(*E*)-α-Bromovinylselenides as Convenient Precursors for Stereoselective Synthesis of Trisubstituted Alkenes

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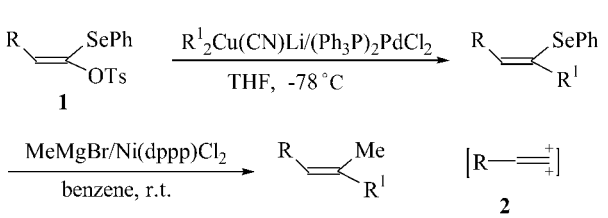
Based on the different reactivity of selanyl and bromo groups, (*E*)-α-bromovinylselenides can undergo sequential cross coupling reactions with nucleophiles in the presence of transition metal complexes to form two carbon-carbon bonds in the same olefinic carbon leading to trisubstituted alkenes stereoselectively in good yields.

Keywords (*E*)-α-bromovinylselenide, cross coupling reaction, trisubstituted alkene, stereoselective synthesis

Introduction

The stereocontrolled synthesis of trisubstituted alkenes is of considerable interest in organic chemistry since many biologically active compounds occurring in nature possess the structural skeleton of trisubstituted alkenes.[1-3] Difunctional group reagents, which have two different functional groups linked to the olefinic carbon atoms, for example, Se-Zr,[4] Te-Zr,[5] Se-Sn,[6] Se-B[7] and Te-Br[8] combinations, play an important role in organic synthesis, especially in developing many convenient methods for the stereoselective synthesis of substituted alkenes. Vinylselenides are important intermediates, but the difunctional group reagent containing selenium and bromine has rarely roused extensive attention. Recently, Tingoli *et al*.[9] reported that *p*-toluenesulfonic acid underwent *cis* addition with alkynylselenides to give (*Z*)-α-selanylvinyl *p*-toluenesulfonates **1**. On the basis of the different reactivity of the selanyl group and *p*-toluenesulfonate group, compounds **1** can undergo sequential cross coupling reactions in the presence of transition metal complexes, providing a convenient method for the stereoselective synthesis of trisubstituted alkenes[9] (Scheme 1). These reactions show that (*Z*)-α-selanylvinyl *p*-toluenesulfonates (**1**) represent the synthetic equivalent of the dication synthon **2**. Herein we report that stereodefined trisubstituted alkenes could be synthesized by the sequential cross coupling reactions of (*E*)-α-bromovinylselenides with nucleophiles in the presence of transition metal complexes.

Scheme 1



Results and discussion

(*E*)-α-Bromovinylselenides (**3**) can be conveniently prepared in good yields with high stereoselectivity by the addition of hydrogen bromide to alkynylselenides.[10] Compounds **3** are difunctional group reagents in which two synthetically versatile groups are linked to the same olefinic carbon atom and can be considered both as vinylselenides and vinyl bromides. Vinylselenides have been employed to effect Ni(0)-catalyzed cross coupling reactions with Grignard reagents.[11] Besides, the bromo groups in vinyl bromides can be easily substituted by transition metal catalyzed coupling reactions.[12] Based on the different reactivity of selanyl and bromo groups, (*E*)-α-bromovinylselenides (**3**) can undergo sequential cross coupling reactions with Grignard reagents in the presence of transition metal complexes to form two carbon-carbon bonds in the same olefinic carbon. Therefore, we carried out the palladium(0)-catalyzed cross coupling reaction of compounds **3** with Grignard reagents. We found that when (*E*)-α-bromovinylselenides (**3**) were allowed to react with Grignard reagents in the presence of catalytic amount of tetrakis(triphenylphosphine) palladium(0) in THF at room temperature, the corresponding disubstituted alkenylselenides (**4**) were obtained in good yields according to Scheme 2 and Table 1.

