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Regiochemistry in Electrophilic Reactions of Propanedithio-Substituted Allylic Anions Influenced by the γ-Substituents

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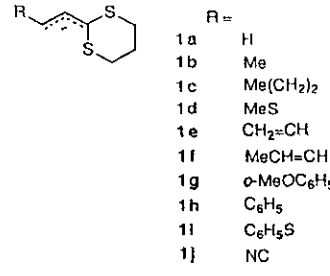
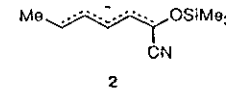
The dienyl anion **1f**, generated from metallation of 2-(1,3-pentadienyl)-1,3-dithiane with *n*-BuLi in THF, reacted exclusively at the C-1 position (α-site) with alkylating agents and ketones, but it showed some tendency toward the C-3 position (γ-site) in the reactions with benzyl bromide and aliphatic aldehydes. No reaction at the C-5 position (ε-site) was observed in any studied case. Examination of the related propanedithio-substituted allylic anions having various γ-substituents revealed that the regiochemistry was remarkably influenced by the γ-substituents and the attacking electrophiles. The electronic effect according to the principle of hard and soft acids and bases is proposed to account for the observed regiochemistry, while the steric factor was minor. Two trienes, obtained by alkylations of the dienyl anion **1f** with 4-bromo-1-butene and 5-pentenyl methanesulfonate, were applicable to intramolecular Diels-Alder reactions to give bicyclic compounds.

INTRODUCTION

The sulfur-substituted allylic anions are useful synthons for formation of carbon-carbon bonds, because they are easily accessible and because the reaction products can be further elaborated to other functional compounds.[1] For example, a propanedithio-substituted allylic anion **1a** can function either as an equivalent of the acyl anion when it reacts at the α-site with an electrophile, or as an equivalent of a β-anion of propionic acid when it reacts at the γ-site.[2] Previous reports of the electrophilic reactions of propanedithio-substituted anions indicated that the regiochemistry can be affected by several factors, including substituent of the allylic anion,[3] the attcking electrophile,[4] the counter cation,[5] the solvent,[4,5] the Lewis acid,[6] and the reaction temperature.[7] The reactions of propanedithio-substituted allylic anions with various γ-substituents such as





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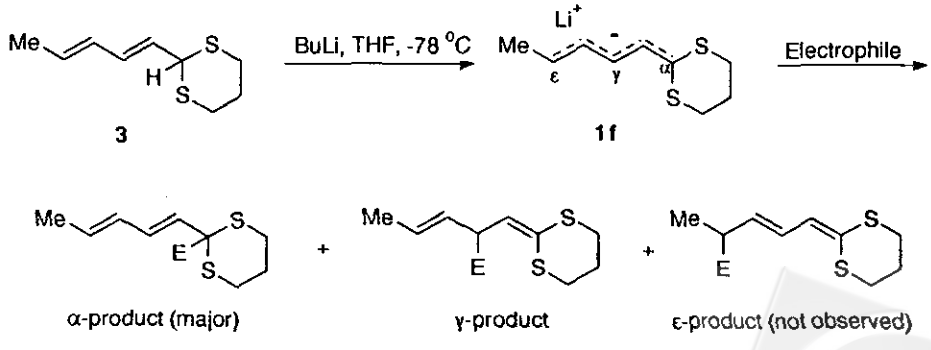
Me,[4,5] C_6H_5,[4] *o*-MeC_6H_4,[8] MeS,[9] C_6H_5S,[3,10] or CN groups[11] have been studied. We investigated an analogous anion **1f** having an alkenyl group at the γ-position. The anion **1f** can be considered a pentadienyl anion, which may have three reactive sites at the α-, γ- or ε-carbon. Methylation of a related pentadienyl anion **1e** is reported to occur exclusively at the α-site,[12] and alkylations of a 1-cyano-1-trimethylsilyloxy dienyl anion **2** show the same α-selectivity.[13]

Scheme I



RESULTS AND DISCUSSION

Condensation of 2,4-hexadienal and 1,3-propanedithiol in the presence of $Mg(ClO_4)_2$ gave a 82% yield of 2-(1,3-pentadienyl)-1,3-dithiane (**3**). Treatment of **3** with *n*-BuLi at -78 °C in THF solution resulted in the corresponding dienyl anion **1f**, which was subsequently reacted with a variety of electrophiles. The reactions with electrophiles such as propylene oxide and carbonyl compounds were performed at -78 °C, whereas the alkylation reactions were allowed to warm to room temperature. All reactions occurred mainly at the α-site of **1f** to give invariably the α-products having the 2*E*,4*E*-configurations as shown in Scheme I and Table 1. The α-selectivity of **1f** was qualitatively in agreement with the regiochemistry displayed in the electrophilic reactions of the dienyl anions **1e** and **2**.[12,13] Loss of α-regioselectivity was noted when the anion **1f** reacted with benzyl bromide and aliphatic aldehydes. These reactions also yielded significant amounts of γ-products, but no reaction at the ε-site was observed. The anion **1f** reacted at both the α- and γ-sites with 2-cyclopentenone to give the 1,4-addition products **17**α and **17**γ in nearly equal amounts. The structures of the α- and γ-products were easily distinguished from their ^{1}H NMR spectra. The vinyl protons H-2′ and H-3′ in the conjugated diene system of compound **3** and the α-products usually exhibited the resonances at fields below δ 6, whereas the most downfield signal of H-1′ proton in the non-conjugated γ-products only appeared at approximately δ 5.8.

Table 2 lists a comparison of several propanedithio-substituted allylic anions in reactions with the representative electrophiles, such as iodomethane, benzyl bromide, cyclopentanone, cyclohexanone, 2-butanone, propanal, butanal and benzaldehyde. The α/γ ratios of products were apparently influenced by the γ-substituents and by the attacking electrophiles. The parent propanedithio allylic anion **1a** and those with γ-substitution of an alkyl or an alkenyl group (**1b-1f**) gave exclusively the α-methylations. The anions **1g-i** having γ-substitution of a phenyl, an *o*-methoxyphenyl or a phenylthio group gave both the α- and γ-methylations. The percentages of γ-alkylations were increased when benzyl bromide was used as the alkylating agent. Furthermore, alkylations of the anion **1j** having a γ-cyano group occurred exclusively at the γ-site.[11] Similar α-selectivity was found in the addition reactions of **1a-g** with 2-butanone and cycloalkanones, but the anions **1h** and **1i** (R = C_6H_5 and C_6H_5S) showed ambident reactivity. However, the regiochemistry in the addition reactions with aldehydes changed dramatically with the γ-substitution. The parent anion **1a** and that with a γ-Me substituent (**1b**) reacted with aldehydes to afford exclusive γ-regioselectivity. These results contrast with the α-selectivity observed in their reactions with ketones. The anions **1f**, **1g** and **1i** all showed a preference for α-additions to aldehydes, whereas the anion **1h** showed no regioselectivity toward aldehydes.

