Stereoselective Addition Reactions of Alkynes with Benzenetellurinyl Trifluoromethanesulfonate in Acetonitrile: Organotellurium-mediated One-pot Synthesis of Oxazoles from Internal Alkynes

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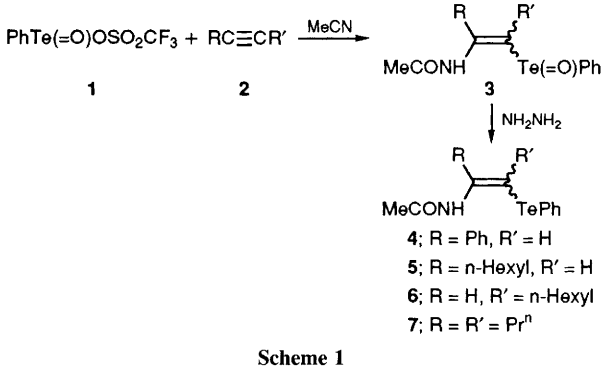
Benzenetellurinyl trifluoromethanesulfonate in conjunction with acetonitrile underwent an *E*-stereoselective amidotellurinylation reaction with alkynes, but the addition products from terminal alkynes tended to isomerize thermally to (*Z*)-β-acetamidovinyl phenyl telluroxide, whereas those from internal alkynes were transformed into oxazoles *via* a spontaneous intramolecular cyclization.

Benzenetellurinic mixed anhydrides such as benzenetellurinyl acetate, trifluoroacetate, and trifluoromethanesulfonate serve as superior electrophiles towards alkenes to undergo addition reactions such as amidotellurinylation,[1] aminotellurinylation[2] and oxytellurinylation.[3] The aminotellurinylation and amidotellurinylation at a high temperature are, however, accompanied by a spontaneous intramolecular displacement of the introduced tellurinyl group to give oxazolidin-2-ones[1] and 4,5-dihydrooxazoles,[2] respectively. If a similar reaction sequence occurs with alkynes, the corresponding unsaturated five-membered heterocycles might be formed in one-pot. We now report the amidotellurinylation of alkynes with benzenetellurinyl trifluoromethanesulfonate **1** in acetonitrile.

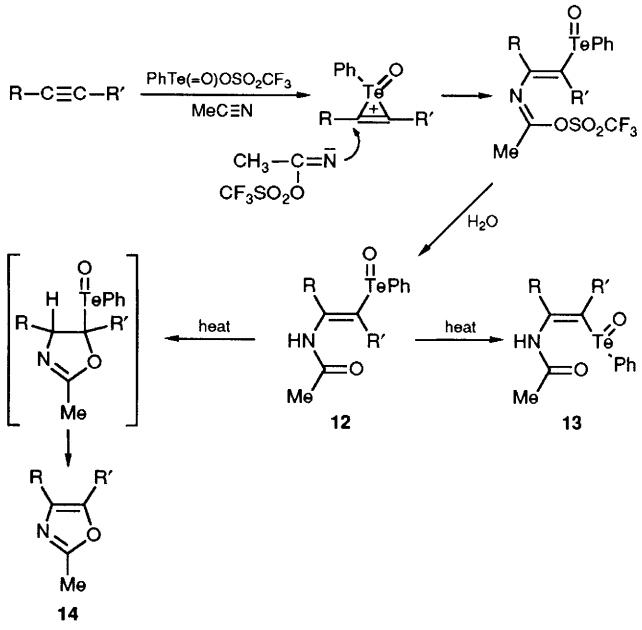
Treatment of phenylacetylene **2** (R = Ph, R′ = H) with **1** in



Scheme 1

acetonitrile at reflux temperature for 12 h gave an amidotellurinylation product **3**, which was isolated as β-acetamidostyryl phenyl telluride **4**† in 16% yield after reduction with hydrazine hydrate in methanol (Scheme 1). An addition of trifluoromethanesulfonic acid fairly accelerated the reaction to enhance the yield up to 43% after 2 h (Table 1). The structure of **4** was confirmed by an X-ray crystallographic analysis to have the *Z* configuration with the phenyltelluro group at the terminal position‡ (Fig. 1). Neither regioisomer nor *E*-stereoisomer was detected. On the other hand, a similar reaction of oct-1-yne gave an isomeric mixture (2:3) of 2-acetamido-1-octenyl phenyl telluride **5**† with the terminal telluro group and 1-(acetamidomethylene)heptyl phenyl telluride **6**† with the internal telluro group in 30% yield. The former compound consisted of only the *Z*-isomer. On the other hand, the latter compound was mostly the *E* isomer, and contained a trace amount of the *Z*-isomer. The configurations of these *Z*-isomers were confirmed by a ^{1}H NMR experiment which showed a nuclear Overhauser effect between the alkenic methine signal and the allylic methylene signal.

