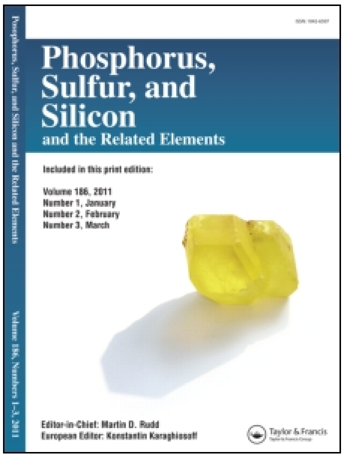

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THE REACTION OF LAWESSON'S REAGENTS WITH 3,6-PYRIDAZINEDIONE AND 1,4-PHTHALAZINEDIONE

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2-Methyl-1-phenyl-1,2-dihydro-3,6-pyridazinedione (II) reacted with Lawesson's reagent (I) in different molar ratio, to give the dithione V and the monothiones VI and VII. 1-Phenyl-1,2-dihydro-3,6-pyridazinedione (III) reacted with reagents Ia-c to give the disulphide VIII, the dithione IX and 1,3,2-oxathiophosphole derivative XII. 2-Phenyl-2,3-dihydro-1,4-phthalazinedione (IV) reacted with reagents Ia-c to give the dithione XIV and monothione XV.

Keywords: Pyridazinediones; Phthalazinediones; Lawesson's Reagent; 1,3,2-Oxathiophosphole; Disulphides; Monosulphides

INTRODUCTION

Little is known about the chemistry of 1,2-dihydro-3,6-pyridazinediones as they show low reactivity due to strain and conjugation. These compounds are useful intermediate in the synthesis of insecticides,[1-5] acaricides,[1-5] and ectoparasiticides.[6] They are used in polymer industry,[7,8] and they have been also reported as antiinflammatory[9] and antifouling agents.[10]

In view of these observations and in continuation of our recent study on the behavior of tertiary phosphite esters on pyridazinediones,[11] we have investigated the behaviors of Lawesson's reagents (I) on 2-methyl-1-phenyl-1,2-dihydro-3,6-pyridazinedione (II) and 1-phenyl-1,2-dihydro-3,6-pyridazinedione (III) in an effort to prepare new compounds as potential pesticides. The study was extended to include 2-phenyl-2,3-dihy-

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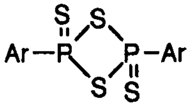
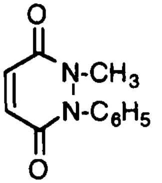
* Correspondence author.

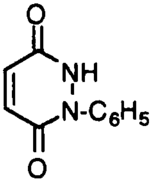
dro- 1,4-phthalazinedione (IV). To the best of our knowledge, no information about such work has appeared in the literature.



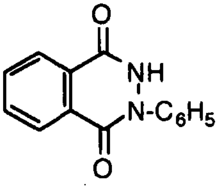
Ia, Ar = C_6H_4-OCH_3-p
b, Ar = C_6H_4-OC_6H_5-p
c, Ar = S-C_6H_5



II



III

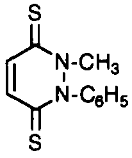


IV

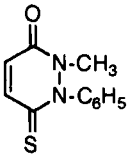
RESULTS AND DISCUSSIONS

We have found that the product of the reaction of compound II with 2,4-bis(p-methoxyphenyl)1,3,2,4-dithiadiphosphetane-2,4-disulphide (Ia)[12,13] depends on experimental conditions. Thus, when 1 mole equivalent of compound II was allowed to react with 1 mole equivalent of compound Ia in dry benzene or toluene, 2-methyl-1-phenyl-1,2-dihydro-3,6-pyridazinedithione (V) was formed quantitatively. The same compound V is likewise formed when compound II was allowed to react with 2,4-bis(p-phenoxyphenyl)-1,3,2,4-dithiadiphosphetane-2,4-disulphide (Ib),[12] and/or 2,4-bis-(thiophenoxy)- 1,3,2,4-dithiaphosphetane-2,4-disulphide (Ic)[13] under the same experimental conditions. The identity of compound V was verified by spectroscopic evidences (cf. experimental).

