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Toluene-*p*-sulfonyl-mediated radical cyclization of bis(allenes) utilizing *p*-TsBr and *p*-TsSePh

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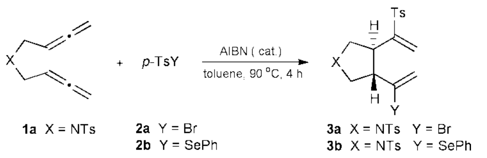
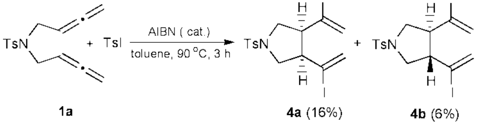
The regio- and stereoselective toluene-*p*-sulfonyl-mediated radical cyclization of bis(allenes) with *p*-TsBr and *p*-TsSePh was carried out in the presence of a catalytic amount of AIBN to afford the *trans*-fused five-membered ring containing vinyl sulfones and bromide or selenide functionalities.

Recently the use of radical cyclization for carbon–carbon bond forming reactions has become widespread in organic chemistry[1] for the construction of carbocyclic and heterocyclic natural products.[2] The majority of commonly employed methods utilize tributyltin hydride to induce homolysis of an organic halide or alcohol derivative in forming the reactive carbon radical species. An alternative approach is to use the addition of a free-radical to two carbon–carbon double bonds, one double bond and one triple bond, or two triple bonds, which has the advantage of incorporating some useful additional functional groups into the cyclized products. The utility of this type of method using dienes,[3,4] enynes,[3a,5] and diynes[5e,6] with sulfonyl halides, thiols, sulfonyl selenides, and tin hydrides *etc.* has been demonstrated. However the radical reaction of allenic derivatives has received little attention,[7,8] because the addition reaction to allenes will be complicated in terms of chemo-, regio-, and stereoselectivity. To the best of our knowledge the radical induced cyclization of bis(allenes) is not known and we reasoned that the radical cyclization addition reaction of bis(allenes) is appealing because useful functionality is introduced in one simple step in which new carbon–carbon bond formation occurs stereoselectively coupled with two unsaturated appendages with distinguished reactivity.[9] The resulting cyclic compounds would be particularly useful to allow further synthetic transformations. Here we report the diastereoselective tosyl-mediated radical cyclization[10] of bis(allenes) **1** with *p*-tosyl bromide[11] and TsSePh[12] in the presence of a catalytic amount of AIBN to afford the *trans*-fused cyclopentane compounds **3**,† in which vinyl sulfones and vinyl bromides, or selenophenyl functionalities are introduced (Scheme 1).



Scheme 1

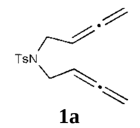
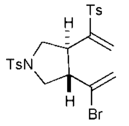
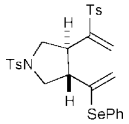
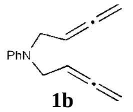
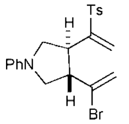
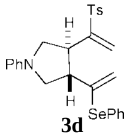
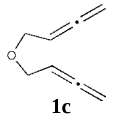
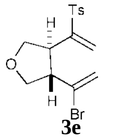
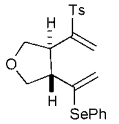
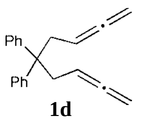
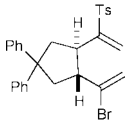
Our initial work began with TsCl and benzoyl peroxide (BPO).[3b] However, it turned out to be unpromising. The reaction of **1a**[9] with TsI and AIBN in a sealed tube gave the cyclized products **4a** and **4b**‡ as a separable mixture in a low (22%) yield in the ratio of *cis* and *trans* (8 : 3). With sulfonyl iodides the chain transfer step seems to be too fast to allow efficient stereoselective cyclization (Scheme 2).



