, 2'-H, 6'-H); ^{13}C NMR ($CDCl_3$): δ 13.8 (CH_3), 24.2 (CH_2), 38.5 (2-C), 108.9 (5-C), 118.4 (CN), 126.1 (1'-C), 129.4, 129.6 (2'-C, 3'-C, 5'-C, 6'-C), 137.8 (4'-C), 143.2 (6-C), 188.6 (C=S); ms: m/z (EI) (%) 312 (17), 311 (M^+, 31), 271 (18), 155 ($ClC_6H_4CS^+$, 100), 111 ($ClC_6H_4^+$, 30), 75 (16). The fraction 6:4, v/v gave triphenylphosphine oxide (60%), mp 156 °C.

Anal. Calcd. for $C_{13}H_{10}ClNS_3$ (311.9): C, 50.06; H, 3.23; Cl, 11.37; N, 4.49; S, 30.84. Found: C, 49.99; H, 3.17; Cl, 11.43; N, 4.45; S, 30.91%.

Reaction of **1** with Phosphonium Salts **11a** and **11b**.

A mixture of 0.8 g (2.97 mmoles) of **1** and 2.12 g (5.94 mmoles) of methyl- (**11a**) or 2.21 g (5.94 mmoles) of ethyltriphenylphosphonium bromide (**11b**) in 40 ml DMF containing 10 ml (0.5 *M*) of LiOH was refluxed for 10 h. After the usual workup, the residue was applied to a column chromatography, which was developed with light petroleum containing increasing amounts of ethyl acetate. Pure light petroleum eluted colorless crystals of triphenylphosphine, mp 77-80 °C. The fraction (9.5:5, v/v) yielded colorless needles of triphenylphosphine sulfide (ca 62%), mp 162 °C.

4-(4-Chlorophenyl)-3-cyano-2-methylthiophene (**16a**).

Compound **16a** was obtained (8:2, v/v) as colorless needles (110 mg, 16 %), mp 164-166 °C ($CHCl_3$); IR 2198 cm^{-1} (CN), ^1H NMR ($CDCl_3$): δ 1.38 (s, 3H, CH_3), 7.41, 7.42 (2d, J = 8.1 Hz, 2H, 3'-H, 5'-H), 7.58, 7.61 (2d, J = 8.1 Hz, 2H, 2'-H, 6'-H), 7.79 (s, 1H, 5-H); ^{13}C NMR ($CDCl_3$): δ 14.8 (CH_3), 110.4 (3-C), 118.2 (CN), 122.6 (5-C), 125.8 (1'-C), 129.3, 129.8 (2'-C, 3'-C, 5'-C, 6'-C), 138.4 (4'-C), 139.2 (2-C); ms: m/z (EI) (%) 234 (37), 233 (M^+, 62), 218 (14), 207 (29), 192 (23), 111 (100), 75 (19).

Anal. Calcd. for $C_{12}H_8ClNS$ (233.7): C, 61.67; H, 3.45; Cl, 15.17; N, 5.99; S, 13.72. Found: C, 61.59; H, 3.38; Cl, 15.24; N, 5.93; S, 13.77%.

6-(4-Chlorophenyl)-5-cyano-4-methylidene-1,3-dithiacyclohexene (**14a**).

Compound **14a** was obtained (6:4, v/v) as light yellow crystals (410 mg, 52 %), mp 192-194 °C (MeCN); IR 2222 (CN), 1619 cm^{-1} (C=C, exocyclic); ^1H NMR ($CDCl_3$): δ 2.78 (s, 2H, 2-CH_2), 5.76 (s, 2H, =CH_2), 7.42, 7.44 (d, J = 8.1 Hz, 2H, 3'-H, 5'-H), 7.58, 7.61 (d, J = 8.1 Hz, 2H, 2'-H, 6'-H); ^{13}C NMR ($CDCl_3$): δ 29.1 (2-C), 107.1 (=CH_2), 110.2 (5-C), 117.6 (CN), 126.2 (1'-C), 129.2, 129.8 (2'-C, 3'-C, 5'-C, 6'-C), 139.1 (4'-C), 139.7 (6-C), 149.7 (4-C); ms: m/z (EI) (%) 266 (10), 265 (M^+, 18), 249 (33), 155 (100, $ClC_6H_4CS^+$), 111 (41), 75 (22).

