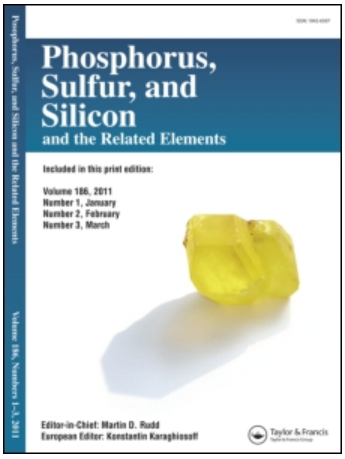

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THE BEHAVIOR OF TERTIARY PHOSPHITE ESTERS TOWARDS 1,2-DIHYDRO-3,6-PYRIDAZINEDIONES AND 2,3-DIHYDRO-1,4-PHTHALAZINEDIONES

A. A. Nada[a]; N. Khir El-din[a]; S. T. Gaballah[a]; M. F. Zayed[a]
[a] National Research Centre, Cairo, Egypt

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THE BEHAVIOR OF TERTIARY PHOSPHITE ESTERS TOWARDS 1,2-DIHYDRO-3,6-PYRIDAZINEDIONES AND 2,3-DIHYDRO-1,4-PHTHALAZINEDIONES

A. A. NADA, N. KHIR EL-DIN, S.T. GABALLAH and M.F. ZAYED*

National Research Centre, Dokki, Cairo, Egypt

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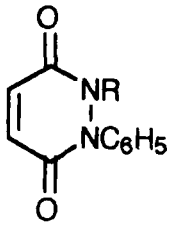
2-Methyl-1-phenyl-1,2-dihydro-3,6-pyridazinedione (Ia) reacts with trialkyl phosphites (III) in the absence of solvent to give compounds IVa,b. 1-Phenyl-1,2-dihydro-3,6-pyridazinedione (Ib) reacts with III in the abscence of solvent whereby alkylation products VIIa,b are formed. Alkylation products IXa,b and Xa–c are similarly formed upon reacting 2,3-dihydro-1,4-phthalazinediones IIa,b with the same phosphite ester under the same experimental conditions.

Keywords: Pyridazinediones (I); phthalazinediones (II); trialkylphosphites (III); phosphonates (IV); pyridazinones (VII); phthalazinones (IX; X); alkylation

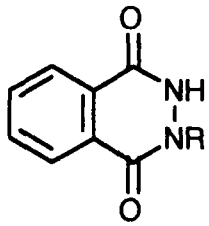
INTRODUCTION

In view of the potential utility of 1,2-dihydro-3,6-pyridazinediones in the synthesis of pesticides[1–5], we have investigated the behavior of 2-methyl-1-phenyl-1,2-dihydro-3,6-pyridazinedione (Ia) and 1-phenyl-1,2-dihydro-3,6-pyridazinedione (Ib) towards alkyl phosphites. The study was further extended to include 2-phenyl-2,3-dihydro-1,4-phthalazinedione (IIa) and 2,3-dihydro-1,4-phthalazinedione (IIb). No work on compounds I and II has hitherto been performed.

*Corresponding author.



I a, R = CH_3
b, R = H



II a, R = C_6H_5
b, R = H

RESULTS AND DISCUSSIONS

We have found that compound Ia did not react with trimethyl phosphite (IIIa) or triethylphosphite (IIIb) in boiling benzene, methylene chloride or acetonitrile. In the absence of solvent, however these phosphite reagents react with compound Ia at 90 °C to produce the colorless crystalline compounds formulated as IV.

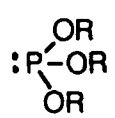
Structure elucidation for compound IVa, for example, was accomplished with the following evidence:

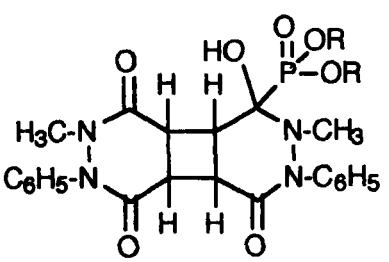
(a)- The ^{31}P NMR spectrum of compound IVa has a signal at δ = 20 which corresponds to phosphonate structure[6,7].