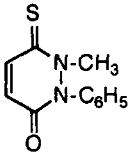
When 1 mole equivalent of compound II was allowed to react with 0.5 mole equivalent of compound I(a-c), 2-methyl-1-phenyl-3-oxo-1,2-dihydropyridazin-6-thione (VI) and 2-methyl-1-phenyl-6-oxo-1,2-dihydropyridazin-3-thione (VII) were isolated as the main reaction products. Together with these compounds, the dithione (V) was



V

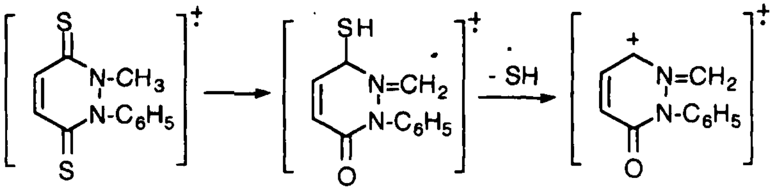


VI



VII

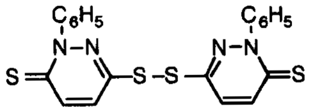
also isolated in a very low yield. Compounds VI and VII were differentiated by a comparative MS study. Both MS of compounds VI and VII showed an ion peak at $m/z = 218$ (M^+). However, only the spectrum of compound VII showed an ion peak at $m/z = 185$ (M^+-SH). It is therefore safe to conclude that the elemination of SH under the MS condition is governed by the presence of the neighbouring labile NCH_3 group (cf. Scheme 1).



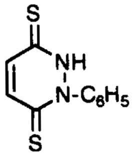
SCHEME 1

Additional support was gained from a comparative ^{1}H-NMR study. Whereas, the spectrum of compound VII revealed the presence of a signal at $\delta = 3.50$ (3 H, s) which is in accordance with the value measured for the $N\text{-}CH_3$ protons of compound V ($\delta = 3.60$), the spectrum of compound VI showed a signal at $\delta = 3.10$ (3 H, s) which is also in accordance with the value of the $N\text{-}CH_3$ protons of compound II ($\delta = 3.15$). Moreover, both compounds VI and VII yielded V upon treatment with phosphorus pentasulphide.

Next, we investigated the behaviour of 1-phenyl-1,2-dihydro-3,6-pyridazinedione (III0 towards reagents Ia-c. When 1 mole equivalent of compound III was allowed to react with 1 mole equivalent of Ia, the disulphide VIII was formed in high yield. The same compound VIII, together with the dithione IX, were formed when 1 mole of compound III was reacted with 1 mole of compound Ib.



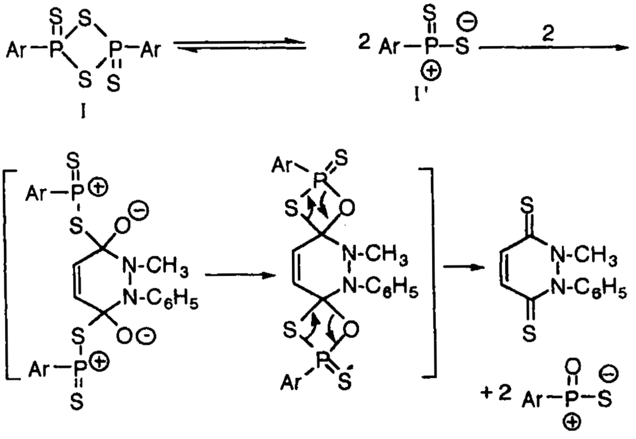
VIII



IX

The assigned structures (VIII and IX) were based on spectroscopic evidences (cf. experimental).

