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Hydrotelluration of aminoalkynes†

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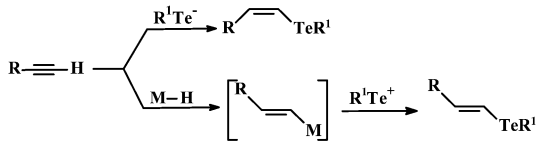
Metal tellurolates (M = B^{3+}; BuTeTeBu/$NaBH_4$/EtOH; Li^{3+}, Te^0/BuLi/THF; In^{3+}, BuTeTeBu/InI/EtOH) react with aminoalkynes to produce vinylic tellurides containing amino groups; the regio-, and stereo-chemistry of the hydrotelluration reaction depend on the metallic counter ion and on the nature of the amino group substituent.

Vinylic tellurides, useful intermediates in organic synthesis, have been prepared by several different routes.[1] *Z*-Vinylic tellurides were obtained by hydrotelluration of alkynes with boron tellurolate (BuTeTeBu/$NaBH_4$/EtOH)[2] or lithium tellurolate (Te^0/BuLi/THF) (Scheme 1).[3] *E*-Vinylic tellurides were prepared by stereospecific *cis* hydrometallation of alkynes, followed by transmetallation of the *E*-vinylorganometallic complexes with organotellurenyl halide (Scheme 1).[4] Due to their easier preparation, the *Z*-isomers have been employed more frequently as intermediates in organic synthesis.[5] One of the most important reactions of vinylic tellurides is the transmetallation.[6] The vinyl organometallics obtained were shown to react with carbonyl compounds,[7] α,β-unsaturated systems[8] and epoxides.[9] Recently, we have found new applications for *Z*-vinylic tellurides using palladium catalyzed cross-coupling to obtain enynes and enediynes; in these cases, the tellurides were shown to act as an equivalent of an aryl or vinyl carbocation.[10] Total synthesis of natural products with biological activity such as macrolactins[11] and polyacetylenic compounds were also achieved *via* vinylic tellurides.[12]



Scheme 1

To the best of our knowledge, there is only one reported preparation of vinylic tellurides functionalized with amino groups.[13] Motivated by our interest in the preparation and applications of vinylic tellurides in organic synthesis, we have investigated the hydrotelluration of aminoalkynes, promoted by the tellurolate nucleophile generated from dibutylditelluride/$NaBH_4$/EtOH and from Te/BuLi/THF. Our initial efforts focused on the reaction of aminoalkynes **1** with boron butyl tellurolate. Thus, dibutylditelluride was added dropwise into a solution containing aminoalkynes **1a**, $NaBH_4$ and ethanol. The resulting solution was refluxed for 24 h and monitored by TLC. Under these conditions, the corresponding vinylic tellurides **2a** were obtained as a minor product (20%). However, when $NaBH_4$ was added in small portions, under argon, to a solution of dibutylditelluride in EtOH (5 mL) at room temperature, we observed, after 10 minutes, the consumption of the red ditelluride. A solution of the aminoalkyne **1a** in EtOH (10 mL) was added and the mixture was heated at reflux for 24 h. This procedure afforded the desired vinylic tellurides **2a**.

† Electronic supplementary information (ESI) available: spectroscopic data and detailed experimental procedures for all new compounds. See http://www.rsc.org/suppdata/cc/b3/b301857a/

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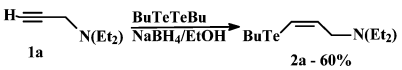
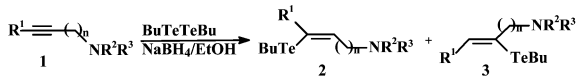
An optimized yield (60% after purification by column chromatography) was obtained from $NaBH_4$ (0.057 g; 1.5 mmol), dibutylditellurides (0.18 g; 0.5 mmol) in EtOH (5 mL), and aminoalkyne **1a** (1 mmol) at reflux (Scheme 2). The vinylic tellurides **2** and **3** prepared using this procedure were obtained in moderate to good yields (Table 1).



Scheme 2

Table 1 Hydrotelluration of aminoalkynes by BuTeTeBu/$NaBH_4$

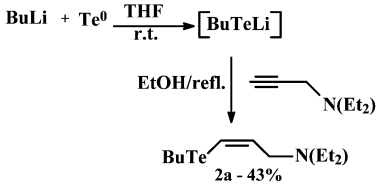


	R^1	R^2	R^3	*n*	Yield (%)	Ratio **2** : **3**
a	H	C_2H_5	C_2H_5	1	60	1 : 0
b	H	H	H	1	50	2 : 1
c	H	H	CH_3	1	60	3 : 1
d	H	cyclo-$(CH_2)_4$		1	67	1 : 0
e	H	cyclo-$(CH_2)_5$		1	57	1 : 0
f	H	$(CH_2)_2$–O–$(CH_2)_2$		1	71	1 : 0
g	MeS	C_2H_5	C_2H_5	1	50	0 : 1
h	BuSe	C_2H_5	C_2H_5	1	n.r.	—
i	C_4H_9	C_2H_5	C_2H_5	1	n.r.	—
j	H	H	H	5	35	1.4 : 1
k	H	C_2H_5	C_2H_5	5	55	1.6 : 1

