

ELECTROPHILIC REACTIONS OF DITHIO-SUBSTITUTED *o*-METHOXYCINNAMYLLITHIUM

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The dithio-substituted *o*-methoxycinnamylithium **3L** reacted at the α -site with D_2O and most of carbonyl compounds in extents of 70–100 %, while it reacted with halides at either the α - or γ -site, depending on the nature of respective halide.

INTRODUCTION

Use of allylic anions in organic synthesis has attracted chemists' attention.¹ The allylic anion having heteroatom substituents is even more versatile for further elaboration to products containing various functional groups.² If an unsymmetric allylic anion can react with electrophiles in a regioselective manner, its practical utility is obvious. Following these guidelines, we have studied the electrophilic reactions of dithio-substituted crotyllithium **1L**³ and cinnamylithium **2L**⁴. Theoretically, these bidentate anions may exist as η_1 and/or η_3 forms to react at the α - and/or γ -sites with an electrophile (Scheme 1).⁵ It is observed that crotyllithium **1L** reacts at the

α -site with halides, but reacts at the γ -site with aldehydes. The regioselectivity in reactions of **1L** and ketones is dependent on the nature of respective ketone, i.e. occurring at the α -site with modest size ketones but at the γ -site with bulky and unsaturated ketones.³ The α -substitution products are successfully transformed into α,β -unsaturated ketones, and the γ -substitution products are converted to derivatives of carboxylic acid (Scheme 2).⁶ On the other hand, cinnamylithium **2L** preferred to react at the α -site only with halides of great hardness,⁷ but it does not exhibit any significant regioselectivity in reactions with carbonyl compounds.⁴ The effect of γ -substituent on the regiochemistry of bidentate anions **1L** and **2L** was apparent, we further tested a related

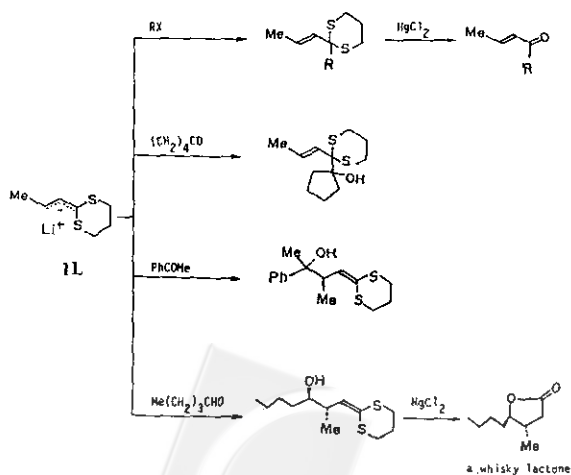
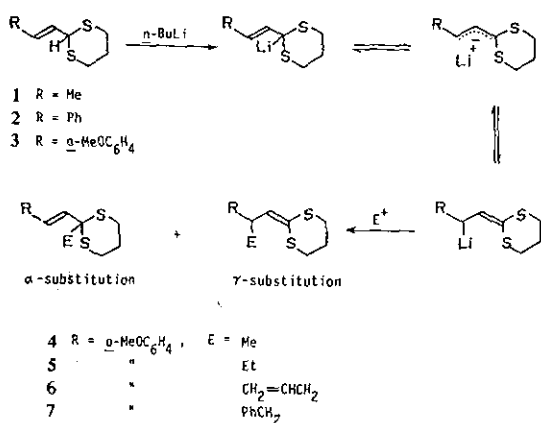


Table 1 Electrophilic reactions of *o*-methoxycinnamyl lithium 3L.

Entry	Electrophile	Products, α : γ	Total Yield (%)
1	D ₂ O	100 : 0	90
2	MeI	55 : 45	85
3	EtI	42 : 58	82
4	CH ₂ =CHCH ₂ Br	42 : 58	88
5	PhCH ₂ Br	0 : 100	90
6	MeCH ₂ CHO	72 : 28 (50/50) ^a	90
7	Me(CH ₂) ₂ CHO	75 : 25 (50/50)	88
8	Me ₂ CHCHO	71 : 29 (50/50)	91
9	MeCH=CHCHO	75 : 25 (62/38)	89
10	PhCHO	72 : 28 (78/22) ^b	85
11	(CH ₂) ₄ CO	90 : 10	85
12	(CH ₂) ₅ CO	88 : 12	76
13	Me ₂ CO	100 : 0	90
14	MeCH ₂ COMe	97 : 3 (55/45)	92
15	Me(CH ₂) ₄ COMe	100 : 0	90
16	Ph ₂ CO	75 : 25	80
17	(MeCH ₂) ₂ CO	0 : 100	37 ^c
18	(Me ₂ CH) ₂ CO		d
19	PhCOMe	37 : 63 (55/45)	87
20	MeCOCO ₂ Et	50 : 50 (55/45)	82

(a) The numbers in parentheses represent the ratio of diastereomers of the γ -addition products. (b) The ratio was inferred from that of spirodithiane derivatives 23. (c) A 58% of the starting material 3 was recovered. (d) No addition reaction occurred. The anion 3L underwent oxidative dimerization to give a 70% yield of 22.

anion generated from dithiane 3 to see their correlations.

RESULTS AND DISCUSSION

A THF solution of *o*-methoxycinnamyl lithium 3L was treated with a variety of electrophiles at -78°C . The results are listed in Table 1. The anion 3L reacted exclusively at the α -site with D₂O, while

at the γ -site with benzyl bromide. When 3L reacted with iodomethane, iodoethane or allyl bromide, no significant regioselection resulted. The regiochemical outcome was qualitatively in agreement with the reactions of cinnamyl lithium 2L.⁷ The percentage of α -alkylation was inclined to increase as the hardness of respective halide increases.

