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Synthesis of β-organotelluro vinylphosphine oxides by hydrotelluration of 1-alkynylphosphine oxides and their palladium-catalyzed cross-coupling with alkynes

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Abstract—β-Organotelluro vinylphosphine oxides **2** can be prepared by treatment of 1-alkynylphosphine oxides **1** with tellurolate anions in satisfactory yields. Compound **2d** undergoes direct coupling reaction with terminal alkynes in the presence of $PdCl_2$/CuI, triethylamine and methanol at room temperature to give β-alkynyl vinylphosphine oxides **3** with retention of configuration in good yields.

The synthesis of stereospecifically substituted alkenes is one of the major challenges in organic synthesis. This remarkable interest in the preparation of these compounds together with the possibility to prepare enynes from them have attracted researches in this field.[1]

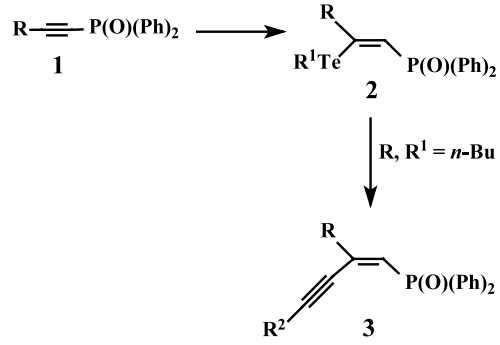
We have prepared several functionalized vinylic compounds[2] and also described the use of palladium-catalyzed reactions to prepare some types of enynes and enediynes by using cross-coupling of α-bromo-vinyl chalcogenides,[3] α-thio-vinyl tosylates[4] and vinyl tellurides[5] with terminal alkynes.

On the other hand, unsaturated phosphorus compounds represent a class of important synthetic intermediates.[6,7] For example, vinyl phosphine oxides have been used to synthesize functionalized phosphine oxides by adding nucleophiles to the electrophilic double bound[8] and also undergo cycloaddition reactions.[9]

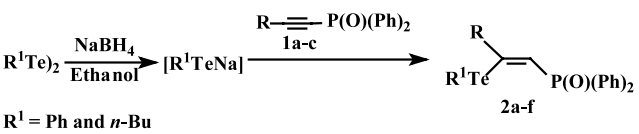
Previously, we have shown that 1-alkynylphosphonates can be used to prepare β-organochalcogeno vinylphosphonates[10] by hydrochalcogenation and enynephosphonates from cross-coupling reaction of β-organotelluro vinylphosphonates with alkynes.[11] In connection with our continued work on this class of compounds, we decided to expand the scope of these methodologies to phosphine oxides derivatives (Scheme 1).

The β-organotelluro vinylphosphine oxides **2** were prepared by addition of alkynylphosphine oxides **1** to a solution of sodium organyl tellurolate, prepared by reduction of ditellurides with sodium borohydride in ethanol at room temperature[12] (Scheme 2).

The products **2a–f** were obtained in satisfactory yields with high *Z*-stereoselectivity (Table 1). In the case of Ph_2Te_2, only β-organotelluro vinylphosphine oxides **2a**,



Scheme 1.



R¹ = Ph and *n*-Bu
R = Ph; *n*-Bu; cyclohexenyl

Scheme 2.

Keywords: phosphine oxide; tellurium; enyne; palladium; cross-coupling.

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Table 1. Synthesis of β-organotelluro vinylphosphine oxides **2** according to Scheme 2

Entry	1-alkynylphosphine oxide **1**	Product **2**	*E*:*Z*[b]	Reaction Time / h	Product **2**[a] Yield %
1	Ph—≡—P(O)(Ph)$_2$	Ph, PhTe, P(O)(Ph)$_2$ **2a**	0:100	5	65
2	Ph—≡—P(O)(Ph)$_2$	Ph, *n*-BuTe, P(O)(Ph)$_2$ **2b**	25:75	6	54
3	*n*-Bu—≡—P(O)(Ph)$_2$	*n*-Bu, PhTe, P(O)(Ph)$_2$ **2c**	0:100	5	62
4	*n*-Bu—≡—P(O)(Ph)$_2$	*n*-Bu, *n*-BuTe, P(O)(Ph)$_2$ **2d**	15:85	7	52
5	P(O)(Ph)$_2$	PhTe, P(O)(Ph)$_2$ **2e**	0:100	6	55
6	P(O)(Ph)$_2$	*n*-BuTe, P(O)(Ph)$_2$ **2f**	15:85	7	50

[a] Isolated yield.
[b] The ratios of *E*- and *Z*-isomers were estimated on the basis of ^{1}H NMR data.

