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Coupling of butyl vinyl tellurides with metal acetylides catalyzed by nickel complexes

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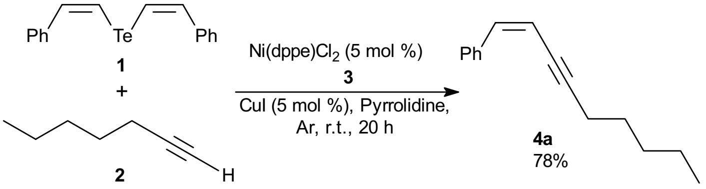
Abstract—*Z*-Vinylic tellurides react with metal acetylides under nickel complexes catalysis to give *Z*-enynes and *Z*-enediynes in good yields.

The transformation of *Z*-vinylic tellurides into reactive *Z*-vinylic organometallics is nowadays well established[1] and found use in the total synthesis of Macrolactin A, a polyunsaturated macrocyclic lactone with anti-viral activity.[2] Recently we turned our attention to the direct transformation of *Z*-vinylic tellurides into *Z*-enynes and *Z*-enediynes through the palladium promoted coupling of *Z*-vinylic tellurides with alkynes.[3] This reaction experienced a rapid growth and found use in the construction of a number of unsaturated systems.[4] In view of the high coast of the palladium reagents, we are in the search for less expensive methods to promote the alkyne–telluride coupling. An alternative should be the use of nickel catalysts[5] and recently one of us found that Ni(dppe)Cl_2 **3** in the presence of CuI promotes the coupling of bis-vinylic tellurides **1** with alkynes **2** (Scheme 1), leading to enynes **4a** in good yields.[6]

However, the preparation of bis-vinylic tellurides by hydrotelluration of alkynes is not general, specially for the preparation of telluroenynes **5**. Attempts to prepare **5** by this method led to the formation of tellurophenes **6**, as described earlier.[7] The hydrotelluration leading to butyltelluroenynes **7**, on the contrary, is quite general producing the desired *Z*-vinylic tellurides in good yields[1] (Scheme 2).

In view of this we attempted the coupling of *Z*-butyl vinyl telluride **8a** with 1-heptyne using the conditions shown in the Scheme 1.[6] To our surprise the coupling did not occur. Then, instead of an alkyne we used an alkynoate **9**, this time using Ni(PPh_3)$_2$$Cl_2$ as the catalyst in the absence of CuI (Scheme 3).

The reaction occurred in good yields giving the enyne **4a** with retention of the *Z* stereochemistry. As can be



Scheme 1.

Keywords: *Z*-Butyl vinyl tellurides; Nickel complexes catalysis; Coupling reaction.

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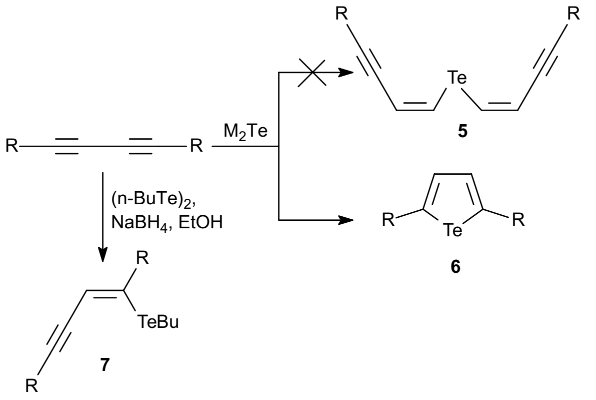
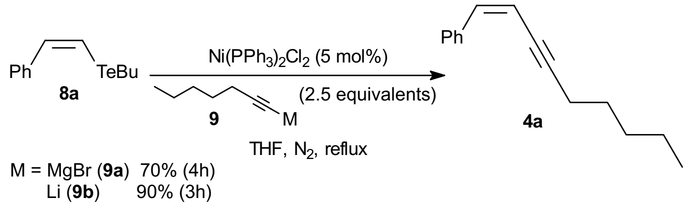


Scheme 2.

