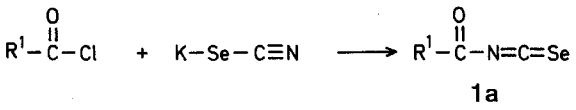
Reaction of Carbonyl Isothio(seleno)cyanates with Trivalent Phosphorus Esters

Wojciech J. STEC*, Krystyna LESIAK, Marek SUDOL**

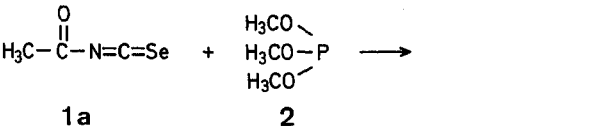
Polish Academy of Sciences, Centre of Molecular and Macromolecular Studies, 90-362 Łódź, Poland

Recently it has been reported that reaction of dialkyl phosphoroisoselenocyanatidate with triethyl phosphite leads to dialkyl phosphoroisocyanidate[1]. In such a way the first acidic isonitrile was obtained. It was of interest to examine the reaction of acyl isoselenocyanates with trivalent phosphorus esters as a route leading to acyl isonitriles, a so far unknown class of organic compounds. Acetyl isoselenocyanate[2] (**1a**; $R^1=CH_3$) was obtained from the reaction of acetyl chloride with potassium selenocyanate. Due to its instability **1a** was not isolated, but its identity was proved by means of I.R. spectroscopy; $\nu_{CO}=1740\,cm^{-1}$ (s), $\nu_{NCSe}=1960\,cm^{-1}$ (vs), (solvent: dimethoxyethane).

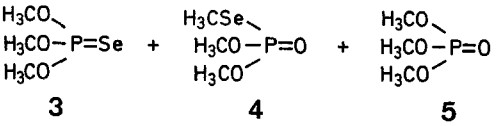


1a

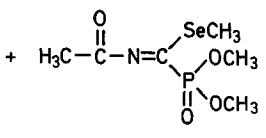
The exothermic reaction of **1a** with equimolar amount of trimethyl phosphite (**2**) was followed by I.R. spectroscopy. A decrease in the intensity of $\nu_{NCSe}=1960\,cm^{-1}$ (br, s) and $\nu_{CO}=1740\,cm^{-1}$ (s) was accompanied by the appearence of $\nu_{CO}=1715\,cm^{-1}$ (s) and $\nu_{C=N}=1605\,cm^{-1}$ (s) but the expected bands characteristic for —NC or —CN near $2200\,cm^{-1}$ were not observed. ^{31}P-N.M.R. spectrum (DME solution) revealed the presence of *O,O,O*-trimethyl phosphoroselenoate (**3**, 15%) *O,O,Se*-trimethyl phosphoroselenoate (**4**, 5%) trimethyl phosphate (**5**, 10%), and a new organophosphorus compound **6a**.



