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First Examples of the Atherton–Todd-Like Reaction in the Absence of Bases

Boris A. Trofimov, Nina K. Gusarova, Pavel A. Volkov, Nina I. Ivanova, and Kseniya O. Khrapova

E. Favorsky Irkutsk Institute of Chemistry, Siberian Branch of the Russian Academy of Sciences, 1 Favorsky Str., 664033, Irkutsk, Russian Federation

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ABSTRACT: *Oxidative cross-coupling between secondary phosphine chalcogenides and alcohols or phenols proceeds in CCl_4 medium at 80–82°C to afford phosphinochalcogenoic O-esters in up to 92% yield. These couplings represent first examples of the Atherton–Todd-like reaction occurring in the absence of bases.* © 2015 Wiley Periodicals, Inc. Heteroatom Chem. 27:44–47, 2016; View this article online at wileyonlinelibrary.com. DOI 10.1002/hc.21299

INTRODUCTION

The Atherton–Todd reaction [1] continues to attract the attention of researchers as a convenient tool to prepare diverse derivatives of phosphoric and phosphinic acids [2]. This reaction has been discovered as an example of the synthesis of phosphoramidates from dialkylphosphites and primary or secondary amines. Later, the Atherton–Todd reaction has been extended to alcohols and thiols as well as to secondary phosphine oxides [2b-d, [3]]. Recently, secondary phosphine sulfides and phosphine selenides were also used in the reactions with NH-, OH-, and SH-compounds for the synthesis of amides, ethers, and thioethers of chalcogenophosphinic acids [2c, [4]]. To the best of our knowledge, all hitherto known variants of the Atherton–Todd reaction are only realized in the presence of the oxidative system base/polyhaloalkane (as a rule, in the Et_3N/CCl_4 system) [1–3]. According to the latest data [2c, [5]], the role of this system is in its interactions with dialkylphosphites by two pathways (i and ii) to produce intermediate chlorophosphate **A** (Scheme 1).

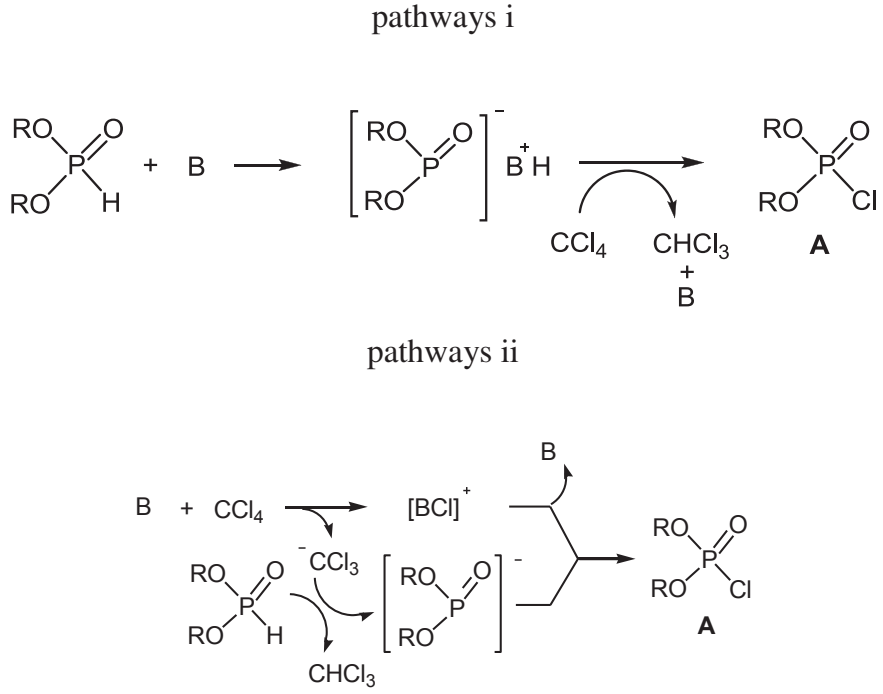
Chlorophosphates **A** react further with NH-, OH-, and SH-compounds to give amides, ethers, and thioethers of phosphoric acid, respectively [1, 2].

