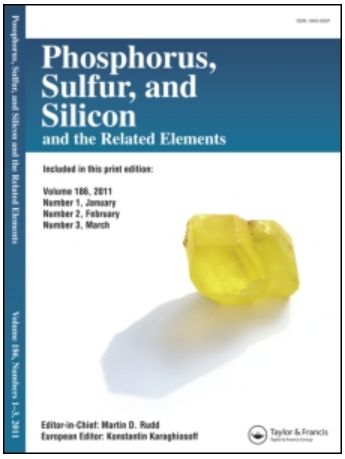

Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

STUDIES ON ORGANOPHOSPHORUS COMPOUNDS REACTIONS OF 1,3,2,4-DITHIADIPHOSPHETANE-2,4-DISULFIDES AND ALKYL PHOSPHITES WITH COUMARIN DERIVATIVES

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To cite this Article Fahmy, A. A. , Hafez, T. S. , El-farargy, A. F. and Hamad, M. M.(1991) 'STUDIES ON ORGANOPHOSPHORUS COMPOUNDS REACTIONS OF 1,3,2,4-DITHIADIPHOSPHETANE-2,4-DISULFIDES AND ALKYL PHOSPHITES WITH COUMARIN DERIVATIVES', Phosphorus, Sulfur, and Silicon and the Related Elements, 57: 3, 211 — 215
To link to this Article: DOI: 10.1080/10426509108038852
URL: http://dx.doi.org/10.1080/10426509108038852

Phosphorus, Sulfur, and Silicon, 1991, Vol. 57, pp. 211–215
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STUDIES ON ORGANOPHOSPHORUS COMPOUNDS REACTIONS OF 1,3,2,4-DITHIADIPHOSPHETANE-2,4-DISULFIDES AND ALKYL PHOSPHITES WITH COUMARIN DERIVATIVES

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(Received June 11, 1990; in final form August 30, 1990)

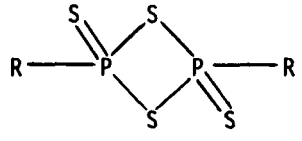
1,3,2,4-Dithiadiphosphetane-2,4-disulfides, $\mathbf{I_a}$ and $\mathbf{I_b}$ react with coumarin **II** and 4-hydroxy coumarin **III** to give thiocoumarin compounds **V** and **VI** respectively. But $\mathbf{I_a}$ and $\mathbf{I_b}$ react with 3-acetyl coumarin **IV** to give cyclic compounds $\mathbf{VII_a}$ and $\mathbf{VII_b}$ respectively. **IV** reacts also with alkyl phosphites $\mathbf{VIII_{a,b}}$ and $\mathbf{IX_{a,b}}$ to give $\mathbf{X_a}$ and $\mathbf{X_b}$ respectively. The given structures were based upon analytical, chemical and spectroscopic results.

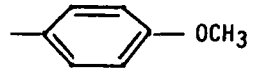
Key words: 1,3,2,4-Dithiadiphosphetane; 2,4-disulfides; alkyl phosphites; 4-hydroxy coumarin; 3-acetyl coumarin.

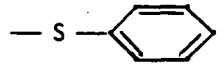
INTRODUCTION

Coumarin itself, has very little physiological action upon human being. Derivatives of coumarin are more important as chemotherapeutic agents.[1] Therefore, we have endeavoured the synthesis of some new coumarin derivatives for their expected biological evaluation.[2,3,4]

It is widely realized that 2,4-bis(4-methoxyphenyl)-1,3,2,4-dithiadiphosphetane, LR (Lawesson reagent), $\mathbf{I_a}$ and 2,4-bis(thiophenol)-1,3,2,4-dithiadiphosphetane, 2,4-disulfide, JR (Japaness reagent), $\mathbf{I_b}$ are potent thiating agents for diverse carbonyl compounds e.g., ketones,[5] esters[6] and lactans.[7]