Anal. Calcd. for $C_{12}H_8ClNS_2$ (265.8): C, 54.23; H, 3.03; Cl, 13.34; N, 5.27; S, 24.13. Found: C, 54.29; H, 3.11; Cl, 13.28; N, 5.35; S, 24.23%.

4-(4-Chlorophenyl)-3-cyano-2-ethyl-5-methylthiophene (**16b**).

Compound **16b** was obtained (8:2, v/v) as colorless needles (132 mg, 17 %), mp 178-180 °C ($CHCl_3$); IR 2200 cm^{-1} (CN), ^1H NMR ($CDCl_3$): δ 0.92 (t, J = 7.4 Hz, 3H, C-CH_3), 1.46 (s, 3H, 5-CH_3), 2.72 (q, J = 7.4 Hz, 2H, 2-C-CH_2), 7.45, 7.46 (2d, J = 8.1 Hz, 2H, 3'-H, 5'-H), 7.71, 7.73 (2d, J = 8.1 Hz, 2H, 2'-H, 6'-H); ^{13}C NMR ($CDCl_3$): δ 12.8 (C-CH_3), 14.6 (CH_3), 24.8 (CH_2), 110.1 (3-C), 118.1 (CN), 126.3 (1'-C), 128.7, 129.3 (2'-C, 3'-C, 5'-C, 6'-C), 139.4 (4'-C), 138.8, 139.6, 139.9 (2-C, 4-C, 5-C); ms: m/z (EI) (%) 262 (32), 261 (M^+, 56), 245 (33), 231 (21), 205 (44), 111 (100), 75 (24).

Anal. Calcd. for $C_{14}H_{12}ClNS$ (261.8): C, 64.24; H, 4.62; Cl, 13.54; N, 5.35; S, 12.25. Found: C, 64.31; H, 4.66; Cl, 13.48; N, 5.40; S, 12.31%.

6-(4-Chlorophenyl)-5-cyano-4-ethylidene-1,3-dithiacyclohexene (**14b**).

Compound **14b** was obtained (7:3, v/v) as pale yellow needless (435 mg, 50%), mp 198-201 °C (EtOH); IR 2218 (CN), 1622 cm^{-1} (C=C, exocyclic); ^1H NMR ($CDCl_3$): δ 1.34 (d, J = 7.3 Hz, 3H, 2-C.CH_3), 1.95 (d, J = 6.8 Hz, 3H, 4-C=C.CH_3), 4.51 (q, J = 7.3 Hz, 1H, 2-H), 5.89 (q, J = 6.8 Hz, 1H, =CH), 7.46, 7.48 (2d, J = 8.3 Hz, 2H, 3'-H, 5'-H), 7.68, 7.78 (2d, J = 8.3 Hz, 2H, 2'-H, 6'-H); ^{13}C NMR ($CDCl_3$): δ 14.2, 18.3 (2 x CH_3), 33.2 (2-C), 110.9 (5-C), 116.8 (=CH), 117.9 (CN), 139.6 (6-C), 147.4 (4-C), 126.6 (1'-C), 129.2, 129.8 (2'-C, 3'-C, 5'-C, 6'-C), 139.4 (4'-C); ms: m/z (EI) (%) 294 (13), 293 (M^+, 25), 278 (11), 267 (24), 263 (18), 155 (100, $ClC_6H_4CS^+$), 111 (37), 75 (15).

Anal. Calcd. for $C_{14}H_{12}ClNS_2$ (293.8): C, 57.23; H, 4.12; Cl, 12.07; N, 4.77; S, 21.83. Found: C, 57.29; H, 4.18; Cl, 12.14; N, 4.68; S, 21.79%.

Reaction of Tetramethylthiuram Disulfide (**17**) with Phosphonium Salts **2a,b** and **11a,b**.

A mixture of 1.0 g (4.16 mmoles) of **17** [18] and 4.2 mmoles of **2a** (1.55 g), **2b** (1.61 g), **11a** (1.5 g) or **11b** (1.56 g) in 40 ml of CH_2Cl_2 containing 10 ml (0.5 *M*) of LiOH solution was stirred at r.t. for 12-24 h (TLC). Following the same procedure and workup were used in the general procedure, compounds **19, 20, 22a** and **22b** were obtained.

1,2-(bis-Dimethyldithiocarbamyl)ethylene (**19**).