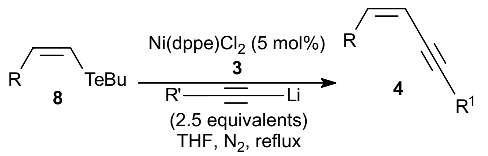
observed in Scheme 3, reaction with the lithium alkynoate **9b** gave higher yield than the reaction with the corresponding magnesium alkynoate **9a**. By changing $Ni(PPh_3)_2Cl_2$ for $Ni(dppe)Cl_2$ (**3**) a substantial increase in the yield was observed (Table 1, entry 1). In view of this fact we adopted the use of $Ni(dppe)Cl_2$ (**3**) (5 mol %) and the lithium alkynoate (**9b**) (2.5 equiv) to perform a systematic study of the coupling reaction. The yields of the coupled products were high in most cases (Table 1, Eq. 1).[8]

As can be observed in Table 1, the vinylic telluride **8e** with a OTBS group at C_3 did not give the coupling reaction (entries 8 and 9), suggesting some steric influence of the bulky group at C_3 of the vinylic telluride. The vinylic telluride **8d** coupled efficiently with the lithium alkynoate and the protecting group was removed during the reaction leading to the alcohol **4g** in quantitative yield. Attempts to reduce the amount of the lithium alkynoate (**9b**) from 2.5 to 1.5 equiv using **8a** and $Ni(dppe)Cl_2$ (**3**) (5 mol %) was satisfactory, however, the



Scheme 3.

Table 1.



(1)

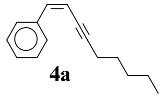
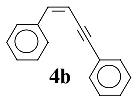
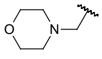
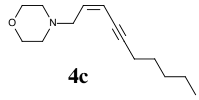
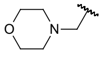
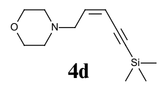
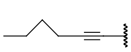
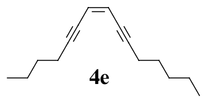
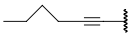
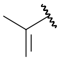
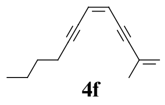
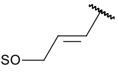
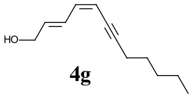
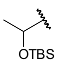
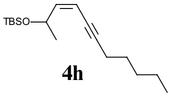
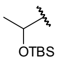
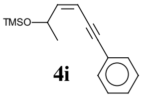
Entry	R	R^1	Product	Reaction time (h)	Yield (%)[a,b]
1	Ph **8a**	n-C_5H_{11}	 **4a**	3	100
2	Ph **8a**	Ph	 **4b**	12	93
3	 **8b**	n-C_5H_{11}	 **4c**	7	100
4	 **8b**	Me_3Si	 **4d**	4	64
5	 **8c**	n-C_5H_{11}	 **4e**	5	97
6	 **8c**		 **4f**	5	75

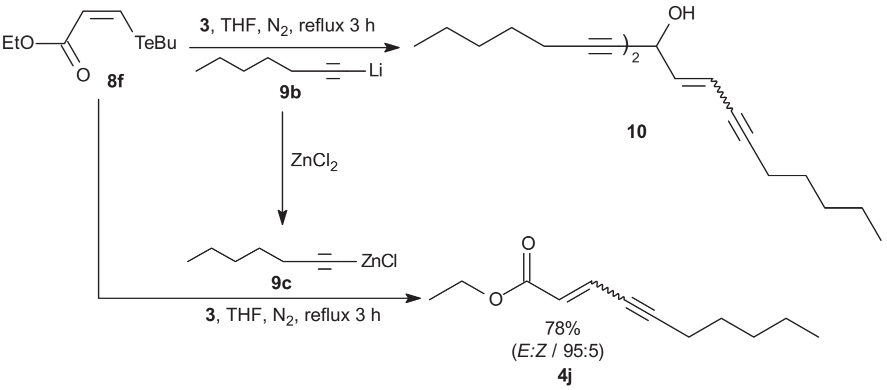
Table 1 (*continued*)

Entry	R	R^1	Product	Reaction time (h)	Yield (%)[a,b]
7	 **8d**	n-C_5H_{11}	 **4g**	12	100
8	 **8e**	n-C_5H_{11}	 **4h**	12	Nr[c]
9	 **8e**	Ph	 **4i**	12	Nr[c]

[a] Isolated yield after column chromatography in silica gel.