Although the present experimental data are limited, one aspect should be mentioned. As the propanedithio substituent is constrained in a ring, its steric influence becomes less important compared to the 1,1-bis-phenylthio substituents.[3,5a] The electronic effect by the principle of hard and soft acids and bases (HSAB principle)[14] has been evoked to explain the trend of regiochemical selectivity.[2c,4] Accordingly, the α-carbons of the allylic anions **1a-f** are

Table 1. Reactions of the Propanedithio-substituted Anion **1f** (*n*-BuLi, THF) with Electrophiles

Electrophile	Products, yield (%, diastereomeric ratio)	E =
iodomethane	**4**α (81)	Me
allyl bromide	**5**α (83)	$CH_2=CHCH_2$
4-bromo-1-butene	**6**α (78)	$CH_2=CH(CH_2)_2$
5-pentenyl methanesulfonate	**7**α (59) + **7**γ (9)	$CH_2=CH(CH_2)_3$
benzyl bromide	**8**α (42) + **8**γ (28)	$PhCH_2$
2-methyloxirane	**9**α (86)	$MeCH(OH)CH_2$
propionaldehyde	**10**α (65) + **10**γ (16, 76:24)	$MeCH_2CH(OH)$
acrolein	**11**α (41) + **11**γ (22, 55:45)	$CH_2=CHCH(OH)$
crotonaldehyde	**12**α (57) + **12**γ (33, 80:20)	$MeCH=CHCH(OH)$
benzaldehyde	**13**α (87)	$PhCH(OH)$
acetone	**14**α (75)	$Me_2C(OH)$
3-pentanone	**15**α (72)	$(MeCH_2)_2C(OH)$
cyclopentanone	**16**α (82)	$(CH_2)_4C(OH)$
2-cyclopentenone	**17**α (32) + **17**γ (30, 75:25)	

Table 2. The α/γ Ratio in Electrophilic Reactions of the Propanedithio-substituted Allylic Anions **1** (with Lithium Counterion in THF)

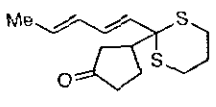
	Electrophile					
Anion[a]	MeI α:γ	$PhCH_2Br$ α:γ	$(CH_2)_nCO$ α:γ	$MeCH_2COMe$ α:γ	$Me(CH_2)_nCHO$ α:γ	PhCHO α:γ
1a, R = H	100:0	100:0	100:0 (n = 4) 85:15 (n = 5)			0:100
1b, R = Me	100:0	100:0[b]	100:0 (n = 4) 82:18 (n = 5)	84:16	< 5:95 (n = 1) < 5:95 (n = 2)	0:100
1d, R = MeS	100:0[c]	100:0	80:20 (n = 5)			
1f, R = MeCH = CH	100:0	60:40	100:0 (n = 4)	100:0	80:20 (n = 1)	100:0
1g, R = *o*-$MeOC_6H_5$	55:45	0:100	90:10 (n = 4) 88:12 (n = 5)	97:3	72:28 (n = 1) 75:25 (n = 2)	72:28
1h, R = C_6H_5	56:44	14:86	64:36 (n = 4) 77:23 (n = 5)	53:47	56:44 (n = 1) 38:62 (n = 2)	51:49
1i, R = C_6H_5S	63:37	57:43	50:50 (n = 4) 60:40 (n = 5)	23:77	100:0 (n = 1)	100:0

[a] Both the anions **1c** (R = $MeCH_2CH_2$) and **1e** (R = CH_2 = CH) reacted exclusively at the α-sites with iodomethane.[9,12] The anion **1j** (R = CN) reacted exclusively at the γ-site with iodoethane and 2-bromopropane.[11] The pertinent data for the anions **1a**,[2,12] **1b**,[4] **1d**,[9] **1g**,[8] **1h**[4,6] and **1i**[3,10] are adapted from literature.

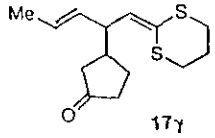
[b] This ratio refers to the exclusive α-alkylation with *m*-$MeOC_6H_4CH_2Br$.[4]

[c] This ratio refers to the exclusive α-alkylation with iodohexane.

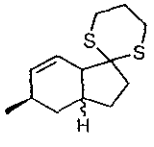
considered relatively hard nucleophilic centers owing to polarization by the propanedithio substituent. The reactions of **1a-f** with hard electrophiles, such as D_2O [15] and Me_3SiCl,[16] afforded consistently α-subsitution products. Since the carbonyl carbon ($O=C^{2+}/2R^-$) of a ketone (R_2CO) is considered as a hard electrophilic center,[4b,14a] the reactions of 2-butanone and cycloalkanones with **1a-f** also showed high α-selectivities. However, when an electron-withdrawing group, such as a phenyl or a phenylthio group, was introduced into the γ-position, the difference of hardness between the α- and γ-carbons was reduced, so that both regioisomers were formed in the reactions of **1g-i** with iodomethane and ketones. Murphy and Wattanasin have shown that percentage of alkylation at the α-site of the anion **1h** increases as the hardness of electrophile RX (X = I, Br, Cl and OTs) increases.[4a] We have also demonstrated that the lithiated 1h reacts exclusively at the α-site with ketones in the presence of a Lewis acid $BF_3 \cdot Et_2O$.[6b] These experiments indicate that the α-carbon of the allylic anion **1h** is a relatively hard nucleophilic center.