(b)- The MS of this adduct showed ion peaks at m/z = 514 [M^+], 423 [$M^+ - NC_6H_5$], 313 [M^+ − Ia] and 91 [NC6H5]$^+$.

(c)- The IR spectrum, in KBr, revealed the presence of bands at 1680 cm^{-1} (C═O), 1250 cm^{-1} (P═O) and at 1020 cm^{-1} (P-OCH_3).

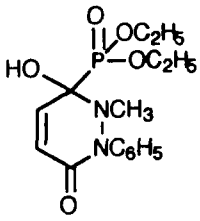
(d)- The 1H-NMR spectrum showed a multiplet at δ = 3.45–3.95 due to the 4 protons of the cyclobutane ring. The spectrum disclosed the presence of 2 doublets centered at δ = 3.15 and = 3.01 (J = 10 Hz)[8], indicating that the



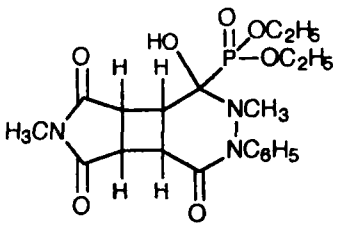


IIIa, R = CH_3
b, R = C_2H_5

IVa, R = CH_3
b, R = C_2H_5



V

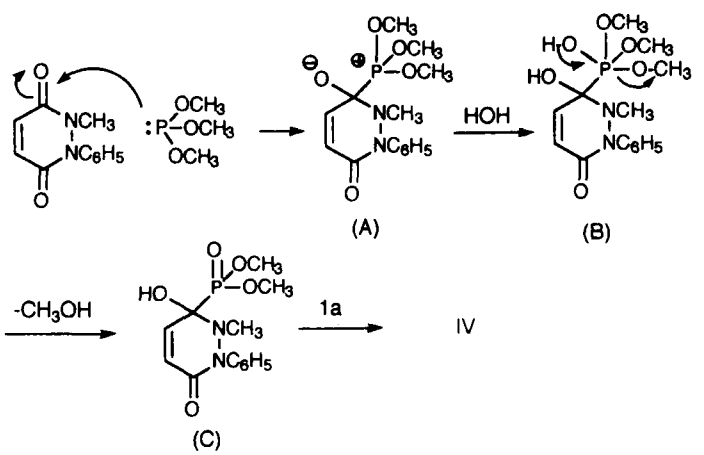


VI

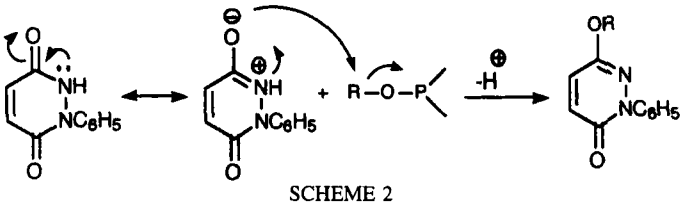
phosphorus is attached to a chiral carbon and thus the methyls are diastereriotopic, whereas the two NCH_3 groups appeared as 2 singlets at δ = 3.05 and 3.03. The aromatic protons appeared as a multiplet centered at δ = 7.45 (10H).

A possible explanation for the course of the reaction of trimethyl phosphite with compound Ia is shown in "Scheme 1". This involves a nucleophilic attack of the phosphorus of trimethyl phosphite on the carbonyl carbon of compound Ia yielding the dipolar intermediate (A)[9,10]. Addition of the elements of water, which is unavoidably present in the medium, to (A) produces a transient intermediate (B) with pentacovalent phosphorus[11]. The latter then collapses to produce (C). The formation of compound 4a is effected by a mechanism including species (C) and compound 1a. Thermal dimerization of pyridazine derivatives through the formation of a cyclobutane ring was formerly reported[12,13].