In this work, on the example of oxidative phosphorylation of alcohols and phenols with the system secondary phosphine chalcogenides/CCl_4, we first report on a new variant of the Atherton–Todd reaction proceeding in the absence of any bases.

The experiments have shown that bis(2-phenethyl)phosphine sulfide **1** and bis(2-phenethyl) phosphine selenide **2** react with alcohols **3, 4** or phenols **5, 6** in CCl_4 medium at 80–82°C to form phosphinochalcogenoic *O*-esters **7** in 85–92% yields, when selenide **2** in used (Table 1, entries 2–5), and in 26% yield in the case of sulfide **1** (Table 1, entry 1).

The oxidative phosphorylation of alcohols and phenols with the system secondary phosphine chalcogenide/CCl_4 in the absence of bases can be rationalized as follows. On the first step, P,X-ambident secondary phosphine chalcogenides **1, 2** react with CCl_4 as tautomers **A** to give phosphonium salts **B**. The latter are in equilibrium with phosphorane **C**, in which the cleavage of the C–P and X–H bonds occurs to deliver chlorophosphinechalcogenides **D** and chloroform. The former reacts further with ROH to afford phosphinochalcogenoic *O*-esters **7a–e** (Scheme 2).

Correspondence to: Boris A. Trofimov; e-mail: boris_trofimov@irioch.irk.ru.



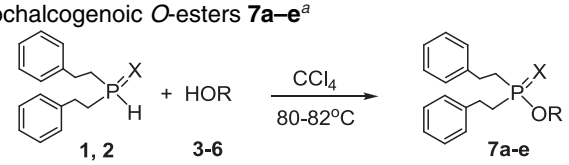
SCHEME 1 Two pathways (i and ii) of chlorophosphate A formation.

To conclude, the direct phosphorylation of alcohols or phenols with the secondary phosphine chalcogenides/carbon tetrachloride system in the absence of bases affording phosphinochalcogenoic *O*-esters fundamentally contributes to the development for the Atherton–Todd reaction.

EXPERIMENTAL

All reactions were carried out under an argon atmosphere. Carbon tetrachloride was purified according to the standard procedure [6]. Secondary phosphine chalcogenides **1**, **2** were prepared from styrene and elemental phosphorus as previously reported [7]. NMR spectral data of esters **7d**,**e** are identical to those of samples described in earlier publication [4a]. The ^{1}H, ^{13}C, ^{31}P, and ^{77}Se NMR spectra were recorded on a Bruker DPX 400 spectrometer (400.13, 100.61, 161.98, and 76.31 MHz, respectively) in $CDCl_3$ solutions and referenced to TMS (^{1}H NMR, ^{13}C NMR), H_3PO_4 (^{31}P NMR) and Me_2Se (^{77}Se NMR). IR spectra were run on a Bruker Vertex 70 instrument. Melting points (uncorrected) were measured on a Kofler micro hot-stage

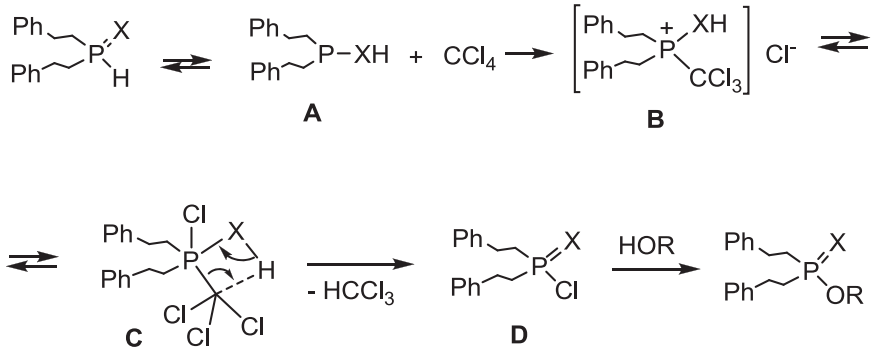
TABLE 1 Synthesis of Phosphinochalcogenoic *O*-esters **7a–e**[a]



