Novel, Readily occurring, and Stereoselective Synthesis of Conjugated Trienes using 2-Trialkylstannyl-2,5-dihydrothiophene *S,S*-Dioxides

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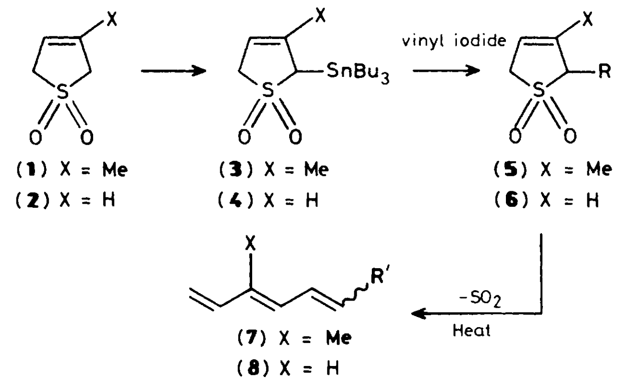
Conjugated trienes have been synthesised readily and stereoselectively by the coupling reaction of 2-tri-n-butylstannyl-2,5-dihydrothiophene *S,S*-dioxides with vinyl iodides in the presence of tetrakis(triphenylphosphine)palladium(0), followed by desulphonylation.

Recently, considerable attention has been focused on the synthesis of conjugated trienes in connection with the synthesis of leukotriene derivatives,[1] vitamin D,[2] and many other natural products.[3] In the course of our studies on the chemistry of 2,5-dihydrothiophene *S,S*-dioxides (**1**) and (**2**), we have established a simple and stereoselective method for synthesizing (*E*)-, (*E,Z*)-, and (*E,E*)-conjugated dienes using the *S,S*-dioxides as diene synthons.[4] If vinyl groups are stereoselectively introduced into the 2- (5-) position of the *S,S*-dioxides, the method can be extended to provide a stereoselective synthesis of the conjugated trienes (**7**) and (**8**) by thermal desulphonylation of the vinyl substituted 2,5-dihydrothiophene *S,S*-dioxides. We report here a novel stereoselective synthesis of conjugated trienes by the reaction of the stannyl derivatives† (**3**) and (**4**),[5] derived from the reaction of 2,5-dihydrothiophene *S,S*-dioxide α-carbanion with tri-n-butylstannyl chloride, with stereo defined vinyl iodides in the presence of $(Ph_3P)_4Pd$ (Scheme 1).

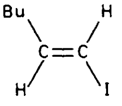
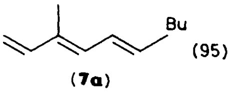
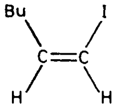
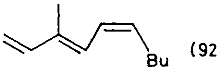
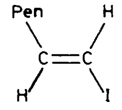
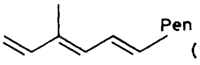
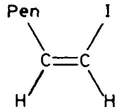
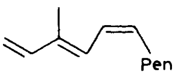
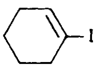
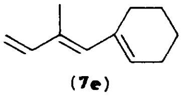
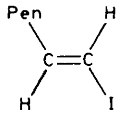
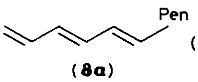
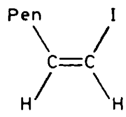
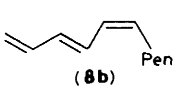
A typical experiment is as follows: to a solution of the *S,S*-dioxide (**3**) (0.32 mmol) and $(Ph_3P)_4Pd$ (0.05 equiv.) in anhydrous tetrahydrofuran (THF) was added (*E*)-1-iodohex-1-ene[6] (1 equiv.) at room temperature under argon. The mixture was stirred for 24 h at room temperature, poured into water, and extracted with ethyl acetate. Silica gel chromatography gave the vinyl substituted *S,S*-dioxide (**5a**) in 41% yield. The yields of the reactions of (**3**) with other vinyl iodides are in Table 1 (entries 2—5). Compounds (**6**) were obtained similarly (entries 6, 7).

The vinyl compounds (**5**) and (**6**) thus obtained were desulphonylated ($NaHCO_3$, 95% EtOH, 60 °C, 1 h) to give the corresponding trienes (**7**) and (**8**) respectively, with >95% stereoselectivity in high yields (see Table 1). The stereoselec-



Scheme 1

Table 1. Reaction of the stannylated *S,S*-dioxides (**3**) and (**4**) with vinyl iodides in the presence of $(Ph_3P)_4Pd$ and desulphonylation of the adducts.

Entry	X	Vinyl iodide[a]	Products[b] (% yield) Reaction with vinyl iodides	Desulphonylation
1	Me		(**5a**) (41)[c,d]	 (95)[d] (**7a**)
2	Me		(**5b**) (40)	 (92) (**7b**)
3	Me		(**5c**) (36)	 (95) (**7c**)
4	Me		(**5d**) (39)	 (95) (**7d**)
5	Me		(**5e**) (33)	 (84) (**7e**)
6	H		(**6a**) (34)	 (88) (**8a**)
7	H		(**6b**) (32)	 (83) (**8b**)

[a] Ref. 6; Pen = pentyl. [b] The ^{13}C n.m.r. spectra of (**7**) and (**8**) and the ^{1}H n.m.r. spectra of all products were in agreement with the proposed structures. [c] The yields were not optimized. [d] Isolated yields.

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† Compounds (**3**) and (**4**) were prepared as follows. The *S,S*-dioxide (1.5 equiv.) in dry tetrahydrofuran (THF; 3 ml) was treated with n-butyl-lithium (1.6 M hexane solution; 1.0 equiv.) in the presence of hexamethylphosphoramide (HMPA, 4.0 equiv.) with stirring for 2 min at −110 °C under argon. Tri-n-butylstannyl chloride (1.0 equiv.) was added, and the stirred mixture was allowed to warm slowly to room temperature during 1 h. The mixture was poured into water, and the products were extracted with ethyl acetate. The extract was washed with brine and dried over Na_2SO_4, and the solvent was removed *in vacuo*. The residue was chromatographed on silica gel with ethyl acetate–hexane (1 : 4 v/v) as eluant to give the stannylated *S,S*-dioxide as a colourless oil in 35—40% yield: (**3**), ^{1}H n.m.r. ($CDCl_3$): δ 0.95 (9H, s), 1.00—1.85 (18H, m), 1.90 (3H, s), 3.81 (3H, m), 5.71 (1H, d, *J* 2.0 Hz); (**4**), ^{1}H n.m.r. ($CDCl_3$): δ 0.96 (9H, m), 1.00—1.86 (18H, m), 3.85 (3H, m), 6.15 (2H, m). Satisfactory analytical and spectroscopic data were obtained for all new compounds.

tivity of the reactions giving (**7**) and (**8**) was established by ^{1}H and ^{13}C n.m.r. spectroscopy.‡ The trienes (**8**) are natural compounds, isolated from *Galbanum* and *Dictyoperis* (Hawaiian seaweed), and have interesting olfactive properties.[7]

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‡ The stereoselectivity of the reactions giving (**7**) was established by the ratio of the integrated intensity of the six unsaturated C protons to the three C-3 methyl protons: for example the methyl protons of (**7a**) appeared at δ 1.78 and those of (**7b**) at δ 1.83. Furthermore, their ^{13}C n.m.r. spectra showed only signals which could reasonably be assigned to sp^2 carbons. The stereointegrity of (**8**) was determined by the ratio of the integrated intensity of the C-7 methylene protons [δ 2.10 for (**8a**) and δ 2.22 for (**8b**)].