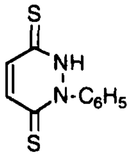
When the previous reactions were conducted using 1 mole of compound III and 0.5 mole of compound Ia and /or Ib, no change in the nature of the product was observed, but the presence of the starting dione (ca. 20%) was noted. A mechanism accounting for the formation of the dithione V is depicted in Scheme 2. It seems likely that the highly reactive dithiophosphine ylide 1′, rather than Lawesson's reagent itself, may be the active thionating agent.[14]



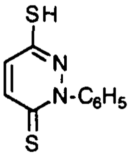
SCHEME 2

The formation of the monothiones VI and VII, when a molar ratio 0.5 : 1 reagent/ reactant was performed, lend credibility to the proposed betaine mechanism.

The disulphide VIII may be formed via the dithione IX which is generated first by a similar betaine mechanism. This is not surprising since the dithione IX would likely be present in the thiol form IX′ due to the lower stabilization of the thiocarbonyl group reflecting a more pronounced tendency to undergo tautomeric changes. The formation of disulphide from thiols via thiyl radicals was reported.[15] The separation of a small amount of the dithione in this reaction (cf. experimental) supports this mechanism.

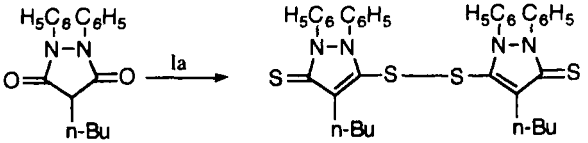


IX



IX'

Disulphides of similar structures were previously noted.[15] El-Barbary and Lawesson reported the formation of 3,3′-dithio-bis(4-butyl-1,2-diphenyl-5-thioxo-3-pyrazoline) (XI) upon reacting 4-butyl-1,2-diphenyl-3,5-pyrazolidinedione (X) with reagent Ia.[15]

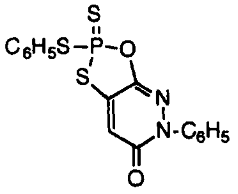


X XI

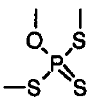
The reaction of compound III with reagent Ic gave a compound to which the 1,3,2-oxathiaphosphole structure XII was assigned. Together with this compound, the disulphide VIII was also formed.

The assigned 1,3,2-oxathiaphosphole structure XII was based on the following:

1) The MS of compound XII showed peaks at $m/z = 390$, M^+; $m/z = 281$, M^+-SC_6H_5 (ion a); $m/z = 249$, ion a -S; $m/z = 109$, -SC_6H_5.



XII

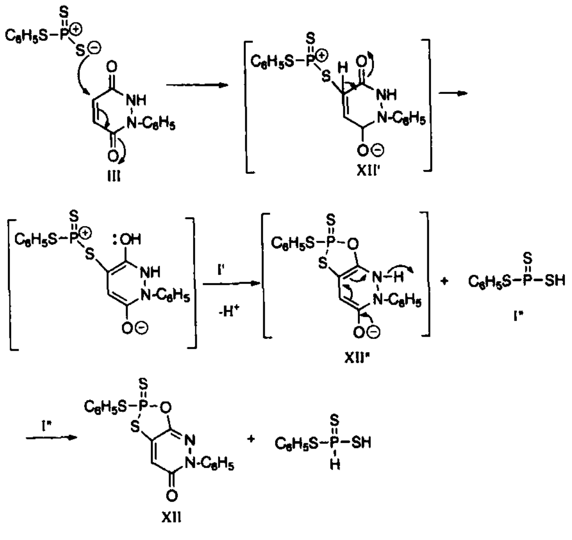


XIII

2) The ^{31}P-NMR chemical shift for compound XII was +93.25 ppm which is in accordance with shifts recorded for structures encorporating moiety XIII.[16]

3) The ^{1}H-NMR spectrum of compound XII showed a multiplet due to the 11 aromatic protons at $\delta = 7.59–7.46$. The spectrum revealed the absence of the 2 doublets corresponding to the 2 olefinic protons of the pyridazine ring, which appeared at $\delta = 7.05$ and $\delta = 7.6$ in the spectrum of the starting compound III.