1, 2 **3-6** **7a-e**

Entry	*$[Ph(CH_2)_2]_2P(X)H$* ***1, 2***	*X*	*HOR* ***3–6***	*R*	*Time (h)*	*Product* ***7a–e***	*Yield (%)*
1[b]	**1**	S	**4**	Amyl	74	**7a**	26
2	**2**	Se	**3**	Bu	22	**7b**	92
3	**2**	Se	**4**	Amyl	12	**7c**	86
4	**2**	Se	**5**	Ph	12	**7d**	85
5	**2**	Se	**6**	1-Napht	22	**7e**	87

[a]All experiments were carried out under argon atmosphere at 80–82°C for 74 h (in the case of phosphine sulfide **1**) and 12–22 h (when phosphine selenide **2** was used); phosphine chalcogenides **1, 2** (1 mmol), HOR (1.1 mmol) and CCl_4 (4 ml) were used. Under these conditions, chloroform is also formed.
[b]In this experiment, significant amount (yield 58%) of bis(2-phenethylthiophosphoryl)oxide is formed.



SCHEME 2 A plausible mechanism for the formation of *O*-esters **7a–e**.

apparatus. The microanalyses were performed on a Flash EA 1112 Series elemental analyzer.

The reaction was monitored using ^{31}P NMR spectra by the disappearance of peaks of the initial bis(2-phenethyl)phosphine sulfide **1** (δ_P 21.3 ppm) [7a], bis(2-phenethyl)phosphine selenide **2** (δ_P 2.2 ppm) [7b], and appearance of new peaks corresponding to *O*-esters 7**a–e**. Chlorophosphinechalcogenides **D** (Scheme 2) were identified using an authentic sample [8] by ^{31}P NMR.

*Phosphinochalcogenoic O-Esters **7a–e** (General Procedure)*

A mixture of bis(2-phenethyl)phosphine chalcogenide (1.0 mmol) and alcohol or phenols (1.1 mmol) in 4 ml of CCl_4 was stirred at 80–82°C for 74 h (in the case of phosphine sulfide **1**) and 12–22 h (when phosphine selenide **2** was used) (see also Table 1). The formation of chloroform in the reaction mixture was detected by ^{13}C NMR. The solvent was removed under the reduced pressure; the precipitate was purified by column chromatography (Al_2O_3, hexane:Et_2O:$CHCl_3$ = 10:2:1) and dried in vacuum to afford esters **7a–b**. Bis(2-phenethylthiophosphoryl)oxide [3b] (in the case of phosphine sulfide **1**) was isolated in 58% yield.

*Bis(2-phenethyl)phosphinothioic O-1-Pentyl Ester (**7a**).* Waxy product; yield: 94 mg (26%). IR (neat): 1214 (P–O–C), 612 cm^{-1} (P=S). ^1H NMR (400.13 MHz, $CDCl_3$) δ: 0.89 (t, 3H, Me, $^3J_{HH}$ 6.5 Hz), 1.31–1.34 (m, 4H, CH_2Me, CH_2Et), 1.59–1.63 (m, 2H, CH_2Pr), 2.16–2.25 (m, 4H, CH_2P), 2.87–3.98 (m, 4H, $PhCH_2$), 3.94 (dt, 2H, OCH_2, $^3J_{HH}$ 6.8 Hz, $^3J_{PH}$ 8.8 Hz), 7.16–7.21, 7.26–7.29 (m, 10H, Ph). ^{13}C NMR (100.61 MHz, $CDCl_3$) δ: 13.5 (Me), 21.8 (CH_2Me), 27.4 (CH_2Et), 28.4 (d, $PhCH_2$, $^2J_{PC}$ 2.2 Hz), 29.8 (d, CH_2Pr,$^3J_{PC}$ 6.5 Hz), 35.8 (d, CH_2P,$^1J_{PC}$ 68.1 Hz), 64.6 (d, OCH_2, $^2J_{PC}$ 6.9 Hz), 126.0 (C_p), 127.8 (C_o), 128.2 (C_m), 140.3 (d, C_i, $^3J_{PC}$ 15.1 Hz). ^{31}P NMR (161.98 MHz, $CDCl_3$) δ: 101.1. Anal. Calcd for $C_{21}H_{29}OPS$: C, 69.97; H, 8.11; P, 8.59; S, 8.90. Found: C, 69.69; H, 7.99; P, 8.13; S, 8.78.