Scheme 2

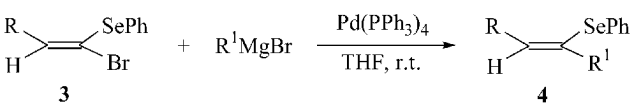


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Table 1 Disubstituted vinylselenides (**4**) prepared according to Scheme 2

Entry	R	R^1	Product	Yield[a] (%)
1	*n*-C_4H_9	C_6H_5	**4a**	72
2	*n*-C_4H_9	4-$CH_3C_6H_4$	**4b**	85
3	*n*-C_4H_9	4-ClC_6H_4	**4c**	69
4	C_6H_5	C_6H_5	**4d**	78
5	C_6H_5	4-$CH_3C_6H_4$	**4e**	79
6	C_6H_5	*n*-C_4H_9	**4f**	75
7	*n*-C_6H_{13}	C_6H_5	**4g**	80
8	*n*-C_6H_{13}	4-$CH_3C_6H_4$	**4h**	71

[a] Isolated yield based on **3** used.

Because of the reactivity difference of bromo and *p*-toluenesulfonate groups as compared to Tingoli's method we could use easily available Grignard reagents instead of organocopper reagents which are difficult to prepare. Moreover, the reaction takes place smoothly at room temperature instead of at low temperature (−78 ℃) and the yields are higher in our case than in Tingoli's method.

Vinylselenides are important synthetic intermediates owing to the versatile reactivity of the selanyl group and the carbon-carbon double bond.[13] (*Z*)-Dialkyl substituted vinylselenides (**4**) are also effective precursors for preparing stereodefined trisubstituted alkenes. In the presence of the catalyst bis(triphenylphosphine) nickel(II) chloride they can easily undergo cross coupling reaction with Grignard reagents providing an effective method to synthesize trisubstituted alkenes. Thus, the cross coupling reaction of compounds **4** with Grignard reagents in the presence of catalytic amount of $(Ph_3P)_2NiCl_2$ afforded the selenium free trisubstituted alkenes (**5**) in good yields (Scheme 3). The experimental results are summarized in Table 2.

Scheme 3

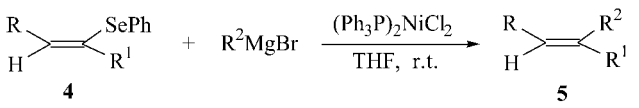

Table 2 Stereodefined trisubstituted alkenes (**5**) prepared according to Scheme 3

Entry	R	R^1	R^2	Product	Yield[a] (%)
1	C_6H_5	*n*-C_4H_9	*n*-C_6H_{13}	**5a**	70
2	C_6H_5	C_6H_5	*n*-C_4H_9	**5b**	66
3	C_6H_5	C_6H_5	CH_3	**5c**	65
4	*n*-C_4H_9	C_6H_5	CH_3	**5d**	60

[a] Isolated yield based on **4** used.

As (*E*)-α-bromovinylselenides (**3**) undergo a two-step cross coupling reaction to form two carbon-carbon bonds on the same olefinic carbon and allow the synthesis of trisubstituted alkenes stereoselectively, **3** can also be regarded as the equivalent of the dication synthon **2**.

In conclusion, compared to other that have been reported, methods[9,14] the present methodology for the synthesis of stereodefined trisubstituted alkenes has the advantages of steadily available starting materials, straightforward and simple procedure, mild reaction conditions and good yields.

Experimental

Tetrahydrofuran (THF) was distilled from sodium-benzophenone immediately prior to use. $(Ph_3P)_4Pd$[15] and $(Ph_3P)_2NiCl_2$[16] were prepared according to the reported procedure. IR spectra were obtained on a Perkin-Elmer 683 instrument as neat films. ^1H NMR spectra were recorded on a Bruker AC-300 (300 MHz) spectrometer using $CDCl_3$ as solvent. ^1H chemical shifts are reported relative to TMS. Elemental analyses were carried out on a Carlo Erba EA 1110 instrument.

Syntheses of disubstituted vinylselenides **4a—4h**

General procedure To a stirred solution of (*E*)-α-bromovinylselenide (**3**) (1.0 mmol) and $Pd(PPh_3)_4$ (0.05 mmol) in THF (2 mL) was added R^1MgBr (1.3 mmol) in THF (2 mL) under nitrogen at room temperature and the mixture was stirred for 24 h. The reaction mixture was diluted with diethyl ether (30 mL) and treated with sat. aq. NH_4Cl (15 mL). The organic layer was washed with water (3 × 20 mL) and dried ($MgSO_4$). After removal of solvent under reduced pressure, the residue was purified by column chromatography on silica gel using light petroleum as eluent.

