Mechanistic aspects of the isomerization of Z-vinyllic tellurides double bonds in the synthesis of potassium Z-vinyltrifluoroborate salts

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Abstract

Through direct transmetalation reaction of Z-vinyllic tellurides with nBuLi was observed the unexpected isomerization of double bonds leading to potassium E-vinyltrifluoroborates salts in low to moderate yields. Using EPR spin trapping experiments the radical species that promoted the stereoinversion of Z-vinyllic organometallic species during the preparation of potassium vinyltrifluoroborate salts was identified. The experiments support the proposed mechanism, which is based on the homolytic cleavage of the Te-nBu bond.

Background

Boronic acids and boronate esters are the most commonly used derivatives in Suzuki-Miyaura cross-coupling reactions. Recently, Molander et al. [1] and our group [2] have explored the use of potassium organotrifluoroborate salts as an alternative to the usual organoboron reagents in alkenyl-alkenyl,[3] aryl-aryl,[4] alkenyl-alkenyl,[5] and alkenyl-aryl [6] cross-coupling reactions.

Distinct from the most commonly explored hydrometallation reactions, the hydrotellurilation of alkynes exclusively forms Z-vinyllic tellurides. [7] Vinylic tellurides have the ability to undergo tellurium-metal exchange reactions with several different commonly used, commercially available, or easily prepared organometallic reagents, leading to Z-vinylolithiums and Z-vinylcyanocuprates. In reactions promoted by Pd or Ni, these compounds undergo stereospecific coupling with a wide range of organic species. [8] The vinylic organometallic species obtained in this way can also react with carbonyl compounds, α, β-unsaturated systems, or epoxides [9-11] with complete retention of the double-bond stereochemistry.

Taking advantage of the regio- and stereocontrol of the preparation of Z-vinyllic tellurides,[12] and of the unique features of the transmetallation with complete retention of the original double bond geometry, we report herein the synthesis of potassium vinyltrifluoroborate salts by means of the Te-Li exchange reaction. To the best of our knowledge, this is the first reported preparation of potassium E-vinyltrifluoroborate salts from Z-vinyllic tellurides.

Results and discussion

Functionalized Z-vinyllic tellurides were prepared by hydrotellurilation of alkynes. [13] Using phenyl vinyl telluride, we performed a series of test reactions to establish
the best reaction conditions for the lithium-boron exchange step (Table 1; ii, Scheme 1). Optimum yield was obtained with B(OiPr)₃ as the electrophile and ether as the solvent (entry 6).

Using the optimized conditions (Table 1, entry 6), all the Z-vinyllic tellurides were, to our surprise, transformed into potassium E-vinyltrifluoroborate salts exclusively (see additional file 1) (Figure 1).

The ¹H NMR spectra of the products showed the presence of the salt nBuBF₃K as a by-product (30–50% of the total yield). Use of 1.0 equiv. of nBuLi instead of 1.5 equiv. as in the optimized protocol gave the same proportion of nBuBF₃K.

With ¹H NMR, we tried to observe the coupling constants of the vinylic hydrogens for each intermediate of the reaction route. Using this approach, we could prove the cis geometry of the vinylic hydrogens of the intermediate 2 (Scheme 1), which presented a coupling constant of 18.09 Hz. [14,15] Unfortunately, the boronic "ate" complex 4 (Scheme 1) is an insoluble species and no ¹H NMR spectra were obtained. However, these results indicated that the double bond geometry isomerization occurred only after the formation of the intermediate 4(Scheme 1).

We suggest that homolytic cleavage of the Te-Bu bond, from 3 (ii, Scheme 1), generates nBu*, which is responsible for the cis-trans isomerization. The butyl radical attack occurs at the boronic "ate" complex 4(Scheme 1),[16] yielding the nBuBF₃K salt as a final product.

Table 1: Lithium-Boron Test Reaction Conditions.

| Entry | Electrophile (eq) | Solvent | Yield (%) |
|-------|------------------|---------|-----------|
| 1     | B(OMe)₃ (1.5)    | THF     | 18        |
| 2     | B(OiPr)₃ (1.5)   | THF     | 47        |
| 3     | BF₃OEt (1.5)     | THF     | -         |
| 4     | B(OiPr)₃ (1.5)   | THF/HMPA| 25        |
| 5     | B(OiPr)₃ (1.5)   | THF/TMEDA| -        |
| 6     | B(OiPr)₃ (1.5)   | Et₂O    | 51        |
| 7     | B(OiPr)₃ (1.5)   | Et₂O    | 15        |

In order to verify the presence of radical species in the reaction mixture, we performed EPR spin trapping experiments using 3,5-dibromo-4-nitrosobenzenesulfonate (DBNBS), which is an appropriate spin trap for tellurium centered radicals. [17] Radical species were detected at the i and ii steps of the proposed route. In the first step (i, Scheme 1), the detected spectra contained a mixture of DBNBS radical adducts (Figure 2A). The triplet of triplets (aₙ = 21.6 G, aₕ = 0.7 G) is the DBNBS/ nBuTe radical adduct [17] and the broadened triplet (aₙ = 9.1 G, aₕ = 1.0 G) can be attributed to another DBNBS radical adduct. The intensity of the broadened triplet started to decay after 5 min incubation, and was barely detected in the 15 min incubation spectrum (Fig. 2B). The DBNBS/TeBu signal maintained its intensity during the course of the EPR analysis.

