Tetrahedron Letters,Vol.25,No.45,pp 5173-5176,1984 0040-4039/84 $3.00 + .00
Printed in Great Britain

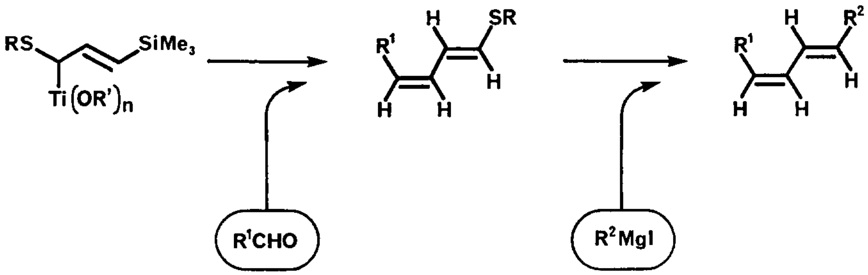
STEREOSELECTIVE SYNTHESIS OF 1,4-DISUBSTITUTED 1,3-DIENE

Junzo Ukai, Yoshihiko Ikeda, Nobuo Ikeda, and Hisashi Yamamoto*
Department of Applied Chemistry, Nagoya University
Chikusa, Nagoya 464, Japan

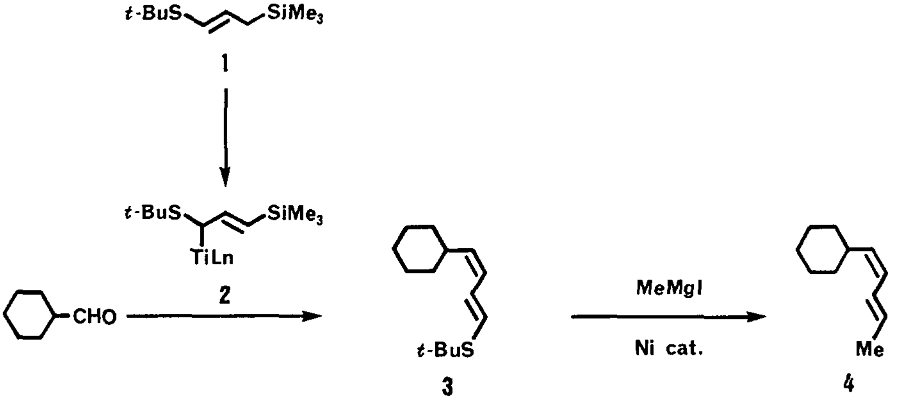
Summary: New synthetic methods for the preparation of 1,3-dienes are described.

We have recently described stereoselective syntheses of 1,3-dienes from aldehydes using allyltitanium reagents derived from allyldiphenylphosphine or allyl sulfides.[1,2] It was also pointed out that alkylthio group has an excellent potential for the further elaborations of carbon chain.[2] The high stereoselectivity of allyltitanium reagent[3] made it apparent that routes to other alkylthio 1,3-diene would be highly desirable. One of the most important processes would be a route for the transformation of aldehydes to 1-alkylthio 1,3-dienes from which 1,4-disubstituted 1,3-dienes[4] would be prepared stereoselectively (Scheme 1). We now describe a new method which responds to this need.

Scheme I



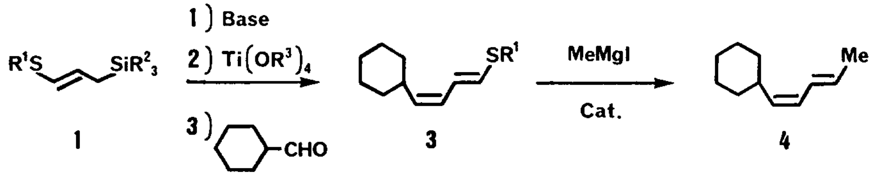
t-Butyl 3-trimethylsilyl-1-propenyl sulfide (1)[5,6] was prepared in ca. 50% yield by metallation of allyl t-butyl sulfide (t-butyllithium) and subsequent silylation. Reaction of 1 with 1 equiv of t-butyllithium in THF results in deprotonation to form lithiated 1 which can be converted to allyltitanium reagent **2** by simple treatment of titanium tetraisopropoxide. Addition of cyclohexanecarbaldehyde to the resulting titanium derivative **2** in THF at -78°C followed by gradual warming to room temperature, extractive isolation and purification by silica gel chromatography afforded the *E*,*Z*-diene **3**[7] in 62% yield with >20:1 *E*,*Z*/ *Z*,*Z* + *E*,*E* + *E*,*Z* stereoselectivity (gc analysis after alkylation).[8,9]



