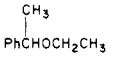
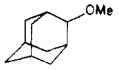
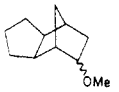
**Table II. Nafion-H Catalyzed Reductive Conversion of Aldehydes and Ketones into Ethers**

| compound | reacn temp[e] | reacn time, h | product | yield, %[a] |
|---|---|---|---|---|
| PhCHO | rt | 2[b] | $PhCH_2OCH_2CH_3$ | 94.6 |
| | reflux | 3[c] | | |
|  | rt | 2[b] |  | 91.0 |
| | reflux | 3[c] | | |
|  | rt | 2[b] |  | 93.0 |
| | reflux | 3[c] | | |
|  | rt | 4[b] |  | 88.0[d] |
| | reflux | 6[c] | | |

[a] Isolated yield are shown. [b] With orthoformate. [c] With triethylsilane. [d] Bp 84 °C (2.2 mm), endo/exo mixture (93:7). [e] Room temperature = rt.

product was purified by distillation to provide corresponding ethers.

**One-Pot Conversion of Benzaldehyde into Benzyl Ethyl Ether.** A mixture of benzaldehyde (3.18 g, 30 mmol), triethyl orthoformate (4.44 g, 30 mmol), and Nafion-H (500 mg) in dichloromethane (20 mL) was stirred at room temperature for 2 h. Then to the reaction mixture was added triethylsilane (3.84 g, 33 mmol) followed by gentle reflux for 3 h. The solid resinsulfonic acid was filtered, and the solvent was evaporated. The crude product was distilled to obtain benzyl ethyl ether: yield, 3.8 g (95%); bp 67–68 °C (3 torr).

**Regeneration of Nafion-H Catalyst.** The used catalyst was washed several times with acetone and deionized water, followed by drying at 105 °C for 10 h. The catalytic activity of regenerated catalyst was as good as that of fresh catalyst.

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**Registry No.** Nafion-H, 63937-00-8; triethylsilane, 617-86-7; (dimethoxymethyl)benzene, 1125-88-8; (diethoxymethyl)benzene, 774-48-1; (1,1-dimethoxyethyl)benzene, 4316-35-2; (1,1-diethoxyethyl)benzene, 4316-37-4; 1,1-dimethoxycyclohexane, 933-40-4; 1,1′-(dimethoxymethylene)bisbenzene, 2235-01-0; 2,2-dimethoxytricyclo[3.3.1.$^{3,7}$]decane, 52776-45-1; 2,2-dimethoxybicyclo-[2.2.1]heptane, 10395-51-4; 1,1-dimethoxydecane, 7779-41-1; (methoxymethyl)benzene, 538-86-3; (ethoxymethyl)benzene, 539-30-0; (1-methoxyethyl)benzene, 4013-34-7; (1-ethoxyethyl)-benzene, 3299-05-6; methoxycyclohexane, 931-56-6; 1,1′-(methoxymethylene)bisbenzene, 1016-09-7; 2-methoxytricyclo-[3.3.1.1$^{3,7}$]decane, 19066-23-0; *endo*-2-methoxybicyclo[2.2.1]heptane, 10395-55-8; 1-methoxydecane, 7289-52-3; 1,1′-methylenebisbenzene, 101-81-5; *exo*-2-methoxybicyclo[2.2.1]heptane, 10395-53-6; benzaldehyde, 100-52-7; 1-phenylethanone, 98-86-2; tricyclo[3.3.1.1$^{3,7}$]decanone, 700-58-3; (3a$\alpha$,4$\alpha$,7$\alpha$,7a$\alpha$)octahydro-4,7-methano-2*H*-inden-5-one, 19138-60-4; (3a$\alpha$,4$\alpha$,5$\beta$,7$\alpha$,7a$\alpha$)-5-methoxyoctahydro-4,7-methano-2*H*-indene, 102518-93-4; (3a$\alpha$,4$\alpha$,5$\alpha$,7$\alpha$,7a$\alpha$)-5-methoxyoctahydro-4,7,-methano-2*H*-indene, 102518-94-5.