[b] The analytical data agree with the structures proposed.

[c] The product was not formed.



Scheme 4.

yield dropped to 87%. Use of 1.5 equiv of **9b** and 1 mol% of Ni(dppe)Cl_2 gave only trace amounts of the product **4a** after 24 h. By performing the reaction at room temperature the product **4a** was obtained also in trace amounts after 72 h.

The functionalized vinylic telluride **8f** on reaction with the lithium alkynoate **9b** gave the coupling product, however, besides the coupling reaction, the addition of the alkynoate to the ester group also occurred, leading to **10** (Scheme 4). To avoid this undesired side reaction the more selective zinc alkynoate **9c**, prepared by a transmetallation reaction between the lithium alkynoate **9b** and $ZnCl_2$, was used. Reaction of **9c** with **8f** under the coupling conditions gave the functionalized enyne **4j** in 78% yield.[9] However, under the reaction conditions used, the configuration of the *Z*-vinylic telluride **8f** was not maintained and **4j** was obtained as a diastereomeric mixture of *E* and *Z* olefins in a 95:5 ratio (Scheme 4). Probably the long heating of the reaction mixture promotes the isomerization of the conjugated system present in **4j**. The stereoisomeric ratio was determined by analysis of the ^1H NMR spectrum. The *E*-vinylic hydrogens resonate as a double triplet at 6.75 ppm with coupling constants of 15.8 and 2.2 Hz and as a doublet at 6.13 ppm with a coupling constant of 15.8 Hz, typical values for *trans*-olefins. A low intensity doublet at 6.01 ppm with coupling constant of 11.4 Hz indicate the presence of the *Z* isomer. The 95:5 ratio was confirmed by a GC analysis.

In conclusion, the results reported in this communication show that the coupling of *Z*-vinylic tellurides with metal alkynoates under nickel complexes catalysis is a convenient method to synthesize enynes and enediynes, being less expensive than our previous method,[3] which make use of palladium chloride.

Acknowledgements

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8. *Typical procedure for the preparation of lithium alkynoates: preparation of 1-heptynyl lithium*: To a 50 mL two-necked round-bottomed flask under nitrogen atmosphere were added THF (10 mL) and 1-heptyne (11 mmol, 1.10 g, 1.5 mL). Then *n*-BuLi (7.7 mL; 10 mmol of a 1.3 M solution in hexane) was added dropwise at −70 °C. The mixture was stirred for 10 min. After this time the solution of 1-heptynyl lithium is ready for use.

   Typical procedure for the coupling reaction: preparation of compound ***4a***: To a 25 mL two-necked round-bottomed flask under nitrogen atmosphere were added Ni(dppe)Cl_2 (0.05 mmol, 0.026 g), THF (10 mL), the *Z*-vinylic telluride **8a** (1 mmol, 0.288 g) and then 1-heptynyl lithium (4.8 mL; 2.5 mmol of the solution prepared above) via syringe. The mixture was refluxed for 3 h. Then the reaction was quenched with brine (50 mL) followed by extraction with ethyl acetate (3 × 50 mL). The extracts were dried over $MgSO_4$ and then filtered and evaporated. The residue was purified by column chromatography on silica gel eluting with hexane to give **4a** in quantitative yield (0.198 g). ^1H NMR (300 MHz, $CDCl_3$, ppm) 7.88–7.85 (m, 2H), 7.37–7.24 (m, 3H), 6.55 (d, $J = 12.0$ Hz, 1H), 5.70 (dt, $J = 12.0$, 2.4 Hz, 1H), 2.43 (td, $J = 7.0$, 2.4 Hz, 2H), 1.61 (quint, $J = 7.0$ Hz, 2H), 1.49–1.29 (m, 4H), 0.92 (t, $J = 7.0$ Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) 137.21, 136.69, 128.43, 128.12, 128.09, 108.20, 97.88, 79.16, 31.16, 28.28, 22.25, 19.87, 13.99; IR near (film) (cm^{-1}) 3058, 3021, 2990, 2863, 2200, 1494, 1455, 1422, 783, 692; LRMS *m/z* (relative intensity) 198 (M^+, 36.8%), 183 (5.2%), 169 (10.4%), 155 (23.3%), 141 (100.0%), 128 (42.9%), 115 (66.3%), 102 (4.8%), 91 (33.6%), 79 (14.5%), 63 (12.3%), 55 (11.0%), 51 (10.2%), 41 (16.3%).