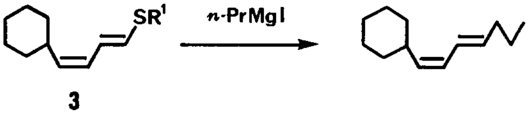
The results of several experiments are summarized in the accompanying Table. It is clear that because of the bulk of *t*-BuS- group, a greater measure of stereochemical control and position selectivity in carbon-carbon bond forming processes might result from the use of this group rather than the more common MeS- group. Although the triphenylsilyl derivative (entry 1-6) undergoes clean metallation with *n*-butyllithium at -78°C to form lithio propene, the condensation of which with aldehyde give rise to a mixture of stereoisomers with low selectivities.

A typical procedure is as follows: To a solution of *t*-butyl 3-trimethylsilyl-1-propenyl sulfide (0.304 g, 1.50 mmol)[5] in dry THF (3 ml) was added *t*-butyllithium (0.85 ml of a pentane solution, 1.5 mmol) dropwise at -78°C, and the mixture was stirred at -78°C for 10 min, and then at 0°C for 1 h. Titanium tetraisopropoxide (0.45 ml, 1.50 mmol) was added dropwise at -78°C, and the resulting mixture was stirred for 30 min. Cyclohexanecarbaldehyde (0.12 ml, 1.0 mmol) was added at -78°C, and the mixture was stirred at -78°C for 2 h and at room temperature overnight. After usual workup, the product was purified by column chromatography on silica gel to give the *E*,*Z*-sulfide **3** (0.139 g, 62%).[7] To a mixture of the sulfide **3** (275 mg, 0.96 mmol), $Ni(PPh_3)_2Cl_2$ (0.0654 g, 0.1 mmol), and DPPP (0.0414 g, 0.1 mmol) in benzene (10 ml) was added MeMgI (9.6 mmol in 4 ml of ether) at room temperature under N_2 and the mixture was heated at reflux for 25 min. After usual workup, the product was purified by chromatography to give 1-cyclohexyl-1,3-pentadiene (**4**, 0.103 g, 71%).[9]

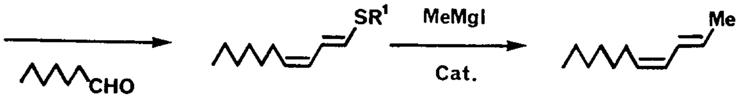
Table 1. Synthesis of 1,4-disubstituted 1,3-diene[a]



Entry	1^3		Base	Reagent	3	Catalyst[b]	4	
					Yield		Yield	Ratio[c]
	R^1	R^2		R^3	(%)		(%)	Z,E:Z,Z:E.E:E,Z
1	n-Pr	Ph	n-BuLi	i-Pr	(69)[d]	A	85	62:24: 9: 5
2	i-Pr	Ph	n-BuLi	i-Pr	(67)[d]	A	53	74:17: 6: 5
3	t-Bu	Ph	n-BuLi	i-Pr	97	B	68	83: 6: 9: 2
4	t-Bu	Ph	n-BuLi	i-Bu	90	B	71	90: 8: 2: -
5	t-Bu	Ph	n-BuLi	t-Bu	29	B	75	57:30:10: -
6	t-Bu	Ph	n-BuLi	none	23	B	—	66:25: 7: 2
7	t-Bu	Me	t-BuLi	i-Pr	62	B	75	98: 2: -: -
8	t-Bu	Me	t-BuLi	i-Bu	29	B	—	97: 3: -: -
9	t-Bu	Me	t-BuLi	i-Pr	55[e]	C	75	94: 2: 4: -
10	t-Bu	Me	t-BuLi	i-Pr	54	C	93	96: 2: -: 3



11	t-Bu	Me	t-BuLi	i-Pr	62	C	93	>95: <5



12	t-Bu	Me	t-BuLi	i-Pr	55	C	-	98: 1: 1: -

[a] All reactions were carried out on a 1-2 mmol scale as described in the text. The products were identified by PMR and IR spectra, and/or comparison with authentic samples. [b] A: $Ni(PPh_3)_2Cl_2$; B: $Ni(PPh_3)_2Cl_2$ + DPPP; C: $Ni(DPPP)Cl_2$. [c] All four possible isomers were independently synthesized using Wittig reactions. [d] Over-all yields of two step sequence. Thus, the intermediary hydroxyl silane was isolated and treated with KO^{t}Bu. [e] Using HMPA (1 equiv) as a co-solvent.