2c and **2e** with (*Z*)-configuration were obtained, while β-butyltelluro vinylphosphine oxides **2b**, **2d** and **2f**, with predominant (*Z*)-stereoselectivity, were isolated using *n*-Bu_2Te_2. The regiochemistry and the exclusive or predominant *Z*-stereochemistry of compounds **2** obtained were readily determined by NMR spectral analysis, especially NOESY experiments.

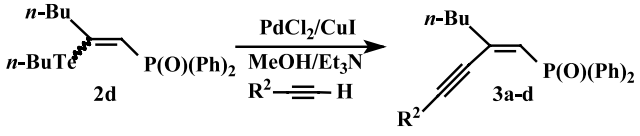
The required starting 1-alkynylphosphine oxides **1**[13] were prepared in a one-pot procedure from diphenylphosphinic chloride and alkynyllithium, in a method similar to the preparation of alkynylphosphonate.[14]

With the β-organotelluro vinylphosphine oxides **2** in hand, we chose one of them to study the coupling reaction with 1-alkynes. The selected compound **2d** (as a mixture of isomers *Z*:*E* 85:15) was treated with appropriated alkynes under cross-coupling conditions[5] to give the β-alkynyl vinylphosphine oxides **3** (70–78% yields, Scheme 3, Table 2).

Our initial goal in the study of this reaction was to investigate the effects of a variety of reaction conditions including solvent (THF, dichloromethane, benzene, methanol and *N*,*N*-dimethylformamide), amine (pyridine, pyrrolidine, diethylamine, triethylamine and diisopropylamine) and catalysts [$Pd(OAc)_2$, $Pd(PPh_3)_4$, $PdCl_2$ and CuI]. We found that the optimum condition for the cross-coupling reaction was the use of $PdCl_2$/CuI (20 mol% each), Et_3N (1 mmol), methanol (10 mL), β-organotelluro vinylphosphine oxide **2d** (1 mmol) and the appropriated 1-alkyne (2 mmol) at room temperature,[15] as recently described by us in the preparation of enynephosphonates.[11] Compounds **3a–d** were isolated as oils or solids after flash chromatography on silica gel, using a mixture of hexane–ethyl acetate as eluent.

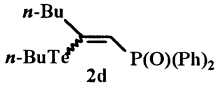
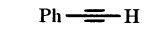
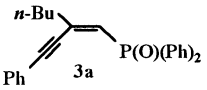
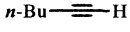
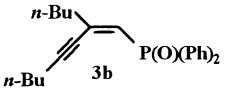
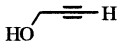
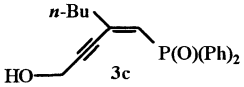
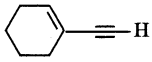
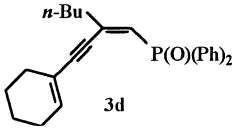
As indicated by NMR analysis, only the *Z*-isomer of the enynes **3** was obtained and no signal of *E*-isomer was observed. Also, none of the starting *E*-isomer of β-organotelluro vinylphosphine oxide **2d** was recovered at the end of reaction.

We do not know with certainty what the fate of the *E*-isomer is, since it is consumed in the reaction but does not furnish the corresponding coupling product. We suppose that the *E*-isomer decomposes and does not isomerize under the coupling conditions. For example, the treatment of an 85:15 mixture of isomers of **4d**,



Scheme 3.

Table 2. Synthesis of β-alkynyl vinylphosphine oxides **3** according to Scheme 3

Entry	β-organotelluro vinylphosphine **2d**	1-alkyne	Product **3**	Reaction Time / h	Product **3**[a] Yield %
1	 **2d**		 **3a**	8	72
2	**2d**		 **3b**	7	78
3	**2d**		 **3c**	7	70
4	**2d**		 **3d**	6	73

[a]Isolated yield.

under the reaction conditions but in the absence of the Pd catalyst, furnished only starting materials, at the same previous ratio. To address correctly the problem, a good alternative would be using **4d** in a different ratio than the 85:15, as isolated. Unfortunately, even after several different experiments, such as isomerizations, changing of reaction conditions or inverse addition of reagents, we always obtained basically the same thermodynamic ratio. Because of this, experiments with different *E*:*Z* ratios, or the use of pure *E*-isomer could not be performed. To our knowledge, the preparation of (*E*)-β-organotelluro vinylphosphine oxides have not been described.

