



Direct Michael addition to electron-deficient alkenes using diorganyl dichalcogenides (Te/S) and NaBH₄/PEG-400



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ABSTRACT

Nucleophilic species of tellurium and sulfur were generated in situ from the reaction of the respective diorganyl dichalcogenides with NaBH₄ in PEG-400 as solvent and selectively added to electron-deficient alkenes. Chalcogenolate anions were directly added at mild conditions by this simple procedure and in all cases furnished the respective Michael adducts in short reaction times and good yields.

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The addition of nucleophilic species of tellurium and sulfur to electron-deficient alkenes represents a very useful method for the formation of new carbon–chalcogenium bond in organic synthesis. Regarding organosulfur compounds, several methods were described using readily available thiols in thia-Michael additions to form C–S bonds.¹ On the other hand, the formation of C–Te bond via Te-Michael addition was scarcely studied, because the generation and use of the analog organyltelluro are not trivial. Both adducts, β-organylthio- and β-organyltellurocarbonyl compounds, are interesting intermediates in organic synthesis, for example, in the synthesis of sulfones and sulfoxides,² in the total synthesis of gercalin A,³ and in the preparation of tetrazoles with antifungal activity.⁴

Among the methods included for the formation of C–Te bonds via telluro-Michael addition is the use of nucleophilic species generated in situ from C₆H₅TeSiMe₃/SmI₂,⁵ (ArTe)₂/Sm/ZrCl₄,⁶ BuLi/Te/EtOH,⁷ (ArTe)₂/Zn/ZrCl₄,⁸ and Te/BuLi/H₂O.⁹ However, most of these methods present some drawbacks like the use of strong base, addition of stoichiometric quantities of ^tBuOH or BuOH, acidic extraction, and expensive reagents. In others cases, the preparation of the nucleophilic species involves several steps, making them time consuming and costly protocols. Besides scarce, these methods make intensive use of Volatile Organic Compounds (VOCs) as solvent. In this sense, the development of practical, selective, and

efficient methods to prepare β-organyltellurocarbonyl compounds is justifiable.

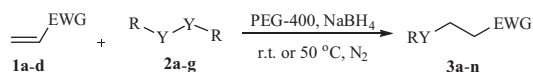
Recently, we developed a new method for the in situ generation of chalcogenolate anions by using the system (RY)₂/NaBH₄/PEG-400 (Y = S, Se, Te). The nucleophilic species were successfully added to alkynes to prepare selectively bis-chalcogen alkenes.¹⁰ More recently, we describe the direct Michael-type addition of nucleophilic species of selenium generated in situ, using diorganyl diselenide and NaBH₄.¹¹

However, to our knowledge, the direct hydrotelluration of α,β-carbonyl compounds using diorganyl ditelluride and NaBH₄ to afford Michael adducts was not yet described. In continuation to our studies on the formation of carbon–chalcogenium bonds, here we describe the addition of nucleophilic species of tellurium and sulfur generated in situ using NaBH₄/PEG-400 to electron-deficient alkenes (Scheme 1).^{12,13}

Initially, we chose as standard starting materials methyl acrylate **1a** and diphenyl ditelluride **2a** to perform the optimization studies under N₂ atmosphere (Table 1). We studied the temperature, amounts of methyl acrylate, diphenyl ditelluride, reaction time, and the nature of the solvent. When the nucleophilic tellurium species was generated using 0.25 mmol of the ditelluride **2a** in PEG-400 (3.5 mL) in the presence of 0.5 mmol of acrylate **1a** at room temperature, the desired product **3a** was obtained in 42% yield after 1 h (Table 1, entry 1). To our surprise, by increasing the temperature to 50 °C, a decrease in the yield of the desired product **3a** was observed (Table 1, entry 2). Next, experiments were carried out varying the amount of **1a** and **2a** at room

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Scheme 1. General scheme of the reaction.

temperature (Table 1, entries 3–5). When an excess of ditelluride **2a** was used (0.5 mmol) there was no increase in the yield of **3a** (Table 1, entry 3). However, in another experiment, it was observed that by using 1.0 mmol of alkene **1a**, the product **3a** was obtained in 75% yield (Table 1, entry 4). Similar result was obtained by further increasing the amount of acrylate **1a** to 1.5 mmol (Table 1, entry 5).

Subsequently, we studied the influence of the reaction time and it was observed that the yield of **3a** decreased both, when **1a** and **2a** reacted for 0.5 h (Table 1, entry 6) and for 1.5 h (entry 7). When the reaction mixture was stirred for a longer reaction time, its color turned reddish and a large amount of diphenyl ditelluride was recovered. Aiming to verify the influence of the solvent, the reaction was performed also using ethanol, glycerol, and a mixture ethanol/THF (Table 1, entries 8–10). The best result was obtained using a 1:1 mixture of ethanol/THF (Table 1, entry 10); however, the yields of **3a** were inferior to that obtained using PEG-400 (entry 4).