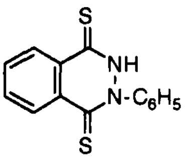
A mechanism accounts for the formation of the 1,3,2-oxathiaphosphole structure is depicted in Scheme 3. It is based on the assumption of the addition of the monomeric species I′ to compound III to yield intermediates XII′ and XII″. The latter rearranges finally to produce XII.



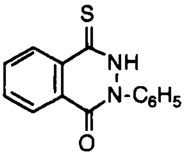
SCHEME 3

It is worthy to mention that the abstraction of a proton by species I′ in the aforementioned mechanism finds analogy in the literature.[17] The formation of similar species is reported to be implicated in the process of demethylation of thiokhellin to produce desmethylthiokhellin exploring a new potentiality for reagent I.[17]

We have also investigated the reaction of 2-phenyl-2,3-dihydro-1,4-phthalazinedione (IV) with Lawesson's reagent Ia. 2-Phenyl-2,3-dihydro-1,4-phthalazinedithione (XIV) was obtained when equal molar ratios of the reactants were used. On the other hand, when 1 mol of compound IV was allowed to react with 0.5 mol of compound Ia, both the dithione XIV and 2-phenyl-1-oxo-2,3-dihydro-4-phthalazinedione (XV) were formed. Compound XV was converted to compound XIV upon treatment with phosphorus pentasulphide. The identity of compounds XIV and XV were verified by spectroscopic evidences (cf. experimental).



XIV



XV

EXPERIMENTAL

All melting points were uncorrected. Toluene and petroleum ether were dried over sodium. Pyridazinediones II and III[18] and Lawesson's reagent[12,13] were prepared according to established procedures and recrystallized before use. The reaction mixtures were resolved into their individual constituents by column chromatography on silica gel G [particle size 0.2–0.5 mm, 37–70 mesh (ASTM) E Merck, Darmstadt] through elution with petroleum ether (40–60 °C), toluene and ethyl acetate in suitable ratios.

The IR spectra were recorded with a Zeiss Infrared spectrophotometer IMR 16. The ^{1}H-NMR spectra were run in DMSO or $DCCl_3$ on a Jeol JNM-EX 270 MH FT NMR system (National Research Centre, Dokki, Cairo) using TMS as an internal reference. ^{31}P-NMR spectra were taken in

$DCCl_3$ (vs 85% H_3PO_4 as external reference) on a Varian CET 20, 32 MHz spectrometer. The MS spectra were preformed at 70 eV on a Schimadzu-GC MS-QP1000 EX (Faculty of Science, Cairo University, Cairo). The microanalysis for the new compounds were in good agreement with the calculated values (C, H, ± 0.1; N, ± 0.05; P, ± 0.05).

Reaction of 2-Methyl-1-phenyl-1,2-dihydro-3,6-pyridazinedione (II) with Lawesson's reagent (Ia)

(a) To a solution of II (0.2. g; 0.01 mole) in dry toluene (30 ml) was added Ia (0.4 g; 0.001 mole). The reaction mixture was refluxed for 30 minutes. The solvent was evaporated, and the residue was applied to a column prepared by packing a slurry of silica gel (30 g) in petroleum ether (40–60 °C). Ethyl acetate-petroleum ether (2:8, v:v) eluted 2-methyl-1-phenyl-1,2-dihydro-3,6-pyridazinedithione (V) as reddish crystals (0.21 g), mp 164 °C, recrystallized from petroleum ether (60–80 °C). IR: 1230 cm^{-1} (C=S), absence of C=O band at 1640 cm^{-1} in the spectrum of compound II. MS: *m/z* 234 (M^+). ^1H-NMR: singlet at $\delta = 3.6$ (3 H, s).