In summary, we have demonstrated by our studies the hydrotelluration of alkyne bearing diphenylphosphoryl group and disclosed a new class of vinylphosphine oxide and its synthetic application. The synthesized β-organotelluro vinylphosphine oxide **2d** was used to prepare β-alkynyl vinylphosphine oxides **3**, an important class of enynes. It is expected that this class of vinylphosphine oxides and enynes will find considerable application in organic synthesis, since the phosphine oxides are well-known to be a good ligand for transition metal complexes[16] and some derivatives of vinylphosphine oxides can be used as biologically active compounds.[6,7e,17]

Acknowledgements

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12. **Preparation of β-organotelluro vinylphosphine oxides 2a–f. General procedure:** To a solution of R′TeNa [generated in situ from R′TeTeR′ (0.5 mmol) and $NaBH_4$ (1.1 mmol)] in absolute ethanol (5 mL) the 1-alkynylphosphine oxide **1** (1.0 mmol) dissolved in ethanol (5 mL) was added dropwise at room temperature. The reaction mixture was stirred for the time indicated in Table 1. Then the mixture was poured into a saturated aqueous solution of NH_4Cl (5 mL) and the aqueous layer was extracted with ethyl acetate (2×20 mL). The organic layer was dried over $MgSO_4$ and evaporated. The residue was purified by flash chromatography on silica gel with hexane/ethyl acetate (6:4) to give the product **2**. **Selected spectral data for 2e**: mp 149–151°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80–7.51 (m, 6H), 7.42–7.19 (m, 6H), 7.18–7.02 (m, 3H), 6.68 (d, 1H, $J_{P-H}=28.12$ Hz), 5.47–5.44 (m, 1H), 2.02–1.55 (m, 4H), 1.14–0.85 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 156.06 (d, $^3J_{P-C}=1.5$ Hz), 141.04, 140.81 (d, $^2J_{P-C}=17.9$ Hz), 133.04 (d, $^1J_{P-C}=103.3$ Hz, Ph_2PO), 131.49, 130.89 (d, $^3J_{P-C}=9.9$ Hz, Ph_2PO), 128.35 (d, $^2J_{P-C}=12$ Hz, Ph_2PO), 128.07, 127.75, 126.42, 119.24 (d, $^1J_{P-C}=105.5$ Hz), 118.13, 29.20, 24.52, 21.41, 21.21; IR (KBr; cm^{-1}) 3052, 2922, 2915, 1546, 1476, 1434 (P–Ph), 1176 (P=O), 1120, 795, 720, 692, 544.
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15. **Preparation of β-alkynyl vinylphosphine oxides 3a–d. General procedure**: To a solution of $PdCl_2$ (20 mol%, 0.035 g), CuI (20 mol%, 0.038 g), Et_3N (1 mmol) in MeOH (10 mL) at 25°C under an argon atmosphere, was added β-butyltelluro vinylphosphine oxide **2d** (1 mmol) and the appropriate alkyne (2 mmol). The mixture was stirred at room temperature for the time indicated in Table 2, treated with saturated aqueous solution of NH_4Cl (10 mL), extracted with ethyl acetate (2×20 mL). The organic layer was washed with brine and dried over $MgSO_4$. The solvent was evaporated and the residue was purified by flash chromatography on silica gel eluting with hexane/ethyl acetate (1:1) to give the product β-alkynyl vinylphosphine oxide **3**. **Selected spectral data for 3d**: mp 68–70°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87–7.69 (m, 4H), 7.52–7.39 (m, 6H), 6.26 (d, 1H, $J_{P-H}=18$ Hz), 5.79–5.75 (m, 1H), 2.36 (t, 2H, $J=7.6$ Hz), 2.09–2.00 (m, 2H), 1.80–1.75 (m, 2H), 1.65–1.33 (m, 8H), 0.91 (t, 3H, $J=7.6$ Hz); ^{13}C NMR (100 MHz, $CDCl_3$): δ 144.75, 137.28 (d, $^2J_{P-C}=2$ Hz), 133.84 (d, $^1J_{P-C}=104.8$ Hz, Ph_2PO), 131.26, 131.21 (d, $^3J_{P-C}=9.8$ Hz, Ph_2PO), 128.27 (d, $^2J_{P-C}=12.1$ Hz, Ph_2PO), 125.14 (d, $^1J_{P-C}=102.5$ Hz), 120.12, 103.25, 85.05 (d, $^3J_{P-C}=10.6$ Hz), 40.41 (d, $^3J_{P-C}=13.8$ Hz), 30.08, 28.12, 25.64, 22.01, 21.93, 21.19, 13.80; IR (KBr; cm^{-1}) 2934, 2859, 2190 (C≡C), 1570, 1435 (P–Ph), 1187 (P=O), 1117, 754, 722, 696, 602, 536. MS m/z 338 (M^+).
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