## Regio- and Diastereoselective Reactions of Dithio-Substituted Crotyllithium and Aldehydes

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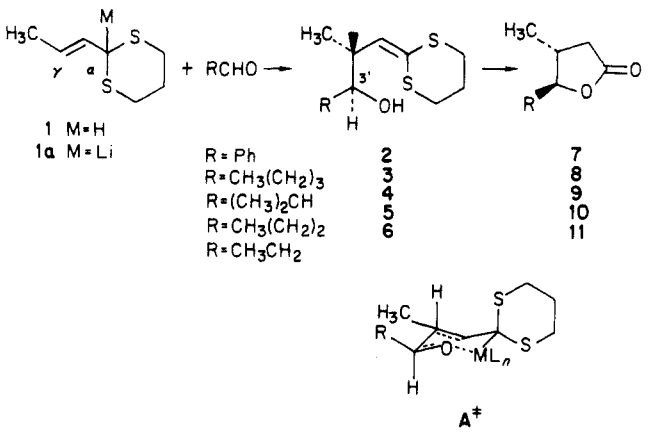
In syntheses of macrolide and polyether antibiotics, crotyl anion, especially with counter cations of boron, aluminum, tin, and titanium, has been shown to react with aldehydes in a highly diastereoselective fashion.[1] However, the corresponding crotyllithium compound, presumably existing as an equilibrating $E/Z$ mixture, reacts less selectively with aldehydes. We thought the process of $E/Z$ isomerization might be impeded by the dithioacetal substituent in the crotyl ion **1a** derived from (*E*)-2-(1-propen-1-yl)-1,3-dithiane,[2] and thus the **1a** ion would react stereoselectively with aldehydes. According to precedent,[3,4] the ambident crotyl ion **1a** should react regioselectively at the $\gamma$-site, and it would function as a useful synthon of a $\beta$-butyrate anion equivalent. The above speculation was realized as demonstrated in this note.

**Scheme I**




The desired vinylogous dithiane **1** was prepared by treating crotonaldehyde with an equivalent amount of 1,3-propanedithiol in the presence of magnesium perchlorate. The purity of the resultant dithiane, containing 98% *E* isomer, was superior to that prepared under conventional conditions ($BF_3$-$Et_2O$, HOAc).[2] Contrary to the counterpart of 2-propylidene-1,3-dithiane,[4] metalation of vinylogous dithiane **1** was readily effected by treatment with *n*-BuLi (THF, −30 °C, 1 h) in the absence of HMPA.[5] Thus, subsequent reaction with appropriate aldehydes (−78 °C, 20 min) was achieved in a highly regio- and stereoselective manner without the interference of HMPA.[5]

In all cases (Scheme I), crotyllithium **1a** reacted with the aldehyde exclusively at the $\gamma$-site as evidenced by $^1$H NMR analysis. The reaction with benzaldehyde gave a diastereomeric mixture (77:23) of the $\gamma$-addition products **2** (95% total yield) as revealed by HPLC and $^1$H NMR analyses. Since both the H-3′ resonances (C*H*OH) of diastereomers **2** (at $\delta$ 4.40 and 4.60) exhibited similar coupling constants (6 Hz), the structural elucidation was based on elaboration of **2** to $\gamma$-lactones **7**. Hydrolysis ($HgCl_2$, aqueous MeOH) of the minor isomer (**2**-*erythro*) gave **7**-*cis* lactone, which was characterized by the unusually high field of the methyl group (at $\delta$ 0.66) owing to the shielding effect of the adjacent phenyl group.[6] On the other hand, hydrolysis of the major isomer (**2**-*threo*) afforded the **7**-*trans* lactone, which displayed the methyl resonance at the normal position ($\delta$ 1.17). The $\gamma$-H resonance of **7**-*trans* lactone, presumably shielded by the $\beta$-$CH_3$ group, exhibited the resonance (d, $J$ = 9 Hz) at relatively higher field ($\delta$ 4.95) than that of **7**-*cis* lactone ($\delta$ 5.62, d, $J$ = 6 Hz).