Examining Table 1, we first note that the hydrotelluration of tertiary propargyl amines of terminal alkynes (entries a, d–f) produces regio-, and stereo-selectively the corresponding product (*Z*)-1-butyltellurio-3-dialkylamino-1-propene, **2**. Considerable loss of the regiochemical control was verified for primary (entry b) and secondary (entry c) amines, which produced a mixture of the corresponding vinylic tellurides **2** and its regioisomer **3**. Again, loss of the regiochemistry was observed when the length of the methylene chain was increased in the aminoalkynes (entries j and k). Internal alkynes (entries h and i) resisted the hydrotelluration, and this is the major drawback of the protocol. The only internal alkyne that was hydrotellurated was 3-dimethylamino-1-methylthio-1-propyn (entry g) that leads to the exclusive formation of the corresponding derivative **3g**. The structures of the vinylic tellurides **2** and **3** were confirmed by ^1H and ^{13}C NMR spectroscopy. As an illustrative example, compound **2a** exhibits a pair of doublet of triplets centered at 6.32 ppm (J = 9.2, 5.6 Hz) and at 6.77 ppm (J = 9.2, 1.2 Hz) attributed to the *cis*-related olefinic protons.

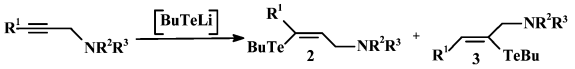
Some of the aminoalkynes, **1** were also allowed to react with the tellurolate anion prepared by addition of BuLi to elemental tellurium (Scheme 3).

Thus, a solution of compound **1a** in deoxygenated ethanol was added dropwise to a solution containing $BuTe^-$ (generated by addition of BuLi to a suspension of elemental tellurium and THF at room temperature). The resulting solution was refluxed



Scheme 3

Table 2 Hydrotelluration of aminoalkynes by [BuTeLi]



	R^1	R^2	R^3	Yield (%)	Ratio **2** : **3**
a	H	C_2H_5	C_2H_5	43	1 : 0
b	H	H	H	48	2 : 1
c		Cyclo-$(CH_2)_5$		40	1 : 0
d		$(CH_2)_2$–O–$(CH_2)_2$		58	1 : 0
e	MeS	C_2H_5	C_2H_5	32	0 : 1
f	C_4H_9	C_2H_5	C_2H_5	n.r.	

for 24 h and monitored by TLC. This procedure gave the corresponding vinylic tellurides **2a** in 43% yield. The reactions listed in Table 2 show the same trends as the cases discussed above obtained from the tellurolate generated by $NaBH_4$, and no improvements in the regio-, and stereo-selectivity were achieved.

The reaction pathways leading to products **2** and **3** seem to depend on the metallic counter ion and on the substitution pattern of the amino group. Compounds **2** are formed by a Michael-type addition of a tellurolate anion onto the triple bond with a subsequent trapping of the vinyl anion with a proton from the alcohol. To support this mechanistic description, we have carried out the reaction of **1a** under the conditions described in Table 1 in EtOH d_6, and (*Z*)-1-butyltellurio-1,2-dideuterio-3-diethylamino-1-propene was isolated as the major product.

Products **3** were obtained from aminoalkynes containing primary and secondary amino substituents. The potentially acidic amino group protons seem to play an important role in the formation of derivatives **3**. A mechanistic description based on the coordination of the aminoalkyne to the tellurolate through the nitrogen atom with a subsequent Markovnikov addition of the tellurol, BuTeH, constituents across the triple bond accommodates the observed experimental facts. This description was proposed recently to explain the chemio-, regio-, and stereo-selective hydroselenation of 2-alkyn-1-ol derivatives promoted by indium(III) selenolates.[14] Accordingly, we have observed the exclusive production of **3c** (Table 2) when the aminoalkyne **1c** was hydrotellurated with an indium(III) tellurolate obtained from the oxidation of indium(I) iodide by BuTeTeBu in EtOH. Further, we point out that no tertiary aminoalkynes could be hydrotellurated by the indium complex.

In summary, we present here the first hydrotelluration reaction of aminoalkynes by metal tellurolates. Both the nature of the metallic counter ion and the degree of substitution (steric effect) on the amino substituent play important roles in the regio-, and stereo-chemistry of the reaction. Metal tellurolates derived from $NaBH_4$ and BuLi produce mainly the anti-Markovnikov adducts of (*Z*) stereochemistry, **2**; and a Michael-type mechanism initiated by the attack of a tellurolate nucleophile onto the triple bond seems to govern the process. In these reactions, Markovnikov adducts **3** were obtained as secondary products from alkynes containing primary and secondary amino group substituents while these compounds were formed exclusively with indium(III) tellurolate. The reaction pathway leading to **3** is governed by coordination of the aminoalkyne to the metal-tellurolate complex. We expect that these findings would be useful to assist in the choice of a method for hydrotelluration of acetylenes containing different functional groups. These reactions associated with the palladium-catalyzed cross-coupling of vinyl tellurides with organometallics and alkynes can constitute an interesting alternative route to the regio-, and stereo-selective preparation of allylic amines and derivatives. The pharmacological activity of these compounds is under study in our laboratory.

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