The reactions of 3L and carbonyl compounds usually completed in 20 min at -78°C to give high yields of addition products. The α -selectivity was in the range of 72% when an aldehyde was used as the electrophile. Anion 3L had the highest tendency to react at the α -site with aldehydes by comparison with 1L and 2L, which gave respectively < 5% and < 56% of α -additions. The reactions of 3L with cyclopentanone, cyclohexanone, acetone, 2-butanone, 2-heptanone, and benzophenone followed the α -selection (75–100%). However, the reactions with acetophenone and ethyl pyruvate did not take place in this fashion. The addition of 3L to 3-pentanone was rather sluggish. No addition reaction to diisopropyl ketone ever occurred, instead a dimer 22 was obtained from the oxidative α , γ -coupling of 3L.⁷

The γ -addition reactions of 3L with aldehydes and unsymmetric ketones usually resulted in nearly equal amounts of two diastereomers, except for the reactions with crotonaldehyde and benzaldehyde (entries 9 and 10). In most of cases, two diastereomers of γ -addition products were inseparable, but their ratio was determined from the ¹H NMR spectrum. However, the stereochemistry could not be unambiguously assigned at this stage. A mixture of α -12 and γ -12 resulted from the reaction of 3L with benzaldehyde was gradually converted to α -12 and spirodithianes 23 (trans/cis = 72 : 28). Owing to the shielding effects of the phenyl and methoxyphenyl groups, the β - and γ -protons of trans-23 appeared at relatively higher fields (δ 3.92 and 5.29) than corresponding protons of the cis isomer, occurring at δ 4.56 and 5.65.⁴ The trans spirodithiane was conceivably be obtained from the acid catalyzed

cyclization of γ -12 anti addition product, and the cis spirodithiane should be derived from γ -12 syn isomer.³

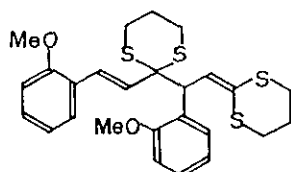
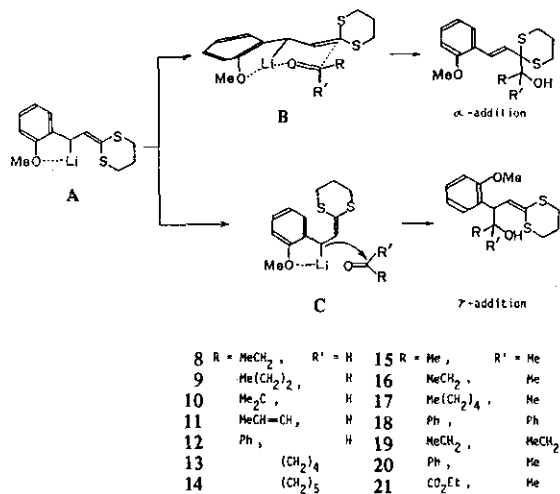
The α -carbon of 3L having three substituents is considered a relatively hindered site. Thus, the preference of α -site over γ -site in reactions with carbonyl compounds should not be attributed to the steric effect.³ The methoxy group may paly two kinds of electronic effect: As an electron-donating group, it would disfavor the accumulation of negative charge on the γ -site, whereas it might stabilize the γ -anion as well by coordination with Li^+ as shown in the chelate form A. This type of chelation with the neighboring amino or methoxy group is well known in literature.⁸ Although the real reaction mechanism is unclear, the observed regiochemistry can be interpreted by postulation of a cyclic transition state B to give the α -addition product (Scheme 3).⁹ The γ -addition products were presumably formed whenever access to the α -site became less effective owing to bulkiness of respective ketone.¹⁰

In summary, the γ -substitution in dithio-substituted allylic anions (1L–3L) displayed remarkable influence on their regiochemistry. The anion 3L showed highest percentages of α -addition than 1L and 2L. The observed regiochemistry is neither consistent with the steric effect of γ -substituents nor parallel to the electron-donating properties of methyl-, *o*-methoxyphenyl-, and phenyl-groups. We propose that the coordination property of *o*-methoxy group functions as the major factor to enhance the α -selectivity while the electron-donating effect appears to be insignificant. However, this rationale is only suggestive rather than conclusive.

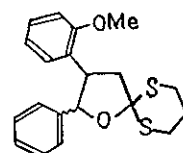
EXPERIMENTAL

Melting points were measured on a Yanaco micro melting point apparatus, and are uncorrected. Elemental analyses were carried out on a Perkin-Elmer 240c elemental analyzer. Infrared spectra

Scheme 3



22



23

were run on a Perkin-Elmer 985 infrared spectrophotometer. The nuclear magnetic resonance spectra were recorded on a Varian EM-390 (90 MHz) spectrometer. Mass spectra were recorded on a Finnigan TSQ 46c spectrometer operating at an ionizing voltage of 70 eV. Merck silica gel 60 F sheets were used for analytic thin-layer chromatography. Flash chromatography was performed as described by Still.¹¹