The reactions of internal alkynes with **1** in acetonitrile proceeded differently from those of terminal alkynes. The reaction of oct-4-yne at room temperature for 12 h or at 50 °C for 2 h gave a mixture of an addition product (*Z*)-**7** (19–36% yield) and 2-methyl-4,5-dipropyloxazole **8**† (54–57% yield). On the other hand, the reaction at −10 °C for 24 h gave, besides oxazole **8** (13% yield), another addition product (*E*)-**7**† (63% yield). In addition, the treatment of oct-4-yne at −10 °C for 24 h and then at room temperature for 24 h gave (*Z*)-**7** (10% yield) and **8** (72% yield). The stereochemistry of **7** was also confirmed by an NOE experiment. The reactions of diphenylacetylene, 1-phenylprop-1-yne, and 1-phenylbut-1-yne gave only the corresponding oxazoles **9**–**11**† in good yields. The reactions leading to **10** and **11** were also regioselective.

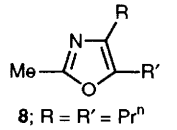


Scheme 2

Table 1 Reactions of benzenetellurinyl trifluoromethanesulfonate **1** with alkynes **2** in acetonitrile[a]

Alkyne	Conditions	Product	Yield (%)[b]
R = Ph, R′ = H	Reflux, 2 h	(*Z*)-**4**	43
R = n-Hexyl, R′ = H	50 °C, 12 h	(*Z*)-**5** + (*E*)-**6**[c]	30
R = R′ = Pr^n	50 °C, 2 h	(*Z*)-**7**	19
		8	57
R = R′ = Pr^n	Room temp, 12 h	(*Z*)-**7**	36
		8	54
R = R′ = Pr^n	−10 °C, 24 h	(*E*)-**7**	63
		8	13
R = R′ = Ph	Reflux, 2 h	**9**	75
R = Ph, R′ = Me	Reflux, 2 h	**10**	44
R = Ph, R′ = Et	Reflux, 2 h	**11**	57

[a] Typical procedure: a mixture of alkyne (1.0 mmol), benzenetellurinyl trifluoromethanesulfonate (1.2 mmol), and trifluoromethanesulfonic acid (0.6 mmol) in acetonitrile (5 ml) was refluxed for 2 h under nitrogen atmosphere followed by treatment with hydrazine hydrate in methanol at 60 °C for 10 min. [b] Yields of products isolated after chromatographic separation. [c] Isomeric ratio **5**:**6** = 2:3, and product **6** contained a trace amount of the *Z*-isomer.



8; R = R′ = Pr^n
9; R = R′ = Ph
10; R = Ph, R′ = Me
11; R = Ph, R′ = Et

† *Selected ^{1}H NMR data* (at 270 MHz in $CDCl_3$, δ, *J*/Hz) for (*Z*)-**4**: 2.16 (s, 3H, CH_3), 6.80 (bs, 1H, NH), 7.09 (s, 1H, CH), 7.2–7.4 (m, 8H, ArH), 7.76 (d, *J* 7.3, 2H, ArH).

For (*Z*)-**5**: 0.88 (t, *J* 6.4, 3H, CH_3), 1.2–1.35 (m, 6H, CH_2), 1.46 (m, 2H, CH_2), 2.01 (s, 3H, CH_3CO), 2.65 (t, *J* 7.4, 2H, CH_2), 6.13 (s, 1H, CH), 7.1–7.3 (m, 4H, NH and ArH), 7.59 (dd, *J* 7.4, 1.5, 2H, ArH).

For (*Z*)-**6**: 0.85 (t, *J* 6.6, 3H, CH_3), 1.15–1.3 (m, 6H, CH_2), 1.49 (m, 2H, CH_2), 1.98 (s, 3H, CH_3CO), 2.44 (t, *J* 7.4, 2H, CH_2), 6.95 (d, *J* 11.2, 1H, CH), 7.15–7.3 (m, 3H, ArH), 7.54 (d, *J* 6.3, 2H, ArH), 7.62 (bd, *J* 11.2, 1H, NH).

For (*E*)-**6**: 0.85 (t, *J* 6.9, 3H, CH_3), 1.15–1.3 (m, 6H, CH_2), 1.45 (m, 2H, CH_2), 2.08 (s, 3H, CH_3CO), 2.32 (t, *J* 7.2, 2H, CH_2), 7.15–7.3 (m, 3H, ArH), 7.49 (d, *J* 10.9, 1H, CH), 7.67 (d, *J* 6.3, 2H, ArH), 8.10 (bs, 1H, NH).

For (*Z*)-**7**: 0.83 (t, *J* 6.9, 3H, CH_3), 0.92 (t, *J* 7.3, 3H, CH_3), 1.48 (sex, *J* 6.8, 4H, CH_2),1.89 (s, 3H, CH_3CO), 2.32 (t, *J* 6.6, 2H, CH_2), 2.66 (t, *J* 6.9, 2H, CH_2), 7.05 (bs, 1H, NH), 7.15–7.3 (m, 3H, ArH), 7.63 (d, *J* 6.9, 2H, ArH).

