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General Approach for Regioselective Synthesis of Fused Phosphono Substituted-Oxadiazines

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ABSTRACT: *A series of fused 1,3,4-oxadiazines were regioselectively prepared in reasonable yields as major products from the reactions of the corresponding α-carbonyl hydrazones with tetraethyl 1,3-dithietane-2,4-diylidene-bis(cyanomethylphosphonate)* (**1**). *Side products were also observed wherein the dimeric products* **8** *or* **17** *and/or different types of N-heterocycles such as pyrazole* **24** *or pyridazines* **28** *or* **29** *were isolated and identified. A comparative study on the chemistry of* **1** *toward α-aminonitrile* **30** *is also described.* © 2000 John Wiley & Sons, Inc. Heteroatom Chem 11:196–204, 2000

INTRODUCTION

Diverse biological/pharmacological activities have been reported for diazines and their related compounds. For instance, many pyridazines are in clinical use [1, 2], while many thiadiazines exhibit antiprotozoal, antiviral, bactericidal, and fungicidal properties [3, 4], probably by virtue of the presence of the toxopheric (-N=C–S) grouping. The oxygen analog, namely oxadiazines, on the other hand, are very few in the published literature [5]. That is the reason why the research on new oxadiazine derivatives has been stimulated during the last two decades. The synthesis of phosphono substituted-oxadiazines, which are practically unknown, should be of great interest, because organophosphorus compounds often possess antibiotic, antineoplastic, antibacterial, or antiviral attributes [6]. In connection with a previous communication [7], we report on the reactions of tetraethyl 1,3-dithietane-2,4-diylidene-*bis*(cyanomethylphosphonate) (**1**), easily obtained (in high yield, ca. 70%) by the method developed by Neidlein and Eichinger [8], with several substituted-α-carbonylmonohydrazones, yielding mainly fused oxadiazines. The investigation was extended to the chemistry of the same reagent **1** toward anthranilonitrile **30** to study the influence of replacement of the hydroxyl group with a nitrile moiety. The reactions studied and the products obtained are depicted in Schemes 2–7.

The reaction of phosphono substituted-1,3-dithietane **1** with hydrazones would be expected to be parallel to the reactions of 1,3-dithietane **2** with H-nucleophiles, for example, to methylene- or amino-species. In this case, according to the Peseke [9] and Neidlein [10–12] mechanisms (Scheme 1), the first formed addition product **5** and/or **6** is either stable or undergoes further transformations. Indeed, adducts from hydrazones and **1** fall within this latter group and the mode of transformation depends on the nature of the substrates.

RESULTS AND DISCUSSION

An ethyl alcohol solution of oxindole-3-hydrazone (**7**) (also known as isatin-3-hydrazone and indolin-2-one-3-hydrazone) and a half equivalent of 1,3-dithietane **1** was heated under reflux for 6 hours. The light brown material that precipitated was collected and

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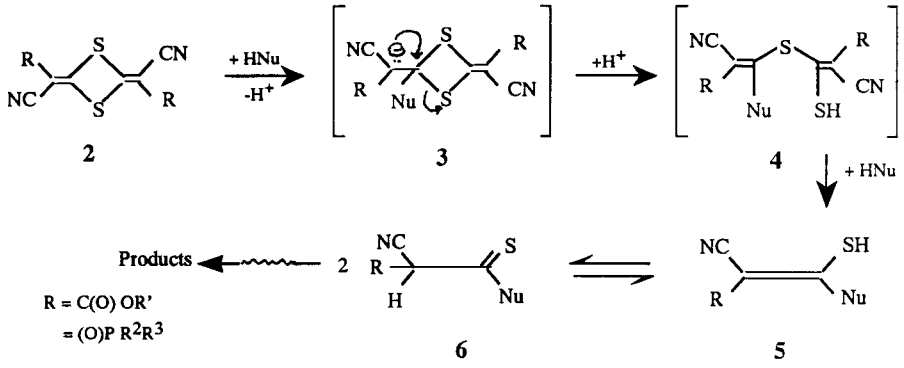
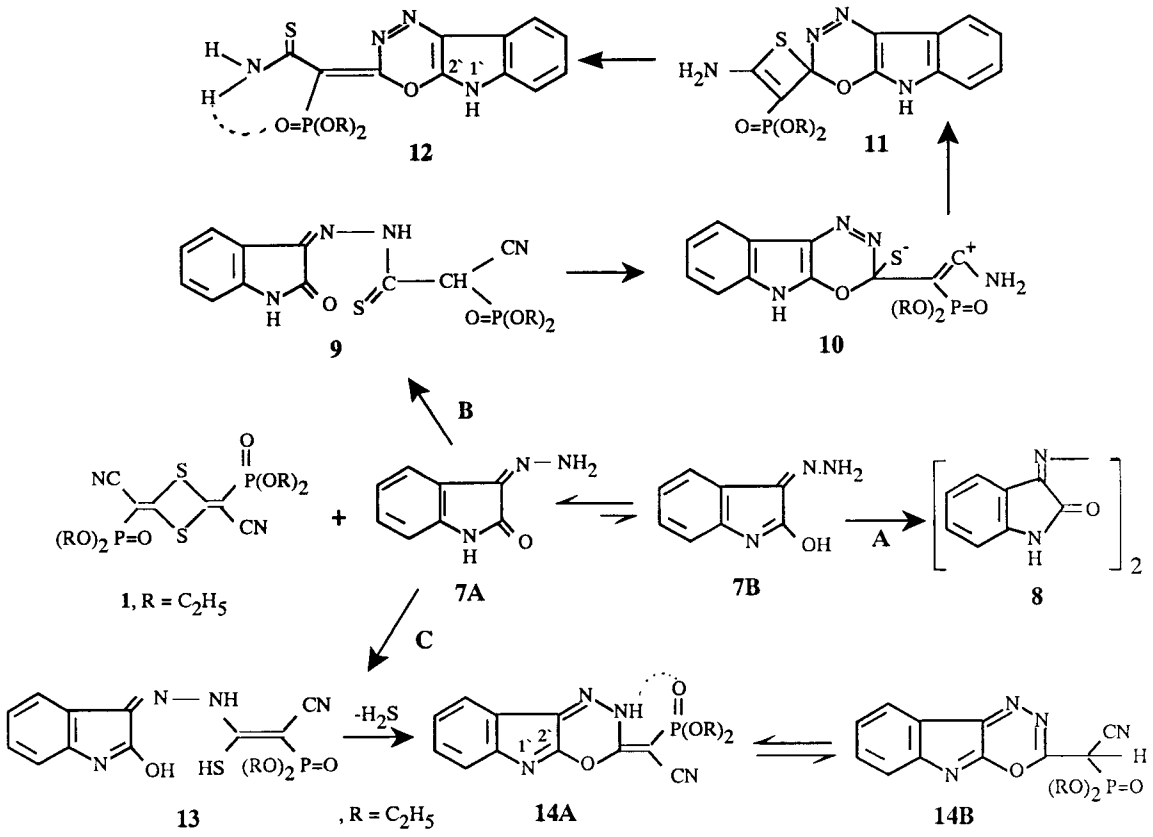
identified as oxindole azine (**8**) (13%). For the known azine **8**, its properties agreed with those reported in the literature [13]. Direct disproportionation of hydrazones to azines through the Wolff-Kishner reaction is well documented [13, 14] (Scheme 2, A).