Preparation of 2-[2-(*o*-Methoxyphenyl)ethenyl]-1,3-dithiane (3). A CHCl_3 solution (10 mL) of *o*-methoxycinnamaldehyde (8.1 g, 50 mmol) was added dropwise to a mixture of 1,3-propanedithiol (5 mL, 50 mmol), 0.6 g of anhydrous $\text{Mg}(\text{ClO}_4)_2$, and a drop of conc. H_2SO_4 in CHCl_3 (100 mL) at 0°C . The mixture was stirred for 1 h, and 100 mL of 10% KOH was added. After 10 min, the organic phase

was separated, washed twice with water, dried over Na_2SO_4 and concentrated to give 11.6 g (92%) of 3 as colorless solids. mp $76\text{--}77^\circ\text{C}$ (from Et_2O); R_f 0.33 (5% EtOAc in hexane); $^1\text{H NMR}$ (CDCl_3) δ 1.86–2.20 (2 H, *m*), 2.87–2.98 (4 H, *m*), 3.83 (3 H, *s*), 4.84 (1 H, *d*, $J = 7.5$ Hz), 6.23 (1 H, *dd*, $J = 16.5$, 7.5 Hz), 6.77–6.97 (2 H, *m*), 7.01 (1 H, *d*, $J = 16.5$ Hz), 7.14–7.44 (2 H, *m*); MS m/z (rel. intensity) 252 (100, M^+), 219 (6), 205 (1), 177 (19), 173 (2), 168 (18), 147 (41), 131 (3), 115 (2), 106 (4), 91 (3). Anal. Calcd for $\text{C}_{13}\text{H}_{16}\text{OS}_2$: C, 61.80; H, 6.39. Found: C, 61.60; H, 6.40.

General Procedure for Electrophilic Reactions of 3.

Under an atmosphere of N_2 , a solution of *n*-BuLi (0.8 mL, 1.6 M in hexane) was added dropwise to a THF solution (5 mL) of 3 (252 mg, 1 mmol) at -78°C . The dark red solution was stirred for 10 min, and an appropriate electrophile (1.3 mmol) was added. After a suitable period (20 min for carbonyl compounds and 1 h for halides), the reaction completed as monitored by the TLC analysis. The resulting yellow mixture was quenched with aqueous NH_4Cl and concentrated. The residue was partitioned between CHCl_3 and water. The aqueous layer was separated and extracted twice with CHCl_3 . The combined organic phase was dried over Na_2SO_4 , concentrated and chromatographed to give the desired products (Table 1).

Reaction with Deuterium Oxide. 3-*d*: IR (neat) 3039, 2931, 1594, 1483, 1243, 1026, 752 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) δ 1.73–2.25 (2 H, *m*), 2.80–2.96 (4 H, *m*), 3.81 (3 H, *s*), 6.23 (1 H, *d*, $J = 16.5$ Hz), 6.73–7.05 (2 H, *m*), 7.07 (1 H, *d*, $J = 16.5$ Hz), 7.10–7.45 (2 H, *m*); MS m/z (rel. intensity) 253 (100, M^+), 220 (10), 206 (3), 192 (8), 178 (39), 164 (49), 148 (85), 132 (4), 116 (3), 106 (6), 91 (3).

Reaction with Methyl Iodide. α -4: white solid, mp $94\text{--}95^\circ\text{C}$; R_f 0.36 (5% EtOAc in hexane); IR (KBr) 3001, 2909, 1593, 1484, 1243, 758 cm^{-1} ; $^1\text{H NMR}$

(CDCl_3) δ 1.70 (3 H, *s*), 1.80 (2 H, *m*), 2.59–3.17 (4 H, *m*), 3.88 (3 H, *s*), 6.32 (1 H, *d*, $J = 15.5$ Hz), 7.13 (1 H, *d*, $J = 15.5$ Hz), 7.12–7.58 (4 H, *m*); MS m/z (rel. intensity) 266 (100, M^+), 251 (7), 233 (12), 192 (20), 177 (22), 161 (74), 145 (7), 115 (13), 91 (6). Anal. Calcd for $\text{C}_{14}\text{H}_{18}\text{OS}_2$: C, 63.12; H, 6.81. Found: C, 62.86; H, 6.81. γ -4: oil; R_f 0.40 (5% EtOAc in hexane); IR (neat) 2929, 1596, 1488, 1241, 1029, 753 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) δ 1.27 (3 H, *d*, $J = 6.0$ Hz), 1.97–2.22 (2 H, *m*), 2.73–2.94 (4 H, *m*), 3.80 (3 H, *s*), 4.28 (1 H, *dq*, $J = 9.5$, 6.0 Hz), 6.15 (1 H, *d*, $J = 9.5$ Hz), 6.75–7.00 (2 H, *m*), 7.01–7.24 (2 H, *m*); MS m/z (rel. intensity) 266 (37, M^+), 251 (55), 177 (23), 145 (10), 135 (100), 121 (20), 105 (22), 91 (19). Anal. Calcd for $\text{C}_{14}\text{H}_{18}\text{OS}_2$: C, 63.12; H, 6.81. Found: C, 62.56; H, 6.78.

Reaction with Ethyl Iodide. α -5: oil; R_f 0.22 (4% EtOAc in hexane); IR (neat) 2910, 1593, 1483, 1242, 1025, 759 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) δ 1.01 (3 H, *t*, $J = 6.0$ Hz), 1.75–2.12 (4 H, *m*), 2.45–3.10 (4 H, *m*), 3.84 (3 H, *s*), 6.13 (1 H, *d*, $J = 15.0$ Hz), 6.70–7.24 (4 H, *m*), 7.37–7.50 (1 H, *br. d*, $J = 8$ Hz); MS m/z (rel. intensity) 280 (100, M^+), 251 (46), 205 (20), 191 (24), 175 (96), 145 (9), 131 (6), 115 (8), 91 (9). γ -5: oil; R_f 0.25 (4% EtOAc in hexane); IR (neat) 2925, 1594, 1458, 1274, 1050, 756 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) δ 0.88 (3 H, *t*, $J = 6.0$ Hz), 1.56–1.96 (4 H, *m*), 2.00–2.29 (2 H, *m*), 2.80–2.94 (4 H, *m*), 3.83 (3 H, *s*), 4.13 (1 H, *m*), 6.19 (1 H, *d*, $J = 9.0$ Hz), 6.79–6.97 (2 H, *m*), 7.05–7.26 (2 H, *m*); MS m/z (rel. intensity) 280 (52, M^+), 251 (100), 205 (18), 190 (37), 175 (47), 145 (16), 131 (8), 115 (10).