The reaction of crotyl ion **1a** and pentanal gave exclusively threo product **3** in 90% yield; no erythro isomer

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could be detected by HPLC or $^1H$ NMR spectroscopy. Hydrolysis of **3** afforded γ-lactone **8**, which was determined to have the trans configuration by comparison with the reported quercus lactones.[7] The γ-H resonance of **8** appeared at δ 3.87 (lit.[7] 3.88), while the corresponding resonance of cis quercus lactone appeared at lower field (δ 4.37).[8] The analogous reactions with 2-methylpropanal, butanal, and propanal followed the same threo selectivity, giving **4–6** in high yields (>90%). Hydrolyses of **4–6** afforded trans lactones **9–11**, which displayed γ-H protons at δ 3.80, 3.88, and 3.80 in the $^1H$ NMR spectra, respectively.

Therefore, the chelation and chair-like transition state **A*** is proposed to account for the γ and threo selectivities in the reaction of crotyllithium **1a** with aldehydes.[9] The methyl and R groups in **A*** orient at favorable equatorial positions and the original *E* configuration of **1** is reatined in the chair form.

## Experimental Section

Elemental analyses were carried out on the Perkin-Elmer 240c elemental analyzer. Infrared spectra were run on the Jasco Model IRA-1 spectrometer. The proton nuclear magnetic resonance spectra were recorded on the Varian EM-390 (90 MHz) spectrometer or the JEOL JNM-FX100 (100 MHz) spectrometer, and chemical shifts are reported in parts per million downfield from tetramethylsilane. Mass spectra were recorded on the JEOL JMS-D300 spectrometer operating at an ionizing voltage of 70 eV. High pressure liquid chromatography was carried out on the Waters Associates M45 liquid chromatograph using the ultraviolet and refractive index detectors.

**(*E*)-2-(1-Propen-1-yl)-1,3-dithiane (1).** In a flask were placed a mixture of 1,3-propanedithiol (5 mL, 50 mmol), anhydrous magnesium perchlorate (0.6 g, 2.5 mmol), concentrated sulfuric acid (1 drop), and anhydrous chloroform (80 mL). The mixture was cooled to −10 °C and vigorously stirred, while a solution of crotonaldehyde (3.5 g, 50 mmol) in chloroform (18 mL) was added dropwise over a period of 20 min. After stirring for 2 h, the reaction mixture was poured into an ice-cold 10% KOH solution. After stirring for 15 min, the organic phase was separated and washed successively with KOH solution and water. After drying over anhydrous $K_2CO_3$, the volatiles were removed in vacuo, and the residue was distilled at 72 °C (0.4 mmHg) to give 7.6 g (47.5 mmol) of vinylogous dithiane **1** (95% yield), accompanied by 0.16 g of *Z* isomer. Dithiane **1**: IR (neat) 3030, 2960, 2920, 1660 $cm^{-1}$; MS, *m/z* (rel intensity) 160 (83, $M^+$), 145 (8), 86 (50), 85 (100); $^1H$ NMR ($CDCl_3$) δ 1.73 (3 H, d, *J* = 6 Hz), 1.85–2.27 (2 H, m), 2.77–2.97 (4 H, m), 4.59 (1 H, d, *J* = 6 Hz), 5.50 (1 H, dd, *J* = 15, 6 Hz), 5.84 (1 H, dq, *J* = 15, 6 Hz). *Z* isomer: $^1H$ NMR ($CDCl_3$, partial) 4.94 (d, *J* = 9 Hz).

**2-(2-Methyl-3-hydroxy-3-phenylpropylidene)-1,3-dithiane (2).** Under an atmosphere of nitrogen, *n*-BuLi (1.1 mmol, 1.6 M in hexane) was added dropwise to a solution of dithiane **1** (1.0 mmol) in anhydrous THF at −30 °C. After stirring for 1 h, the mixture was cooled to −78 °C and a solution of benzaldehyde (1 mmol) in THF (1 mL) was added dropwise. After being stirred for 20 min, the reaction was quenched by addition of methanol. The mixture was concentrated in vacuo, and the residue was taken up with ether. The ethereal solution was washed 3 times with brine, dried ($Na_2SO_4$), and concentrated in vacuo to give adducts **2** as a diastereomeric mixture (threo:erythro = 77:23). Separation was accomplished by HPLC on a μ-Porasil column (0.78 cm × 25 cm) with elution of ethyl acetate/hexane (1:9) to afford 194 mg of **2**-*threo* and 58 mg of **2**-*erythro* isomers. **2**-*threo*: IR (neat) 3440, 1600, 1580 $cm^{-1}$; MS, *m/z* (rel intensity) 266 (10, $M^+$), 159 (57), 106 (100); $^1H$ NMR ($CDCl_3$) δ 0.85 (3 H, d, *J* = 6 Hz), 1.97–2.25 (2 H, m), 2.70–2.97 (4 H, m), 3.00–3.23 (1 H, m), 4.40 (1 H, d, *J* = 6 Hz, C*H*OH), 5.85 (1 H, d, *J* = 9 Hz, vinyl), 7.35 (5 H, br s). Anal. Calcd for $C_{14}H_{18}OS_2$: C, 63.11; H, 6.81. Found: C, 62.89; H, 6.77. **2**-*erythro*: $^1H$ NMR ($CDCl_3$) δ 0.98 (3 H, d, *J* = 6 Hz), 2.01–2.28 (2 H, m), 2.72–2.98 (4 H, m), 3.02–3.23 (1 H, m), 4.60 (1 H, d, *J* = 6 Hz), 5.78 (1 H, d, *J* = 10 Hz), 7.35 (5 H, br s).