The IR, ^{31}P and ^{1}H NMR spectra of compound IVb have assignments analogous to that of compound IVa. However, the GC/MS of this compound exhibited two distinct peaks corresponding to structure V and VI.



SCHEME 1



SCHEME 2

The first (V) has an ion peak at m/z = 341 [M^+ + 1], 25% and fragment ion at m/z = 204 [M^+ − O═P(OC_2H_5)$_2$]. The second (VI) has an ion peak at m/z = 451 [M^+], 75% and fragment at m/z 313 [M^+ − O═P(OC_2H_5)$_2$]. It seems reasonable that compound IVb is decomposed in the GC part of the experiment to species V and VI.

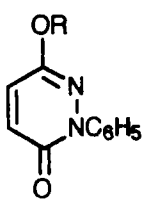
Next, we have investigated the behavior of 2-phenyl-1,2-dihydro-3,6-pyridazinedione (Ib) towards trialkyl phosphites. The alkyl derivatives VIIa and VIIb were the main reaction products produced when compound Ib was allowed to react with trimethyl and/or triethyl phosphites, respectively. Compounds VI-Ia,b were formed in relatively low yields when dialkyl phosphites VIIIa,b were used instead of trialkyl phosphites.

The reaction may be viewed as occurring via the attack of the oxygen atom of the pyridazinone on the alkyl group of the phosphite reagent as depicted in "Scheme 2".

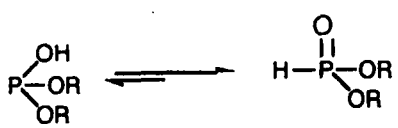
In a similar manner, trialkyl- and/or dialkyl phosphites effected O-alkylation of 2-phenyl-2,3-dihydro-1,4-phthalazinedione (IIa) whereby compounds IXa and IXb were formed, respectively.

On the other hand, trialkyl and/or dialkyl phosphites effected both O- and N-alkylation when allowed to react with 2,3-dihydro-1,4-phthalazinedione (IIb) under the same experimental conditions with the formation of compounds Xa and Xb. Compound Xc was also produced in case of triethyl phosphite.

The identity of compounds VII, IX and X were verified by spectroscopic tools (cf. Experimental).



VII a, R = CH_3
b, R = C_2H_5



VII a, R = CH_3
b, R = C_2H_5

The relatively low yield of compounds VII, IX and X produced when dialkyl phosphites were utilized is in accordance with that reported about the lower alkylation power of these reagents in comparison with trialkyl phosphites.[14]

EXPERIMENTAL

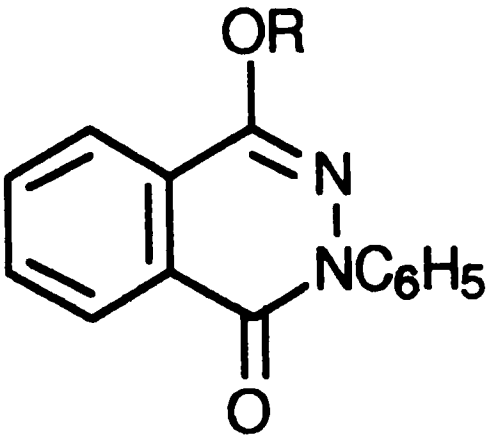
All melting points were uncorrected. The appropriate precautions in handling moisture-sensitive compounds were taken. Trialkyl phosphites[15] were purified by treatment with sodium followed by fractional distillation. Dialky phosphites[16,17] were freshly distilled. Pyridazinediones (Ia,b)[18] and phthalazinediones[18] were prepared by established procedures.