Subjection of the filtrate to column chromatography afforded the phosphono substituted-oxadiazines **12** and **14**, respectively (Scheme 2).

Diethyl 2-thiocarbamoyl(2′,3′-dihydroindole) [3′,2′-*b*](1,3,4-oxadiazin-2-ylidene) methylphosphonate (**12**) was obtained as the main product (in 37% yield). Its mass spectrum displayed a molecular ion peak at *m/z* (%) 380 (18) [M^+], and related peaks at 347 (25) [M^+-33, −SH], 321 (20) [M^+ −59, HNCS] and at 276 (100) [(M^+ −59) −45, $-C_2H_5O$]. The ^{31}P-NMR ($CDCl_3$) spectrum showed a sharp signal at δp = 15.4 ppm [12]. The ^{1}H-NMR spectrum (270 MHz) of **12** revealed three types of NH- protons with different chemical shifts at δ_H 9.55, 10.53, and 11.13 ppm based upon intramolecular hydrogen



SCHEME 1



SCHEME 2

bond formation between one of the hydrogens of the NH_2-group and the oxygen atom of the P=O bonding in the phosphonate group [10]. The spectrum also showed signals at δ 1.21 (d of t, J_{HH} = 7.1, J_{HP} = 2.6 Hz, 6H, C-**C**H_3), 4.25 (d of q, J_{HH} = 7.1, J_{HP} = 3.4 Hz, 4H, O-**C**H_2). The ^{13}C-NMR spectrum of **12** exhibited a doublet ($^1J_{cp}$ = 210 Hz) at δc 78.8 ppm, which was attributed to the unsaturated carbon bearing no hydrogens and conjugated to phosphorus as indicated from the large coupling constant. Signals at δc 17.3 (d, C-**C**H_3), 59.6 (d, O**C**H_2) and 194.5 (**C**=S) were also observed among others.

Diethyl 1′,2′-dihydroindole[3′,2′-*b*](1,3,4-oxadiazin-2-ylidene)cyanomethylphosphonate (**14**) (13%) was found to be present in two different tautomeric structures **14A** and **14B** as indicated by the NMR spectra. The ^{1}H-NMR spectrum of **14** ($CDCl_3$, δ) showed the exocyclic methine proton (**14B**) as a doublet ($^2J_{HP}$ = 22.7 Hz) at 5.25 ppm. The presence of the exocyclic methine proton also attested to a doublet ($^1J_{cp}$ = 183.4 Hz) at 53.6 (−**C**H–P, **14B**) in the ^{13}C-NMR spectrum of **14,** a value that coincides with an expected shift for a deshielded methine carbon due to the electron withdrawing cyano-and phosphonate groups. Furthermore, the doublet ($^1J_{cp}$ = 213 Hz) at δc 73.6 was assigned for (=**C**–P, **14A**). The presence of an NH group in **14B** was strongly supported by a signal at 10.35 ppm in the ^{1}H-NMR spectrum of **14** and the frequency absorption band at ν 3330 cm^{-1} in its IR spectrum.

Scheme 2 shows the probable mechanism for the reaction of 1,3-dithietane **1** with oxindole-3-hydrazone (**7**), which is consistent with the data presented thus far. However, the structural products **12** and **14** indicate that 2,3-dihydrooxindole derivative **7** reacts with **1** in both lactim-**7A** and lactam-**7B** forms [15]. Even though it has been established that the preference of these compounds exists for the lactim structure, they undergo reactions characteristic of both forms **7A** ⇋ **7B** [15]. Following this, compound **12** should mechanistically be explained by the initial nucleophilic attack on the 1,3-dithietane carbon by the β-N atom of isatin-3-hydrazone (**7A**) to give the first intermediate **9.** Subsequent prototropic rearrangement, cyclization, and transformations led to the formation of **12** (Scheme 2, B). The formation of **14,** on the other hand, could be rationalized in terms of the carbophilic attack by the β-N of χisatin-3-hydrazone **7B** (lactam form) on the 1,3-dithietane carbon to give the first thiol intermediate **13,** which could easily be transformed into the observed oxadiazine **14** (**14A** ⇌ **14B**) with elimination of H_2S (Scheme 2, C).

It should be noted that reactions of isatins and their derivatives with other different teravalent and pentavalent phosphorus reagents were previously studied by us [16–18].

A parallel fused oxadiazine **16** (56%) and the known [19] ketazine **17** (12%) (Scheme 3) were likewise obtained by reacting phosphono substituted-1,3-dithietane **1** with acenaphthenequinonemonohydrazone (**15**) under the conditions previously mentioned for the reaction of **7** with **1.** Identification of **16** was confirmed by combustion analysis, mass, NMR-spectroscopy, and by analogy with **12** (Scheme 2, B). Closely related to the latter reaction is the formation of acenaphthene [*a*] fused with pyrano-derivatives from the reaction of 1-dicyanomethyleneacenaphthen-2-one with several phosphorus ylides [20].