**2-(2-Methyl-3-hydroxyheptylidene)-1,3-dithiane (3):** IR (neat) 3700–3100, 3000–2800, 1580 $cm^{-1}$; MS, *m/z* (rel intensity) 246 (8, $M^+$), 159 (100), 85 (23); $^1H$ NMR ($CDCl_3$) δ 0.80–1.05 (6 H, m, two methyls), 1.10–1.60 (6 H, m), 1.92–2.30 (2 H, m), 2.68–2.98 (4 H, m, $SCH_2$), 3.20–3.52 (1 H, m, C*H*OH), 5.72 (1 H, d, *J* = 10 Hz).

**2-(2,4-Dimethyl-3-hydroxypentylidene)-1,3-dithiane (4):** IR (neat) 3440, 2950, 2910, 1570 $cm^{-1}$; MS, *m/z* (rel intensity) 232 (14, $M^+$), 159 (100), 85 (28); $^1H$ NMR ($CDCl_3$) δ 0.95 (6 H, d, *J* = 6 Hz), 0.98 (3 H, d, *J* = 6 Hz), 1.60–1.87 (2 H, m), 1.95–2.28 (2 H, m), 2.78–2.98 (4 H, m), 3.10 (1 H, t, *J* = 6 Hz, C*H*OH), 5.89 (1 H, d, *J* = 10 Hz). Anal. Calcd for $C_{11}H_{20}OS_2$: C, 56.85; H, 8.67. Found: C, 56.92; H, 8.75.

**2-(2-Methyl-3-hydroxyhexylidene)-1,3-dithiane (5):** IR (neat) 3440, 2960, 2920, 2870, 1580 $cm^{-1}$; MS, *m/z* (rel intensity) 232 (0.03, $M^+$), 159 (100), 85 (30); $^1H$ NMR ($CDCl_3$) δ 0.85–1.10 (6 H, m), 1.20–1.65 (4 H, m), 1.95–2.32 (2 H, m), 2.65– 3.00 (4 H, m), 3.20–3.50 (1 H, m, C*H*OH), 5.75 (1 H, d, *J* = 10 Hz).

**2-(2-Methyl-3-hydroxypentylidene)-1,3-dithiane (6):** IR (neat) 3700–3100, 1560 $cm^{-1}$; MS, *m/z* (rel intensity) 218 (11, $M^+$), 159 (100), 85 (27); $^1H$ NMR ($CDCl_3$) δ 0.88–1.15 (6 H, m), 1.28–1.72 (2 H, m), 2.02–2.32 (2 H, m), 2.68–3.00 (4 H, m), 3.22–3.44 (1 H, m, C*H*OH), 5.85 (1 H, d, *J* = 10 Hz).