17α



17γ



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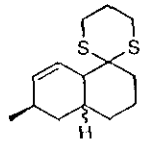

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When a relatively soft alkylating agent such as benzyl bromide was employed as the electrophile, its reactions with anions **1f-h** resulted in modest to high γ-regioselectivities. The degree of γ-selectivity roughly parallels the anion-stabilizing aptitude of the γ-substituent (Me < MeS < MeCH = CH < *o*-$MeOC_6H_5$ < C_6H_5 < C_6H_5S). At the extreme, the anion **1j** having a strongly electron-withdrawing cyano group at the γ-carbon caused exclusively γ-alkylations with iodoethane and 2-bromopropane.[11] In contrast, the γ-selectivity was obvious in the reactions of the anions **1a** and **1b** (R = H and Me) with relatively soft aldehydes ($O=C^{2+}/R^-$, H^-),[4b,14a] but other anions **1f-i** did not operate with the same regiochemistry.

In summary, the regiochemistry in electrophilic reactions of a series of the propanedithio-substituted allylic anions seemed to be finely tuned by different γ-substituents. The electronic effect according to the principle of hard and soft acids and bases is proposed to account for the observed regiochemistry, whereas the steric factor was minor. This rationale is applicable to interpret most ex-

perimental results, but question remains especially when the hardness of the attacking electrophile, such as iodomethane, is not well defined. Revelation of the real reaction pathway should await further experimental evidence.

The alkylation products **6**α and **7**α were applicable to intramolecular Diels-Alder reactions. Thus, the trienes **6**α and **7**α in toluene were respectively heated to 190 °C in sealed tubes to give the tetrahydroindan **18** and the octahydronaphthalene **19**. Although three asymmetric centers were created in each reaction, only two epimers as depicted were obtained. The stereochemistry was tentatively assigned under the assumption that the reaction proceeded in a concerted and stereospecific manner as generally accepted for Diels-Alder reactions.

EXPERIMENTAL SECTION

Melting points (Yanaco micro melting point apparatus) are uncorrected. Elemental analyses were carried out on a Perkin-Elmer 240c elemental analyzer. Infrared spectra were measured on a Perkin-Elmer 985 infrared spectrophotometer. The nuclear magnetic resonance spectra were recorded on a Varian EM-90 or a Bruker AM-300 WB spectrometer. Mass spectra were recorded on a Finnigan TSQ 46c spectrometer operating at an ionizing voltage 70 eV. Merck silica gel 60F sheets were used for analytical thin-layer chromatography. Column chromatography was performed on SiO_2 (70-230 mesh) with elution of gradients of EtOAc and *n*-hexane. High-pressure liquid chromatography was carried out on a liquid chromatograph, equipped with a refractive index detector. The samples were analyzed and separated on a μ-Porasil column (25 cm x 0.78 cm) by the indicated eluent with flow rate 5 mL/min. THF was distilled from sodium benzophenone ketyl under N_2.

2-(1,3-Pentadienyl)-1,3-dithiane (3)

To a mixture of 1,3-propanedithiol (1 mL, 10 mmol), of anhydrous $Mg(ClO_4)_2$ (0.12 g) and conc. H_2SO_4 (1 drop) in $CHCl_3$ (50 mL) was added dropwise a solution of 2,4-hexadienal (1.2 mL, 11 mmol) in $CHCl_3$ (20 mL) at 0 °C. The reaction completed in 2 h as indicated by TLC analysis. Excess KOH aqueous solution (10%) was added to quench the reaction. The aqueous phase was extracted with $CHCl_3$, the combined $CHCl_3$ solution was concentrated in vacuo. The residue was separated on a SiO_2 column by elution with *n*-hexane to give the dienyl dithiane **3** (1.52 g, 82%): Liquid; TLC (hexane) R_f 0.10; IR (neat) 2904, 1647, 1419, 1273, 1110, 986 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.68 (3 H, *d*, J = 6.6 Hz, Me), 1.80 (1 H, *m*, SCH_2CH_2), 2.03 (1 H, *m*, SCH_2CH_2), 2.71-2.89 (4 H, *m*, SCH_2 x 2), 4.59 (1 H, *d*, J = 7.7 Hz), 5.51 (1 H, *dd*, J = 15.0, 7.7 Hz, H-1'), 5.67 (1 H, *dq*, J = 15.0, 7.0 Hz, H-4'), 5.95 (1 H, *dd*, J = 15.0, 10.4 Hz, H-3'), 6.26 (1 H, *dd*, J = 15.0, 10.4 Hz, H-2'). MS m/z (rel. int.) 186 (38, M^+), 161 (11), 145 (12), 123 (32), 111 (31), 97 (100), 84 (27), 79 (38); Anal. Calcd for $C_9H_{14}S_2$: C, 58.01; H, 7.57. Found: C, 58.41; H, 7.45.

General Procedure for Electrophilic Reactions of 3

Under an atmosphere of N_2, a solution of *n*-BuLi (0.4 mL, 1.6 M in hexane) was added dropwise to a THF solution (5 mL) of **3** (93 mg, 0.5 mmol) at -78 °C. The yellow solution was stirred for 20 min, and an appropriate electrophile (0.6 mmol) was added. After a suitable period (20 min for carbonyl compounds, 45 min for epoxide and the alkylation reactions were allowed to warm to room temperature for 3 h), the reaction was quenched with sat. NH_4Cl. THF was removed by rotary evaporator, the residue was partitioned between EtOAc and water. The aqueous phase was extracted with EtOAc, the combined organic phase was dried (Na_2SO_4), concentrated, and separated on a SiO_2 column by elution with gradients of EtOAc in hexane as indicated in compounds **4-17**.

2-Methyl-2-(1,3-pentadienyl)-1,3-dithiane (4α**)**

Liquid; TLC (hexane) R_f 0.20; IR (neat) 2929, 1645, 1419, 1373, 1130, 985 cm^{-1}; ^1H NMR ($CDCl_3$, 90 MHz) δ 1.27 (3 H, *s*, Me), 1.60-2.01 (2 H, *m*, SCH_2CH_2), 1.78 (3 H, *d*, J = 6.7 Hz, Me), 2.50-3.05 (4 H, *m*, SCH_2 x 2), 5.53 (1 H, *d*, J = 15.3 Hz, H-1'), 5.75 (1 H, *dq*, J = 15.3, 6.9 Hz, H-4'), 6.10 (1 H, *dd*, J = 15.3, 10.4 Hz, H-3'), 6.37 (1 H, *dd*, J = 15.3, 10.4 Hz, H-2'). ^{13}C NMR ($CDCl_3$, 50 MHz) δ 26.2 (CH_3), 27.8 (CH_3), 28.1 (CH_2), 42.8 (CH_2), 55.2 (C), 130.4 (CH), 131.2 (CH), 134.1 (CH), 134.4 (CH). MS m/z (rel. int.) 200 (8, M^+), 185 (48), 167 (72), 153 (58), 126 (70), 111 (100), 106 (55), 77 (50); Anal. Calcd for $C_{10}H_{16}S_2$: C, 59.95; H, 8.05. Found: C, 59.96; H, 8.15.