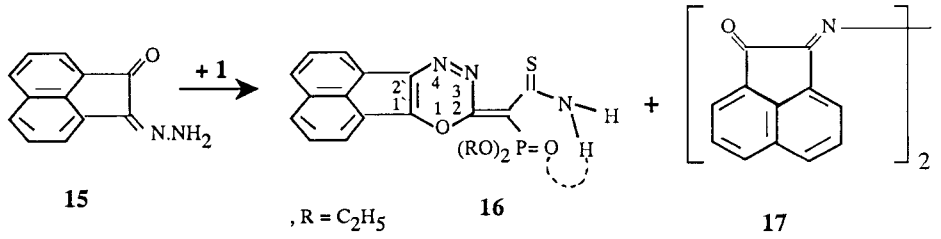
The reaction of 3,5-di-*tert*-butyl-1,2-benzoquinone-1-monohydrazone (**18**) with phosphono substituted-1,3-dithietane **1** proceeded as anticipated, with the involvement of the enol substrate form **18B** [21] being indicated by the formation of diethyl (6,8-di-*tert*-butyl-9,10-dihydrobenzo[*a*](1,3,4-oxadiazin-2-ylidene)cyanomethylphosphonate (**20**) (64%) as the sole adduct from the product mixture. There was no indication of the formation of a dimeric product from this reaction (Scheme 4).

As with the reaction between **1** and the hydrazone **7** (Scheme 2, C), further intramolecular cyclization of the initially formed thiol intermediate **19** yields the oxadiazine **20** accompanied by the loss of H_2S (Scheme 4).

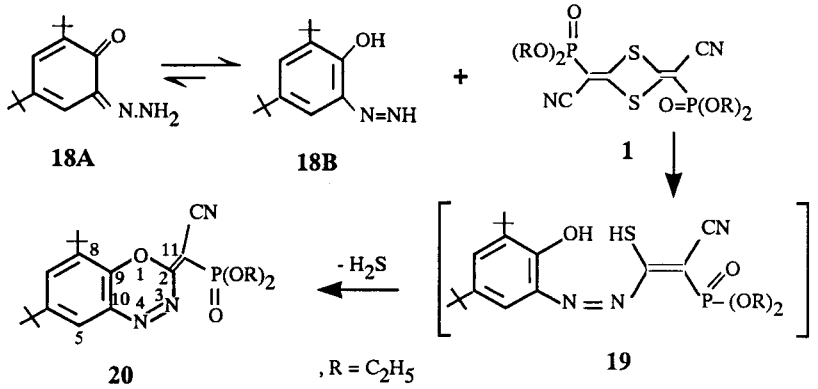
Similarly, 3,5-di-*tert*-butyl-benzene 2,1-fused with oxazines, pyridazines, and pyrazoles have also been synthesized by us [22], on treatment of *N*-phenyl-3,5-di-*tert*-butyl-1,2- benzoquinone monohydrazone with different types of phosphorus ylides.

1,3-Indandion-2-hydrazone (**21**), on treatment with 1,3-dithietane **1,** gave the unexpected diethyl 2-imino-3H-4-thioxo(11,12-dihydroindan-10-one)[12,11-*a*](5,13,1-oxadiazole)[13,1-*b*](1,13-pyrazole-3-yl) phosphonate (**24**) (49%) along with the expected 1,3,4-oxadiazine derivative **25** as a minor product (11%) (Scheme 5). The nuclear magnetic resonance study of **24** and **25** gave results in agreement with the proposed structures.

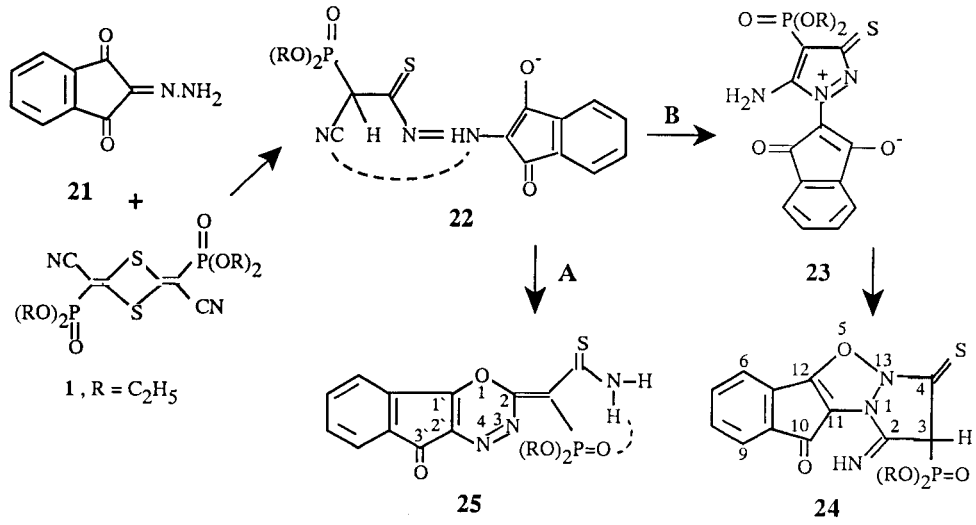
The formation of the reaction products **24** and **25** can be rationalized by the generally accepted mechanism of the initial formation of the reactive intermediate **22.** Stabilization of **22** could be attained by two different pathways of intramolecular cyclization (Scheme 5, A and B) to give either the oxadiazine **25** (Scheme 5, A) or else the oxadiazole **24** via the dipolar intermediate **23** (Scheme 5, B). Similar 1,2-dihydroindan-3-one [2,1-*a*] fused with oxazole and/or oxadiazole systems were previously