$\mathbf{I_a}$, R = 

$\mathbf{I_b}$, R = 

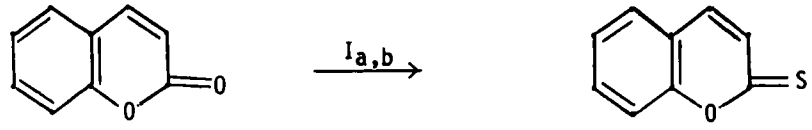
The reagents $\mathbf{I_a}$ and $\mathbf{I_b}$ are easily available and undergo also ring-closure reactions with substrates containing two functional groups.[8,9,10]

We report in this paper the reaction of coumarin **II**, 4-hydroxy coumarin **III** and

3-acetyl coumarin **IV**, with I_a and I_b, in addition to the reaction of di- and trialkyl phosphites on **IV**.

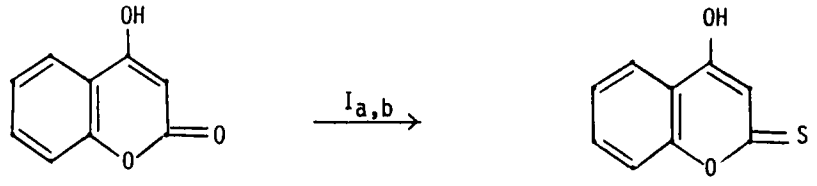
RESULTS AND DISCUSSIONS

We have found that the reaction of I_a and I_b with coumarin **II** in boiling dry toluene gave chromatography pure product encorporating sulfur (elemental analyses). The obtained product was superimposable with 2-thiocoumarin **VII** (m.p. and mixed m.p. 101°C).



III V

The reaction of I_a (or I_b) with 4-hydroxy coumarin **IV** proceeds in boiling dry toluene to give 2-thio-4-hydroxy coumarin **VI** which was confirmed by elemental analyses (Table I), molecular weight determination MS, IR and ^{1}H-NMR spectra.



III VI

IR spectrum lacked to C=O group absorption, in the same time it revealed the presence of absorption bands at 3000 cm^{-1} (OH) and at 1240 cm^{-1} (C=S). The NMR spectrum of VI (in $CDCl_3$) showed signal at δ 12 ppm due to the —OH

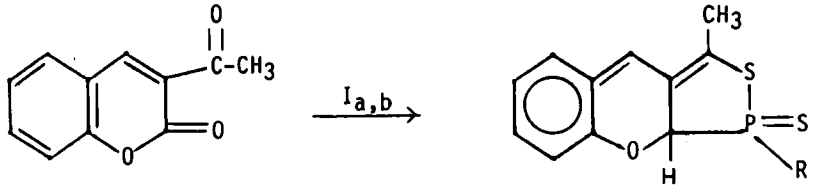
TABLE I

Physical constants of analytical data of new compounds

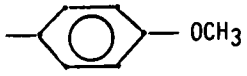
Compound	M.P. °C	Solvent of crystallization	Yield %	Formula mol. wt.	Analysis calc./found C	H	S	P
VI	180	Ethyl acetate	85	$C_9H_6So_2$ (178)	60.67 60.70	3.37 3.38	17.98 17.95	— —
VII$_a$	144	Toluene	60	$C_{18}H_{16}S_2PO_2$ (359)	60.72 60.43	4.45 4.29	17.82 17.81	8.63 8.38
VII$_b$	150	Toluene	65	$C_{17}H_{14}S_3PO$ (361)	56.51 56.90	3.85 3.76	26.59 26.75	8.58 8.29
X$_a$	125	Ethanol	80	$C_{13}H_{15}PO_6$ (298)	52.35 52.33	5.03 5.02	— —	10.40 10.42
X$_b$	139	Ethanol	75	$C_{15}H_{19}PO_6$ (326)	55.22 55.24	5.83 5.85	— —	9.51 9.50

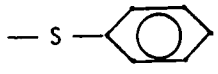
proton which disappeared when deuterated, showed multiplet at δ 6.9–7.7 ppm (5H) due to the aromatic protons. The mass spectra showed a molecular ion peak at 178.