1a **2**

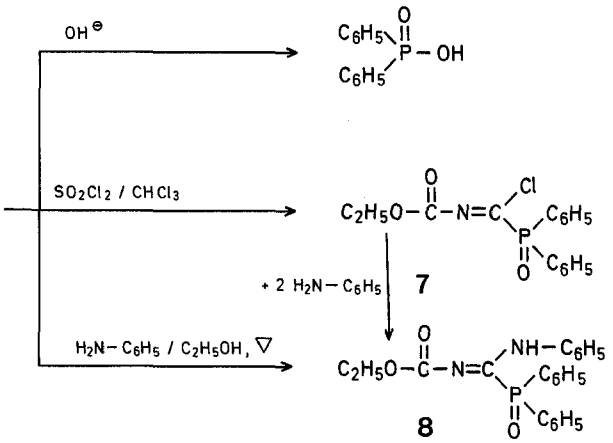


3 **4** **5**



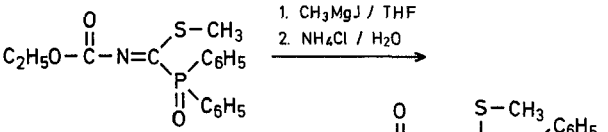
6a

Full characteristic data for **6a** are included in the Table. On the basis of the mass spectral analysis and other data included in the Table the structure of **6a** has been assigned as *N*-acetyl-*O,O*-dimethylphosphonoselenoimidic acid methyl ester. Further results from reactions of compounds of general formulas R-C(O)-NCY[3] with trivalent phosphorus esters are summarized in the Table. Base-catalysed hydrolysis of **6e** led to diphenylphosphinic acid[4]. Treatment of **6e** with an equimolar amount of sulphuryl chloride in chloroform solution gave *N*-ethoxycarbonyldiphenylphosphinoxyimidoyl chloride (**7**). Its reaction with aniline (molar ratio 1:2) was exothermic and produced *N*-ethoxycarbonyl-*N'*-phenyldiphenylphosphinoxyamidine (**8**, yield 72%). The same compound was obtained when **6e** was refluxed in absolute ethanol in the presence of equimolar amount of aniline (yield 79%). Both, the chlorinolysis reaction of **6e** and substitution at the azomethine carbon atom are typical for this type of compound[5].



7 **8**

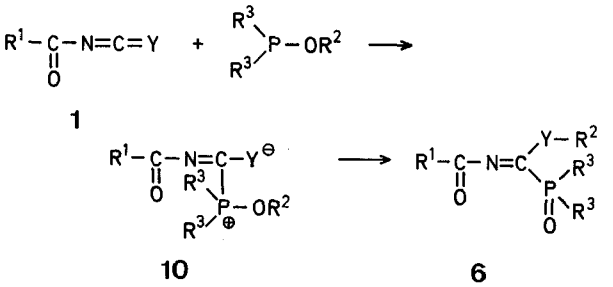
The reaction of **6e** with methylmagnesium iodide took, however, a different course and instead of the product of substitution at the azomethine carbon atom, the compound resulting from formal addition of the Grignard reagent to the C=N bond was obtained (**9**). Such course of reaction of a Grignard reagent with a Schiff-base type compound has been previously reported by Dessy, et al.[6].



6e **9**

It is worthwhile to emphasise that the attempts to bring about reaction of phenyl isothiocyanate with trimethyl phosphite in boiling toluene resulted in formation of phenyl isonitrile, in agreement with earlier findings of Mukaiyama and coworkers[7]. However, in reactions of compounds of general formulas R-C(O)-NCY with trivalent phosphorus esters, no traces of acyl (alkoxycarbonyl) isonitriles as well as nitriles were observed. These observations speak for sensitivity of the reaction behaviour of isothio(seleno)cyanates on the chemical surrounding of thio(seleno)carbonyl group[8,9].

The results from reactions of acyl(alkoxycarbonyl) isothio(seleno)cyanates with trivalent phosphorus esters can be well accounted for by assuming the formation of the betain intermediate[10] **10**.



1 **10** **6**

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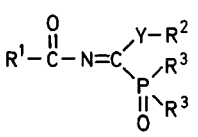
Table. Physical Data for Compounds of Structure