SCHEME 3



SCHEME 4

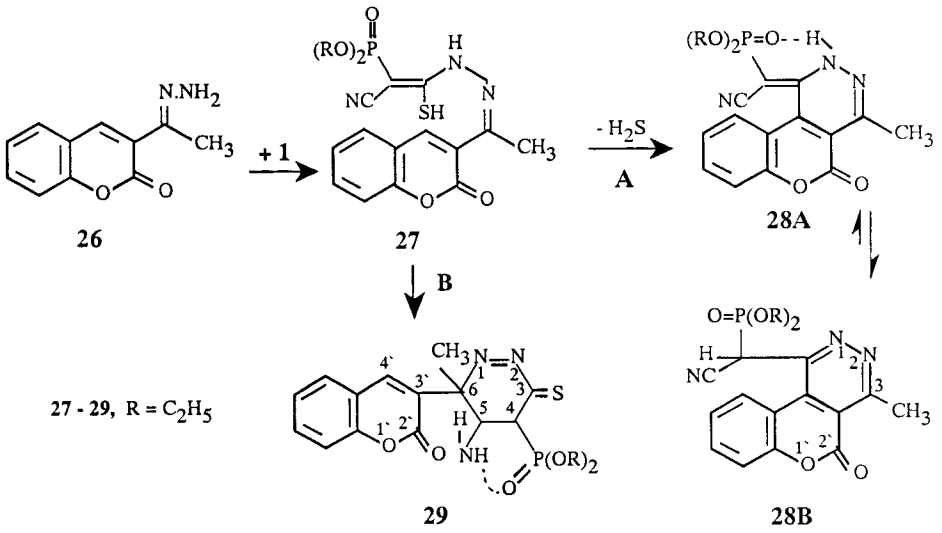


SCHEME 5

reported [23,24], for example, by treatment of indantrione (or other triketones) [23] with phenylalanine.

Furthermore, we have studied the reaction of the dithietane **1** with 3-(1-hydrazoethyl) coumarin (**26**). When a mixture of **26** and **1** was caused to react in boiling ethyl alcohol for 18 hours, diethyl 3-methyl (2′-oxo-3′,4′-dihydro-2′-oxo-benzopyran)[4′,3′-*c*] (1,2-pyridazin-6-ylidene) cyanomethylphosphonate (**28**) (23%), which exists in the equilibrium **28A** ⇋ **28B,** and diethyl 5-amino-6-methyl-3-thione 6 (2′-oxo-benzopyran- 3′-yl) 1,2-pyridazin-4-yl-phosphonate (**29**) (38%) were isolated and identified as depicted in Scheme 6.

The presence of the two tautomeric structures **28A** and **28B** in solution could be detected by NMR spectroscopy. In the ^{1}H-NMR ($CDCl_3$, δ) spectrum of



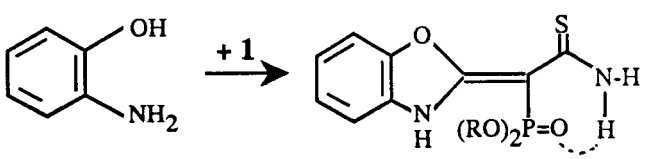
SCHEME 6

28, the presence of the exocyclic methine proton (**28B**) is found as a doublet ($^1J_{HP}$ = 21.4 Hz) at δ_H 5.26 (1H) and at δc 73.2 ppm (d, $^1J_{cp}$ = 183 Hz, **28B**) along with the NH proton (**28A**) at δ_H 8.55 ppm. Moreover, the signal at δc 85.5 (d, $^1J_{cp}$ = 208 Hz), is attributed to (=C–P, **28A**). The weak signals for the NH group in PMR and IR spectra indicates **28B** as the main tautomer.

The formation of **28** and **29** is believed to occur via the initial nucleuphilic condensation of **1** with **26** to produce the thiole intermediate **27,** which, by further usual transformations, yields either the adduct **29** (Scheme 6, B) [9a] or else the pyridazine derivative **28.**

It is worthwhile to mention that compounds consisting of chromene [4,3-*c*] fused with different cyclic and heterocyclic derivatives were previously obtained [25] by the reaction of the parent, 3-acetyl coumarin, with some phosphorus ylides.

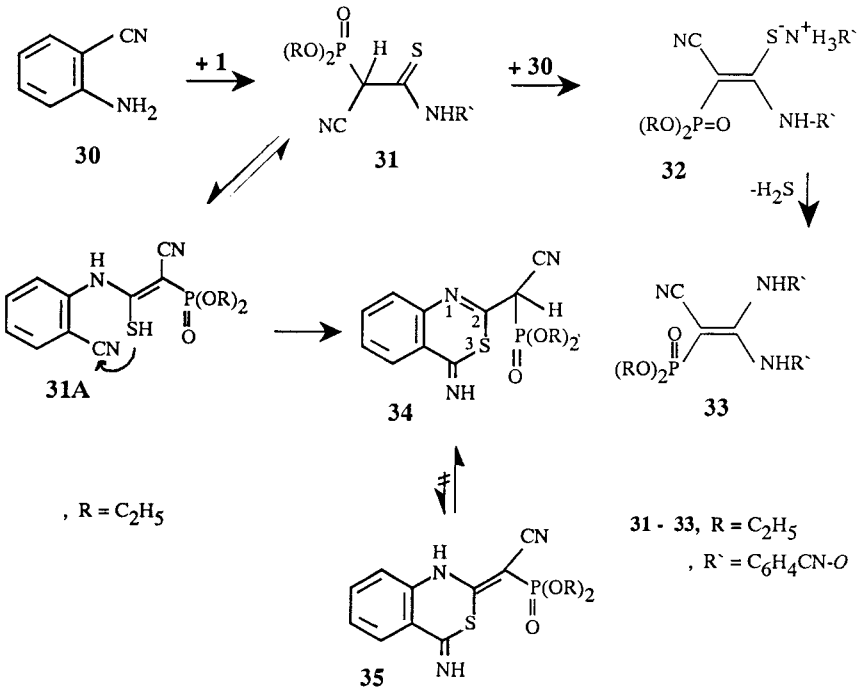
The reaction of the phosphorus reagent **1** with anthranilonitrile (**30**) was investigated next in an effort to search for possible chemical dissimilarities that might occur when another electronegative group (CN) is introduced in lieu of the hydroxyl moiety in *o*-aminophenol [26] (Equation 1).