But we have found that the reaction of $\mathbf{I_a}$ and $\mathbf{I_b}$ with 3-acetyl coumarin IV proceeds in boiling dry toluene to give cyclic structures $\mathbf{VII_a}$ and $\mathbf{VII_b}$[7,10] respectively.

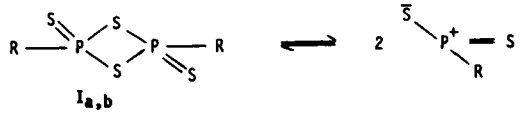


IV VII

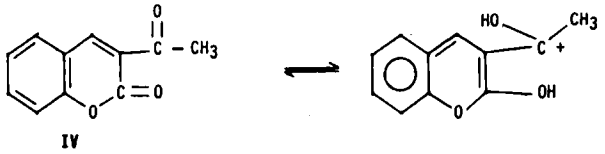
$\mathbf{VII_a}$, R = 

b, R = 

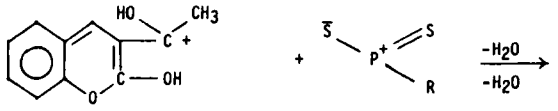
A possible explanation of the reaction of $\mathbf{I_{a,b}}$ with **IV** is illustrated in "Scheme A."

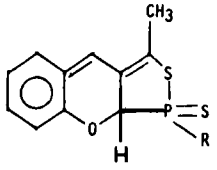


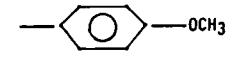
$\mathbf{I_{a,b}}$

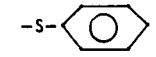


IV





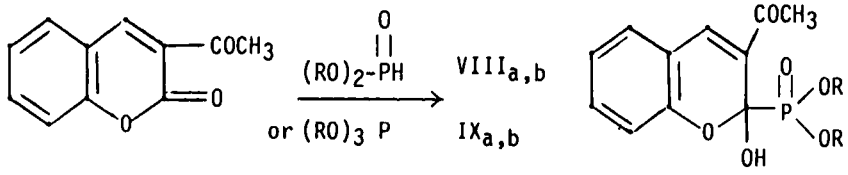
$\mathbf{VII_a}$, R = 

b, R = 

" Scheme A "

The structures of aforementioned compounds were confirmed by elemental analyses (Table I), molecular weight determination (MS), IR, ^{1}H-NMR and ^{31}P-NMR, taking **VII$_a$** as example, its elemental analyses corresponded to $C_{18}H_{16}S_2PO_2$, IR spectrum lacked the C=O group absorption which is recorded in the spectra of 3-acetyl coumarin **IV** at (1730 cm^{-1}), the spectrum however showed strong absorption bands in the region 1600–1500 cm^{-1} due to aromatic C=C stretching vibrations and showed absorption band at 650 cm^{-1} due to $\overset{S}{\diagdown}P{=}S$, the NMR spectrum of **VII$_a$** showed signals at δ 3.9 ppm (3H, OCH_3, singlet) and at δ 2.5 ppm (3H, CH_3, singlet). The aromatic protons gave multiplet at δ 6.9–7.7 ppm region (10 H, multiplet), in ^{31}P-NMR spectrum there is a singlet at 39.8 ppm, the MS spectrum showed m/e 359 (M^+).

The work of coumarin derivatives was extended to include also the reaction of 3-acetyl coumarin **IV** with di- and tri-methyl phosphites, DMP, **VIII$_a$** and TMP, **VIII$_b$** respectively together with di- and triethyl phosphites, DEP **IX$_a$** and TEP, **IX$_b$** respectively.



