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Stereoselective Formation of (2-Thenyl)-substituted Alkenes from 2-Chloromethylthiophene and Lithium Trialkylalkynylborates

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ABSTRACT

The reactions of 2-chloromethylthiophene (an analog of a benzyl halide) with lithium trialkylalkynylborates gave, after protonation, E-alkenes with a (2-thenyl) substituent in good yields, and the reaction stereoselectivity was different from that of the reaction of benzyl bromide with an alkynylborate.

The highly stereoselective reaction of a lithium trialkylalkynylborate with various electrophiles [1] is attractive as an effective approach for the formation of a carbon-carbon bond in organic synthesis. In a typical reaction, the β-carbon of the alkynyl group in the lithium trialkylalkynylborate attacks the electrophile, with subsequent migration of an alkyl group from boron to the α-carbon of the alkynyl group, stereoselectivity in the formation of the alkenyl derivative generally being observed. In the case of some electrophiles, such as dimethyl sulfate, allyl bromide, benzyl bromide, [2] bromoacetone, ethyl bromoacetate, ethyl iodoacetate [3], and carbon dioxide [4], the incoming group (electrophile) and the migrating group (alkyl group) became located on the same side of the double bond in the resulting alkene; however, with other electrophiles, such as chlorodialkylborane, [5] chlorotrimethylsilane, [6] halodiorganophosphine, [7] chlorotributyltin, phenylselenenyl chloride [8], and allyl ethyl carbonate [9], the incoming group and the migrating group ended up on the opposite sides of the double bond. Thus, the effect of the structure of the electrophile on the reaction stereoselectivity is obviously of interest. Recently, we became interested in expanding the scope of the reaction to include some heterocycle systems and in studying the influence of the heterocycle structure on the stereoselectivity of the reaction [10]. Pelter investigated in detail the reaction of various active alkylation reagents, including benzyl bromide, with lithium trialkylalkynylborates [2]. Considering that 2-chloromethylthiophene, an analog of a benzyl halide, is more reactive than benzyl halides generally, we have studied the reaction of 2-chloromethylthiophene with the organoborates in a preliminary manner, and we herein report the results.

RESULTS AND DISCUSSION

Under mild conditions, 2-chloromethylthiophene can readily react with a lithium trialkylalkynylborate. The reaction occurred at the β-carbon of the alkynyl group in the organoborate, with subsequent stereoselective migration of an alkyl group from boron to the α-carbon of the alkynyl group to afford in good yield the intermediates (I and II) that were protonated to give (E)- and (Z)-alkenes containing the 2-thenyl group, as shown in Scheme 1.

All of the products could readily be isolated by silica gel column chromatography. In glc of the products, two peaks with a ratio of about 70:30 appeared. The structure of the major product was

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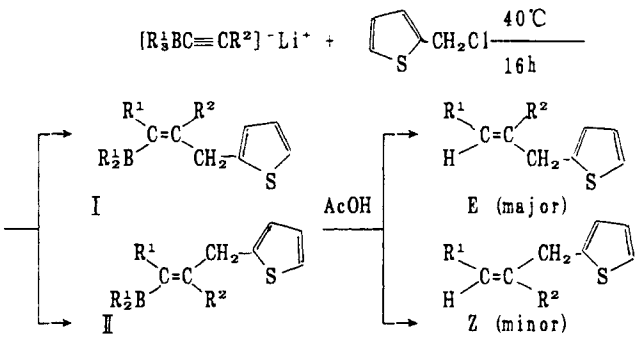