No.	Compound[a]	R^1	Y	R^2	R^3	B.p. or m.p. $[n_D^{20}]$	δ_P ppm (H_3PO_4)	δ_H ppm (R^2)	I.R. ν_{CO}	ν_{max} cm^{-1} ν_{CN}	ν_{PO}	Mass spectrum	Yield (%)
1	**6a**[b]	H_3C	Se	H_3C	H_3CO	105°/0.2 torr [1.5180]	−3.0 (neat)	2.30	1715 (film)	1605	1200	273 ($M^{\oplus}$, 0.2%) 136 (100%)	56
2	**6b**	H_3C	Se	C_2H_5	C_2H_5O	110°/0.1 torr [1.5135]	0.0 (neat)	2.23 (—Se—CH_2—)	1715 (film)	1605	1200	315 ($M^{\oplus}$, 1%) 164 (100%)	29
3	**6c**	H_3C	S	H_3C	H_3CO	95°/0.1 torr [1.4954]	−2.5 (neat)	2.40	1720 (film)	1605	1230	225 ($M^{\oplus}$, 0.4%) 136 (100%)	52
4	**6d**	C_2H_5O	S	H_3C	H_3CO	98°/0.1 torr [1.5028]	−1.8 (neat)	2.45	1730 (film)	1605	1230	255 ($M^{\oplus}$, 8.9%) 136 (100%)	57
5	**6e**	C_2H_5O	S	H_3C	C_6H_5	m.p. 112.5–113.5°	−22.5 ($CHCl_3$)	2.38	1720 (KBr)	1580	1220	347 ($M^{\oplus}$, 1.7%) 201 (100%)	59
6	**7**[c]	C_2H_5O	Cl	—	C_6H_5	—	−24.0 (CCl_4)	—	1755 (CCl_4)	1665	1230	335 ($M^{\oplus}$, 0.8%) 201 (100%)	—
7	**8**	C_2H_5O	NH	C_6H_5	C_6H_5	m.p. 150–151.5°	−28.5 ($CHCl_3$)	—	1690 (nujol)	1595	1220	392 ($M^{\oplus}$, 2.4%) 201 (100%)	79[d] 72[e]

[a] M.ps and b.ps are uncorrected; ^{1}H-N.M.R. spectra recorded at 80 MHz, reference internal TMS, using $CDCl_3$ as a solvent; ^{31}P-N.M.R. spectra recorded at 24.3 MHz with H_3PO_4 as the reference (negative chemical shift values for compounds absorbing at lower fields than H_3PO_4); G.C.-M.S. analyses were performed with LKB 9000 S instrument at 70 eV, ion source temp. 250°. All compounds gave satisfactory analytical data.

[b] U.V. spectrum exhibits an absorption at 286 mu, $\varepsilon = 4000$ (dioxan).

[c] Compound not isolated. Identified on the basis of G.C.-M.S. analysis.

[d] Yield of **8** obtained in reaction of **6e** with aniline.

[e] Yield of **8** obtained in reaction of **7** with aniline.

A solvent-dependent equilibrium between tributylphosphine and various isothiocyanates, involving this type of betain was reported recently[8]. In the next step, attack of a "soft" sulphur or selenium nucleophile on the carbon atom of the alkoxycarbonyl group attached to phosphorus causes the alkyl group transfer with formation of the final product. We wish to emphasize that although *syn*- and *anti* isomers could be expected for compounds **6, 7, 8** in all studied cases only one isomer was observed at room temperature by ^{1}H-N.M.R. and ^{31}P-N.M.R. spectroscopy.

Reactions of Acetyl Isoselenocyanate (1a) with Trialkyl Phosphites:
Into the solution of potassium isoselenocyanate (14.4 g, 0.1 mol) in dimethoxyethane (150 ml) acetyl chloride (7.9 g, 0.1 mol) was added dropwise at 10–15°. Vigorous stirring was continued for 15 minutes and followed by addition of corresponding trialkyl phosphite (0.11 mol) at a temperature not exceeding 40°. The reaction was exothermic and cooling with ice-water was required. Potassium chloride was filtered off and the solvent evaporated from the filtrate. The residue was distilled under reduced pressure and fractions of boiling points shown in the Table were collected (entries nos. 1 and 2).

Reaction of Acyl (Ethoxycarbonyl) Isothiocyanates with Trivalent Phosphorus Esters:
Trimethyl phosphite (13.6 g, 0.11 mol) or methyl diphenylphosphinite (23.78 g, 0.11 mol) was added at the room temperature to a solution of ethoxycarbonyl isothiocyanate (13.1 g, 0.1 mol) in dimethoxyethane (150 ml) and the reaction mixture was left at room temperature for 16 h. The solvent was evaporated and the residue distilled under reduced pressure (entry no. 4) or crystallised (entry no. 5) from ether.