Compound **19**, 756 mg (70%) of (*E/Z* ratio, 3:1) was obtained (from **17** + **2a**) as yellow crystals after chromatographic separation (hexane /AcOEt, 7:3, v/v), ^1H NMR ($CDCl_3$): δ 3.42 (br, 12H, 2N(CH_3)$_2$], 6.65 (d, *E*-isomer, J = 16 Hz, 2 x 1H, CH=CH), 6.81 (d, *Z*-isomer, J = 12 Hz, 2 x 1H). The mixture of the isomers were re-dissolved in CH_2Cl_2 and kept at 0 °C for 2 days. The solvent was decanted and the procedure was repeated with fresh CH_2Cl_2. Crystals that separated out were collected and proved to be the major isomer *E*-**19** (0.4 g, 37%), m.p. 114-116 °C; IR 1616 (HC=CH), 1487 cm^{-1} (C=S); ^1H NMR ($CDCl_3$): δ 3.27, 3.45 [2s, 2 x 6H, 2N(CH_3)$_2$], 6.64 (d, J = 16 Hz, 2 x 1H, CH=CH-*homotopic*); ^{13}C NMR ($CDCl_3$): δ 31.7, 33.8 (2s, 2 x [N(CH_3)$_2$]), 130.4, 131.8 (CH=CH), 191.2, 191.5 (2x C=S); ms: m/z (EI) (%) 266 (M^+, 11), 88 (100).

Anal. Calcd. for $C_8H_{14}N_2S_4$ (266.47): C, 36.06; H, 5.29; N, 10.51; S, 48.13. Found: C, 36.13; H, 5.24; N, 10.43; S, 48.21%.

1,3-(bis-Dimethyldithiocarbamyl)allene (**20**).

Compound **20**, 793 mg (68%) of (*E* and *Z* isomers) was obtained (from **17** + **2b**) as yellow crystals after chromatographic separation (hexane/AcOEt, 7:3, v/v). The mixture of diastereomers **20** is tested first by ^1H NMR spectrum whereby they present in ratio 3:1. Likewise with **19**, fractional crystallization from CH_2Cl_2 afforded a pure sample of the major isomer *E*-**20** (315 mg, 27 %), m.p. 126-128 °C; IR 1622 (HC=CH), 1485 cm^{-1} (C=S); ^1H NMR ($CDCl_3$): δ 3.40, 3.45 [2s, 2 x 6H, 2N(CH_3)$_2$], 3.86 (d, J = 6.5 Hz, 2H, CH_2S), 5.93 (m, 1H, CH^a), 6.52 (d, J = 16.5 Hz, 1H, CH^b); ^{13}C NMR ($CDCl_3$): δ 24.7 (CH_2), 31.3, 31.6, 33.5, 34.1 (4s, 2 x [N(CH_3)$_2$]), 120.6 (=CH^a), 126.7 (=CH^b), 188.3, 190.6 (2 x C=S); ms: m/z (EI) (%): 280 (M^+, 16), 88 (100).

Anal. Calcd. for $C_9H_{16}N_2S_4$ (280.5): C, 38.54; H, 5.75; N, 9.99; S, 45.73. Found: C, 38.46; H, 5.66; N, 10.03; S, 45.67%.

bis-(Dimethyldithiocarbamyl)methane (**22a**).

Compound **22a**, 688 mg (65%) was obtained (from **17** + **11a**) as straw yellow crystals after chromatographic separation (hexane/AcOEt, 8:2, v/v), m.p. 138-140 °C (cyclohexane); IR 1484 cm^{-1} (C=S); ^1H NMR ($CDCl_3$): δ 3.12, 3.28 [2s, 2 x 6H, 2N(CH_3)$_2$], 4.21 (s, 2H, SCH_2); ^{13}C NMR ($CDCl_3$): δ 22.8 (CH_2S), 31.4, 33.6 (NCH_3), 190.8, 192.4 (C=S); ms: m/z (EI) (%) 254 (M^+, 14), 88 (100).

Anal. Calcd. for $C_7H_{14}N_2S_4$ (254.46): C, 33.04; H, 5.55; N, 11.0; S, 50.41. Found: C, 33.09; H, 5.48; N, 11.07; S, 50.47%.

bis-(Dimethyldithiocarbamyl)ethane (**22b**).