For (*E*)-**7**: 0.76 (t, *J* 7.3, 3H, CH_3), 0.88 (t, *J* 7.3, 3H, CH_3), 1.44 (sex, *J* 7.4, 4H, CH_2), 2.03 (s, 3H, CH_3CO), 2.26 (t, *J* 7.4, 2H, CH_2), 2.68 (t, *J* 7.6, 2H, CH_2), 7.1–7.3 (m, 3H, ArH), 7.69 (d, *J* 6.9, 2H, ArH), 7.82 (s, 1H, NH).

For **8**: 0.92 (t, *J* 7.4, 3H, CH_3), 0.93 (t, *J* 7.4, 3H, CH_3), 1.61 (sex, *J* 7.3, 2H, CH_2), 1.62 (sex, *J* 7.4, 2H, CH_2), 2.35 (t, *J* 7.2, 2H, CH_2), 2.37 (s, 3H, CH_3), 2.51 (t, *J* 7.4, 2H, CH_2).

For **9**: 2.48 (s, 3H, CH_3), 7.2–7.3 (m, 6H, ArH), 7.55 (dd, *J* 7.9, 1.6, 2H, ArH), 7.64 (dd, *J* 8.1, 1.5, 2H, ArH).

For **10**: 2.44 (s, 3H, CH_3), 2.47 (s, 3H, CH_3), 7.27 (t, *J* 7.3, 1H, ArH), 7.39 (t, *J* 7.9, 2H, ArH), 7.60 (d, *J* 7.3, 2H, ArH).

For **11**: 1.30 (t, *J* 7.6, 3H, CH_3), 2.47 (s, 3H, CH_3), 2.86 (q, *J* 7.6, 2H, CH_2), 7.2–7.5 (m, 5H, ArH).

‡ *Crystal data* for **4**: $C_{16}H_{15}NOTe$, *M* = 364.90, monoclinic, space group $P2_1/c$, *a* = 16.591(1), *b* = 10.149(1), *c* = 8.726(1) Å, β = 91.42(1)°, *V* = 1468.9(3) Å^3, *Z* = 4, D_x = 1.651 g cm^{-3}, graphite-monochromated Cu-Kα radiation, crystal dimensions 0.60 × 0.05 × 0.04 mm, μ(Cu-Kα) = 154.8 cm^{-1}. Rigaku AFC-6C diffractometer, 2061 unique reflections having $|F_o| \geq 1.0\sigma(F_o)$. The intensity of the three standard reflections, which were measured every 100 reflections, showed certain decay which finally reached 24%, and was used for intensity corrections of the collected data. The structure was solved by the Monte-Carlo direct method using MULTAN78 program system for the selection of the initial set of phase, and refined by the full-matrix least-squares program without absorption correction. Anisotropic temperature factors were used for the refinement, and hydrogen atoms were not included in the refinement (*i.e.* number of parameters = 172), *R* = 0.068, R_w = 0.063. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Notice to Authors, Issue No. 1.

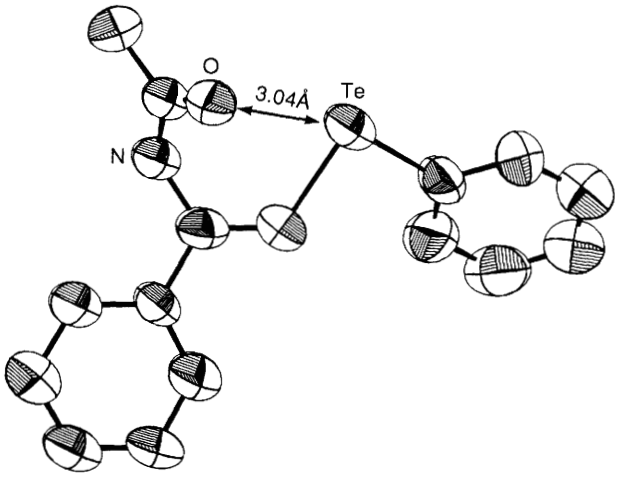


Fig. 1 ORTEP drawing of (*Z*)-β-acetamidostyryl phenyl telluride

The reaction study of oct-4-yne indicates that the amidotellurinylation of alkynes proceeds in a *trans* fashion to initially give the *E*-addition product **12**, which thermally isomerizes to the *Z*-isomer **13** or changes to the oxazole **14** *via* an intramolecular cyclization (Scheme 2). The different paths for the reactions of terminal alkynes and internal alkynes presumably depend on the following two factors. The higher stability of the *Z*-isomer **13** than the *E*-isomer **12** is ascribable to an intramolecular nonbonded Te–O interaction, being supported by the short distance (3.04 Å) between Te and O in adduct **4** (Fig. 1). On the other hand, the intramolecular cyclization of **12** to **14** presumably involves a telluroxide elimination reaction, which occurs more readily with highly branched alkyl telluroxides,[4] favouring the formation path of **14** from internal alkyne. In conclusion, the present organotellurium-mediated reaction provides a convenient one-pot synthetic method of oxazoles from internal alkynes.

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