Chlorinolysis of 6e:
Into the solution of **6e** (3.47 g, 0.01 mol) in chloroform (30 ml) freshly distilled sulphuryl chloride (1.35 g, 0.01 mol) was added dropwise at room temperature. Reaction mixture was left for 2 h at this temperature, the solvent was evaporated, and the undistilled **7** was analysed by means of G.C.-M.S. and ^{1}H-N.M.R. spectroscopy (entry no. 6).

Reaction of 7 with Aniline:
Aniline (1.86 g, 0.02 mol) was added at room temperature to the solution of **7** (3.35 g, 0.01 mol) in benzene (30 ml). The reaction was slightly exothermic and after 15 minutes of stirring, aniline hydrochloride was filtered off, the solvent evaporated, and the solid residue crystallized from ethanol to give a crystalline compound; m.p. 150–151.5°; which was identified as **8** (entry no. 7, footnote e).

Reaction of 6e with Aniline:
A mixture of **6e** (3.47 g, 0.01 mol) and aniline (0.93 g, 0.01 mol) in ethanol (40 ml) was refluxed during two hours. The evolution of methanethiol was observed. The solvent was removed and the oily residue solidified. It was crystallised from ethanol to give **8**. (entry no. 7, footnote d).

Reaction of 6e with Methylmagnesium Iodide:
Into a vigorously stirred solution of methylmagnesium iodide (0.02 mol) in ether (150 ml), a solution of **6e** (3.47 g, 0.01 mol) in tetrahydrofuran (50 ml) was dropped at temperature −10 to −5°. Stirring was continued until the mixture reached a temperature of 15°. Then the mixture was cooled to 0° and a saturated solution of ammonium chloride in water (50 ml) was carefully added. The organic layer was separated and the aqueous phase was extracted twice with chloroform (2 × 40 ml). The combined organic layers were dried over anhydrous magnesium sulphate, the solvents were evaporated, and the oily residue solidified when ethyl ether (10 ml) was added. Two crystallisations from ether/chloroform (3:1) gave [1-(*N*-ethoxycarbonylamino)-1-thiomethyl]-ethyl-diphenyl phosphine oxide (**9**); yield: 2.6 g (70%); m.p. 102–103°.

$C_{18}H_{22}NO_3PS$ (363.4)	calc.	C 59.50	H 6.06	N 3.85	P 8.54
	found	59.21,	6.26	4.01	8.80

I.R. (nujol): $\nu = 3380$ (N—H), 1735 (C=O) cm^{-1}

^{31}P-N.M.R. ($CHCl_3$): $\delta = -38$ ppm (H_3PO_4)

^{1}H-N.M.R. ($CDCl_3$): $\delta = 1.92$ (s, 3H, —P—C—CH_3), 2.15 ppm (s, 3H, —SCH_3).

Mass spectrum: $m/e = 363$ ($M^{\oplus}$), 201.

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* To whom all correspondence should be addressed.

** On leave of absence from Pedagogical University, Opole, during 1974.

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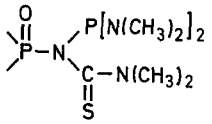
[9] According to patent literature (G. Oertel, H. Malz, H. Holtschmidt, E. Degener, *BRD-Patent* 1155433, Ref. *J. Chem. (USSR)* **1965** 15H 415) reaction of dialkyl phosphoroisothiocyanatidates with tris[dimethylamino]phosphine gave the products with formula:



[10] Very recently Yoshida, et al. (Z. Yoshida, T. Kawase, S. Yoneda, *Tetrahedron Lett.* **1975,** 235; **1975,** 331) published results on the reaction of thioketones with trialkyl phosphites and the same type of intermediate was postulated.

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