2-(2-Propen-1-yl)-2-(1,3-pentadienyl)-1,3-dithiane (5α**)**

Liquid; TLC (hexane) R_f 0.18; IR (neat) 3037, 2906, 1633, 1419, 1373, 1243 cm^{-1}; ^1H NMR ($CDCl_3$, 90 MHz) δ 1.87 (3 H, *d*, J = 6.3 Hz, Me), 1.67-2.23 (2 H, *m*, SCH_2CH_2), 2.50-2.98 (6 H, *m*, SCH_2 x 2 + H-1"), 5.03 (1 H, *m*, H-3"), 5.19 (1 H, *m*, H-3"), 5.56 (1 H, *d*, J = 15.6 Hz, H-1'), 5.48-6.14 (3 H, *m*, H-2", 3', 4'), 6.44 (1 H, *dd*, J = 15.6, 10.5 Hz, H-2'); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 18.2 (CH_2), 25.3 (CH_2), 27.0 (CH_3), 46.4 (CH_2), 53.8 (C), 118.6 (CH_2), 130.2 (CH), 130.4 (CH), 132.0 (CH), 133.2 (CH), 133.7 (CH); MS m/z (rel. int.) 226 (11, M^+), 185 (100), 173 (15), 151 (32), 137 (46), 119 (23), 111 (39), 106 (60), 91 (29), 77 (42);

HRMS Calcd for $C_{12}H_{18}S_2$ (M^+) 226.0850, Found 226.0860.

2-(3-Buten-1-yl)-2-(1,3-pentadienyl)-1,3-dithiane (6α)

Liquid; TLC (hexane) R_f 0.26; IR (neat) 3072, 3012, 2905, 1635, 1419, 1273 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.72 (3 H, *d*, J = 6.6 Hz, Me), 1.76-1.88 (2 H, *m*, SCH_2CH_2), 1.89-2.00 (2 H, *m*), 2.08-2.16 (2 H, *m*), 2.57-2.64 (2 H, *m*, SCH_2), 2.77-2.88 (2 H, *m*, SCH_2), 4.88 (1 H, *dd*, J = 10.7, 1.5 Hz, H-4"), 4.95 (1 H, *dd*, J = 17.1, 1.5 Hz, H-4"), 5.49 (1 H, *d*, J = 15.1 Hz, H-1'), 5.70-5.78 (2 H, *m*, H-3", 4'), 6.09 (1 H, *dd*, J = 15.2, 10.4 Hz, H-3'), 6.35 (1 H, *dd*, J = 15.1, 10.4 Hz, H-2'); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 18.0 (CH_2), 25.3 (CH_2), 27.0 (CH_3), 28.0 (CH_2), 40.5 (CH_2), 54.4 (C), 114.7 (CH_2), 129.9 (CH), 130.4 (CH), 133.2 (CH), 133.6 (CH), 137.6 (CH); MS m/z (rel. int.) 240 (10, M^+), 225 (1), 197 (7), 185 (100), 165 (12), 151 (12), 111 (21), 91 (46); HRMS Calcd for $C_{13}H_{20}S_2$ (M^+) 240.1006, Found 240.0989.

2-(4-Pentenyl)-2-(1,3-pentadienyl)-1,3-dithiane (7α)

Liquid; TLC (hexane) R_f 0.12; IR (neat) 3071, 2906, 1635, 1418, 1274, 991 cm^{-1}; ^1H NMR ($CDCl_3$, 90 MHz) δ 1.36-2.27 (8 H, *m*, CH_2 x 4), 1.78 (3 H, *d*, J = 6.6 Hz, Me), 2.43-3.07 (4 H, *m*, SCH_2 x 2), 4.89-5.08 (2 H, *m*, H-5" x 2), 5.57 (1 H, *d*, J = 15.3 Hz, H-1'), 5.70-6.10 (2 H, *m*), 6.33 (1 H, *dd*, J = 15.2, 10.4 Hz, H-3'), 6.42 (1 H, *dd*, J = 15.3, 10.4 Hz, H-2'); MS m/z (rel. int.) 254 (1, M^+), 221 (3), 185 (4), 179 (6), 165 (5), 106 (5), 91 (6), 83 (100); HRMS Calcd for $C_{14}H_{22}S_2$ (M^+) 254.1163, Found 254.1166.

2-(2-Propenyl-6-heptenyliden-1-yl)-1,3-dithiane (7γ)

Liquid; TLC (hexane) R_f 0.16; IR (neat) 3053, 2925, 1672, 1432, 1275, 965 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.62-1.77 (2 H, *m*), 1.64 (3 H, *dd*, J = 5.4, 1.1 Hz, Me), 1.79-1.87 (2 H, *m*, SCH_2CH_2), 1.99-2.21 (4 H, *m*), 2.81-2.89 (4 H, *m*, SCH_2 x 2), 3.75 (1 H, *m*, H-2'), 4.94-5.04 (2 H, *m*, H-7'), 5.26-5.31 (1 H, *m*), 5.36-5.42 (1 H, *m*), 5.73-5.86 (1 H, *m*), 5.77 (1 H, *d*, J = 9.6 Hz, H-1'); MS m/z (rel. int.) 254 (3, M^+), 221 (2), 185 (100), 179 (16), 132 (17), 111 (20), 105 (21), 91 (19); HRMS Calcd for $C_{14}H_{22}S_2$ (M^+) 254.1163, Found 254.0929.