***trans*-β-Methyl-γ-phenyl-γ-butyrolactone (7).** A mixture of adduct **2**-*threo* (133 mg, 0.5 mmol), mercuric chloride (0.41 g, 1.5 mmol), and 10% methanol (20 mL) was refluxed for 5 h under a nitrogen atmosphere. After removal of methanol, the residue was extracted 3 times with ethyl acetate. The combined extracts were washed with brine, dried ($Na_2SO_4$), concentrated, and purified by the flash chromatography to give 66 mg of **7**-*trans* lactone (75% yield): IR (neat) 3080, 1780, 1600 $cm^{-1}$; MS, *m/z* (rel intensity) 176 (54, $M^+$), 107 (100), 105 (81), 77 (25); $^1H$ NMR ($CDCl_3$) δ 1.17 (3 H, d, *J* = 6 Hz, $CH_3$), 2.19–2.63 (3 H, m), 4.95 (1 H, d, *J* = 9 Hz, γ-H), 7.34 (5 H, br s). Anal. Calcd for $C_{11}H_{12}O_2$: C, 74.98; H, 6.86. Found: C, 74.25; H, 6.65.

***cis*-β-Methyl-γ-phenyl-γ-butyrolactone:** MS, *m/z* (rel intensity) 176 (50, $M^+$), 107 (100), 105 (75), 77 (30); $^1H$ NMR ($CDCl_3$) δ 0.66 (3 H, d, *J* = 6 Hz, $CH_3$), 2.70–2.97 (3 H, m), 5.62 (1 H, d, *J* = 6 Hz, γ-H), 7.34 (5 H, br s).

***trans*-β-Methyl-γ-butyl-γ-butyrolactone (8):** IR (neat) 3000–2800, 1780 $cm^{-1}$; MS, *m/z* (rel intensity) 156 (3, $M^+$), 99 (100), 71 (34); $^1H$ NMR ($CDCl_3$) δ 0.80–1.03 (3 H, m), 1.10 (3 H, d, *J* = 6 Hz, β-$CH_3$), 1.20–1.75 (6 H, m), 1.85–2.70 (3 H, m), 3.87 (1 H, m, γ-H).

***trans*-β-Methyl-γ-isopropyl-γ-butyrolactone (9):** IR (neat) 2960, 1780 $cm^{-1}$; MS, *m/z* (rel intensity) 142 (18, $M^+$), 99 (50), 71 (100); $^1H$ NMR ($CDCl_3$) δ 0.95 (3 H, d, *J* = 6 Hz), 0.97 (3 H, d, *J* = 6 Hz), 1.25 (3 H, d, *J* = 6 Hz), 1.67–2.05 (1 H, m), 1.97–2.73 (3 H, m), 3.80 (1 H, t, *J* = 6 Hz, γ-H). Anal. Calcd for $C_8H_{14}O_2$: C, 67.57; H, 9.92. Found: C, 67.10; H, 9.92.

***trans*-β-Methyl-γ-propyl-γ-butyrolactone (10):** IR (neat) 2940, 2910, 2860, 1790 $cm^{-1}$; MS, *m/z* (rel intensity) 142 (11, $M^+$), 71 (100); $^1H$ NMR ($CDCl_3$) δ 0.80–1.03 (3 H, m), 1.13 (3 H, d, *J* = 6 Hz, β-$CH_3$), 1.30–1.75 (4 H, m), 1.85–2.75 (3 H, m), 3.88 (1 H, m).

***trans*-β-Methyl-γ-ethyl-γ-butyrolactone (11):** IR (neat) 3000–2800, 1780 $cm^{-1}$; $^1H$ NMR ($CDCl_3$) δ 1.01 (3 H, t, *J* = 7 Hz), 1.13 (3 H, d, *J* = 6 Hz), 1.35–1.75 (2 H, m), 1.85–2.75 (3 H, m), 3.80 (1 H, m).

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**Registry No.** **1**, 84307-59-5; **2** (isomer 1), 102587-15-5; **2** (isomer 2), 102587-16-6; **3**, 102587-17-7; **4**, 102587-18-8; **5**, 102587-19-9; **6**, 102587-20-2; *trans*-**7**, 26704-17-6; *cis*-**7**, 26620-41-7; **8**, 39638-67-0; **9**, 85710-97-0; **10**, 102587-21-3; **11**, 34405-51-1; PhCHO, 100-52-7; $CH_3(CH_2)_3CHO$, 110-62-3; $(CH_3)_2CHCHO$, 78-84-2; $CH_3(CH_2)_2CHO$, 123-72-8; $CH_3CH_2CHO$, 123-38-6; 1,3-propanedithiol, 109-80-8; crotonaldehyde, 4170-30-3.

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