References and Notes

1. J. Ukai, Y. Ikeda, N. Ikeda, and H. Yamamoto, *Tetrahedron Lett.*, **24**, 4029 (1983).
2. Y. Ikeda, K. Furuta, N. Meguriya, N. Ikeda, and H. Yamamoto, *J. Am. Chem. Soc.*, **104**, 7663 (1982).
3. (a) F. Sato, Y. Suzuki, and M. Sato, *Tetrahedron Lett.*, **23**, 4589 (1982); (b) M. T. Reetz and B. Wenderoth, *ibid.*, **23**, 5259 (1982); (c) Y. Yamamoto, Y. Saito, and K. Maruyama, *ibid.*, **23**, 4597 (1982); *J. Chem. Soc., Chem. Commun.*, **1982**, 1326. As a general review of allylic carbanions substituted by heteroatoms, see J.-F. Biellmann and J.-B. Ducep, *Organic Reactions*, **27**, 1 (1982).
4. Recent general review: G. Pattenden In "Comprehensive Organic Chemistry, Vol. 1"; Sir D. H. R. Barton and W. D. Ollis, Eds.; Pergamon Press, Oxford, 1979; pp 171-186.
5. The reagent **1** was prepared as follows: To a solution of allyl *t*-butyl sulfide and HMPA (1 equiv) in dry THF was added *t*-BuLi (1 equiv) at -78^{o}C and the mixture was stirred for 1 h at that temperature. Chlorotrimethylsilane (1 equiv) was added at -78^{o}C and the mixture was stirred for 20 min. The reaction was terminated by pouring into ice-cold dil. HCl and the product was extracted with ether. The organic layers were washed with brine and concentrated in vacuo to leave an oil which was purified by column chromatography on silica gel (hexane)(44-56% yield). IR (neat) 2970, 1370, 1260, 1160, 870 cm^{-1} ; PMR ($CDCl_3$)δ5.93 (2H, m), 1.82-1.62 (2H, m), 1.41 (9H, s), 0.16 (9H, s); R_f 0.28 (hexane); Anal. Found: C, 59.2;H, 11.1%.
6. *t*-Butyl 3-trimethylsilyl-2-propenyl sulfide may be an alternative starting material which was prepared by DIBAH addition (*Z*/*E* = 1:4.2 and the *E*-isomer was separated by column chromatography and used for the reaction) to *t*-butyl 3-trimethylsilyl-2-propeynl sulfide(67%) which in turn was prepared by silylation of *t*-butyl propargyl sulfide (80%).
7. IR (CCl_4) 2930, 1430, 1370, 1250, 1160, 840 cm^{-1}; PMR ($CDCl_3$) δ 6.57 (1H, dd, 14 and 10 Hz), 6.13 (1H, d, 14 Hz), 5.77(1H, dd, 10 Hz), 5.10 (1H,dd, 10 Hz), 2.79-0.96 (20H).
8. H. Okamura, M. Miura, H. Takei, *Tetrahedron Lett.*, 43 (1979); E. Wenkert, T. W. Ferreira, E. L. Michelotti, *J. Chem. Soc., Chem. Commun.*, **1979**, 637.
9. IR (neat) 2930, 1455, 985, 950, 830 cm^{-1}; PMR ($CDCl_3$) δ 6.29 (1H, dd, 16 and 11 Hz, 5.81 (1H, dq), 5.61(1H, dd, 10 Hz),5.18 (1H, dd, 10 Hz); GC (25-m PEG-HT capillary column, 80^{o}C) t_R 8.25 min (*Z*,*E*) (t_R of other isomers: *Z*,*Z*: 8.73; *E*,*E*: 9.24; *E*,*Z*: 9.48 min). Anal. Found: C, 87.8; H, 12.2%.

(Received in Japan 30 July 1984)