SCHEME 1

determined by the NOE technique of ^{1}H NMR spectroscopy. For example, in the ^{1}H NMR spectrum of 9-(2-thenyl)-9-phenyl-8-nonene (**9**), there are two single peaks at δ = 3.96 and 3.78 for the CH_2 group of the 2-thenyl group of two different isomers (with a ratio of 74:26), which is in accord with the ratio of two peaks found by glc. When the larger peak (δ = 3.96) was simultaneously irradiated, a 26.3% increase of intensity of the vinyl proton (δ = 5.88) was observed; however, on simultaneous irradiation of the smaller peak (δ = 3.78), there was hardly any increase in the intensity of the vinyl proton (δ = 5.54). In the case of the preparation of 7-(2-thenyl)-7-hexadecene (**3**), the same phenomenon appeared. There were two single peaks at δ = 3.47 and 3.52 with a ratio of 60:40. When the former peak (δ = 3.47) was simultaneously irradiated, the intensity of the vinyl proton (δ = 5.28) was increased about 17.1 pct, and on simultaneous irradiation of the latter peak (δ = 3.52), the signal intensity of the vinyl proton did not increase. These facts suggest that the thenyl group and the vinyl proton are on the same side of the double bond in the major product; *i.e.*, the incoming group (2-thenyl) and the migrating group (alkyl) are on the opposite sides of the double bond, which is different from the result obtained by using benzyl bromide as the electrophile [2].

The reaction results are listed in Table 1. From Table 1, it is apparent that the reaction of the organoborates having a cyclo or side-chain alkyl or phenyl group resulted in higher stereoselectivity than those of the organoborates with normal alkyl groups, but the yields of the former were lower than those of the latter. This might be due to steric hindrance effects. We will continue to study such reactions in detail.

2-Chloromethylthiophene can be prepared readily either by halomethylation of a suitable thiophene or by side-chain halogenation of an alkyl thiophene [11], and the reaction of 2-chloromethylthiophene with lithium trialkylalkynylborates appears to be general and the yields moderate to good. Thus, this reaction may be attractive as a new entry to thiophene derivatives.

TABLE 1 (E/Z)-(2-Thenyl)-Substituted Alkenes from 2-Chloromethylthiophene and Trialkylalkynylborate

Entry	R^1	R^2	*Z:E*[a]	*Yield* (%)[b]
1	*n*-heptyl	*n*-hexyl	38:62	88
2	*n*-octyl	*n*-butyl	37:63	74
3	*n*-octyl	*n*-hexyl	43:57	98
4	*n*-hexadecyl	*n*-hexyl	36:64[c]	92
5	2-methyl-1-pentyl	*n*-butyl	26:74	92
6	2-methyl-1-pentyl	*n*-hexyl	25:75	67
7	cyclopentyl	*n*-butyl	26:74	77
8	cyclopentyl	*n*-hexyl	30:70	66
9	*n*-pentyl	phenyl	22:78	78

[a]Obtained from capillary column (OV-101, 125 m) chromatography.
[b]Isolated yields.
[c]Obtained from ^{1}H NMR, with a JEOL FX-90Q spectrometer.

EXPERIMENTAL

IR spectra were recorded on an IR-440 spectrometer. ^{1}H NMR spectra and NOE were taken on a JEOL FX-90Q instrument with $CDCl_8$ as the solvent and TMS as the internal standard. MS were taken on a Finnigan 4021 spectrometer. GC results were recorded on a Varian 3700 gas chromatography instrument installed with a capillary column (OV-101, 126 m).

Typical Procedure for Synthesis of (2-Thenyl)alkenes

Into a solution of a lithium trialkylalkynylborate [2] (5 mmol) in THF (10 mL) contained in a dry 50 mL flask under argon at −78°C was added 2-chloromethylthiophene [11] (5 mmol) in THF (5 mL). After a 30 minute period for the addition, stirring was continued for 16 hours at 40°C. Then the reaction mixture was treated with acetic acid (4 mL) for another 6 hours at 25°C. The organic layer was washed until it was neutral, dried, and evaporated to give a residue that was separated into its components by silica gel column chromatography (petroleum ether as eluant).

7-(2-Thenyl)-7-pentadecene (**1**)

Anal. $C_{20}H_{34}S$ calcd: C, 78.36; H, 11.11. Found: C, 78.11; H, 11.18. IR(film) ν_{max}: 3100 (m), 2900, 2850 (s), 1780 (w), 1475 (s), 855, 820 (m), 725 (m), 695 (s) cm^{-1}. ^{1}HNMR (CCl_4/TMS) δ = 7.00–6.56 (m, 3H, thenyl-H), 5.33–5.10 (t, 1H, –CH=C), 3.45 (unsolved, d, 2H, $-CH_2-$thenyl), 2.10–1.80 (m, 4H, $-CH_2C{=}C{-}CH_2-$), 1.26 (m, 18H, $C-(CH_2)_5C-C{=}C-C-(CH_2)_4-C$), 0.86 (t, 6H, 2 × CH_3-). MS (*m/z*): 306 (M^+, 36), 97 (100).