(*Z*)-1-*Phenyl*-1-*phenylseleno*-1-*hexene* (**4a**) ^1H NMR δ: 7.59—7.08 (m, 10H), 6.13 (t, *J* = 7.5 Hz, 1H), 2.14—2.02 (m, 2H), 1.49—1.18 (m, 4H), 0.87 (t, *J* = 7.2 Hz, 3H); IR (film) ν: 3056, 3017, 2925, 2856, 1595, 1577, 1488, 1438, 1378, 735, 690 cm^{-1}. Anal. calcd for $C_{18}H_{20}Se$: C 68.57, H 6.35; found C 68.34, H 6.19.

(*Z*)-1-(4-*Methylphenyl*)-1-*phenylseleno*-1-*hexene* (**4b**) ^1H NMR δ: 7.55—6.98 (m, 9H), 6.03 (t, *J* = 7.5 Hz, 1H), 2.23 (s, 3H), 2.15—2.01 (m, 2H), 1.48—1.17 (m, 4H), 0.85 (t, *J* = 7.1 Hz, 3H); IR (film) ν: 3054, 3021, 2923, 2856, 1607, 1577, 1475, 1437, 815, 734, 689 cm^{-1}. Anal. calcd for $C_{19}H_{22}Se$: C 69.30, H 6.69; found C 69.41, H 6.52.

(*Z*)-1-(4-*Chlorophenyl*)-1-*phenylseleno*-1-*hexene* (**4c**) ^1H NMR δ: 7.45—7.16 (m, 9H), 6.18 (t, *J* = 7.5 Hz, 1H), 2.10—2.01 (m, 2H), 1.40—1.17 (m, 4H), 0.83 (t, *J* = 7.3 Hz, 3H); IR (film) ν: 3058, 3014, 2926, 2857, 1589, 1578, 1486, 1437, 1090, 870, 821, 736, 690 cm^{-1}. Anal. calcd for $C_{18}H_{19}ClSe$: C 61.80, H 5.44; found C 61.62, H 5.25.

(*Z*)-1,2-*Diphenyl*-1-(*phenylseleno*)*ethene* (**4d**) ^1H NMR δ: 7.59—6.92 (m); IR (film) ν: 3056,

3021, 1596, 1577, 1493, 1443, 1022, 930, 760 cm^{-1}. Anal. calcd for $C_{20}H_{16}Se$: C 71.64, H 4.78; found C 71.40, H 4.64.

(*Z*)-1-(4-*Methylphenyl*)-1-*phenylseleno*-2-*phenylethene* (**4e**) ^1H NMR δ: 7.62—6.91 (m, 15H), 2.25 (s, 3H); IR (film) ν: 3055, 3021, 1597, 1578, 1506, 1476, 812, 692 cm^{-1}. Anal. calcd for $C_{21}H_{18}Se$: C 72.21, H 5.16; found C 72.35, H 5.22.

(*Z*)-1-*Phenyl*-2-*phenylseleno*-1-*hexene* (**4f**) ^1H NMR δ: 7.65—6.95 (m, 11H), 2.38 (t, J = 7.4 Hz, 2H), 1.62—1.24 (m, 4H), 0.90 (t, J = 7.1 Hz, 3H); IR (film) ν: 3057, 3023, 2929, 2870, 1598, 1578, 1493, 1438, 1022, 735, 690 cm^{-1}. Anal. calcd for $C_{18}H_{20}Se$: C 68.57, H 6.35; found C 68.33, H 6.22.

(*Z*)-1-*Phenyl*-1-*phenylseleno*-1-*octene* (**4g**) ^1H NMR δ: 7.57—6.93 (m, 10H), 6.13 (t, J = 7.5 Hz, 1H), 2.12—2.01 (m, 2H), 1.47—1.18 (m, 8H), 0.85 (t, J = 7.1 Hz, 3H); IR (film) ν: 3057, 3017, 2924, 2854, 1596, 1578, 1488, 1475, 1377, 735, 690 cm^{-1}. Anal. calcd for $C_{20}H_{24}Se$: C 69.97, H 7.00; found C 69.74, H 6.82.