In an optimized reaction, NaBH₄ was added to a reddish mixture of diphenyl ditelluride **2a** and PEG-400. The heterogeneous reaction mixture was stirred for 40 min at room temperature under N₂ atmosphere. After that, the color turned white, indicating the cleavage of the Te–Te bond. Then, methyl acrylate **1a** was added and the mixture was stirred for additional 1.0 h, affording methyl 3-phenyltellanylpropanoate **3a** in 75% yield. A plausible mechanism for this reaction is similar to that proposed for the hydrochalcogenation of terminal alkynes using PEG-400, with the solvent acting as a proton-donor in the reaction.¹⁴

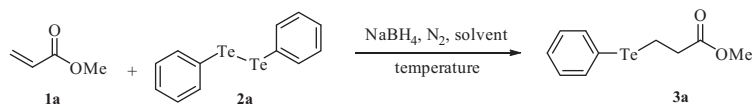
Extending the scope of our methodology, the possibility of performing the reaction with other ditellurides was investigated and, in most cases, the reaction proceeded smoothly to give the respective 3-organyltellurium esters **3a–e** and nitrile **3f–i** in good yields (Table 2, entries 2–9). It was observed that the presence of electron-withdrawing and electron-donating groups in the aryl ditelluride affects the reactivity of the tellurium species (Table 2, entries 2–4 and 7–8). Thus, when 4-chlorophenylditelluride **2c**

was used, methyl 3-(4-chlorophenyltellanyl)propanoate **3c** and 3-(4-chlorophenyltellanyl)propanenitrile **3g** were obtained, respectively, in 51% and 60% yields respectively (Table 2, entries 3 and 7). In contrast, the presence of electron-donors in the aromatic ring of the ditelluride favors the reaction. Thus, when 4-methoxyphenylditelluride **2b** and 4-methylphenylditelluride **2d** were used, the desired products **3b**, **3d**, and **3h** were obtained in 80%, 69%, and 71% yields, respectively, (Table 2, entries 2, 4, and 8). We observed that our new protocol is also suitable for dialkyl ditelluride **2e**. Methyl 3-butyltelluropropanoate **3e** and methyl 3-butyltelluro propanonitrile **3i** were obtained in 80% and 95% yields under our conditions (Table 2, entries 5 and 9). However, when 1,2-disubstituted alkene was used, such as aryl acrylate, no adduct was formed, with the starting material being recovered even after 24 h of reaction.

We also tested the system NaBH₄/PEG-400 using diorganyl disulfide as chalcogenium source in the thia-Michael addition to electron-deficient alkenes. To generate the nucleophilic species, NaBH₄ (0.6 mmol) was added to a mixture of diphenyl disulfide **2f** or didodecyl disulfide **2g** (0.6 mmol) in PEG-400 (3.5 mL) and the mixture was stirred for 40 min at 50 °C under N₂. Differently to the ditelluride analog, in this case it was not possible to observe a change in the color of the reaction mixture due the cleavage of the S–S bond. Then, methyl acrylate **1a** (0.5 mmol) was added and the mixture was stirred for additional 2 h at 50 °C, affording methyl 3-phenylthiopropoate **3j** in 87% yield (Table 2, entry 10). When a smaller amount of **2f** (0.25 mmol) was used, **3j** was obtained only in 35% yield. The yield of **3j** increased to 55% when 0.5 mmol of **2f** was used. Thus the use of an excess of the nucleophilic species was necessary to prepare the sulfur analogs. The best reaction conditions were extended to other α,β -unsaturated alkenes and, except for acrylic acid **1c**, in all the tested examples the products were obtained in good yields (Table 2, entries 11–13). Besides, using dialkyl disulfide **2g**, the product methyl 3-dodecylthiopropoate **3n** was obtained in 82% yield (Table 2, entry 14).

Due to our interest in the synthetic applications of organochalcogen compounds, we performed the synthesis of the thiofunctionalized hydrazide **4a**,¹⁵ a member of a class of compounds that have gained importance because of their biological and pharmacological activities (Scheme 2).¹⁶ More recently, hydrazides containing the group organo-sulfur or tellurium, were used for the synthesis of vinyl-substituted 1,3,4-oxadiazoles,¹⁷ and of Cy-NTE, a reversible

Table 1
Optimization of the synthesis of methyl 3-phenyltellanylpropanoate **3a**^a



Entry	1a (mmol)	2a (mmol)	Solvent	Time (h)	Yield ^b (%)
1	0.5	0.25	PEG-400	1.0	42
2	0.5	0.25	PEG-400	1.0	30 ^c
3	0.5	0.5	PEG-400	1.0	32 ^d
4	1.0	0.25	PEG-400	1.0	75
5	1.5	0.25	PEG-400	1.0	76
6	1.0	0.25	PEG-400	0.5	60
7	1.0	0.25	PEG-400	1.5	50
8	1.0	0.25	Ethanol	1.0	45
9	1.0	0.25	Glycerol	1.0	Traces
10	1.0	0.25	Ethanol/THF	1.0	65

^a Reactions performed in the presence of **1a**, **2a**, NaBH₄ (0.6 mmol), and solvent (3.5 mL) under N₂ atmosphere at room temperature.

^b Yields are given for isolated product **3a**.

^c Reaction performed at 50 °C.

^d 1.2 mmol of NaBH₄ was used.

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