2-(Phenylmethyl)-2-(1,3-pentadienyl)-1,3-dithiane (8α)

Liquid; HPLC (2% EtOAc in hexane) R_t 6.9 min; IR (neat) 3057, 2920, 1685, 1490, 1275, 1029 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.77 (3 H, *d*, J = 6.6 Hz, Me), 1.86-2.20 (2 H, *m*, SCH_2CH_2), 2.59-2.72 (2 H, *m*, SCH_2), 2.74-2.93 (2 H, *m*, SCH_2), 3.12 (2 H, *s*, H-1"), 5.50 (1 H, *d*, J = 15.0 Hz, H-1'), 5.69 (1 H, *dq*, J = 15.1, 6.6 Hz, H-4'), 6.13 (1 H, *dd*, J = 15.1, 10.8 Hz, H-3'), 6.22 (1 H, *d*, J = 15.0, 10.8 Hz, H-2'), 7.20-7.32 (5 H, *m*, PhH); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 18.5 (CH_2), 25.3 (CH_2), 27.2 (CH_3), 48.9 (CH_2), 55.6 (C), 127.0 (CH), 127.6 (CH), 130.2 (CH), 130.4 (CH), 131.1 (CH), 133.1 (CH), 134.3 (CH), 138.6 (C); MS m/z (rel. int.) 276 (35, M^+), 235 (6), 201 (1), 185 (100), 173 (13), 111 (8), 91 (12), 77 (6).

2-[2-(Phenylmethyl)-3-pentenyliden-1-yl]-1,3-dithiane (8γ)

Liquid; HPLC (2% EtOAc in hexane) R_t 6.3 min; IR (neat) 3021, 2952, 1668, 1490, 1275, 1029 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.62 (3 H, *dd*, J = 6.0, 0.8 Hz, Me), 2.03-2.13 (2 H, *m*, SCH_2CH_2), 2.54-2.80 (6 H, *m*, SCH_2 x 2 + H-1"), 3.57-3.76 (1 H, *m*, H-2'), 5.28-5.38 (2 H, *m*, H-3', 4'), 5.85 (1 H, *d*, J = 9.6 Hz, H-1'), 7.13-7.30 (5 H, *m*, PhH); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 18.0 (CH_2), 25.3 (CH), 29.7 (CH_3), 30.5 (CH_2), 41.8 (CH_2), 44.2 (CH_2), 125.4 (CH), 125.8 (CH), 127.9 (CH), 129.4 (CH), 132.0 (CH), 136.7 (CH), 139.2 (C), 140.7 (C); MS m/z (rel. int.) 277 (4, $[M + 1]^+$), 235 (3), 201 (2), 185 (100), 111 (11), 91 (17), 77 (5).

2-(2-Hydroxypropyl)-2-(1,3-pentadienyl)-1,3-dithiane (9α)

Oil; TLC (10% EtOAc in hexane) R_f 0.30; IR (neat) 3445, 2906, 1644, 1419, 1274, 991 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.18 (3 H, *dd*, J = 6.3, 2.1 Hz, Me), 1.20-1.42 (2 H, *m*, H-1"), 1.79 (3 H, *d*, J = 6.6 Hz, Me), 1.84-2.14 (2 H, *m*, $SCCH_2$), 2.74-3.00 (4 H, *m*, SCH_2 x 2), 4.16 (1 H, *dd*, J = 9.1, 6.3 Hz, H-2"), 5.62 (1 H, *d*, J = 15.2 Hz, H-1'), 5.70-5.95 (1 H, *dq*, J = 15.0, 6.6 Hz, H-4'), 6.14 (1 H, *dd*, J = 15.0, 10.3 Hz, H-3'), 6.47 (1 H, *dd*, J = 15.2, 10.3 Hz, H-2'); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 16.9 (CH_3), 18.1 (CH_2), 22.4 (CH_3), 23.6 (CH_2), 49.0 (CH_2), 51.9 (C), 63.4 (CH), 128.9 (CH), 129.6 (CH), 131.8 (CH), 132.2 (CH); MS m/z (rel. int.) 244 (18, M^+), 229 (1), 200 (4), 185 (12), 169 (72), 155 (20), 125 (22), 112 (71), 106 (22), 97 (43), 91 (69), 77 (76); Anal. Calcd for $C_{12}H_{20}OS_2$: C, 58.97; H, 8.25. Found: C, 58.96; H, 8.15.

2-(1-Hydroxypropy)-2-(1,3-pentadienyl)-1,3-dithiane (10α)

Oil; TLC (10% EtOAc in hexane) R_f 0.18; IR (neat) 3469, 2927, 1678, 1419, 1275, 1122 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 0.90 (3 H, *t*, J = 6.6 Hz, Me), 1.18-1.43 (2 H, *m*), 1.65 (3 H, *d*, J = 6.6 Hz, Me), 1.67-1.87 (2 H, *m*, SCH_2CH_2), 2.59-2.77 (4 H, *m*, SCH_2 x 2), 3.54 (1 H, *ddd*, J = 6.3, 4.2, 2.1 Hz, H-1"), 5.50 (1 H, *d*, J = 15.3 Hz, H-1'), 5.66 (1 H, *dq*, J = 15.5, 6.6 Hz, H-4'), 6.02 (1 H, *dd*, J = 15.5, 10.4 Hz, H-3'), 6.40 (1 H, *dd*, J = 15.3, 10.4 Hz, H-2'); MS m/z (rel. int.) 244 (2, M^+), 185 (100, $[M-C_3H_7O]^+$), 174 (2), 155 (2), 145 (2), 139 (9), 111 (28), 97 (10), 77 (18): Anal. Calcd for $C_{12}H_{20}OS_2$: C, 58.97; H, 8.25. Found: C, 58.56; H, 8.22.

2-[2-(1-Hydroxypropyl)-3-pentenyliden-1-yl]-1,3-dithiane (10γ)

Oil; TLC (10% EtOAc in hexane) R_f 0.15; IR (neat) 3435, 2925, 1668, 1419, 1275, 1113 cm^{-1}; ^1H NMR ($CDCl_3$,

300 MHz) δ 0.88 (3 H, *t*, J = 5.8 Hz, Me), 1.28-1.38 (1 H, *m*), 1.43-1.52 (1 H, *m*), 1.63 (3 H, *d*, J = 6.6 Hz, Me), 2.06-2.14 (2 H, *m*, SCH_2CH_2), 2.78-2.84 (4 H, *m*, SCH_2 x 2), 3.32 (1 H, *m*), 3.40 (1 H, *m*), 5.32 (1 H, *dd*, J = 10.2, 5.7 Hz, H-3′), 5.50 (1 H, *m*), 5.88 (1 H, *d*, J = 9.6 Hz, H-1′); another isomer: 1.61 (3 H, *d*, J = 6.6 Hz, Me), 5.79 (1 H, *d*, J = 9.6 Hz, H-1′); MS m/z (rel. int.) 244 (3, M^+), 227 (1), 185 (100, $[M-C_3H_7O]^+$), 171 (1), 139 (6), 111 (21), 105 (8), 77 (16); Anal. Calcd for $C_{12}H_{20}OS_2$: C, 58.97; H, 8.25. Found: C, 58.93; H, 8.19.