Compound **22b**, 720 mg (60%) was obtained (from **17** + **11b**) as sandy yellow crystals after chromatographic separation (hexane /AcOEt, 8:2, v/v), m.p. 126-128 °C (MeCN); IR 1484 cm^{-1} (C=S); ^1H NMR ($CDCl_3$): δ 1.26 (d, J = 6.8 Hz, 3H, CH_3), 3.23, 3.27 [2s, 2 x 6H, 2N(CH_3)$_2$], 4.88 (q, 1H, SCH); ^{13}C NMR ($CDCl_3$): δ 15.3 (CH_3), 30.1 (SCH), 31.3, 33.8 (NCH_3), 194.2, 196.2 (C=S); ms: m/z (EI) (%) 268 (M^+, 13), 88 (100).

Anal. Calcd. for $C_8H_{16}N_2S_4$ (268.49): C, 35.79; H, 6.01; N, 10.43; S, 47.77. Found: C, 35.84; H, 6.04; N, 10.37; S, 47.85%.

Reaction of **1** and **17** with α-Alkylthiomethyl Phosphonates **24a,b**.

Compounds **25a, 25b, 26a** and **26b** were prepared by adding a solution of 3 mol equiv of NaOEt in 30 ml absolute ethanol to a stirred solution of one mol equiv of **24a** or **24b** in 20 ml EtOH at -10 °C. Stirring is continued for 20 min and a solution of 0.8 g (2.97 mmoles) of **1** (or 0.8 g, 3.33 mmoles of **17**) in 20 ml EtOH is then added at -10 °C. After stirring for 1 h at 0 °C, and further

for ~ 12 h (TLC) at r.t., the solvent is concentrated to its half *in vacuo* and then poured onto ice, extracted with $CHCl_3$, dried and evaporated. The residue is then purified by chromatography (light petroleum /AcOEt gradient as eluents).

5-(4-Chlorophenyl)-4-cyano-(3*H*)-1,2-dithiol-3-(α-diethylphosphorylmethylene)thiomethyl (**25a**).

Compound **25a**, 592 mg (46%) was obtained (7:3, v/v) as yellow fine needles, m.p. 150-152 °C (MeCN); IR 2210 (CN), 1254 (P=O), 1030 cm^{-1} (P-O-C); ^1H NMR ($CDCl_3$): δ 1.22, 1.26 (2dt, J_{HH} = 7.2, J_{HP} = 4.8 Hz, 6H, 2OC-CH_3), 2.27 (d, J_{HP} = 4.2 Hz, 3H, SCH_3), 4.09, 4.18 (2q, J = 8.7, 2 x 2H, 2-OCH_2), 7.42, 7.77 (2d, J = 8.2 Hz, 2 x 2H, H-Ar); ^{13}C NMR ($CDCl_3$): δ 13.5 (SCH_3), 18.32 ($OCCH_3$), 63.3 (OCH_2), 110.4 (4-C), 118.1 (CN), 121.5 (d, J_{CP} = 122.8 Hz, =C-P), 126.5, 129.3, 129.6, 139.5, 141.2 (C'-Ar), 151.3 (3-C); ^{31}P NMR ($CDCl_3$): δ 17.84 ppm, ms: m/z (EI) (%) 432 (18), 433 (M^+, 33), 407 (16), 386 (15), 360 (31), 396 (28), 349 (55), 155 (100, $ClC_6H_4CS^+$).

Anal. Calcd. for $C_{16}H_{17}ClNO_3PS_3$ (433.94): C, 44.29; H, 3.95; Cl, 8.17; N, 3.23; P, 7.14; S, 22.17. Found: C, 44.35; H, 3.99; Cl, 8.24; N, 3.18; P, 7.22; S, 22.10%.

5-(4-Chlorophenyl)-4-cyano-(3*H*)-1,2-dithiol-3-(α-diethylphosphorylmethylene)thioethyl (**25b**).

Compound **25b**, 665 mg (50%) was obtained (7:3, v/v) as pale yellow needles, m.p. 143-145 °C (cyclohexane); IR 2218 (CN), 1282 (S-S), 1254 (P=O), 1030 cm^{-1} (P-O-C); ^1H NMR ($CDCl_3$): δ 1.13, 1.24 (2dt, J_{HH} = 7.2, J_{HP} = 4.6 Hz, 6H, $OCCH_3$), 1.35 (t, J_{HH} = 6.8 Hz, $SCCH_3$), 3.98 (q, J_{HP} = 4.2 Hz, 2H, SCH_2), 4.11, 4.23 (2q, J = 8.7, 2 x 2H, 2-OCH_2), 7.43, 7.76 (2d, J = 8.1 Hz, 2 x 2H, H-Ar); ^{13}C NMR ($CDCl_3$): δ 14.3, 15.1 ($2CH_3$), 29.4 (SCH_2), 62.4 (OCH_2), 111.2 (4-C), 118.4 (CN), 128.8 (d, J_{CP} = 124.8 Hz, =C-P), 126.1, 130.2, 130.5, 139.1, 141.5 (C'-Ar), 151.5 (3-C); ^{31}P NMR ($CDCl_3$): δ 18.3 ppm, ms: m/z (EI) (%) 446 (14), 447 (M^+, 24), 421 (9), 386 (21), 360 (33), 310 (37), 249 (58), 155 (100, $ClC_6H_4CS^+$).