Scheme 2

Although with *p*-TsBr and AIBN simple heating did not give the clean product, by the use of a pressure tube (30 mL) capped

Table 1 Radical cyclization of bis(allenes) with TsBr and TsSePh in the presence of AIBN

Entry[a]	Bis(allenes)	TsX	Product	Isolated yield (%)
1	 **1a**	TsBr **2a**	 **3a**	73
2	**1a**	TsSePh **2b**	 **3b**	59
3	 **1b**	**2a**	 **3c**	48
4	**1b**	**2b**	 **3d**	65
5	 **1c**	**2a**	 **3e**	64
6	**1c**	**2b**	 **3f**	55
7	 **1d**	**2a**	 **3g**	63

[a] All reactions were carried out at 90 °C for 4 h with AIBN (20 mol%) in toluene.

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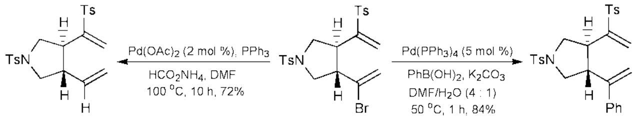

5a **3a** **5b**

Scheme 3

with a teflon screw§ the reaction of **1a** with TsBr (1.1 equiv.) and AIBN (0.2 equiv.) in toluene at 90 °C for 4 h afforded the *trans*-fused cyclized product **3a** as the sole product in 73% isolated yield (entry 1 in Table 1).¶ The *trans* stereochemistry of the cyclized product **3a** was confirmed by the coupling constant (J = 9.6 Hz) for the protons (δ 2.97 and 2.87 ppm) at the ring junction in COSY experiments and 2D-NOESY experiments of the two protons at ring juncture and two *ortho* protons of the *p*-tosyl group in ^{1}H NMR.[13] It is presumed that the addition of tosyl radical to the central carbon atom of the allene moiety gives the allylic radical intermediates in the propagation step followed by cyclization with the other tethered allene moiety in a *trans* fashion stereoselectively to give the energetically more favorable and more stable *trans* product **3a** (entry 1 in Table 1). More clearly the *trans* stereochemistry of **3a** was determined by X-ray crystallography.

The cyclized product **3a** was transformed to the compounds **5a** and **5b** by the palladium-catalyzed reductive hydrogenolysis and Suzuki coupling reaction, respectively (Scheme 3).

Using *p*-TsSePh[12] as the radical source[14] in a pressure tube with AIBN in toluene, the *trans* cyclized selenide **3b** was obtained as the only isolated product in 59% yield (entry 2 in Table 1). The *trans* stereochemistry of **3b** was confirmed by X-ray crystallography.

We have applied this radical cyclization to the other bis(allenes) **1b**, **1c**, and **1d**, summarized in Table 1. The *N*-phenyl-substituted bis(allene) **1b** was treated with TsBr and TsSePh to give the cyclized products **3c** and **3d** in 48 and 65% yields, respectively (entries 3 and 4). For the bis(allenyl) ether **1c** the radical cyclization with **2a** and **2b** gave oxacycles **3e** and **3f** in 64 and 55% yields, respectively (entries 5 and 6). The *trans* stereochemistry of **3f** was determined by the coupling constant (J = 8.8 Hz) for the protons (δ 3.10 and 3.20 ppm) at the ring junction in COSY experiments. The diphenyl-substituted bis(allene) **1d** was smoothly cyclized to furnish vinyl bromide **3g** in 63% yield (entry 7).

In conclusion, *p*-tosyl-mediated radical cyclization of bis-(allenes) with *p*-TsBr and *p*-TsSePh was accomplished stereoselectively in the presence of a catalytic amount of AIBN to afford the *trans* cyclized rings containing vinyl sulfone and vinyl bromide or vinyl phenylselenide.