2-(1-Hydroxy-2-propen-1-yl)-2-(1,3-pentadienyl)-1,3-dithiane (11α)

Oil; TLC (10% EtOAc in hexane) R_f 0.22; IR (neat) 3457, 2906, 1645, 1419, 1370, 1243 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 1.74 (3 H, *dd*, J = 6.7, 0.9 Hz, Me), 1.90-2.00 (2 H, *m*, SCH_2CH_2), 2.67-3.02 (4 H, *m*, SCH_2 x 2), 4.06 (1 H, *dd*, J = 12.7, 6.4 Hz, H-1″), 4.31 (1 H, *br d*, J = 6.4 Hz, OH), 5.23 (1 H, *dd*, J = 10.4, 1.5 Hz, H-3″), 5.40 (1 H, *dd*, J = 15.2, 1.5 Hz, H-3″), 5.58 (1 H, *d*, J = 15.3 Hz, H-1′), 5.72-6.15 (3 H, *m*, H-2″, 3′, 4′), 6.57 (1 H, *dd*, J = 15.3, 10.4 Hz, H-2′); MS m/z (rel. int.) 242 (1, M^+), 225 (1), 195 (2), 185 (100), 167 (2), 111 (21), 105 (8), 77 (17).

2-[2-(1-Hydroxy-2-propenyl-3-pentenyliden-1-yl]-1,3-dithiane (11γ)

Oil; TLC (10% EtOAc in hexane) R_f 0.18; IR (neat) 3431, 2910, 1580, 1419, 1274, 967 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, two isomers 55:45) δ 1.66 (3 H, *d*, J = 6.1 Hz, Me), 2.10-2.17 (2 H, *m*, SCH_2CH_2), 2.82-2.94 (4 H, *m*, SCH_2 x 2), 3.43 (1 H, *dd*, J = 9.8, 6.0 Hz, H-2′)/3.40 (minor), 4.04 (1 H, *dd*, J = 9.5, 6.3 Hz, H-1″)/3.98 (minor), 5.15 (1 H, *br s*, H-3″), 5.23 (1 H, *br s*, H-3″), 5.28 (1 H, *dd*, J = 15.4, 8.1 Hz, H-3′), 5.44-5.64 (1 H, *m*), 5.78-5.88 (1 H, *m*), 5.85 (1 H, *d*, J = 6.0 Hz, H-1′); MS m/z (rel. int.) 242 (3, M^+), 225 (4, $[M+1-18]^+$), 185 (100), 151 (3), 119 (11), 111 (19), 105 (9), 77 (15).

2-(1-Hydroxy-2-butenyl)-2-(1,3-pentadienyl)-1,3-dithiane (12α)

Oil; TLC (10% EtOAc in hexane) R_f 0.27; IR (neat) 3431, 2909, 1668, 1419, 1081 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.68 (3 H, *d*, J = 6.8 Hz, Me), 1.77 (3 H, *d*, J = 6.9 Hz, Me), 1.80-2.01 (2 H, *m*, SCH_2CH_2), 2.70-2.96 (4 H, *m*, SCH_2 x 2), 4.02 (1 H, *dd*, J = 12.7, 6.4 Hz, H-1″), 4.27 (1 H, *d*, J = 6.4 Hz, OH), 5.42-5.88 (4 H, *m*, H-1′, 4′, 2″, 3″), 6.17 (1 H, *dd*, J = 15.2, 10.4 Hz, H-3′), 6.56 (1 H, *dd*, J = 15.3, 10.4 Hz, H-2′); ^{13}C NMR δ 22.4 (CH_2), 26.6 (CH_3), 27.5 (CH_3), 36.8 (CH_2), 60.2 (C), 72.6 (CH), 126.1 (CH), 127.4 (CH), 129.2 (CH), 130.5 (CH), 134.4 (CH), 135.6 (CH); MS m/z (rel. int.) 272 (1, M^+), 256 (5), 239 (3), 185 (100), 174 (3), 119 (7), 111 (19), 105 (8), 71 (13); Anal. Calcd for $C_{13}H_{20}OS_2$: C, 60.89; H, 7.86. Found: C, 61.20; H, 7.64.

2-[2-(1-Hydroxy-2-propen-1-yl)-3-pentenyliden-1-yl]-1,3-dithiane (12γ)

Oil; TLC (10% EtOAc in hexane) R_f 0.21; IR (neat) 3393, 2909, 1672, 1442, 1232, 952 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz, two isomers 80:20) δ 1.65 (3 H, *d*, J = 6.3 Hz, Me), 1.67 (3 H, *d*, J = 6.4 Hz, Me), 2.08-2.18 (2 H, *m*, SCH_2CH_2), 2.80-2.91 (4 H, *m*, SCH_2 x 2), 3.37 (1 H, *ddd*, J = 9.0, 6.4, 1.6 Hz, H-2′), 3.94 (1 H, *dd*, J = 8.4, 6.4 Hz, H-1″)/3.88 (*t*, J = 6.5 Hz, minor), 5.29 (1 H, *dd*, J = 15.3, 7.0 Hz), 5.38-5.69 (3 H, *m*), 5.82 (1 H, *d*, J = 9.5 Hz, H-1′)/5.78 (*d*, J = 9.2 Hz, minor); MS m/z (rel. int.) 272 (1, M^+), 256 (1), 239 (1), 185 (100), 143 (3), 119 (12), 111 (21), 106 (15), 77 (20); Anal. Calcd for $C_{14}H_{24}OS_2$: C, 60.89; H, 7.86. Found: C, 60.89; H, 7.72.