Reaction with Allyl Bromide. α -6: oil; R_f 0.30 (2.5% EtOAc in hexane); IR (neat) 3070, 2902, 1594, 1483, 1243, 1027, 751 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) 1.80–2.04 (2 H, *m*), 2.51–3.18 (6 H, *m*), 3.81 (3 H, *s*), 5.00–5.22 (2 H, *m*), 5.65–6.03 (1 H, *m*), 6.20 (1 H, *d*, $J = 16.5$ Hz), 6.80–6.97 (2 H, *m*), 7.12 (1 H,

d, $J = 16.5$ Hz), 7.13–7.50 (2 H, *m*); MS m/z (rel. intensity) 292 (27, M^+), 264 (1), 251 (100), 217 (18), 203 (5), 187 (15), 171 (5), 145 (5), 121 (2). γ -6: oil; R_f 0.27 (2.5% EtOAc in hexane); IR (neat) 3068, 2907, 1594, 1487, 1241, 753 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) δ 1.95–2.20 (2 H, *m*), 2.43 (2 H, *dd*, $J = 6.3, 6.3$ Hz), 2.71–2.86 (4 H, *m*), 3.80 (3 H, *s*), 4.27 (1 H, *dt*, $J = 9.6, 6.3$ Hz, ArCH), 4.86–5.17 (2 H, *m*), 5.49–5.95 (1 H, *m*), 6.16 (1 H, *d*, $J = 9.6$ Hz), 6.76–6.90 (2 H, *m*), 7.04–7.20 (2 H, *m*); MS m/z (rel. intensity) 292 (3, M^+), 267 (1), 251 (100), 185 (2), 176 (9), 161 (10), 145 (8), 131 (2), 118 (2), 105 (1).

Reaction with Benzyl Bromide. γ -7: oil; R_f 0.45 (10% EtOAc in hexane); IR (neat) 3022, 2909, 1596, 1488, 1241, 1028, 752 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) δ 1.79–2.02 (2 H, *m*), 2.38–2.78 (4 H, *m*), 2.86–3.18 (2 H, *m*), 3.70 (3 H, *s*), 4.50 (1 H, *m*), 6.21 (1 H, *d*, $J = 9.3$ Hz), 6.67–6.84 (2 H, *m*), 6.99–7.16 (7 H, *m*); MS m/z (rel. intensity) 343 (20, $M^+ + 1$), 267 (5), 251 (100, $M^+ - \text{PhCH}_2$), 211 (4), 177 (11), 145 (8), 91 (12), 71 (3). Anal. Calcd for $\text{C}_{20}\text{H}_{22}\text{O}_2\text{S}_2$: C, 70.13; H, 6.47. Found: C, 70.54; H, 6.25.

Reaction with Propanal. α -8: oil; R_f 0.30 (15% EtOAc in hexane); IR (neat) 3469, 2931, 1594, 1483, 1243, 1027, 752 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) δ 1.03 (3H, *t*, $J = 7.2$ Hz), 1.36–1.78 (2 H, *m*), 1.79–2.16 (2 H, *m*), 2.50 (1 H, *br d*, $J = 3.0$ Hz, OH), 2.67–2.94 (4 H, *m*), 3.60–3.74 (1 H, *m*), 3.85 (3 H, *s*), 6.26 (1 H, *d*, $J = 15.6$ Hz), 7.34 (1 H, *d*, $J = 15.6$ Hz), 6.80–7.50 (4 H, *m*); MS m/z (rel. intensity) 311 (10, $M^+ + 1$), 293 (6), 251 (100), 203 (15), 177 (13), 145 (10), 106 (2), 91 (2), 59 (2). Anal. Calcd for $\text{C}_{16}\text{H}_{22}\text{O}_2\text{S}_2$: C, 61.90; H, 7.14. Found: C, 61.65; H, 6.85. γ -8 (two isomers, 50/50): R_f 0.26 (15% EtOAc in hexane); IR (neat) 3461, 2929, 1594, 1486, 1241, 1026, 754 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) δ 0.83–1.03 (CH_3), 1.16–1.57 (CH_2), 1.73 (*br s* OH), 1.90–2.22 (CH_2), 2.73–2.86 (2 x SCH_2), 3.70–3.95 (CH), 3.82 (*s*, OCH_3), 4.25 (0.5

H, *dd*, $J = 10, 4$ Hz)/4.31 (0.5 H, *dd*, $J = 9, 1.5$ Hz, CH), 6.25 (0.5 H, *d*, $J = 10.5$ Hz)/6.38 (0.5 H, *d*, $J = 10.5$ Hz, CH=), 6.80–7.24 (PhH); MS m/z (rel. intensity) 311 (13, $M^+ + 1$), 251 (100).

Reaction with *n*-Butanal. α -9: oil; R_f 0.30 (10% EtOAc in hexane); IR (neat) 3462, 2954, 1594, 1484, 1243, 751 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) δ 0.94 (3 H, *t*, $J = 6.0$ Hz), 1.27–2.10 (6 H, *m*), 2.50 (1 H, *br s*, OH), 2.65–2.96 (4 H, *m*), 3.72–3.84 (1 H, *m*), 3.82 (3 H, *s*), 6.25 (1 H, *d*, $J = 16.5$ Hz), 6.79–6.98 (2 H, *m*), 7.16–7.49 (3 H, *m*); MS m/z (rel. intensity) 325 (1, $M^+ + 1$), 307 (2), 251 (100), 217 (5), 177 (18), 145 (11), 91 (6), 71 (9), 55 (8). Anal. Calcd for $\text{C}_{17}\text{H}_{24}\text{O}_2\text{S}_2$: C, 62.92; H, 7.45. Found: C, 62.88; H, 7.34. γ -9 (two isomers, 50/50): oil; R_f 0.20 (10% EtOAc in hexane); IR (neat) 3455, 2954, 1594, 1486, 1241, 1027, 753 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) δ 0.95 (CH_3), 1.25–2.40 (CH_2), 2.71–2.90 (2 x SCH_2), 3.75 (*m*, CH), 3.81 (*s*, OCH_3), 4.25 (0.5 H, *dd*, $J = 10, 3$ Hz)/4.31 (0.5 H, *br d*, $J = 9$ Hz), 6.26 (0.5 H, *d*, $J = 10.5$ Hz)/6.39 (0.5 H, *d*, $J = 10.5$ Hz), 6.78–6.96 (PhH), 7.09–7.24 (PhH); MS m/z (rel. intensity) 325 (5, $M^+ + 1$), 251 (100). Anal. Calcd for $\text{C}_{17}\text{H}_{24}\text{O}_2\text{S}_2$: C, 62.92; H, 7.45. Found: C, 63.04; H, 7.78.