Similarly compound II (0.2 g) reacted with reagent Ib (0.5 g) and/or Ic (0.4 g.) to give compound V in quantitative yield.

(b) To a suspension of compound II (0.2 g; 0.001 mole) in dry toluene (30 ml) was added reagent Ia (0.2 g; 0.0005 mole). The reaction mixture was worked up in the same way as in (a). The column was developed first with petroleum ether (40–60 °C)-ethyl acetate (9:1, v:v) which was progressively changed to 6:4, 5:5, 2:8 and finally to ethyl acetate, at 250 ml intervals. Fractions of 50 ml were collected. The first material (10 mg) eluted from the column was purified by recrystallization from petroleum ether (60–80 °C), mp 164 °C, and shown to be compound V (mixed mp with an authentic sample). The second material (80 mg) eluted proved to be VI, mp 133 °C, recrystallized from petroleum ether (60–80 °C). IR: 1220 cm^{-1} (C=S), 1632 cm^{-1}(C=O). MS: *m/z* 218 (M^+). ^1H-NMR: $\delta = 3.10$ (3 H, s). The third material (80 mg) proved to be VII, mp 193 °C, recrystallized from petroleum ether. IR:1220 cm^{-1} (C=S), 1620 cm^{-1} (C=O). MS: *m/z* 218 (M^+), *m/z* 185 (M^+-SH). ^1H-NMR: $\delta = 3.5$ (3H, s). The last compound (20 mg) eleuted proved to be compound II, mp and mixed mp 180 °C.

The reaction of compound II (0.2 g) with reagent Ib (0.25 g) in a similar procedure gave compound V (10 mg), compound VI (90 mg), compound VII (90 mg), and the starting compound II (50 mg). Similarly the reaction of compound II (0.2 g) with reagent Ic (0.2 g) gave compound V (10 mg), compound VI (70 mg), compound VII (70 mg), and unreacted II (40 mg).

Thionation of compound VI with phosphorus pentasulphide

To a solution of 0.3 g of compound VI in 20 ml of pyridine, was added 0.65 g of phosphorus pentasuliphide. The mixture was refluxed for 5–6 hours. After cooling, the reaction mixture was poured onto ice-water containing hydrochloric acid (50 ml). The solid compound was filtered off, dried, and recrystallized from petroleum ether (60–80 °C) as reddish crystals, mp 164 °C, are proved to be compound V (mp, mixed mp). The same compound V was also prepared when the reaction was repeated using compound VII instead of compound VI.

Reaction of 2-phenyl-1,2-dihydro-3,6-pyridazinedione (III) with Lawesson's reagent (Ia)

A suspension of compound III (0.188 g, 0.001 mole) in dry toluene (30 ml) was treated with reagent Ia (0.4, 0.001 mole). The reaction mixture was kept at reflux for 6–7 hours. After cooling, the solvent was evaporated under reduced pressure. The residue was separated to its components by column chromatography on silica gel using petroleum ether-ethyl acetate mixture in a suitable combination as an eluent. Petroleum ether-ethyl acetate(8:2, v:v) eluted compound VIII as red crystalline compound (150 mg), mp 212 °C, IR: 1230 cm^{-1} (C=S), MS: *m/z* = 437 (M^+-1), ion a, *m/z* = 405 (ion a-S), *m/z* = 219 (½ M^+); ^{1}H-NMR: $\delta = 7.04$ (2 H, d), $\delta = 7.15$–7.28 (10 H, m) and $\delta = 7.55$ (2 H, d).