The IR spectra were run on a Zeiss infrared-spectrophotometer IMR 16. The ^{1}H-NMR spectra were recorded on a JEOL JNM-EX 270 FT NMR system, and a Bruker Spectrometer Model 250 and the chemical shifts are recorded in δ (ppm) relative to TMS. The ^{31}P NMR spectra were taken on a Varian CET-20 (vs 85% H_3PO_4). The mass spectra were performed at 70 eV on a Shimadzu-GC/MS-QP 1000 EX spectrometer. The microanalysis for compounds IV, VII, IX and X were in good agreement with the calculated values (C, H ± 0.1; N ± 0.05).

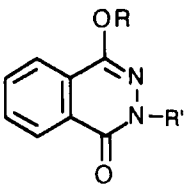
Reaction of Trialkyl Phosphites with 1-Methyl-2-Phenyl-1,2-Dihydro-3,6-Pyridazinedione (Ia)

A suspension of 0.4 g of compound Ia in trimethyl phosphite (3 ml) was heated on a steam bath for 10 hours. After cooling, the excess unreacted trimethyl phosphite was removed under reduced pressure. The oil that was left behind was triturated with petroleun ether whereby a solid compound was separated, filtered off, washed with petroleun ether and recrystallized from chloroform-cyclohexane to give dimethyl (2,5-dimethyl-1,6-diphenyl-3-hydroxy-4,7,8-trioxo-perhydropyridazino-[4′,5′:3,4]-cyclo-buta[1,2-d]pyridazin-3-yl]phosphonate (IVa) as colorless crystals, m.p. 210 °C (dec.).

Similarly, a suspension of 0.4 g of Ia and triethyl phosphite (3 ml) react under the same experimental conditions whereby diethyl (2,5-dimethyl-1,6-diphenyl-3-hydroxy-4,7,8-trioxo-perhydropyridazino[4′,5′:3,4]-cyclobuta[1,2-d]pyridazin-3-yl)-phosphonate IVb was separated as colorless crystals, m.p. 135 °C (dec.). IR: 1255 cm^{-1} (P═O), 1030 cm^{-1} (P-O-C) and 1675 cm^{-1} (C═O). ^{31}P NMR: δ 21.4.



IX a, R = CH_3
b, R = C_2H_5



X a, R = R' = CH_3
b, R = R' = C_2H_5
c, R = C_2H_5; R' = H

Reaction of Trialkyl Phosphites with 2-Phenyl-1,2-Dihydro-3,6-Pyridazinedione (Ib)

A mixture of 0.36 g of compound Ib and trimethyl phosphite (3 ml) was heated for 14 hours on a steam bath. After cooling to room temperature, the excess phosphite ester was removed under reduced pressure. The residue was applied to a silica gel column. Benzene-ethyl acetate (8:2, v/v) eluted 3-methoxy-1-phenyl-6(1H)-pyridazinone (VIIa) as colorless crystals, m.p. 72 °C, yield 90%. IR: 1679 cm^{-1} (C═O). MS: m/z = 202 [M^+]. ^1H NMR: δ 3.85 (OCH_3, s), 7.02 (2H, d. of doublet due to the olefinic protons), 7.35 (1H, m), 7.45 (2H, m), 7.67 (2H, m) for 5 aromatic protons.

Similarly, compound Ib (0.36 g) reacted with triethyl phosphite (3 ml). The reaction mixture was worked up as above. Petroleum ether-ethyl acetate (6:4, v/v) eluted 3-ethoxy-1-phenyl-6(1H)-pyridazinone (VIIb) as colorless crystals,

m.p. 88 °C, yield 85%. IR: 1677 cm^{-1} (C═O). MS: m/z = 216 [M^+]. ^1H NMR: δ 1.35 (CH_3, t), 4.2 (CH_2, q) for ethoxy group, 7.02 (d. of doublet due to the olefinic protons), 7.34 (1H, m), 7.44 (2H, m) and 7.66 (2H, m) for 5 aromatic protons.

Compounds VIIa (yield 10%) and VIIb (yield 15%) were also produced when dimethyl and/or diethyl phosphites were used instead of trialkyl phosphites.