Reaction with Isobutanal. α -10: oil; R_f 0.30 (15% EtOAc in hexane); IR (neat) 3490, 2958, 2049, 1594, 1483, 1275, 1028, 752 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) δ 0.98 (3 H, *d*, $J = 6$ Hz), 1.02 (3 H, *d*, $J = 6$ Hz), 1.75–2.34 (3 H, *m*), 2.56 (1 H, *br s*, $J = 3.0$ Hz, OH), 2.70–2.82 (4 H, *m*), 3.52–3.80 (1 H, *m*), 3.85 (3 H, *s*), 6.37 (1 H, *d*, $J = 16.5$ Hz), 6.80–6.99 (2 H, *m*), 7.07–7.50 (2 H, *m*), 7.28 (1 H, *d*, $J = 16.5$ Hz); MS m/z (rel. intensity) 325 (28, $M^+ + 1$), 307 (10), 251 (100), 217 (19), 177 (9), 145 (10), 71 (2), 55 (2). γ -10 (two isomers, 50/50): oil; R_f 0.25 (15% EtOAc in hexane); IR (neat) 3460, 2920, 1596, 1472, 1226, 1013, 748 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) δ 0.96–1.00 (CH_3), 1.75–2.34 (CH_2), 2.70–2.82 (2 x SCH_2), 3.80 (*s*, OCH_3), 4.35 (0.5 H, *br d*, $J =$

9 Hz)/4.48 (0.5 H, *dd*, $J = 10$, 4 Hz), 6.25 (0.5 H, *d*, $J = 10.5$ Hz)/6.46 (0.5 H, *d*, $J = 10.5$ Hz); MS m/z (rel. intensity) 325 (26, $M^+ + 1$), 251 (100).

Reaction with Crotonaldehyde. α -11: oil; R_f 0.35 (20% EtOAc in hexane); IR (neat) 3447, 2910, 1667, 1593, 1484, 1242, 753 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) δ 1.72 (3 H, *d*, $J = 6.0$ Hz), 1.85–2.10 (2 H, *m*), 2.58 (1 H, *br d*, $J = 3.0$ Hz, OH), 2.73–2.97 (4 H, *m*), 3.86 (3 H, *s*), 4.30 (1 H, *dd*, $J = 5$, 3 Hz, *CHOH*), 5.67–5.83 (2 H, *m*), 6.28 (1 H, *d*, $J = 16.2$ Hz), 6.80–7.00 (2 H, *m*), 7.25 (1 H, *d*, $J = 16.2$ Hz), 7.23–7.50 (2 H, *m*); MS m/z (rel. intensity) 322 (12, M^+), 305 (24), 251 (100), 215 (10), 177 (39), 145 (35), 127 (14), 71 (15). γ -11 (two isomers, 62/38): oil; R_f 0.24 (20% EtOAc in hexane); IR (neat) 3453, 2911, 1668, 1594, 1457, 1241, 1027, 754 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3 , 200 MHz) δ 1.61 (1.14 H, *d*, $J = 6.1$ Hz)/1.69 (1.86 H, *d*, $J = 6.0$ Hz, CH_3), 2.02–2.14 (2 H, *m*), 2.68–2.95 (4 H, *m*), 3.82 (3 H, *s*, OCH_3), 4.32–4.42 (2 H, *m*), 5.35–5.74 (2 H, *m*), 6.24 (0.62 H, *d*, $J = 9.1$ Hz)/6.38 (0.38 H, *d*, $J = 9.1$ Hz), 6.83–6.95 (2 H, *m*), 7.10–7.24 (2 H, *m*); MS m/z (rel. intensity) 322 (1, M^+), 305 (6), 251 (100), 177 (19), 145 (13), 119 (8), 91 (2), 71 (7).

Reaction with Benzaldehyde. Inseparable mixture of α -12 and γ -12 (72/28): oil; R_f 0.33 (15% EtOAc in hexane); IR (neat) 3453, 3026, 2907, 1594, 1484, 1244, 1026, 752 cm^{-1} ; MS m/z (rel. intensity) 359 (1, $M^+ + 1$), 341 (12), 251 (100). $^1\text{H NMR}$ (CDCl_3 , α -12) δ 1.80–2.10 (*m*, CH_2), 2.57–2.92 (*m*, 2 \times SCH_2), 3.07 (*br d*, $J = 3$ Hz, OH), 3.77 (*s*, OCH_3), 4.90 (*br d*, $J = 3$ Hz, *CHOH*), 6.11 (*d*, $J = 16.5$ Hz), 6.86 (1 H, *d*, $J = 16.5$ Hz); $^1\text{H NMR}$ (CDCl_3 , γ -12) δ 3.70 (*s*, OCH_3), 4.56 (*dd*, $J = 9.5$, 6 Hz, ArCH), 4.95 (*br d*, $J = 6$ Hz), 6.47 (*d*, $J = 9.5$ Hz). Spirodi-thiane 23 (trans/cis = 78/22): $^1\text{H NMR}$ (CDCl_3 , 200 MHz) δ 1.85–2.09 (2 H, *m*), 2.55–2.91 (4 H, *m*), 3.43–3.76 (2 H, *m*), 3.56 (2.24 H, *s*)/3.64 (0.66 H, *s*, OCH_3), 3.92 (0.78 H, *ddd*, $J = 10.6$, 8.8, 1.8 Hz)/4.56 (0.22 H, *q*, $J = 8.0$ Hz, β -H), 5.29