5-(2-Thenyl)-5-tetradecene (**2**)

Anal. $C_{19}H_{32}S$ calcd: C, 78.01; H, 11.03. Found: C, 77.53; H, 11.14. IR(film) ν_{max}: 3100 (m), 2900, 2850

(s), 1775 (w), 1475 (s), 850, 820 (m), 720 (m), 695 (s) cm^{-1}. ^1H NMR (CCl_4/TMS) δ = 6.93–6.68 (m, 3H, thenyl-H), 5.26–5.04 (t, 1H, –CH=C), 3.36 (unsolved, d, 2H, $-CH_2-$thenyl), 1.84 (m, 4H, $-CH_2C=C-CH_2-$), 1.18 (m, 16H, $C-(CH_2)_6C-C=C-C-(CH_2)_2-$), 0.77 (t, 6H, 2 × CH_3-). MS (*m/z*): 292 (M^+, 20), 97 (54), 43 (100).

7-(2-Thenyl)-7-hexadecene (**3**)

Anal. $C_{21}H_{26}S$ calcd: C, 78.68; H, 11.32. Found: C, 78.88; H, 11.68. IR(film) ν_{max}: 3050 (m), 2900, 2850 (s), 1780 (w), 1480 (s), 850, 820 (m), 720 (m), 695 (s) cm^{-1}. ^1H NMR (CCl_4/TMS) δ = 7.04–6.72 (m, 3H, thenyl-H), 5.35–5.12 (t, 1H, –CH=C), 3.46 (unsolved, d, 2H, $-CH_2-$thenyl), 1.94 (m, 4H, $-CH_2C=CCH_2-$), 1.28 (m, 20H, $C-(CH_2)_3C-C=C-C-(CH_2)_4-$), 0.88 (t, 6H, 2 × CH_3-). MS (*m/z*): 320 (M^+, 56), 97 (100).

7-(2-Thenyl)-7-tetracosene (**4**)

Anal. $C_{29}H_{52}S$ calcd: C, 80.56; H, 12.11. Found: C, 79.93; H, 12.58. IR(film) ν_{max} 3100 (m), 2900, 2850 (s), 1775 (w), 1470 (s), 855, 820 (m), 725 (m), 695 (s) cm^{-1}. ^1H NMR (CCl_4/TMS) δ = 6.92–6.67 (m, 3H, thenyl-H), 5.32–5.08 (t, 1H, –CH=C), 3.44 (unsolved, d, 2H, $-CH_2-$thenyl), 2.03 (m, 4H, $-CH_2C=CCH_2-$), 1.24 (m, 36H, $C-(CH_2)_{14}C-C=C-C-(CH_2)_4-$), 0.86 (t, 6H, 2 × CH_3-). MS (*m/z*): 432 (M^+, 27), 97 (100).

5-(2-Thenyl)-8-methyl-5-undecene (**5**)

Anal. $C_{17}H_{29}S$ calcd: C, 77.21; H, 10.67. Found: C, 76.82; H, 10.64. IR(film) ν_{max}: 3050 (m), 2950, 2900 (s), 1775 (w), 1465 (s), 850, 820 (m), 725 (m), 695 (s) cm^{-1}. ^1H NMR (CCl_4/TMS) δ = 6.86–6.60 (m, 3H, thenyl-H), 5.27–5.03 (t, 1H, –CH=C), 3.37 (unsolved, d, 2H, $-CH_2-$thenyl), 1.89 (m, 4H, $-CH_2C=CCH_2-$), 1.16 (m, 9H, $C-(CH_2)_2C-CH-C=C-C-(CH_2)_2-$), 0.80 (m, 9H, 3 × CH_3-). MS (*m/z*): 264 (M^+, 76), 137 (100).