IV X

VIII$_a$,= R=CH_3
b, R=C_2H_5

IX$_a$, R=CH_3
b, R=C_2H_5

X$_a$, R=CH_3
b, R=C_2H_5

We have found that **IV** reacts with DMP **VIII$_a$** and TMP **IX$_a$**, in absence of solvents at 100°C to give structure of compound **X$_a$**. Also, **IV** reacts with DEP **VIII$_b$** and TEP **IX$_b$** at the same conditions to give structure **X$_b$**. The structures of aforementioned compounds were confirmed by elemental analyses (Table I) molecular weight determination MS, IR and ^{1}H-NMR spectra. Taking **X$_b$** as example, its IR spectrum was identical to the proposed structure, revealed the presence of strong absorption bands at 1660 cm^{-1} (C=O, acetyl), 1250 cm^{-1} (P=O),[12] 1060 cm^{-1} (P—O—C_2H_5) and 3000 cm^{-1} (OH), the NMR spectrum of **X$_b$** (in $CDCl_3$) showed signals at δ 4.01 ppm (4H, ethoxy —CH_2, q), at δ 1.20 ppm (6H ethoxy —CH_3, t), δ 2.5 ppm (3H, $COCH_3$, s) and the aromatic protons gave multiplet at δ 7.0–7.5 ppm region (5H, multiplet) and δ 11.5 ppm due to the —OH proton which disappeared when deuterated, its MS spectrum showed m/e 298 (M^+).

Compound **X$_a$**, **X$_b$** dissolve freely in dilute aqueous alkali and respond positively to the alcoholic $FeCl_3$ reagent.

EXPERIMENTAL

All melting points were uncorrected. Toluene was dried over sodium. The reagents $\mathbf{I_a}$ and $\mathbf{I_b}$ were prepared according to established procedure.[13-15] Dialkyl phosphites,[16] and trialkyl phosphites[17] were prepared according to established procedures and twice distilled before use.

The IR spectrum (run in KBr and expressed in cm^{-1}) were recorded with Beckman infracord Model 4220 and the ^{1}H-NMR spectra were measured in $CDCl_3$ or DMSO-d_6 and expressed in δ scale at 60 MHz or 90 MHz on a Varian instrument using TMS as an internal standard. The mass spectra were performed at 70 eV using avarian MAT 112 Mass spectrometer.

General procedure for the reactions **II, III** *and* **IV** with $\mathbf{I_a}$ *and* $\mathbf{I_b}$. 0.01 mole of the starting compound and 0.01 mole $\mathbf{I_a}$ (or $\mathbf{I_b}$) was refluxed in 10 ml of anhydrous toluene at 110°C with stirring until no more of the starting material could be detected (TLC). After cooling to room temperature the excess of $\mathbf{I_a}$ (or $\mathbf{I_b}$) was filtered off. Then the reaction mixture was evaporated on silica gel column using ether/light petroleum as eluant. The physical data are summarized in Table I.

General procedure for the reactions of 3-Acetyl coumarin **IV** *with* $\mathbf{VIII_{a,b}}$ *and* $\mathbf{IX_{a,b}}$. A mixture of **IV** (0.005 mol) and alkyl phosphite (0.05 mol) was heated at 100°C for 8 hrs. After removal of the volatile materials in vacuo, the residual substance was collected and recrystallized from the proper solvent to give the adduct, dimethyl (3-acetyl-2-hydroxy-2H-benzopyran-2-yl) phosphonate $\mathbf{X_b}$.

Degradation experiments of $\mathbf{X_a}$.

a) **Thermolysis:** Compound $\mathbf{X_a}$, taken as example (0.2 g) was heated at 200°C (bath temp.) for 30 minutes. The residue was extracted with hot ethanol. After cooling, the ethanol deposited a white crystalline substance which was identified as 3-acetyl coumarin **IV** (m.p. and mixed m.p.).

b) **Action of hydrochloric acid:** Compound $\mathbf{X_a}$ was refluxed with alcoholic hydrochloric acid (5 ml of hydrochloric acid sp.gr. 1.18 and 15 ml ethanol) for 6 hrs. The reaction mixture was cooled and the precipitate was separated after neutralization with sodium bicarbonate, it was collected and crystallized from pet. ether to give 3-acetyl coumarin (**IV**) (m.p. and mixed m.p.).

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