(0.78 H, *d*, $J = 10.2$ Hz)/5.65 (0.22 H, *d*, $J = 9.6$ Hz, $\text{CH}=\text{}$), 6.74–7.06 (2 H, *m*), 7.12–7.30 (5 H, *m*), 7.34–7.44 (2 H, *m*).

Reaction with Cyclopentanone. α -13: white solid, mp 87–88 $^\circ\text{C}$; R_f 0.32 (15% EtOAc in hexane); IR (KBr) 3533, 2951, 1624, 1594, 1458, 1242, 1027, 753 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) δ 1.50–2.25 (10 H, *m*), 2.30 (1 H, *br s*, OH), 2.53–3.13 (4 H, *m*), 3.85 (3 H, *s*), 6.32 (1 H, *d*, $J = 16.5$ Hz), 6.84–7.00 (2 H, *m*), 7.25 (1 H, *d*, $J = 16.5$ Hz), 7.25 – 7.52 (2 H, *m*); MS m/z (rel. intensity) 336 (8, M^+), 319 (20), 252 (100), 229 (17), 177 (31), 147 (18), 106 (19), 85 (5). Anal. Calcd for $\text{C}_{18}\text{H}_{24}\text{O}_2\text{S}_2$: C, 64.25; H, 7.19. Found: C, 64.42; H, 7.05. γ -13: white solid, mp 42–43 $^\circ\text{C}$; R_f 0.30 (15% EtOAc in hexane); IR (KBr) 3420, 2905, 1593, 1484, 1243, 752 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) δ 1.55–2.30 (10 H, *m*), 2.64–3.24 (4 H, *m*), 3.81 (1 H, *d*, $J = 9$ Hz), 3.87 (3 H, *br s*), 6.28 (1 H, *d*, $J = 9$ Hz), 6.85–7.34 (4 H, *m*). Anal. Calcd for $\text{C}_{18}\text{H}_{24}\text{O}_2\text{S}_2$: C, 64.25; H, 7.19. Found: C, 64.53; H, 7.20.

Reaction with Cyclohexanone. α -14: white solid, mp 110–112 $^\circ\text{C}$; R_f 0.40 (10% EtOAc in hexane); IR (KBr) 3515, 2931, 1688, 1594, 1484, 1242, 752 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) δ 1.15–2.20 (10 H, *m*), 2.21–2.42 (2 H, *m*), 2.23 (1 H, *s*, OH), 2.52–3.10 (4 H, *m*), 3.83 (3 H, *s*), 6.33 (1 H, *d*, $J = 16.5$ Hz), 6.84–6.99 (2 H, *m*), 7.18 (1 H, *d*, $J = 16.5$ Hz), 7.15–7.52 (2 H, *m*); MS m/z (rel. intensity) 350 (1, M^+), 333 (5), 251 (100), 221 (5), 177 (36), 162 (4), 145 (20), 118 (10), 106 (32), 81 (22). γ -14: white solid, mp 140–142 $^\circ\text{C}$; R_f 0.30 (10% EtOAc in hexane); IR (KBr) 3481, 2931, 1594, 1484, 1243, 751 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) δ 1.20–2.45 (12 H, *m*), 2.55–3.02 (4 H, *m*), 3.80 (3 H, *s*), 4.33 (1 H, *d*, $J = 9.5$ Hz), 6.50 (1 H, *d*, $J = 9.5$ Hz), 6.73–7.03 (2 H, *m*), 7.04–7.50 (2 H, *m*); MS m/z (rel. intensity) 351 (8, $M^+ + 1$), 333 (31), 251 (100), 243 (13), 221 (5), 177 (14), 147 (18), 106 (5), 99 (1), 81 (8). Anal. Calcd for $\text{C}_{19}\text{H}_{26}\text{O}_2\text{S}_2$: C,

65.10; H, 7.48. Found: C, 64.98; H, 7.49.

Reaction with Acetone. α -15: oil; R_f 0.41 (10% EtOAc in hexane); IR (neat) 3463, 2978, 1594, 1483, 1243, 1026, 752 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) δ 1.40 (6 H, *s*), 1.73–2.10 (2 H, *m*), 2.50 (1 H, *s*, OH), 2.51–3.12 (4 H, *m*), 3.86 (3 H, *s*), 6.32 (1 H, *d*, $J = 16.5$ Hz), 6.84–7.00 (2 H, *m*), 7.23 (1 H, *d*, $J = 16.5$ Hz), 7.17–7.53 (2 H, *m*); MS m/z (rel. intensity) 310 (9, M^+), 292 (9), 279 (5), 251 (100), 203 (9), 177 (24), 145 (15), 135 (21), 121 (15), 106 (14).