9. *Transmetallation reaction between 1-heptynyl lithium (**9b**) and $ZnCl_2$: preparation of **9c***: To 1-heptynyl lithium (14.4 mL; 7.5 mmol of a solution prepared as above) under nitrogen atmosphere, at −70 °C was added $ZnCl_2$ (7.5 mL; 7.5 mmol of a 1 M solution in THF). The mixture was stirred at room temperature for 20 min. After this time the solution of **9c** is ready for use. *Coupling reaction of **8f** with* **9c**: *preparation of compound **4j***: To a 100 mL two-necked round-bottomed flask under nitrogen atmosphere were added Ni(dppe)Cl_2 (0.15 mmol, 0.079 g), THF (30 mL), the *Z*-vinylic telluride **8f** (3 mmol, 0.851 g) and then the zinc alkynoate **9c** (21.9 mL; 7.5 mmol of the solution prepared above) via syringe. The mixture was refluxed for 3 h. The reaction was quenched with brine (100 mL) followed by extraction with ethyl acetate (3 × 100 mL). The extracts were dried over $MgSO_4$. The solvent was filtrated and evaporated and the residue was first purified by flash chromatography eluting with hexane and then with ethyl acetate. The residue was further purified by horizontal distillation under reduced pressure to give 0.455 g (78%) of **4j** as a *E*/*Z* mixture in a 95:5 ratio. *E* stereoisomer: 200 MHz ^1H NMR ($CDCl_3$, ppm) 6.75 (dt, $J = 15.8$, 2.2 Hz, 1H), 6.13 (d, $J = 15.8$ Hz, 1H), 4.20 (q, $J = 7.0$ Hz, 2H), 2.37 (td, $J = 7.0$, 2.2 Hz, 2H), 1.56 (quint, $J = 7.0$ Hz, 2H), 1.44–1.30 (m, 4H), 1.28 (t, $J = 7.0$ Hz, 3H), 0.91 (t, $J = 7.0$ Hz, 3H); 50 MHz ^{13}C NMR ($CDCl_3$, ppm) 165.90, 129.14, 125.92, 100.54, 77.84, 60.33, 30.90, 27.90, 22.00, 19.54, 14.02, 13.71; IR near (film) (cm^{-1}) 3069, 2959, 2934, 2866, 2215, 1719, 1619, 1463, 1368, 1302, 1157, 963; LRMS *m/z* (relative intensity) 194 (M^+, 3.6%), 179 (16.3%), 165 (40.9%), 149 (42.3%), 133 (20.0%), 119 (52.0%), 109 (44.9%), 93 (62.2%), 79 (100.0%), 65 (47.5%), 55 (76.5%), 41 (69.1%). The *Z* isomer was identified in the mixture by its LRMS *m/z* (relative intensity) 194 (M^+, 1.9%), 179 (0.7%), 166 (35.9%), 149 (22.2%), 137 (13.3%), 123 (47.0%), 109 (100.0%), 91 (20.6%), 81 (69.6%), 65 (28.8%), 55 (48.9%), 41 (49.4%) and by a low intensity doublet at 6.01 ppm with a coupling constant of 11.4 Hz in the ^1H NMR spectrum. A GC analysis of the purified product showed that it was constituted by a 95:5 mixture of the *E* and *Z* isomers of **4j**, respectively.