2-(1-Hydroxy-1-phenylmethyl)-2-(1,3-pentadienyl)-1,3-dithiane (13α)

Oil; TLC (10% EtOAc in hexane) R_f 0.30; IR (neat) 3434, 3058, 2927, 1599, 1448, 1043 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz) δ 1.78 (3 H, *dd*, J = 6.7, 1.3 Hz, Me), 1.78-2.12 (2 H, *m*, SCH_2CH_2), 2.54-2.85 (4 H, *m*, SCH_2 x 2), 3.28 (1 H, *br s*, OH), 4.82 (1 H, *d*, J = 3.4 Hz, $PhCH_2$), 5.47 (1 H, *d*, J = 15.6 Hz, H-1′), 5.80 (1 H, *dq*, J = 15.5, 6.6 Hz, H-4′), 6.10 (1 H, *dd*, J = 15.5, 10.4 Hz, H-3′), 6.36 (1 H, *dd*, J = 15.6, 10.4 Hz, H-2′), 7.14-7.36 (5 H, *m*, PhH); MS m/z (rel. int.) 293 (3, $[M+1]^+$), 275 (14, $[M+1-18]^+$), 185 (100, $[M-C_7H_9O]^+$), 164 (7), 147 (29), 107 (69), 91 (9), 79 (51); Anal. Calcd for $C_{16}H_{20}OS_2$: C, 65.71; H, 6.89. Found: C, 65.54; H, 6.55.

2-(1-Hydroxy-1-methylethyl)-2-(1,3-pentadienyl)-1,3-dithiane (14α)

Oil; TLC (5% EtOAc in hexane) R_f 0.16; IR (neat) 3467, 2923, 1644, 1365, 1173, 998 cm^{-1}; ^1H NMR ($CDCl_3$, 90 MHz) δ 1.33 (6 H, *s*, Me x 2), 1.80 (3 H, *d*, J = 6.6 Hz, Me), 1.82-2.02 (2 H, *m*, SCH_2CH_2), 2.44 (1 H, *s*, OH), 2.60-3.02 (4 H, *m*, SCH_2 x 2), 5.50 (1 H, *d*, J = 15.3 Hz, H-1′), 5.66 (1 H, *dd*, J = 15.5, 6.6 Hz, H-4′), 6.02 (1 H, *dd*, J = 15.5, 10.4 Hz, H-3′), 6.40 (1 H, *dd*, J = 15.3, 10.4 Hz, H-2′); MS m/z (rel. int.) 244 (4, M^+), 227 (7), 186 (100, $[M-C_3H_7O]^+$), 171 (6), 139 (32), 111 (55), 97 (28), 77 (31), 59 (54); Anal. Calcd for $C_{12}H_{20}OS_2$: C, 58.97; H, 8.25. Found: C, 58.56; H, 8.34.

2-(1-Hydroxy-1-ethylpropyl)-2-(1,3-pentadienyl)-1,3-dithiane (15α)

Oil; TLC (5% EtOAc in hexane) R_f 0.22; IR (neat) 3510, 2935, 1673, 1456, 1275 cm^{-1}; ^1H NMR ($CDCl_3$, 90 MHz) δ 0.92 (6 H, *t*, J = 6.6 Hz, Me), 1.36 (4 H, *q*, J = 6.3 Hz, CH_2 x 2), 1.66-1.98 (2 H, *m*, SCH_2CH_2), 1.78 (3 H, *d*, J = 6.9 Hz, Me), 2.24 (1 H, *s*, OH), 2.50-3.05 (4 H, *m*, SCH_2 x 2), 5.67 (1 H, *d*, J = 15.3 Hz, H-1′), 5.87 (1 H, *dq*, J = 15.3,

6.9 Hz, H-4'), 6.18 (1 H, *dd*, J = 15.3, 10.4 Hz, H-3'), 6.50 (1 H, *dd*, J = 15.3, 10.4 Hz, H-2'); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 17.7 (CH_3), 24.7 (CH_2), 26.5 (CH_3), 27.2 (CH_2), 30.5 (CH_2), 37.4 (CH_2), 51.8 (C), 68.4 (C), 129.8 (CH), 130.1 (CH), 130.7 (CH), 135.4 (CH); MS m/z (rel. int.) 273 (3, $[M+1]^+$), 255 (9, $[M+1-18]^+$), 243 (3), 186 (100), 139 (38), 132 (17), 111 (41), 97 (25), 87 (76); HRMS Calcd for $C_{14}H_{24}OS_2$ (M^+) 272.1269, Found 272.1273.

2-(1-Hydroxycyclopentyl)-2-(1,3-pentadienyl)-1,3-dithiane (16α)

Oil; TLC (5% EtOAc in hexane) R_f 0.15; IR (neat) 3463, 2953, 1644, 1430, 1276, 1195 cm^{-1}; ^{1}H NMR ($CDCl_3$, 90 MHz) δ 1.10-2.20 (13 H, *m*), 2.33 (1 H, *s*, OH), 2.47-3.30 (4 H, *m*, SCH_2 x 2), 5.51 (1 H, *d*, J = 15.3, H-1'), 5.67 (1 H, *dq*, J = 15.5, 6.6 Hz, H-4'), 6.02 (1 H, *dd*, J = 15.5, 10.4 Hz, H-3'), 6.41 (1 H, *dd*, J = 15.3, 10.4 Hz, H-2'); MS m/z (rel. int.) 270 (2, M^+), 253 (5), 195 (2), 186 (69, $[M-C_5H_9O]^+$), 163 (5), 139 (30), 132 (16), 113 (37), 85 (100), 67 (55); Anal. Calcd for $C_{14}H_{22}OS_2$: C, 62.18; H, 8.20. Found: C, 61.97; H, 8.58.

2-(3-Oxocyclopentyl)-2-(1,3-pentadienyl)-1,3-dithiane (17α)

Oil; TLC (10 % EtOAc in hexane) R_f 0.24; IR (neat) 2907, 1736, 1685, 1440, 1224, 1159 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.76 (3 H, *dd*, J = 6.6, 1.1 Hz, Me), 1.79-1.89 (2 H, *m*), 1.98-2.03 (2 H, *m*), 2.09-2.31 (2 H, *m*), 2.24-2.31 (3 H, *m*), 2.57-2.85 (2 H, *m*, SCH_2), 2.82-2.92 (2 H, *m*, SCH_2), 5.53 (1 H, *d*, J = 15.2 Hz, H-1'), 5.77 (1 H, *dq*, J = 15.1, 6.7 Hz, H-4'), 6.14 (1 H, *dd*, J = 15.1, 10.9 Hz, H-3'), 6.78 (1 H, J = 15.2, 10.9 Hz, H-2'); MS m/z (rel. int.) 268 (18, M^+), 213 (2), 201 (29), 193 (48), 185 (100), 179 (73), 159 (41), 111 (36), 106 (94), 84 (73), 77 (77), 55 (85).