Reaction with 2-Butanone. α -16: white solid, mp 81–82 °C; R_f 0.33 (10% EtOAc in hexane); IR (KBr) 3490, 2933, 1594, 1483, 1243, 1109, 752 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) δ 0.93 (3 H, *t*, $J = 6.3$ Hz), 1.32 (3 H, *s*), 1.60–2.05 (4 H, *m*), 2.17 (1 H, *br s*, OH), 2.52–3.10 (4 H, *m*), 3.81 (3 H, *s*), 6.31 (1 H, *d*, $J = 16.5$ Hz), 6.80–6.99 (2 H, *m*), 7.23 (1 H, *d*, $J = 16.5$ Hz), 7.23–7.51 (2 H, *m*); MS m/z (rel. intensity) 325 (3, $\text{M}^+ + 1$), 307 (9), 295 (1), 251 (100), 217 (12), 177 (38), 147 (31), 106 (21), 73 (23), 55 (15). Anal. Calcd for $\text{C}_{17}\text{H}_{24}\text{O}_2\text{S}_2$: C, 62.92; H, 7.45. Found: C, 62.99; H, 7.45. γ -16 (two isomers, 55/45): oil; R_f 0.20 (10% EtOAc in hexane); IR (neat) 3486, 2930, 1593, 1485, 1241, 1027, 753 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) δ 0.97 (*t*, $J = 7.2$ Hz, CH_3), 3.77 (*s*, OCH_3), 4.34 (0.55 H, *d*, $J = 10.5$ Hz)/4.38 (0.45 H, *d*, $J = 10.5$ Hz), 6.47 (0.55 H, *d*, $J = 10$ Hz)/6.55 (0.45 H, *d*, $J = 10.5$ Hz); MS m/z (rel. intensity) 324 (2, M^+), 251 (100).

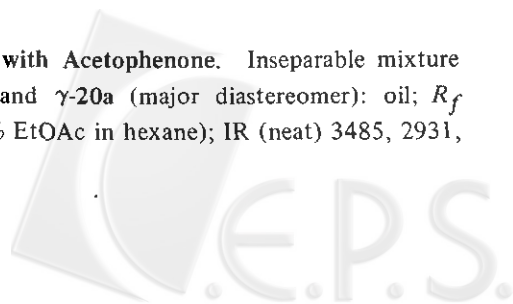
Reaction with 2-Heptanone. α -17: oil; R_f 0.40 (15% EtOAc in hexane); IR (neat) 3493, 2951, 1595, 1458, 1243, 1028, 751 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) δ 0.87 (3 H, *t*, $J = 5.4$ Hz), 1.10–1.60 (8 H, *m*), 1.39 (3 H, *s*), 1.65–2.03 (2 H, *m*), 2.33 (1 H, *s*, OH), 2.55–3.14 (4 H, *m*), 3.85 (3 H, *s*), 6.33 (1 H, *d*, $J = 16.5$ Hz), 6.82–7.00 (2 H, *m*), 7.25 (1 H, *d*, $J = 16.5$ Hz), 7.21–7.53 (2 H, *m*); MS m/z (rel. intensity) 367 (8, $\text{M}^+ + 1$), 349 (45),

252 (100), 221 (7), 177 (12), 147 (13), 106 (4), 91 (2), 71 (2).

Reaction with Benzophenone. α -18: oil; R_f 0.33 (10% EtOAc in hexane); IR (neat) 3488, 3053, 2907, 1593, 1442, 1243, 1027, 752 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) δ 1.75–1.97 (2 H, *m*), 2.44–2.83 (4 H, *m*), 3.58 (1 H, *s*, OH), 3.80 (3 H, *s*), 6.09 (1 H, *d*, $J = 16.5$ Hz), 6.71–6.87 (3 H, *m*), 7.00–7.29 (9 H, *m*), 7.58–7.73 (3 H, *m*); MS m/z (rel. intensity) 435 (10, $\text{M}^+ + 1$), 328 (64), 299 (100), 286 (85), 252 (48), 191 (45), 165 (40), 105 (37), 91 (52), 77 (22). Anal. Calcd for $\text{C}_{26}\text{H}_{26}\text{O}_2\text{S}_2$: C, 71.58; H, 6.03. Found: C, 71.81; H, 5.91. γ -18: white solid, mp 128–129 °C; R_f 0.30 (10% EtOAc in hexane); IR (KBr) 3431, 3056, 2933, 1594, 1487, 1239, 753 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) δ 1.96–2.10 (2 H, *m*), 2.53–2.78 (4 H, *m*), 3.60 (3 H, *s*), 4.24 (1 H, *s*, OH), 5.28 (1 H, *d*, $J = 10.5$ Hz), 6.51 (1 H, *d*, $J = 10.5$ Hz), 6.60–6.76 (2 H, *m*), 6.94–7.45 (10 H, *m*), 7.49–7.65 (2 H, *m*); MS m/z (rel. intensity) 434 (1, M^+), 328 (42), 299 (34), 286 (41), 251 (100), 194 (21), 182 (12), 177 (16), 165 (22), 147 (17), 105 (35), 91 (20), 77 (25). Anal. Calcd for $\text{C}_{26}\text{H}_{26}\text{O}_2\text{S}_2$: C, 71.58; H, 6.03. Found: C, 70.99; H, 6.01.

Reaction with 3-Pentanone. γ -19: oil; R_f 0.30 (15% EtOAc in hexane); IR (neat) 3494, 2961, 1692, 1594, 1485, 1239, 1027, 754 cm^{-1} ; $^1\text{H NMR}$ (CDCl_3) δ 0.90 (6 H, *t*, $J = 7.5$ Hz), 1.13–1.60 (4 H, *m*), 1.83–2.20 (2 H, *m*), 2.54–2.92 (4 H, *m*), 3.80 (3 H, *s*), 4.35 (1 H, *d*, $J = 10$ Hz), 6.53 (1 H, *d*, $J = 10$ Hz), 6.80–6.99 (2 H, *m*), 7.10–7.26 (2 H, *m*); MS m/z (rel. intensity) 339 (2, $\text{M}^+ + 1$), 321 (18), 309 (9), 252 (100), 203 (5), 177 (40), 147 (22), 87 (5), 71 (6).