When compound III (0.188 g, 0.001 mole) was allowed to react with Ib (0.5 g, 0.001 mole) under a similar experimental conditions, compound VIII was produced (80 mg), mp 212 °C. In addition, petroleum ether-ethyl acetate (1:1, v:v) eluted compound IX (95 mg) as a green crystalline compound, mp > 300 °C; IR: 1230 cm^{-1} (C=S). MS, *m/z* = 220 (M^+), *m/z* = 187 (M^+-SH). ^{1}H-NMR $\delta = 7.01$ (1 H, d), $\delta = 7.18$ (1 H, d), $\delta = 7.32$ (5 H, m).

In a similar procedure compound III (0.188 g, 0.001 mole) reacted with reagent Ic (0.2 g, 0.001 mole) whereby two compounds were separated from the column. The first compound eluted (petroleum ether) was a colourless crystalline compound (100 mg), melted at 93 °C and proved to have structure XII. IR: 1620 cm^{-1} (C=O). MS: *m/z*= 390 (M^+), *m/z* 281 (M^+-SC_6H_5), ion a′, *m/z* 249 (ion a -S). ^{1}H-NMR: $\delta = 7.75$–7.51 (m). ^{31}P-NMR: +93.25 ppm. The second compound [petroleum ether-ethyl acetate (8:2, v:v)] proved to be compound VIII (20 mg), mp and mixed mp 212 °C.

2-Phenyl-2,3-dihydro-1,4-phthalazinedione (IV)

To 22.2 g of phthalic anhydride (0.15 mole) in 36.5 g of HCl was added 16.2 g of phenylhydrazine (0.15 mole) in 250 ml water. The mixture was refluxed for 4 hours. After cooling to room temperature, pale yellow crystals were separated, filtered, and dried, mp 215 °C, and proved to be compound IV by comparison with authentic sample (mixed mp).[18]

Reaction of 2-phenyl-2,3-dihydro-1,4-phthalazinedione (IV) with Lawesson's reagent (1a)

A suspension of compound IV (0.238 g, 0.001 mole) in dry toluene (30 ml) was treated with Ia (0.4 g, 0.001 mole). The reaction mixture was refluxed for 2 hours. Working up the reaction mixture in the same mannar as described previously, resulted in the separation of compound XIV (200 mg), as a reddish crystalline compound, which melted at 196 °C. IR: 1250 cm^{-1} (C=S), no C=O band. MS: *m/z* = 270 (M^+), *m/z* = 237 (M^+-SH). ^{1}H-NMR : δ= 7.30 (5 H, m), $\delta = 8.05$ (4 H, m) and $\delta = 8.83$ (1 H, s).

When the same reaction was conducted with 1 mole of compound IV (0.238 g) and 0.5 mole of reagent Ia (0.2 g), two compounds were separated. The first compound eluted by n-hexane-acetone (8:2, v:v), proved to be compound XV, which was a reddish crystalline compound (50 mg) that melted at 73 °C. IR: 1250 cm^{-1} (C=S), 1640 cm^{-1} (C=O). MS: *m/z* 254 (M^+), *m/z* = 221 (M^+-SH). ^{1}H-NMR: $\delta = 6.7$ (3 H, m), $\delta = 7.18$ (2 H, t), $\delta = 7.4$ ppm (1 H, t), $\delta = 7.95$ (3 H, m) and $\delta = 8.96$ (1 H, s). The second compound eluted by chloroform proved to be compound XIV, mp and mixed mp 196 °C.