(1)

As shown in Scheme 7, when anthranilonitrile **30** was treated with 0.4 equivalent of the phosphonato substituted-1,3-dithiethane **1** in refluxing ethanol, diethyl 2-cyano 1,1-di-(*N,N-o*-nitrilophenylamine)ethylene-2-phosphonate (**33**) and diethyl 4-imino-3,1-benzothiazin-2-yl)cyanomethylphosphonate (**34**), in approximate equal yields (~32%), along with other unidentified products of high melting points (>340 °C) were isolated from the product mixture. It is reasonable to assume that the initial addition intermediate, **31,** was formed from **30** and **1** followed by a nucleophilic addition of a second amine species **30,** further elimination of an H_2S molecule from the intermediate **32** affording the ethylene product **33.** Conversely, with respect to the formation of **34,** we presume that the intermediate **31,** possibly present in the equilibrium **31** ⇌ **31A,** via a prototropic rearrangement, is then intramolecularly cyclized to yield the thiazine derivative **34** (Scheme 7, B). However, the deviation of the reaction course for **1** with **30** from what previously had been found for the reactions of **1** with α-hydroxyl amino (or hydrazido-) compounds, presents a diverse reactivity of 1,3-dithietanes toward H-nucleophilic compounds.

Although compound **34** could undergo the tautomeric equilibrium **34** ⇌ **35,** as previously shown with **28B** ⇋ **28A** (Scheme 6), spectroscopic investigation showed only one possible structure **34.** In the ^{1}H NMR spectrum ($CDCl_3$, δ) the presence of a single tautomer **34** was indicated by the presence of one set of signals for the ethoxyl group, the exocyclic hydrogen proton observed as a doublet ($^2J_{HP}$ = 22.1 Hz) at 5.17 ppm (1H) and only one signal for an =NH proton at 8.43 ppm. Furthermore, the characteristic bands at 3155 (weak, NH), 1660 (C=NH) and at



SCHEME 7

1405 cm^{-1} (N=C–S) in the IR spectrum of **34** and the ^{13}C NMR spectrum, which showed, among other signals, a doublet ($^{1}J_{cp}$ = 126 Hz) at 47.6 ppm, a value which coincides with a chemical shift for an sp3-hybridized C-atom bearing a phosphorus of the phosphonate moiety are in a better agreement with the assigned structure.

The previously noted observations show that the previously [7] studied reactions of phosphonato 1,3-dithietane **1** with H-nucleophiles can be considerably extended. However, the reactions of compound **1** with α-carbonyl hydrazones provide an easy route, not only for the expected fused oxadiazines, similar to **12, 14, 16, 20, or 25,** but also for fused pyrazoles, for example, **24;** pyridazines, for example **28** or **29;** and/or other N-heterocyclic derivatives based on the hydrazone species. The nature of the α-substitutent of the hydrazone moiety, on the other hand, seems to be crucial. Following this, although the first step in the reaction of **1** with hydrazones involves an initial nucleophilic attack by the β-N atom of the hydrazone on the 1,3-dithietane carbon (Scheme 1), the consequences of the initial step vary markedly according to the nature of the hydrazone compound. Furthermore, the unexpected behavior of **1** toward the α-nitriloamine compound **30** leading to the thiazine derivative **34** and the ethylene derivative **33** represents a new finding and supplements the promising aspect of utilizing phosphorus reagent **1** in syntheses.

EXPERIMENTAL

All melting points are uncorrected. The IR spectra were recorded with a Perkin Elmer Infracord Spectrometer model 197 (Grating). The ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ or d_6-DMSO as solvents on a Joel-270 MHz Spectrometer using $SiMe_4$ as an internal standard. The ^{31}P NMR spectra were taken with a Varian CFT-20 instrument (**vs.** external 85% H_3PO_4). Mass spectra were performed at 70 eV on a Shimadzu GCS-QP 1000 EX Spectrometer provided with a data system. Elemental analyses were carried out at the Microanalysis Laboratory at Cairo University. The appropriate precautions in handling moisture-sensitive reagents were observed. Solvents were dried by standard techniques.

Reaction of Oxindole-3-hydrazone (**7**) *with Phosphono-Substituted-1,3-Dithietane* **1**

To a stirred solution of the hydrazone **7** [13] (1.6 g, 0.01 mol) in 30 mL of absolute ethyl alcohol was added portionwise 2.2 g (5 mmol) of *tetraethyl 1,3-dithietane-2,4-diylidene-bis*(cyanomethylphosphonate) (**1**) [8]. The stirred reaction mixture was heated under reflux for 6 hours, whereupon the yellow material that had precipitated was collected (250 mg, 13%) recrystallized from pyridine, and proved to be

oxindole azine **(8)** (m.p. and mixed m.p.s 255°C) [13].

The filtrate was subjected to column chromatography on silica gel. Elution with *n*-hexane-chloroform afforded two fractions. The first fraction (6:4, v/v) afforded yellow crystals of diethyl 2-thiocarbamoyl(2′,3′-dihydroindole)[3′,2′-*b*](1,3,4-oxadiazin-2-ylidene)methylphosphonate (**12**) (1.4 g, 37%); m.p. 166.5°C (benzene). IR (KBr) cm^{-1} 3357–3210 (NH=HNH), 1628 (C=C, vinyl), 1555 (N=N), 1445 (N–C=S), 1255 (P=O) and 1060 (P–O–C). NMR ($CDCl_3$): δ_H 1.21 (d of t, J_{HH} = 7.1, J_{HP} = 2.6 Hz, 6H, C.C**H**$_3$), 4.25 (d of q, J_{HH} = 7.1, J_{HP} = 3.4 Hz, 4H, O-C**H**$_2$), 7.35–7.68 (m, 4H, arom.), 9.55, 10.53, 11.13 (3*s, 3*1H, **H**-N-**H,** N**H**); δc 17.3 (d, C–CH_3), 59.6 (d, OCH_2), 78.8 (d, $^1J_{cp}$ = 210 Hz, = C–P), 158.2 (d, $^2J_{cp}$ = 8 Hz, C=CP), 194.5 (d, C=S); δp = 15.4 ppm. MS: *m/z* (%) = 380 (18) [M^+], 347 (22) [M^+ − 33, SH], 321 (25) [M^+ − 59, HCNCS], 276 (100) [(M^+ − 59) − 45, $C_2H_5O^+$].