Anal. Calcd. for $C_{17}H_{19}ClNO_3PS_3$ (447.97): C, 45.58; H, 4.28; Cl, 7.91; N, 3.13; P, 6.91; S, 21.47. Found: C, 45.53; H, 4.21; Cl, 7.84; N, 3.22; P, 6.97; S, 21.52%.

bis-(Dimethyldithiocarbamyl)thiomethyl-α-diethylphosphorylmethane (**26a**).

Compound **26a**, 942 mg (65%) was obtained (8:2, v/v) as colorless crystals, m.p. 170-172 °C (EtOH); IR 1484 (C=S), 1256 (P=O), 1080 cm^{-1} (P-O-C); ^1H NMR ($CDCl_3$): δ 1.32, 1.37 (2dt, J_{HH} = 7.2, J_{HP} = 4.6 Hz, 6H, 2 x $OCCH_3$), 3.24, 3.35 (2s, 2 x 6H, $2N(CH_3)_2$], 2.42 (s, 3H, SCH_3), 4.15, 4.22 (2q, J = 11.5, 2 x 2H, $2OCH_2$); ^{13}C NMR ($CDCl_3$): δ 14.2 (SCH_3), 15.2, 15.4 ($OCCH_3$), 31.2, 31.6, 33.24, 33.29 [$2N(CH_3)_2$], 38.5 (d, J_{CP} = 98 Hz, CP), 61.6 (OCH_2), 188.3 (C=S); ^{31}P NMR ($CDCl_3$): δ 22.4 ppm, ms: m/z (EI) (%) 436 (M^+, 23), 389 (30), 299 (22), 252 (55), 137 (62), 88 (100).

Anal. Calcd. for $C_{12}H_{25}N_2O_3PS_5$ (436.65): C, 33.01; H, 5.77; N, 6.42; P, 7.09; S, 36.72. Found: C, 32.96; H, 5.69; N, 6.35; P, 7.03; S, 36.78%.

bis-(Dimethyldithiocarbamyl)thioethyl-α-diethylphosphorylmethane (**26b**).

Compound **26b**, 900 mg (60%) was obtained (8:2, v/v) as colorless crystals, m.p. 152-154 °C (from benzene); IR 1485 (C=S), 1260 (P=O), 1055 cm^{-1} (P-O-C); ^1H NMR ($CDCl_3$): δ 1.24, 1.37 (2dt, J_{HH} = 7.2, J_{HP} = 4.6 Hz, 2 x 3H, 2 x $OCCH_3$), 1.41 (t, J = 6.8 Hz, 3H, $SCCH_3$), 2.89, 3.12 [2s, 2 x 6H, $2N(CH_3)_2$], 4.27 (q, J = 6.8 Hz, 2H, SCH_2), 4.12, 4.18 (2q, 2 x 2H, $2OCH_2$); ^{13}C NMR ($CDCl_3$): δ 14.7, 15.6, 15.9 ($OCCH_3$, $SCCH_3$), 28.6 (SCH_2), 31.1, 31.5, 33.4, 33.7 (NCH_3), 38.2 (d, J_{CP} = 99.5 Hz, CP), 62.8 (OCH_2), 190.2, 191.7 (2 x C=S); ^{31}P NMR ($CDCl_3$): δ 18.86 ppm, ms: m/z (EI) (%) 450 (M^+, 28), 435 (9), 389 (13), 313 (41), 137 (55), 88 (100).

Anal. Calcd. for $C_{13}H_{27}N_2O_3PS_5$ (450.67): C, 34.65; H, 6.04; N, 6.22; P, 6.87; S, 35.58. Found: C, 34.56; H, 6.11; N, 6.29; P, 6.93; S, 35.52%.

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