*Bis(2-phenethyl)phosphinoselenoic O-Buthyl Ester (**7b**).* Waxy product; yield: 361 mg (92%). IR (neat): 1214 (P–O–C), 581 cm^{-1} (P=Se). ^1H NMR (400.13 MHz, $CDCl_3$) δ: 0.92 (t, 3H, Me, $^3J_{HH}$ 7.3 Hz), 1.32–1.41 (m, 2H, CH_2Me), 1.55–1.63 (m, 2H, CH_2Et), 2.25–2.41 (m, 4H, CH_2P), 2.83–3.00 (m, 4H, $PhCH_2$), 3.95 (dt, 2H, OCH_2, $^3J_{HH}$ 6.6 Hz, $^3J_{PH}$ 9.2 Hz), 7.16–7.21, 7.26–7.29 (m, 10H, Ph). ^{13}C NMR (100.61 MHz, $CDCl_3$) δ: 13.2 (Me), 18.4 (CH_2Me), 28.7 (d, $PhCH_2$, $^2J_{PC}$ 2.0 Hz), 32.0 (d, CH_2Et, $^3J_{PC}$ 6.9 Hz), 36.9 (d, CH_2P,$^1J_{PC}$ 58.2 Hz), 65.8 (d, OCH_2, $^2J_{PC}$ 6.5 Hz), 126.0 (C_p), 127.8 (C_o), 128.2 (C_m), 139.9 (d, C_i,$^3J_{PC}$ 15.5 Hz). ^{31}P NMR (161.98 MHz, $CDCl_3$) δ: 102.0 (s) (+ d satellite, $^1J_{PSe}$ 771.5 Hz). Anal. Calcd for $C_{20}H_{27}OPSe$: C, 61.07; H, 6.92; P, 7.87; Se, 20.07. Found: C, 60.89; H, 6.83; P, 7.69; Se, 19.88.

*Bis(2-phenethyl)phosphinoselenoic O-1-Pentyl Ester (**7c**).* Waxy product; yield: 350 mg (86%). IR (neat): 1213 (P–O–C), 581 cm^{-1} (P=Se). ^1H NMR (400.13 MHz, $CDCl_3$) δ: 0.93 (t, 3H, Me, $^3J_{HH}$ 6.7 Hz), 1.34–1.37 (m, 4H, CH_2Me, CH_2Et), 1.61–1.68 (m, 2H, CH_2Pr), 2.29–2.45 (m, 4H, CH_2P), 2.87–3.06 (m, 4H, $PhCH_2$), 3.97 (dt, 2H, OCH_2, $^3J_{HH}$ 6.7 Hz, $^3J_{PH}$ 9.2 Hz), 7.20–7.25, 7.29–7.33 (m, 10H, Ph). ^{13}C NMR (100.61 MHz, $CDCl_3$) δ: 14.0 (Me), 22.3 (CH_2Me), 24.0 (CH_2Et), 29.2 (d, $PhCH_2$, $^2J_{PC}$ 2.0 Hz), 30.1 (d, CH_2Pr, $^3J_{PC}$ 6.9 Hz), 37.4 (d, CH_2P,$^1J_{PC}$ 57.8 Hz), 66.6 (d, OCH_2, $^2J_{PC}$ 6.5 Hz), 126.5 (C_p), 128.3 (C_o), 128.7 (C_m), 140.4 (d, C_i, $^3J_{PC}$ 15.5 Hz). ^{31}P NMR (161.98 MHz, $CDCl_3$) δ: 102.6 (s) (+ d satellite, $^1J_{PSe}$ 770.5 Hz). Anal. Calcd for $C_{21}H_{29}OPSe$: C,

61.91; H, 7.18; P, 7.60; Se, 19.38. Found: C, 61.79; H, 7.05; P, 7.43; Se, 19.21.