$C_{15}H_{17}N_4O_4PS$ (380.4) Calcd.: C, 47.36; H, 4.5; N, 14.73; P, 8.14; S, 8.43. Found: C, 47.42; H, 4.43; N, 14.64; P, 8.18; S, 8.51.

The second fraction (4:6, v/v) yielded straw yellow crystals of diethyl 2′,3′-dihydroindole[3′,2′-b](1,3,4-oxadiazin-2-ylidene)cyanomethylphosphonate (**14**) (450 mg, 13%), m.p. 183.5°C (acetone). IR (KBr) cm^{-1}: 3330 (NH, **14A**), 2224 (CN) 1250 (P=O), 1062 (P–O–C). NMR ($CDCl_3$): δ_H 1.25, 1.32 (2* d of t, J_{HH} = 6.8, J_{HP} = 2.5 Hz, 2*6 H, 2*C-C**H**$_3$), 4.13, 4.18 (2* d of q, J_{HH} = 6.8, J_{HP} = 3.8 Hz, 2* 4H, 2*-OC**H**$_2$), 5.25 (d, $^2J_{HP}$ = 22.7 Hz, 1H, C**H**-P, **14B**), 7.35–7.82 (m, 2* 4H, arom.), 10.35 (s, 1H, N**H**, **14A**); δc 17.8, 18.6 (2*d, 2* C-CH_3), 53.6 (d, $^1J_{cp}$ = 183.4 Hz, H–C–P, **14B**), 60.2, 62.4 (2*d, 2*OCH_2), 73.6 (d, J_{cp} = 213 Hz, = C-P, **14A**), 158.8 (d, C=C–P, **14B**), δ_p = 14.6 and 15.3 ppm. MS: *m/z* (%) = 346 (60) [M^+].

$C_{15}H_{15}N_{14}O_4P$ (346.3) Calcd.: C, 52.03; H, 4.37; N, 16.18; P, 8.94. Found: C, 52.12; H, 4.32; N, 16.09; P, 9.12.

Reaction of Acenaphthenequinonemonohydrazone (**15**) *with Phosphono-Substituted 1,3-Dithietane* **1**

The reaction between the hydrazone **15** [27] (2 g, 0.01 mol) and the dithietane **1** (2.2 g, 5 mmol) in absolute ethyl alcohol (50 mL) was carried out, and the product mixture was worked up according to the described procedure for the substrate **7.** The pink material that precipitated was collected (220 mg, 12%) and recrystallized from benzene and proved to be acenaphthenequinone ketazine **17** (m.p. and mixed m.p.s 295°C) [19].

The filtrate was subjected to column chromatography on silica gel. Elution with *n*-hexane-chloroform (3:7, v/v) yielded diethyl 2-thiocarbamoyl (1′,2′-dihydro′-acenaphthene)[2′,1′-a](1,3,4-oxadiazin-2-ylidene)methylphosphonate (**16**) (2.4 g, 56%), m.p. 233°C (ethyl acetate). IR (KBr) cm^{-1}: 3445–3350 (H–N–H), 1637 (C=C, exocyclic), 1580 (N=N), 1448 (N–C=S), 1245 (P=O), 1062 (P–O–C). NMR ($CDCl_3$): δ_H 1.23 (d of t, J_{HH} = 7.4, J_{HP} = 2.6 Hz, 6H, –C–C**H**$_3$), 4.27 (d of q, J_{HH} = 7.4, J_{HP} = 3.5 Hz, 4H, –O–CH_2), 7.53–8.14 (m, 6H, arom.), 9.42, 10.67 (2*s, 2*H, **H**-N-**H**); δc 15.8 (d, C-**C**H_3), 63.8 (d, O**C**H_2), 73.6 (d, $^1J_{cp}$ = 210 Hz, = **C**–P), 156.7 (d, $^2J_{cp}$ = 8 Hz, **C**=C–P), 191.7 (d, C=S); δp = 13.3 ppm. MS: *m/z* (%) = 415 (33) [M^+], 382 (37) [M^+ − 33, SH], 356 (28) [M^+ − 59, HNCS], 311 (100) [(M^+ − 59) − 45, $C_2H_5O^+$].

$C_{19}H_{18}N_3O_4PS$ (415.42) Calcd: C, 54.93; H, 4.37; N, 10.11; P, 7.45; S, 7.72. Found: C, 54.87; H, 4.3; N, 10.02; P, 7.52; S, 7.68.

Reaction of 3,5-Di-tert-butyl-1,2-benzoquinone-1-monohydrazone (**18**) *with Phosphono-Substituted 1,3-dithietane* **1**.

A mixture of **1** (2.2 g, 5 mmol) and the freshly prepared hydrazone **18** [21] (2.3 g, 0.01 mol), from equivalent amounts of the parent quinone and hydrazine hydrate, in ethyl alcohol (50 mL) was heated under reflux for 6 hours. The product mixture was evaporated to dryness and then added to a column previously charged with silica gel suspended in light petroleum ether. The column was developed with cyclohexane containing increasing amounts of ethyl acetate. The fraction (9:1 v/v) afforded yellow crystals of diethyl (6,8-di-*tert*-butyl-9,10-dihydrobenzo)[*a*](1,3,4-oxadiazin-2-ylidene)cyanomethylphosphonate (**20**) (2.6 g, ~64%), m.p. 108°C (cyclohexane). IR (KBr) cm^{-1}: 2218 (CN), 1630 (C=C, vinyl), 1265 (P=O), 1050 (P–O–C). NMR ($CDCl_3$): δ_H 1.22 (d of t, J_{HH} = 7.2, J_{HP} = 2.5 Hz, 6H, C.C**H**$_3$), 1.36, 1.51 [2*s, 2*9H, C(C**H**$_3$)$_3$], 4.33 (d of q, J_{HH} = 7.2, J_{HP} = 3.7 Hz, 4H, OC**H**$_2$), 6.23, 6.99 (2*d, J_{HH} = 4.2 Hz, 2*H, 2H, arom.), δc: 17.4 (d, C-**C**H_3), 31.4, 32.2 [2*d, 2*C (CH_3)$_3$], 34.5, 35.5 [2* C(CH_3)$_3$], 58.6 (d, OCH_2), 68.6 (d, $^1J_{cp}$ = 215 Hz, = **C**-P), 118.5 (**C**N), 150.8 (d, $^2J_{cp}$ = 8 Hz, **C** = C-P); δp = 13.7 ppm. MS: *m/z* (%) 419 (66) [M^+].