7-(2-Thenyl)-4-methyl-6-tridecene (**6**)

Anal. $C_{19}H_{32}S$ calcd: C, 78.01; H, 11.03. Found: C, 77.99; H, 11.14. IR(film) ν_{max}: 3050 (m), 2900, 2850 (s), 1780 (w), 1465 (s), 850, 820 (m), 720 (m), 695 (s) cm^{-1}. ^1H NMR (CCl_4/TMS) δ = 6.94–6.65 (m, 3H, thenyl-H), 5.28–5.06 (t, 1H, –CH=C), 3.39 (unsolved, d, 2H, $-CH_2-$thenyl), 1.91 (m, 4H, $-CH_2C=CCH_2-$), 1.16 (m, 13H, $-(CH_2)_2-CH-C-C=C-C-(CH_2)_4-$), 0.81 (m, 9H, 3 × CH_3-). MS (*m/z*): 292 (M^+, 20), 97 (100).

5-(2-Thenyl)-6-cyclopentyl-5-hexene (**7**)

Anal. $C_{16}H_{24}S$ calcd: C, 77.36; H, 9.74. Found: C, 76.84; H, 9.72. IR(film) ν_{max}: 3050 (m), 2900, 2850 (s), 1775 (w), 1470 (s), 850, 820 (m), 725 (m), 695 (s) cm^{-1}. ^1H NMR (CCl_4/TMS) δ = 7.03–6.69 (m, 3H, thenyl-H), 5.21–5.06 (d, 1H, –CH=C), 3.50–3.59 (d, 2H, $-CH_2-$thenyl), 1.96 (m, 3H, $-CHC=CCH_2-$), 1.58 [m, 8H, (Cyclopentyl–$CH_2)_4$], 1.26 (m, 4H, $-C=C-C-(CH_2)_2-$), 0.87 (m, 3H, CH_3-). MS (*m/z*): 248 (M^+, 27), 122 (100), 97 (67).

7-(2-Thenyl)-8-cyclopentyl-7-octene (**8**)

Anal. $C_{18}H_{28}S$ calcd: C, 78.19; H, 10.21. Found: C, 77.86; H, 10.55. IR(film) ν_{max}: 3050 (m), 2950, 2900 (s), 1780 (w), 1470 (s), 855, 820 (m), 725 (m), 695 (s) cm^{-1}. ^1H NMR (CCl_4/TMS) δ = 7.01–6.65 (m, 3H, thenyl-H), 5.20–5.05 (d, 1H, –CH=C), 3.48–3.57 (d, 2H, $-CH_2-$thenyl), 1.98 (m, 3H, $-CHC=CCH_2-$), 1.56 [m, 8H, (Cyclopentyl–$CH_2)_4$], 1.24 (m, 8H, $-C=C-C-(CH_2)_4-$), 0.87 (m, 3H, CH_3-). MS (*m/z*): 276 (M^+, 11), 123 (100), 97 (43).

9-(2-Thenyl)-9-phenyl-8-nonene (**9**)

Anal. $C_{20}H_{26}S$ calcd: C, 80.48; H, 8.78. Found: C, 80.88; H, 9.20. IR(film) ν_{max}: 3050, 3025 (m), 2950, 2900 (s), 166 (w), 1605, 1495 (m), 1455 (m), 850, 820 (m), 760 (m), 700 (s) cm^{-1}. ^1H NMR (CCl_4/TMS) δ = 7.25 (m, 5H, thenyl-H), 6.97–6.71 (m, 3H, thenyl-H), 5.97–5.74, 5.66–5.42 (tt, 1H, Z and E–CH=C–), 3.96, 3.77 (ss, 2H, $-CH_2-$thenyl), 2.34–2.23 (d, 2H, $-CH_2-C=C-$), 1.36 (m, 10H, $-(CH_2)_5-C-C=C-$), 0.92 (t, 3H, CH_3-). MS (*m/z*): 298 (M^+, 43), 97 (100).

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