Stereoselective Synthesis of (*E*)-α-Hydroxy-1,3-dienes *via* the Reaction of 2,5-Dihydrothiophene *S,S*-Dioxides with Carbonyl Compounds

Sachiko Yamada, Hiromasa Suzuki, Hiroyuki Naito, Takashi Nomoto, and Hiroaki Takayama*

Faculty of Pharmaceutical Sciences, Teikyo University, Sagamiko, Kanagawa 199–01, Japan

A stereoselective synthesis of (*E*)-α-hydroxy-1,3-dienes, by thermal extrusion from adducts of 2,5-dihydrothiophene *S,S*-dioxide (**1**) with aldehydes and ketones, is presented and its extension to the synthesis of the dienone, (*E*)-tagetone, and of a 1,3,5-triene system, is illustrated.

Reaction of 2,5-dihydrothiophene *S,S*-dioxides with alkyl iodides followed by thermal desulphonylation provides a facile stereoselective method for synthesizing (*E*)-, (*E,Z*)-, and (*E,E*)-conjugated dienes.[1—4] Extension of this reaction to carbonyl compounds allows 1,3-dienes having a hydroxy group at the α-position to be synthesised stereoselectively; this functionality is present in the key intermediates in the syntheses of biologically important compounds such as compactin,[5] mevinolin,[6] and chlorothricolide.[7] We report here the successful addition of α-carbanions derived from the *S,S*-dioxides (**1**) to carbonyl compounds giving the α-hydroxyalkyl derivatives (**2**) and (**3**),† which by subsequent desulphonylation afford α-hydroxy conjugated dienes.

The reaction of the *S,S*-dioxides (**1**) with carbonyl compounds in hexamethylphosphoramide (HMPA)–tetrahydrofuran (THF) proceeded in moderate to good yields on treatment with lithium hexamethyldisilazide (LiHMDS) in THF (see Table 1). Both aliphatic and aromatic aldehydes and ketones reacted with (**1**) to give the adducts (**2**) or (**3**). The substituent on the double bond of the *S,S*-dioxides (**1**) profoundly affected the regioselectivity of the reaction. Thus, while an electron-donating methyl group promoted exclusive reaction at the 2-position, compound (**1b**), the presence of an electron-withdrawing phenyl substituent resulted in condensation only at C-5, compound (**1c**). Similar substituent effects have been observed in the reaction of compounds of type (**1**) with alkyl iodides.[9]

With α,β-unsaturated ketones, α-carbanions derived from (**1**) underwent conjugate addition giving predominantly the 1,4-adduct (**4**), accompanied by the 1,2-adduct (**2**) (Table 1).

The α-hydroxyalkyl compounds (**2**) and (**3**) and 1,4-adducts (**4**) thus obtained were desulphonylated ($NaHCO_3$, 95% EtOH, 125 °C, 30 min) to give the corresponding (*E*)-α-hydroxydienes (**5**) (X = H or Me) and (**6**) (X = Ph) and (*E*)-γ-oxo-1,3-dienes (**7**) (R^2 = Me, X = H or Me), respectively, with nearly 100% stereoselectivity in high yields (Table 1).

The method can be applied to the synthesis of conjugated trienes and dienones. (*E*)-2,4-Dimethylhexa-1,3,5-triene (**8**) was obtained from the adduct (**2f**) by dehydration ($SOCl_2$, pyridine, 75%) followed by thermal desulphonylation ($NaHCO_3$, $CDCl_3$, 125 °C, 30 min, quantitative). Taking advantage of the regioselective reaction of compound (**1b**) at the 2-position, the head position of the masked isoprene, monoterpene (*E*)-tagetone (**9**)[10] was synthesized in three

† In previous papers, the reaction of (**1**) with aliphatic ketones under basic conditions gave no α-hydroxyalkyl derivatives, but the corresponding dehydrated or isomerized products were obtained.[8]

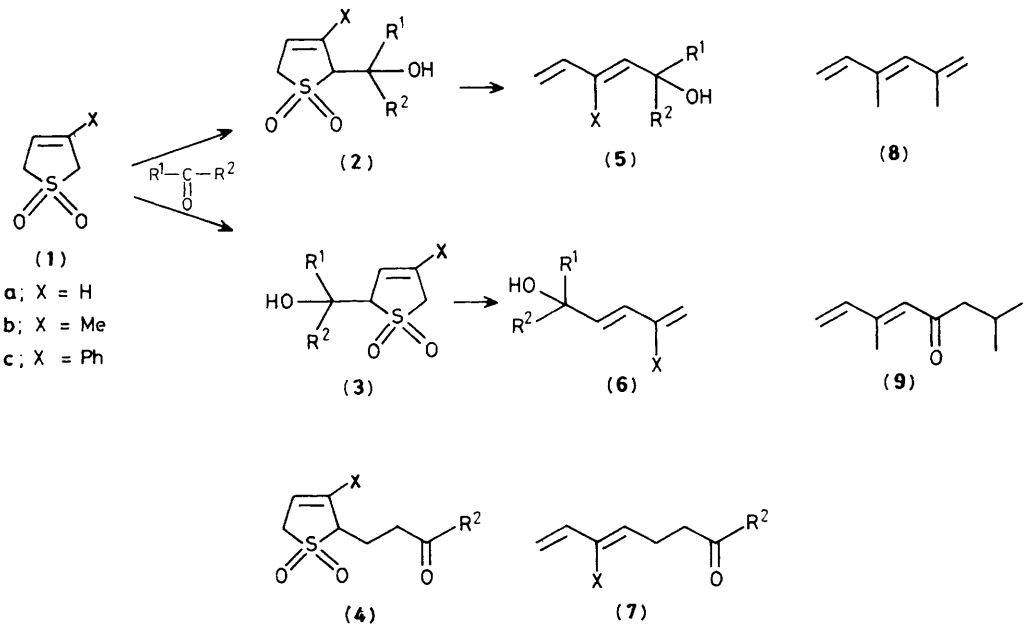

Table 1. Reaction of the *S*,*S*-dioxides (**1**) with ketones and aldehydes,[a] and desulphonylation of the adducts.[b]