Reaction of Trialkyl Phosphites with 2-Phenyl-2,3-Dihydro-1,4-Phthalazinedione (IIa)

A mixture of 0.48 g of compound IIa and trimethyl phosphite (3 ml) was heated for 6 hours on a steam bath. The reaction mixture was worked up in the same manner as described above. Benzene-ethyl acetate (8:2, v/v) eluted 4-methoxy-2-phenyl-1(2H)-phthalazinone (IXa) as a white crystalline solid, m.p. 125 °C, yield 70%. IR: 1632 cm^{-1} (C═O). MS: m/z = 252 [M^+]. ^1H NMR: δ 3.3 (OCH_3, s), 7.35 (5H, m), 7.78 (2H, m) and 8.35 (2H, m) for aromatic protons.

Similarly, compound IIa (0.48 g) reacted with triethyl phosphite (3 ml) under the same experimental conditions and the mixture was worked up in a similar manner. Petroleum ether-ethyl acetate (7:3, v/v) eluted 4-ethoxy-2-phenyl-1(2H)-phthalazinone (IXb) as white crystals, m.p. 98 °C, yield 75%. IR: 1657 cm^{-1} (C═O). MS: m/z = 266 [M^+]. ^1H NMR: δ 1.43 (CH_3, t), 4.38 (CH_2, q) for ethoxy group, 7.33 (1H, t), 7.46 (2H, t), 7.76 (4H, m), 8.03 (1H, m) and 8.46 ppm (1H, m) for aromatic protons.

Compounds IXa (yield 10%) and IXb (yield 10%) were also produced when dimethyl and/or diethyl phosphite were used instead of trialkyl phosphites.

Reaction of Trialkyl Phosphites with 2,3-dihydro-1,4-phthalazinedione (IIb)

A mixture of 0.33 g of compound IIb and trimethyl phosphite (3 ml) and triethylamine (0.2 g/0.2 mol) was heated at 120–130 °C for 11–13 hours (oil bath). The reaction mixture was worked up in a similar manner as described above. Petroleum ether-ethyl acetate (7:3, v/v) eluted 2-methyl-4-methoxy-1(2H)phthalazinone (Xa) as a white crystals, m.p. 98°C, yield 80%. IR: 1645 cm^{-1} (C═O). MS: m/z = 190 [M^+]. ^1H NMR: δ 3.37 (N-CH_3, s), 3.97 (OCH_3, s), 7.75 (2H, m), 7.94 (1H, m) and 8.37 ppm (1H, m) for aromatic protons.

Similarly, triethyl phosphite reacted with compound IIb in the presence of triethylamine. The work up of the mixture separated two compounds. Petroleum ether-ethyl acetate (7:3, v/v) eluted 2-ethyl-4-ethoxy-1(2H)-phthalazinone (Xb)

as colorless crystals, m.p. 81 °C, yield 60%. IR: 1651 cm^{-1} (C═O).MS: m/z = 218 [M^+]. ^1H NMR: δ 1.3 (CH_3, t), 1.45 (CH_3, t), 4.18 (CH_2, q), 4.36 (CH_2, q), for the two ethoxy groups, 7.86 (2H, m), 7.97 (1H, m) and 8.28 ppm (1H, m) for aromatic protons. Petroleum ether-ethyl acetate (6:4, v/v) eluted 4-ethoxy-1(2H)-phthalazinone (Xc) as colorless crystals, m.p. 208 C, yield 30%. IR: 1645 cm^{-1} (C═O) and 3142 cm^{-1} (OH). MS: m/z 190 [M+]. ^1H NMR: δ 1.5 (CH_3, t), 4.38 (CH_2, q), for the ethoxy group, 7.9 (2H, m), 8.00 (1H, m) and 8.2 (1H, m) for aromatic protons, 10.22 ppm (OH, s).

Compounds Xa (30% yield) and Xb (30% yield) were produced when dimethyl and/or diethyl phosphites were used instead of trialkyl phosphites.

Acknowledgment

Dedicated to Professor H.D. Scharf on the occasion of his 65th birthday.

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