(*Z*)-1-(4-*Methylphenyl*)-1-*phenylseleno*-1-*octene* (**4h**) ^1H NMR δ: 7.54—6.98 (m, 9H), 6.09 (t, J = 7.5 Hz, 1H), 2.25 (s, 3H), 2.11—2.02 (m, 2H), 1.48—1.17 (m, 8H), 0.84 (t, J = 7.3 Hz, 3H); IR (film) ν: 3058, 3018, 2925, 2856, 1597, 1579, 1489, 1476, 1378, 690 cm^{-1}. Anal. calcd for $C_{21}H_{26}Se$: C 70.59, H 7.28; found C 70.33, H 7.14.

Syntheses of trisubstituted alkenes **5a—5d**

General procedure To a stirred suspension of $(Ph_3P)_2NiCl_2$ (0.05 mmol) and disubstituted vinylselenide **4** (1.0 mmol) in THF (5 mL) was added a solution of R^2MgBr (3 mmol) in THF (6 mL) under nitrogen at room temperature and the mixture was stirred for 48 h. After the usual workup (see above) the residue was chromatographed through a silica gel column using light petroleum as eluent.

(*Z*)-1-*Phenyl*-2-*butyl*-1-*octene* (**5a**) ^1H NMR δ: 7.42—7.14 (m, 5H, ArH), 6.25 (s, 1H, =CH), 2.25—2.13 (m, 4H, $=CCH_2(CH_2)_4CH_3$ and $=CCH_2(CH_2)_2CH_3$), 1.48—1.21 (m, 12H, $CH_2(CH_2)_4CH_3$ and $CH_2(CH_2)_2CH_3$), 0.97—0.82 (m, 6H, $CH_2(CH_2)_4CH_3$ and $CH_2(CH_2)_2CH_3$); IR (film) ν: 3058, 3024, 2927, 2858, 1647, 1599, 1493, 1465, 1378, 744, 698 cm^{-1}. Anal. calcd for $C_{18}H_{28}$: C 88.52, H 11.48; found C 88.24, H 11.29.

(*E*)-1,2-*Diphenyl*-1-*hexene* (**5b**) ^1H NMR δ: 7.53—7.01 (m, 10H, ArH), 6.68 (s, 1H, =CH), 2.19 (t, J = 5.7 Hz, 2H, $=CCH_2$), 1.41—1.19 (m, 4H, $CH_2(CH_2)_2CH_3$), 0.87 (t, J = 7.1 Hz, 3H, $CH_2(CH_2)_2CH_3$); IR (film) ν: 3057, 3022, 2923, 2858, 1648, 1598, 1493, 1425, 698 cm^{-1}. Anal. calcd for $C_{18}H_{20}$: C 91.53, H 8.47; found C 91.32, H 8.30.

(*E*)-1,2-*Diphenyl*-1-*propene* (**5c**) ^1H NMR δ: 7.54—7.03 (m, 10H, ArH), 6.72 (s, 1H, =CH), 2.15 (d, J = 1.3 Hz, 3H, CH_3); IR (film) ν: 3057, 3023, 1650, 1595, 1530, 1420, 690 cm^{-1}. Anal. calcd for $C_{15}H_{14}$: C 92.78, H 7.22; found C 92.52, H 7.03.

(*E*)-2-*Phenyl*-2-*heptene* (**5d**) ^1H NMR δ: 7.39—7.08 (m, 5H, ArH), 5.71 (t, J = 7.0 Hz, 1H, =CH), 2.41—2.04 (m, 2H, $=CCH_2$), 2.01 (s, 3H, $=CCH_3$), 1.52—1.18 (m, 4H, $CH_2(CH_2)_2CH_3$), 0.89 (t, J = 7.1 Hz, 3H, $CH_2(CH_2)_2CH_3$); IR (film) ν: 3058, 3021, 2925, 2857, 1647, 1597, 1493, 850, 754, 700 cm^{-1}. Anal. calcd for $C_{13}H_{18}$: C 89.66, H 10.34; found C 89.41, H 10.19.

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