			Products[c] (yield,[d] %)	
			Reaction with	
X	R^1	R^2	carbonyl compounds	Desulphonylation
H	Me	Me	(**2a**) (49)	(**5a**) (85)
H	$-[CH_2]_5-$		(**2b**) (57)	
H	Me_2CHCH_2	H	(**2c**) (62)	(**5c**) (87)
H	Ph	H	(**2d**) (42)	
H	CH_2=CH	Me	(**2e**) (9), (**4e**) (45)	(**7e**) (95)
Me	Me	Me	(**2f**) (75)	(**5f**) (84)
Me	$-[CH_2]_5-$		(**2g**) (41)	
Me	Me_2CHCH_2	H	(**2h**) (59)	(**5h**) (84)
Me	Ph	H	(**2i**) (76)	(**5i**) (70)
Me	Ph	Me	(**2j**) (34)[e]	(**5j**) (53)[f]
Me	CH_2=CH	Me	(**2k**) (5), (**4k**) (39)	(**7k**) (96)
Ph	Me	Me	(**3l**) (66)	(**6l**) (81)
Ph	Me_2CHCH_2	H	(**3m**) (44)	(**6m**) (74)

[a] A solution of LiHMDS (1.1 equiv.) in THF was added in one portion to a solution of (**1**) and the carbonyl compound (2 equiv.) in THF–HMPA at −78 °C, and the reaction was quenched after 5 min. [b] A 95% ethanol solution of the adduct (**2**), (**3**), or (**4**) was heated at 125 °C for 30 min in the presence of $NaHCO_3$ in a sealed tube. [c] All new compounds gave satisfactory spectral data. [d] Isolated yields. [e] In addition to (**2j**), an unidentified product (14%) was obtained. [f] Appreciable amounts of elimination products, acetophenone and isoprene, were obtained.

steps in 35% overall yield. The adduct of (**1b**) with isovaleraldehyde (**2h**) was desulphonylated to yield exclusively the (*E*)-diene (**5h**) which upon oxidation [pyridinium chlorochromate (PCC), CH_2Cl_2, 70%] gave (*E*)-tagetone (**9**).

Although a similar method for synthesizing α-hydroxy-1,3-dienes using a Diels–Alder adduct of (**1**), instead of using (**1**) directly, has been reported,[11] our method is advantageous in that the electronic effect of the substituent on the double bond can be transmitted to the reaction centre so that regioselective substitution at the 2- or 5-position is possible depending on the substituent.

Received, 18th August 1986; Com. 1194

References

1 S. Yamada, T. Suzuki, and H. Takayama, *Tetrahedron Lett.*, 1981, **22**, 3085; S. Yamada, T. Suzuki, H. Takayama, K. Miyamoto, I. Matsunaga, and Y. Nawata, *J. Org. Chem.*, 1983, **48**, 3483.
2 S. Yamada, H. Ohsawa, T. Suzuki, and H. Takayama, *Chem. Lett.*, 1983, 1003.
3 S. Yamada, H. Ohsawa, T. Suzuki, and H. Takayama, *J. Org. Chem.*, 1986, **51**, 4934.
4 T.-S. Chou, H.-H. Tso, and L.-J. Chang, *J. Chem. Soc., Perkin Trans. 1*, 1985, 515.
5 M. Hirama and M. Uei, *J. Am. Chem. Soc.*, 1982, **104**, 4251.
6 M. Hirama and M. Iwashita, *Tetrahedron Lett.*, 1983, **24**, 1811.
7 W. R. Roush and S. E. Hall, *J. Am. Chem. Soc.*, 1981, **103**, 5200; W. R. Roush and M. Kageyama, *Tetrahedron Lett.*, 1985, **26**, 4327; J. A. Marshall, J. E. Audia, and J. Grote, *J. Org. Chem.*, 1984, **49**, 5277.
8 C. S. Argyle, K. G. Mason, M. A. Smith, and E. S. Stern, *J. Chem. Soc. (C)*, 1967, 2176; H. J. Backer and J. Strating, *Recl. Trav. Chim., Pays-Bas.*, 1943, **62**, 815.
9 H. Takayama, H. Suzuki, T. Nomoto, and S. Yamada, *Heterocycles*, 1986, **24**, 303; T. Nomoto and H. Takayama, *ibid.*, 1985, **23**, 2913.
10 E. E. Boehm, V. Thaller, and M. C. Whiting, *J. Chem. Soc.*, 1963, 2535; E. Guittet and S. Julia, *Tetrahedron Lett.*, 1978, 1155.
11 R. Bloch, D. Hassan, and X. Mandard, *Tetrahedron Lett.*, 1983, **24**, 4691.