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Notes and references

† A solution containing *p*-TsBr **2a** (94 mg, 0.40 mmol), bis(allene) **1a** (100 mg, 0.36 mmol) and AIBN (0.20 equiv.) in 4.0 mL of toluene was degassed and heated in a pressure tube at 90 °C for 4 h and toluene was evaporated *in vacuo*. The crude product was separated by column chromatography (hexanes–ethyl acetate = 2:1). Spectral data for (**3a**), yield: 135 mg, 73%; white solid; TLC, SiO$_2$, R_f 0.31 (2:1 hexane–EtOAc); mp 158 °C; IR (neat) ν = 3061, 2925, 1596, 1338, 1171, 1012, 812 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$): δ = 2.45 (s, 3H), 2.48 (s, 3H), 2.87 (ddd, 1H, J = 7.8, 8.9, 9.6 Hz), 2.97 (ddd, 1H, J = 8.0, 8.9, 9.6 Hz), 3.04 (dd, 1H, J = 8.9, 10.5 Hz), 3.18 (dd, 1H, J = 8.9, 10.4 Hz), 3.61 (dd, 1H, J = 8.0, 10.4 Hz), 3.65 (dd, 1H, J = 7.8, 10.5 Hz), 5.33 (d, 1H, J = 2.2 Hz), 5.46 (d, 1H, J = 2.2 Hz), 5.77 (d, 1H, J = 1.4 Hz), 6.46 (d, 1H, J = 1.4 Hz), 7.31 (d, 2H, J = 8.1 Hz), 7.37 (d, 2H, J = 8.0 Hz), 7.64 (d, 2H, J = 8.1 Hz), 7.70 (d, 2H, J = 8.0 Hz); ^{13}C NMR (125 MHz, CDCl$_3$): δ = 22.3, 22.4, 43.0, 52.0, 53.2, 54.4, 121.2, 125.0, 128.4, 129.2, 130.5, 130.6, 130.7, 134.1, 135.6, 144.6, 145.5, 149.7; HRMS for $C_{22}H_{24}BrNO_4S_2$; calcd: 509.0330; found: 509.0343.

Spectral data for (**3b**), yield: 59%; white solid; TLC, SiO$_2$, R_f 0.21 (3:1 hexane–EtOAc); mp 100–102 °C; IR (neat) ν = 3058, 2954, 1598, 1347, 1311, 1163, 814 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$): δ = 2.44 (s, 3H), 2.48 (s, 3H), 2.91 (m, 3H), 3.08 (m, 1H), 3.62 (m, 2H), 5.01 (d, 1H, J = 0.9 Hz), 5.23 (d, 1H, J = 0.9 Hz), 5.57 (d, 1H, J = 1.5 Hz), 6.38 (d, 1H, J = 1.5 Hz), 7.26–7.35 (m, 9H), 7.65 (m, 4H); ^{13}C NMR (125 MHz, CDCl$_3$): δ = 21.6, 21.7, 42.2, 50.9, 52.6, 54.1, 120.0, 123.8, 127.6, 128.1, 128.4, 128.6, 129.5, 129.8, 130.0, 133.6, 134.5, 135.1, 138.7, 143.8, 145.1, 149.5; HRMS for $C_{28}H_{29}NO_4S_2Se$; calcd: 587.0703; found: 587.0715.

‡ The *trans* configuration was deduced by the coupling constant of the two protons (J = 9.8 Hz) (δ 2.72 and 2.55 ppm) at the ring junction.

§ The pressure tube (made of borosilicate glass) was purchased from Aldrich Chem. Co., Inc. (Catalog Number Z18,109-9 type B).

¶ However when the same reaction was conducted with *p*-TsBr at threefold higher concentration for a shorter reaction time (1 h), we could isolate the *trans* product **3a**, the kinetic *cis* product and the monoadduct in the ratio 5:1:0.6 in 34% total yield and there remained 46% of the starting material.

1 B. Giese, in *Radicals in Organic Synthesis, Formation of Carbon–Carbon Bonds*, Pergamon Press, Oxford, 1986; D. P. Curran, *Synthesis*, 1988, 417; D. P. Curran, *Synthesis*, 1988, 489; D. J. Hart, *Science*, 1984, **223**, 883; W. P. Neuman, *Synthesis*, 1987, 665; M. Ramaiah, *Tetrahedron*, 1987, **43**, 3541.