Reaction with Acetophenone. Inseparable mixture of α -20 and γ -20a (major diastereomer): oil; R_f 0.36 (10% EtOAc in hexane); IR (neat) 3485, 2931,



1594, 1458, 1241, 1027, 753 cm^{-1} ; MS m/z (rel. intensity) 373 (6, $\text{M}^+ + 1$), 251 (100). ^1H NMR (CDCl_3 , α -20) δ 1.73 (s, CH_3), 3.80 (s, OCH_3), 6.11 (d, $J = 16.5$ Hz, =CH); ^1H NMR (CDCl_3 , γ -20a) δ 1.36 (s, CH_3), 3.79 (s, CH_3), 4.78 (d, $J = 6.5$ Hz, ArCH), 6.43 (d, $J = 6.5$ Hz, =CH). Anal. Calcd for $\text{C}_{21}\text{H}_{24}\text{O}_2\text{S}_2$: C, 67.70; H, 6.49. Found: C, 67.87; H, 6.47. γ -20b (minor isomer): oil; R_f 0.32 (10% EtOAc in hexane); IR (neat) 3465, 2931, 1595, 1487, 1240, 1027, 755 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.60 (3H, s), 2.00–2.23 (2 H, m), 2.70–2.90 (4 H, m), 3.64 (1 H, s, OH), 3.68 (3 H, s), 4.70 (1 H, d, $J = 10.5$ Hz), 6.59 (1 H, d, $J = 10.5$ Hz), 6.67–6.85 (2 H, m), 6.94–7.36 (7 H, m); MS m/z (rel. intensity) 373 (1, $\text{M}^+ + 1$), 355 (11), 265 (1), 251 (100), 237 (2), 223 (1), 177 (8), 162 (2), 145 (7), 121 (2), 105 (2), 91 (2), 71 (2), 43 (9). Anal. Calcd for $\text{C}_{21}\text{H}_{24}\text{O}_2\text{S}_2$: C, 67.70; H, 6.49. Found: C, 67.86; H, 6.48.

Reaction with Ethyl Pyruvate. α -21: oil; IR (neat) 3489, 2934, 1722 (C=O), 1626, 1594, 1483, 1245, 1025, 753 cm^{-1} ; ^1H NMR (CDCl_3) δ 0.85 (3 H, t, $J = 6.5$ Hz), 1.62 (3 H, s), 1.75–2.02 (2 H, m), 2.52–3.05 (4 H, m), 3.85 (3 H, s), 4.24 (2 H, q, $J = 6.5$ Hz), 6.11 (1 H, d, $J = 16.5$ Hz), 6.83–6.96 (2 H, m), 7.13–7.51 (2 H, m), 7.25 (1 H, d, $J = 16.5$ Hz); MS m/z (rel. intensity) 368 (9, M^+), 351 (10), 295 (18), 251 (100), 235 (3), 177 (1), 145 (2), 119 (1). γ -21a (major isomer): oil; IR (neat) 3496, 2933, 1718 (C=O), 1594, 1487, 1240, 1026, 755 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.35 (3 H, t, $J = 6.5$ Hz), 1.65 (3 H, s), 1.95–2.24 (2 H, m), 2.73–2.89 (4 H, m), 3.52 (1 H, s, OH), 3.89 (3 H, s), 4.29 (2 H, q, $J = 6.5$ Hz), 4.84 (1 H, d, $J = 10.5$ Hz), 6.39 (1 H, d, $J = 10.5$ Hz), 6.84–7.00 (2 H, m), 7.15–7.45 (2 H, m); MS m/z (rel. intensity) 369 (5, $\text{M}^+ + 1$), 351 (1), 295 (4), 251 (100), 239 (1), 177 (3), 145 (3), 119 (1). γ -21b (minor isomer): white solid, mp 95–97°C; IR (KBr) 3501, 2977, 1722, 1594, 1487, 1242, 813, 716 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.03 (3 H, t, $J = 6.5$ Hz), 1.45 (3 H, s), 1.96–2.10 (2 H, m), 2.72–2.88 (4 H,

m), 4.65 (1 H, d, $J = 10.5$ Hz), 6.42 (1 H, d, $J = 10.5$ Hz), 6.73–6.90 (2 H, m), 7.10–7.30 (2 H, m); MS m/z (rel. intensity) 369 (1, $\text{M}^+ + 1$), 351 (1), 295 (8), 261 (3), 251 (100), 177 (23), 145 (19), 119 (2). Anal. Calcd for $\text{C}_{18}\text{H}_{24}\text{O}_4\text{S}_2$: C, 58.67; H, 6.56. Found: C, 58.23; H, 6.59.

Dimer 22. White solid, mp 128–129°C; R_f 0.22 (15% EtOAc in hexane); IR (KBr) 2905, 1594, 1484, 1244, 1027, 752 cm^{-1} ; ^1H NMR (CDCl_3) δ 1.79–2.16 (4 H, m), 2.50–3.05 (8 H, m), 3.75 (3 H, s), 3.80 (3 H, s), 5.05 (1 H, d, $J = 9.5$ Hz), 6.18 (1 H, d, $J = 16.5$ Hz), 6.47 (1 H, d, $J = 9.5$ Hz), 6.73–6.96 (3 H, m), 7.05–7.47 (6 H, m); MS m/z (rel. intensity) 502 (78, M^+), 427 (35), 395 (19), 381 (6), 353 (2), 321 (2), 251 (100), 177 (11), 145 (10), 118 (9), 106 (7), 91 (9), 71 (5). Anal. Calcd for $\text{C}_{26}\text{H}_{30}\text{O}_2\text{S}_4$: C, 62.12; H, 6.01. Found: C, 61.98; H, 6.18.

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