After the addition of the B(OiPr)₃ (ii, Scheme 1), the reaction mixture produced a complex EPR spectra that can be attributed to a mixture of radical species (Figure 3). The addition of the boron reagent generated different radical species from those observed in the previous reaction step (Figure 2).
We performed control experiments to exclude the possibility of radical generation by the combination of the boron reagent with \( \text{O}_2 \) [18] or by the self-radical generation of the \( \text{nBuTe} \) reagent. Incubation of \( \text{nBuTe} \), \( \text{nBuLi} \) and DBNBS produced no EPR signals (Table 2, entries 3–5). Equimolar solutions of \( \text{nBuTe} \), \( \text{nBuLi} \) and DBNBS (Table 2, entry 6) produced a radical signal with similar parameters as those detected during the Te-Li exchange (\( \text{i} \), Scheme 1). In the absence of the reducing reagent (\( \text{nBuLi} \)), an equimolar solution of \( \text{nBuTe} \), \( \text{B(OiPr)}_3 \) and DBNBS also did not produce EPR signals (Table 2, entry 8).

To test our proposed mechanism, we repeated the reaction using (\( Z \))-\( \beta \)-bromostyrene, to achieve the desired \( Z \)-vinyllithium, the experiments were performed using \( \text{BuLi} \) in a solution composed of THF/Et\(_2\)O/petrol ether, at -120°C, with and without \( \text{nBuTe} \), instead of \( Z \)-vinylic tellurides to examine the effect of the \( \text{nBuTe} \) as the source of the butyl radical. From this reaction, the expected potassium vinyltrifluoroborate salt was not isolated, probably because it is necessary to use experimental conditions [19] that differ from those that were selected to perform the synthesis of the BF\(_3\)K salts. To maintain the same reaction conditions, other control experiments were performed (Scheme 2).

Instead of having the double bond isomerization as a radical pathway model, evidence of \( \text{nBuTe} \) radical behavior came from the detection of \( \text{nBuBF}_3\text{K} \) as a product only from experiment \( \text{A} \) (Scheme 2). With the control experiments (Scheme 2), it was proven that the generation of \( \text{nBuBF}_3\text{K} \) salt is dependent on the presence of \( \text{nBuTe} \), as well as that that occurs during the reaction to prepare the alkenyltrifluoroborate salts.

The results presented above support a free radical pathway for the trans-cis double bond isomerization. Scheme 3 was proposed to account for the \( E \)-vinylic and \( n \)-BuBF\(_3\)K salts. In the first step, the butyl radical \( \cdot \text{TeBu} \) is formed by homolytic cleavage of the \( n \)-Bu-Te bond of the compound \( \text{3} \), caused by the lithium species present in the reaction medium. The second step consists of an attack of \( \cdot \text{at} \) the boronic "ate" complex \( \text{4} \), leading to the vinylic radical, which undergoes self-isomerization to the most stable isomer \( \text{8} \). In the third step, the vinylic radical \( \cdot \text{8} \) attacks a \( \text{B(OiPr)}_3 \) species, yielding an anionic vinyl boronic "ate" radical. The boron-centered radical is then reduced by a \( \cdot \text{TenBu} \) radical, leading to the \( E \)-vinyltrifluoroborate salt after the reaction work up with aqueous KHF\(_2\).
Conclusion

In conclusion, we have identified the radical species that promoted the stereoinversion of vinylclic compounds during the preparation of potassium vinyltrifluoroborate salts. The above experiments support the proposed mechanism, which is based on the homolytic cleavage of the TenBu bond.

Additional material

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Table 2: Reactions and Control Experiments Performed

| Entry | Reactions | DBNBS radical adducts EPR Hyperfines (G) |
|-------|-----------|------------------------------------------|
|       |           | aN  | aH  | a'N | a'H |
| 1     | BuTeCH = CHPh+ + BuLi + DBNBS | 21.6 | 0.7 | 9.1 | 1.0 |
| 2     | LiCH = CHPh+B(OiPr)3+ + DBNBS | complex signal | no signal | no signal | no signal |
| 3     | BuTeBu + DBNBS | - | - | 9.1 | 1.0 |
| 4     | BuLi+ + DBNBS | - | - | 9.1 | 1.0 |
| 5     | B(OiPr)3+ + DBNBS | - | - | 9.1 | 1.0 |
| 6     | BuTeBu + BuLi+ + B(OiPr)3+ + DBNBS | complex signal | no signal | no signal | no signal |

Scheme 3: Proposed mechanism of the reaction.