2 C. P. Jasperse, D. P. Curran and T. L. Fevig, *Chem. Rev.*, 1991, **91**, 1237.

3 Cyclizations using *p*-TsCl, *p*-TsBr, and *p*-TsSePh: (*a*) J. E. Brumwell, N. K. Simpkins and N. K. Terrett, *Tetrahedron Lett.*, 1993, **34**, 1219; (*b*) with *p*-TsCl and BPO: C.-P. Chuang and T. H. Ngoi, *Tetrahedron Lett.*, 1989, **30**, 6369; (*c*) A. C. Serra, C. M. M. Da Silva Correa and M. L. C. Do Vale, *Tetrahedron*, 1991, **47**, 9463; (*d*) R. Nouguier, C. Lesueur, E. De Riggi, M. P. Bertrand and A. Virgili, *Tetrahedron Lett.*, 1990, **31**, 3541; (*e*) I. De Riggi, S. Gastaldi, J.-M. Surzur, M. P. Bertrand and A. Virgili, *J. Org. Chem.*, 1992, **57**, 6118.

4 The light-induced addition of tosyl bromide to some 1,6-dienes led to a mixture of *cis*- and *trans*-carbocycles and heterocycles was known by Bertrand and Silva Correa. See: I. De. Riggi, J.-M. Surzur and M. P. Bertrand, *Tetrahedron*, 1988, **23**, 7119; A. C. Serra, C. M. M. Da Silva Correa, M. A. M. S. A. Vieira and M. A. Gomes, *Tetrahedron*, 1990, **46**, 3061.

5 Cyclizations using R$_3$SnH: (*a*) G. Stork, Jr. and R. Mook, *J. Am. Chem. Soc.*, 1987, **109**, 2829; (*b*) K. Nozaki, K. Oshima and K. Utimoto, *J. Am. Chem. Soc.*, 1987, **109**, 2547; (*c*) cyclizations using thiols: Y. Ichinose, K. Wakamatsu, K. Nozaki, J.-L. Birbaum, K. Oshima and K. Utimoto, *Chem. Lett.*, 1987, 1647; (*d*) C. A. Broka and D. E. C. Reichert, *Tetrahedron Lett.*, 1987, **28**, 1503; (*e*) A. Padwa, H. Nimmesgern and G. S. K. Wong, *J. Org. Chem.*, 1985, **50**, 5620.

6 Cyclizations using R$_3$SnH: D. Crich and S. M. Fortt, *Tetrahedron Lett.*, 1987, **28**, 2895; cyclizations using *p*-TsBr: S. Caddick, C. L. Shering and S. N. Wadman, *Chem. Commun.*, 1997, 171.

7 Truce *et al.*, reported light-initiated addition of sulfonyl iodides to allenes. See: W. E. Truce, D. L. Heuring and G. C. Wolf, *J. Org. Chem.*, 1974, **39**, 238.

8 Hatem *et al.*, reported only one example of the allylallene **6**, to give the cyclized compounds **6**, and **7**, and **8**, in a ratio which is conditioned by the R substituent steric hindrance. See: F. E. Gueddari, J. R. Grimaldi and J. M. Hatem, *Tetrahedron Lett.*, 1995, **36**, 6685.

9 We have studied the palladium-catalyzed carbocyclization of bis-(allenes). S.-K. Kang, T.-G. Baik, A. Kulak, Y.-H. Ha, Y. Lim and J. Park, *J. Am. Chem. Soc.*, 2000, **122**, 11 529.

10 For review on the sulfonyl radical, see: M. P. Bertrand, *Org. Prep. Proced. Int.*, 1994, **26**, 257.

11 A. C. Poshkus, J. E. Herweh and F. A. Magnotta, *J. Org. Chem.*, 1963, 2766.

12 T. G. Back, S. Collins and M. V. Krishna, *Can. J. Chem.*, 1987, **65**, 38.

13 Recently, Denmark *et al.*, reported the stereostructural assignment of *trans*-3, 4-disubstituted-*N*-(*p*-tolylsulfonyl)pyrrolidines by analysis of their ^{1}H NMR coupling constants. See: S. E. Denmark and L. R. Marin, *J. Org. Chem.*, 1993, **58**, 3857.

14 Light induced addition of TsSePh to allenes is known. See: Y.-H. Kang and J. L. Kice, *Tetrahedron Lett.*, 1982, **23**, 5373.