$C_{21}H_{30}N_3O_4P$ (419.5) Calcd.: C, 60.12; H, 7.21; N, 10.02; P, 7.38. Found: C, 60.04; H, 7.11; N, 9.91; P, 7.44.

Reaction of 1,3-Indandione-2-hydrazone (**21**) *with Phosphono-Substituted 1,3-dithietane* **1**

A stirred mixture of **1** (2.2 g, 5 mmol) and the hydrazone **21** [14] (1.7 g, 0.01 mol) in ethyl alcohol (50

mL) was heated under reflux for 4 hours and then column chromatographed on silica gel (light petroleum ether-ethyl acetate). The fraction (8:2, v/v) yielded yellow crystals of diethyl 2-imino-3H-4-thioxo(11,12-dihydroindan-10-one)[12,11-*a*](5,13,1-oxadiazole)[13,1-*b*](1,13-pyrazole-3-yl)phosphonate (**24**) (1.9 g, 49%), m.p. 236°C (CH_3CN). IR (KBr) cm^{-1}: 3325 (NH, weak), 1685 [C-10 (O)], 1622 (C=NH), 1485 [N–C(S)], 1235 (P=O), 1060 (P–O–C). NMR ($CDCl_3$): δ_H 1.27 (d of t, J_{HH} = 7.4, J_{HP} = 2.8 Hz, 6H, C-C**H**$_3$), 4.18 (d of q, J_{HH} = 7.4, J_{HP} = 3.8 Hz, 4H, O**CH**$_2$), 4.8 (d of d, J_{HH} = 2.5, $^2J_{HP}$ = 18.3 Hz, 1H, P-C-3-**H**), 7.26–7.73 (m, 4H, arom.), 8.22 (s, 1H, N**H**); δc 15.7 (d, C-**C**H$_3$), 54.5 (d, $^1J_{cp}$ = 82.6 Hz, H–C–P), 61.3 (d, O**C**H$_2$), 133.5, 142.2 (**C**-11, **C**-12), 158.3 (**C**=NH), 172.5 [**C**-10(O)], 193.5 [**C**-4(S)]; δp = 14.6 ppm. MS: *m/z* (%) = 393 (33) [M^+].

$C_{16}H_{16}N_3O_5PS$ (393.4) Calcd.: C, 48.85; H, 4.1; N, 10.68; P, 7.87; S, 8.15. Found: C, 48.73; H, 3.93; N, 10.57; P, 7.93; S, 8.21.

The second fraction (6:4, v/v) gave an orange substance of diethyl 2-thiocarbamoyl (1′,2′-dihydroindan-3′-one)[2′,1′-b](1,3,4-oxadiazin-2-ylidene) methylphosphonate (**25**) (148 mg, 11%), m.p. 248°C (benzene). IR (KBr) cm^{-1}: 3320-328 (HNH), 1685 [C-3′ (O)], 1635 (C=C, exocyclic), 1256 (P=O), 1045 (P-O-C). NMR (d_6-DMSO): δ_H 1.24 (d of t, J_{HH} = 7.2, J_{HP} = 2.8 Hz, 6H, C-C**H**$_3$), 4.23 (d of q, J_{HH} = 7.2, J_{HP} = 3.5 Hz, 4H, O**CH**$_2$), 7.33–7.85 (m, 4H, arom.), 9.68, 10.35 (2*s, 2*H, H-N-H); δc 15.2 (d, C-CH$_3$), 60.3 (d, O**C**H$_2$), 82.6 (d, $^1J_{cp}$ = 196.3 Hz, = C-P), 154.5 (d, $^2J_{cp}$ = 8 Hz, C=C-P), 194.2 (d, C=S); δp = 15.4 ppm. MS: *m/z* (%) = 393 (22) [M^+].

$C_{16}H_{16}N_3O_5PS$ (393.4) Calcd.: C, 48.85; H, 4.1; N, 10.68; P, 7.87; S, 8.15. Found: C, 48.92; H, 4.05; N, 10.62; P, 7.91; S, 8.08.

Reaction of 3(1-Hydrazoethyl)coumarin (**26**) *with 1,3-Dithietane* **1**

A stirred mixture of the hydrazone **26** (2 g, 0.01 mol) [28] and phosphonato-reagent **1** (2.2 g, 5 mmol) in ethyl alcohol (50 mL) was heated under reflux for 18 hours. After evaporation of the solvent, the residue was chromatographed on silica gel with *n*-hexane-chloroform (7:3, v/v) as eluent to give first diethyl 5-amino-6-methyl-3-thione 6(2′-oxo-benzopyran-3′-yl) 1,2-pyridazin-4-yl-phosphonate (**29**) (1.55 g, 38%), m.p. 192.5°C (CH_2Cl_2). IR (KBr) cm^{-1}): 3340–3273 (H-N-H), 1707 (C=O, coumarinyl), 1445 (N–C=S), 1255 (P=O), 1055 (P–O–C). NMR (d_6-DMSO): δ_H 1.23 (d of t, J_{HH} = 6.8, J_{HP} = 2.7 Hz, 6H, OCH$_2$C**H**$_3$), 1.89 (s, 3H, C-C**H**$_3$), 4.25 (d of q, J_{HH} = 6.8, J_{HP} = 3.8 Hz, 4H, O**CH**$_2$), 7.28–7.64 (m, 5H, arom), 9.43, 11.18 (diffused, 2*H, **H**-N-**H**); δc 15.6 (d, OC-**C**H$_3$), 19.3 (C-6-**C**H$_3$), 35.2 (**C**-6-CH$_3$), 60.4 (d, O**C**H$_2$), 60.4 (d, O**C**H$_2$), 88.9 (d, $^1J_{cp}$ = 183.7 Hz, **C**-4-P), 156.7 (**C**-5-HNH), 162.8 (**C**=O, coumarin), 193.5 (**C**=S), δp = 16.3 ppm. MS: *m/z* (%) = 421 (66) [M^+].