2-[2-(3-Oxocyclopentyl)-3-penten-1-yliden-1-yl]-1,3-dithiane (17γ)

Major isomer: Oil; HPLC (10% EtOAc in hexane) R_t 15.0 min; IR (neat) 3026, 2929, 1735, 1419, 1232, 1156 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.68 (3 H, *dd*, J = 6.3, 1.4 Hz, Me), 1.89-2.37 (9 H, *m*), 2.83-2.92 (4 H, *m*, SCH_2 x 2), 3.23 (1 H, *m*, H-2'), 5.26 (1 H, *ddd*, J = 15.3, 7.6, 1.4 Hz, H-3'), 5.46 (1 H, *dq*, J = 15.3, 6.3 Hz), 5.82 (1 H, *d*, J = 9.8 Hz, H-1'); MS m/z (rel. int.) 268 (16, M^+), 193 (1), 185 (100), 143 (3), 119 (8), 111 (15), 105 (19), 77 (12). Minor isomer: Oil; HPLC (10% EtOAc in hexane) R_t 16.6 min; IR (neat) 3052, 2929, 1735, 1425, 1220, 1156 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.68 (3 H, *dd*, J = 6.3, 1.3 Hz, Me), 1.89-2.36 (9 H, *m*), 2.83-2.90 (4 H, *m*, SCH_2 x 2), 3.25 (1 H, *m*, H-2), 5.27 (1 H, *ddd*, J = 15.5, 7.7, 1.3 Hz, H-3'), 5.52 (1 H, *dq*, J = 15.5, 6.3 Hz), 5.81 (1 H, *d*, J = 9.8 Hz, H-1'); MS m/z (rel. int.) 268 (15, M^+), 193 (1), 185 (100), 143 (5), 119 (14), 111 (19), 105 (26), 77 (27).

5-Methyl-3a,4,5,7a-tetrahydroindan-1-spiro-2'-(1',3'-dithiane) (18)

The triene **6α** (112 mg, 0.46 mmol) was dissolved in toluene (20 mL), placed in a sealed tube, and heated to 190 °C for 72 h. The mixture was cooled, toluene was removed in vacuo, and the residue was purified on a SiO_2 column by elution with EtOAc/hexane (2:98) to give the bicyclic compound **18** (77.3 mg, 70%), which consisted of two isomers (66:34). Liquid; TLC (2% EtOAc in hexane) R_f 0.25; IR (neat) 3014, 2948, 1636, 1418, 1271 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) major isomer: δ 0.94 (3 H, *d*, J = 7.1 Hz, Me), 1.34 (1 H, *m*), 1.56-1.67 (2 H, *m*), 1.81-1.87 (1 H, *m*), 1.98-2.15 (4 H, *m*), 2.35-2.38 (2 H, *m*), 2.64-2.93 (3 H, *m*), 3.06 (1 H, *m*), 3.07-3.11 (1 H, *m*), 5.71 (1 H, *br d*, J = 10.7 Hz, H-7), 5.78 (1 H, *dq*, J = 10.7, 2.8 Hz, H-6); minor isomer: δ 1.00 (3 H, *d*, J = 7.2 Hz, Me), 5.60 (1 H, *dq*, J = 9.9, 3.2 Hz, H-7), 5.88 (1 H, *br d*, J = 9.9 Hz, H-6); ^{13}C NMR ($CDCl_3$, 50 MHz, two isomers) δ 25.5, 26.0, 26.4, 27.4, 28.7, 28.8, 28.9, 30.0, 30.4, 30.5, 34.7, 35.4, 36.8, 38.1, 41.6 (CH_2), 43.7 (CH_2), 50.6 (CH_2), 56.0 (C), 62.5 (C), 123.4 (CH), 124.5 (CH), 135.0 (CH); 136.7 (CH); MS m/z (rel. int.) 240 (10, M^+), 193 (12), 165 (5), 145 (100), 132 (92), 117 (53), 106 (60, $C_3H_6S_2$), 77 (31); HRMS Calcd for $C_{13}H_{20}S_2$ (M^+) 240.1006, Found 240.1010.

6-Methyl-1,2,3,4,4a,5,6,8a-octahydronaphthalene-1-spiro-2'-(1',3'-dithiane) (19)

A thermal reaction of **7a** (100 mg, 0.39 mmol) in toluene (20 mL) was carried out, by a similar procedure described above, afforded the product **19** (64.4 mg, 65%), which consisted of two isomers (68:32); oil, TLC (2% EtOAc in hexane) R_f 0.21; IR (neat) 3016, 2925, 1636, 1441, 1273 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) major isomer, δ 1.06 (3 H, *d*, J = 7.2 Hz, Me), 1.37-2.34 (11 H, *m*), 2.41-2.73 (1 H, *m*), 2.70-2.83 (2 H, *m*), 2.85-3.02 (2 H, *m*), 3.07-3.27 (1 H, *m*), 5.69-5.81 (2 H, *m*); minor isomer, δ 1.03 (3 H, *d*, J = 7.2 Hz, Me), 5.84-6.14 (2 H, *m*); ^{13}C NMR ($CDCl_3$, 50 MHz, two isomers) δ 19.5, 21.4, 21.5, 22.8, 25.2, 25.4, 25.8, 25.9, 26.3, 28.6, 29.1, 30.2, 30.5, 30.7, 32.9, 33.2, 35.6, 36.4, 37.1, 44.7 (CH_2)/51.6 (CH_2), 54.4 (C)/55.0 (C), 125.4 (CH)/125.9 (CH), 134.0 (CH)/135.6 (CH); MS m/z (rel. int.) 254 (88, M^+), 221 (2), 179 (30), 145 (71), 131 (62), 118 (42), 105 (100), 91 (68), 77 (49); HRMS Calcd for $C_{14}H_{22}S_2$ (M^+) 254.1163, Found 254.1155.

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Dithianes; Allylic anions; Regiochemistry; Hard and soft acids and bases principle.

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