*Bis(2-phenethyl)phosphinoselenoic O-Phenyl Ester (**7d**).* Waxy product; yield: 351 mg (85%). IR (neat): 1198 (P–O–C), 583 cm^{-1} (P=Se). ^1H NMR (400.13 MHz, $CDCl_3$) δ: 2.49–2.58 (m, 4H, CH_2P), 2.97–3.09 (m, 4H, $PhCH_2$), 7.18–7.23, 7.28-7.37 (m, 15H, Ph, OPh). ^{13}C NMR (100.61 MHz, $CDCl_3$) δ: 29.1 ($PhCH_2$), 37.4 (d, CH_2P, $^1J_{PC}$ 56.4 Hz), 121.8 (d, C_o, OPh,$^3J_{PC}$ 4.1 Hz), 125.2 (C_p, OPh), 126.6 (C_p, Ph), 128.3 (C_o, Ph), 128.7 (C_m, Ph), 129.5 (C_m, OPh), 140.1 (d, C_i, Ph,$^3J_{PC}$ 15.5 Hz), 150.5 (d, C_i, OPh,$^2J_{PC}$ 9.6 Hz). ^{31}P NMR (161.98 MHz, $CDCl_3$) δ: 104.3 (s) (+d satellite, $^1J_{PSe}$ 803.1 Hz). ^{77}Se NMR (76.31 MHz, $CDCl_3$) δ: -246.8 (d, $^1J_{PSe}$ 803.1 Hz). Anal. Calcd for $C_{22}H_{23}OPSe$: C, 63.93; H, 5.61; P, 7.49; Se, 19.10. Found: C, 63.82; H, 5.54; P, 7.37; Se, 18.96.

*Bis(2-phenethyl)phosphinoselenoic O-1-Naphthyl Ester (**7e**).* White solid; yield: 403 mg (87%); mp 95–97°C (hexane). IR (KBr): 1228 ν (P–O–C), 587 cm^{-1} ν (P=Se). ^1H NMR (400.13 MHz, $CDCl_3$) δ: 2.64–2.72 (m, 4H, CH_2P), 2.97–3.16 (m, 4H, $PhCH_2$), 7.17–7.20 (m, 4H, H_p), 7.23–7.33 (m, 6H, H_o, H_m), 7.45 (dd, 1H, H-3, Napht,$^3J_{HH}$ 8.1 Hz, $^3J_{HH}$ 7.8 Hz), 7.53–7.56 (m, 2H, H-5, H-8, Napht), 7.69–7.72 (m, 2H, H-2, H-4, Napht), 7.87–7.89 (m, 1H, H-7, Napht), 8.05–8.08 (m, 1H, H-6, Napht). ^{13}C NMR (100.61 MHz, $CDCl_3$) δ: 29.5 ($PhCH_2$), 38.0 (d, CH_2P,$^1J_{PC}$ 58.6 Hz), 116.3 (d, C-2, Napht, $^3J_{PC}$ 5.5 Hz), 121.6 (C-6, Napht), 124.8 (C-4, Napht), 125.2 (C-3, Napht), 126.3 (C-5, C-8, Napht), 126.6 (C_p), 128.0 (C-7, C-10, Napht), 128.3 (C_o), 128.7 (C_m), 134.9 (C-9, Napht), 140.0 (d, C_i,$^3J_{PC}$ 15.8 Hz), 147.1 (d, C-1, Napht,$^3J_{PC}$ 11.0 Hz). ^{31}P NMR (161.98 MHz, $CDCl_3$) δ: 105.1 (s) (+d satellite, $^1J_{PSe}$ 804.2 Hz). ^{77}Se NMR (76.31 MHz, $CDCl_3$) δ: -236.4 (d, $^1J_{PSe}$ 804.2 Hz). Anal. Calcd for $C_{26}H_{25}OPSe$: C, 67.39; H, 5.44; P, 6.68; Se, 17.04. Found: C, 67.27; H, 5.36; P, 6.59; Se, 16.88.

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