References

1. W. Hofer, F. Maurer, H. J. Riebel, L. Rohe, and R. Schroeder, Germ. Offen 2, 534, 893 (CL Co 7F 9165), 17 Feb. 1977, Appl. 05 Aug; *Chem. Abstr.*, **87**, 233139 (1977).
2. R. A. Fuchs, F. Maurer, H. J. Riebel, R. Schroeder, I. Hammonn, W. Behrenz, and B. Homeyer (Bayer A-G); Germ. Offen. 2, 537, 353 (CL CO 7F9165), 03 Mar. 1977, Appl. 21 Aug. 1975, 80 pp; *Chem. Abstr.*, **87**, 23314r (1977).
3. W. Hofer, F. Maurer, H. Riebel, I. Hammonn, and W. Stendel (Bayer A.-G), Germ. Offen 2, 531, 340 (CL Co 7F9165), 27 Jon. 1977, Appl. 12 Jul. 1975, 29 pp.; *Chem. Abstr.*, **86**, 171601b (1977).
4. K. Nitonia, T. Ito, O. Morikawa, and S. Ogawa (Mitsui Toutso Chemical, Inc) Japan, 7312, 973 (CL AO1n, CO 7d), 24 Apr. 1973, Appl. 69, 90, 464, 13 Nov. 1969, 4 pp.; *Chem. Abstr.*, **80**, 14950y (1974).
5. K. Nitonai, T. Ito, O. Morikawa, and S. Ogawa (Mitsui Toutso Chemical, Inc)Japan, 7312, 972 (CL AO1n, CO 7d), 24 Apr. 1973, Appl. 6978, 143, 02 Oct. 1969, 4 pp.; *Chem. Abstr.*, **80**, 14951z (1974).
6. W. Hofer, F. Maurer, H. J. Riebel, and W. Stendel (Bayer A.-G.), Germ. Offen 2737, 486 (CL A 61K 311675), 03 Mar. 1977, Appl., 22 Aug. 1975, 12 pp.; *Chem. Abstr.*, **87**, 233155s (1977).
7. M. Yoshihara, T. Eda, Y. Matsubara and T. Maeshima, *Nippon Kagaka Kaishi* (4), 720–3 (1975); *Chem. Abstr.*, **83**, 43857 (1975).
8. D. C. Allport, Brit. 1, 061, 844 (CL CO 8F), March 15, 1967, Appl. Feb. 19, 1965, 5 pp.; *Chem. Abstr.*, **66**, 116270e (1967).
9. R. Ozegawski and H. Dorn (Akademie der Wessenchaften der DDR), Germ. (East), DD 247, 218 (CL CO 7D237116), 01 Jul. 1987, Appl. 287, 920, 14 Mar. 1988, 6 pp.; *Chem. Abstr.*, **109**, 6532r (1988).
10. Ihara Chemical Industry Co., Ltd, Jpn Kokai Tokyo Koho 80, 89, 205 (CL AO1N 43/58), 05 Jul. 1980, Appl. 78 / 163, 420, 28 Dec. 1978, 4 pp.; *Chem. Abstr.*, **93**, 182042d (1980).
11. A. A. Nada, N. Khir El-Din, S. T. Gaballa and M.F. Zayed, *Phosphorus, Sulfur and Silicon*, **119**, 27 (1996).
12. B. S. Pederson, S. Scheibye, N. H. Nilsson, and S.O. Lawesson, *Bull. Soc. Chim. Belg.*, **87**, 223 (1978).
13. M. Yokoyama, Y. Haregawa, H. Hatanaka, Y. Kawazoe, and T. Imamoto, *Synthesis*, **827** (1984).
14. M. P. Cova, M. I. Levinsan, *Tetrahedron*, **41**, 5061 (1985).
15. A. A. El-Barbary, S. Scheibye, S.O. Lawesson, and M. Fritz, *Acta Chem. Scand.* B **34**, 597 (1980).
16. M. M. Crutchfield, C. H. Dungan, J.H. Letcher, V. Mark, and J. R. Van Wazer, "Topics in Phosphorus Chemistry", Interscience, New York, 1967, Vol. 5, p. 372.
17. T. S. Hafez, Y. O. El-Khoshnieh, and M. R. Mahran, *Phosphorus, Sulfur and Silicon*, **56**, 165 (1991).
18. J. Durrey, Kd. Meier, and A. Staehelin, *Helvetica Chimica Acta*, **62**, 1485 (1962).