$C_{18}H_{20}N_3O_5PS$ (421.43) Calcd.: C, 51.3; H, 4.78; N, 9.97; P, 7.35, S, 7.6. Found: C, 51.37; H, 4.71; N, 9.86; P, 7.46; S, 7.52.

The next fraction (up to 6:4, v/v) gave yellow needles of diethyl 3-methyl (2′-oxo-3′-4′-dihydrobenzopyran)[4′,3′-*c*](1,2-pyridazin-6-ylidene)cyanomethylphosphonate (**28**) (0.88 g, 23%), m.p. 133.5°C (CH_2Cl_2). IR (KBr) cm^{-1}: 3345 (weak, NH, **28A**), 2217(CN), 1710 (C=O, coumarinyl), 1622 (C=C, exocyclic, **28A**), 1255 (P=O), 1055 (P-O-C). NMR ($CDCl_3$) δ_H 1.2, 1.23 (2* d of t, J_{HH} = 7.3, J_{HP} = 2.8 Hz, 2* 6H, 2* C-C**H**$_3$), 2.15, 2.18 (2* s, 2* 3 H, 2* -C**H**$_3$, A, B), 4.22, 4.31 (2* d of q, J_{HH} = 7.3, J_{HP} = 3.5 Hz, 2*4H, 2*OC**H**$_2$), 5.26 (d, $^2J_{HP}$ = 21.4 Hz, 1H, **H**C-P, **28B**), 7.27–7.88 (m, 2* 4H, arom.), 8.55 (br., 1H, N**H**, **28B**), δc: 17.6, 18.3 (2*d, 2* OC.CH$_3$), 23.7, 25.5 (2*C-3, 2*-C**H**$_3$), 60.8, 62.4 (2* d, 2* OCH$_2$), 73.2 (d, $^1J_{cp}$ = 183 Hz, HC-P, **28B**), 85.5 (d, $^1J_{cp}$ = 208 Hz, C=P, **28A**), 117.3, 119.5 (2*-C-**C**N), 160.3, 161.7 (2***C**=O); δp = 11.5 and 13.8 (A & B). MS: *m/z* (%) = 387 (33) [M^+].

$C_{18}H_{18}N_3O_5P$ (387.3) Calcd.: C, 55.82; H, 4.68; N, 10.85; P, 7.99. Found: C, 55.73; H, 4.57; N, 10.77; P, 8.03.

Reaction of Anthranilonitrile (**30**) *with 1,3-Dithietane* **1**

A stirred mixture of compound **30** (1.2 g, 0.01 mol) and phosphenato reagent **1** (1.75 g, 4 mmol) was refluxed in ethyl alcohol for 12 hours. The procedure and the workup were the same as described for the hydrazones, whereby elution with cyclohexane-ethyl acetate (8:2, v/v) afforded diethyl 4-imino-(3,1-benzothiazin-2-yl)cyanomethylphosphonate (**34**) (1g, 30%) as yellow crystals, m.p. 116°C (ether). IR (KBr) cm^{-1}: 3155 (weak, =NH), 2190 (CN), 1660 (C=NH), 1405 (N=C-S), 1260 (P=O) and 1050 (P–O–C). NMR ($CDCl_3$): δ_H 1.24 (d of t, J_{HH} = 7.4, J_{HP} = 2.7 Hz, 6H, C.C**H**$_3$) 4.24 (d of q, J_{HH} = 7.4, J_{HP} = 3.6 Hz, 4H, OCH$_2$), 5.17 (d, $^2J_{HP}$ = 20.5 Hz, 1H, **H**-C-P), 7.25–7.83 (m, 4H, arom.), 8.43 (s, 1H, = NH); δc: 16.2 (d, C-C**H**$_3$), 47.6 (d, $^1J_{cp}$ = 126 Hz, H-**C**-P), 62.3 (d, O**C**H$_2$), 118.7 (**C**N), 124.8 (d, $^2J_{cp}$ = 8.8 Hz, N-C-S) 146.6 (**C**=NH), δp = 15.7 ppm. MS: *m/z* (%) 337 (28) [M^+].

$C_{14}H_{16}N_3O_3PS$ (337.35) Calcd. C, 49.84; H, 4.78; N, 12.46; P, 9.18; S, 9.51. Found: C, 49.77; H, 4.72; N, 12.35; P, 9.24; S, 9.42.

Elution with cyclohexane-ethyl acetate (7:3, v/v) yielded diethyl 2-cyano 1,1-di-(*N*,*N*-*o*-nitrilopheny-

lamine)ethylene-2-phosphonate (**33**) (0.7 g, 33%) as yellow crystals, m.p. 187.5°C (CH_2Cl_2). IR (KBr) cm^{-1} 3420–3350 (br., 2NH); 2222, 2212, 1996 (3 CN), 1618 (C=C, exocyclic), 1255 (P=O), 1058 (P-O-C). NMR ($CDCl_3$): δ_H 1.22 (d of t, J_{HH} = 7.3, J_{HP} = 2.7 Hz, 6H, C-C**H**$_3$), 4.23 (d of q, J_{HH} = 7.3, J_{HP} = 3.5 Hz, 4H, OC**H**$_2$), 7.32–8.2 (m, 8H, arom.), 8.75, 9.13 (2*s, br., 2*H, 2*-NH); δp = 12.6 ppm. MS: *m/z* (%) = 421 (38) [M^+].

$C_{21}H_{20}N_5O_3P$ (421.4) Calcd.: C, 59.85; H, 4.78; N, 16.62; P, 7.35. Found: C, 59.93; H, 4.67; N, 4.67; P, 7.43.

In the next fractions, several unidentified polymeric products with m.p. greater than 340°C were eluted.

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