

## KETENE DITHIOACETALS III<sup>1</sup>: THE CONJUGATE ADDITION OF KETENE DITHIOACETAL ANIONS TO CYCLIC $\alpha,\beta$ -UNSATURATED KETONES

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*Abstract: The relative amounts of 1,2 to 1,4 addition products of several ketene dithioacetal anions to cyclic  $\alpha,\beta$ -unsaturated ketones have been determined. The influence of solvent and counterion is reported.*

Methods have been reported recently which permit the aprotic 1,4 addition of dithiane anions to  $\alpha,\beta$ -unsaturated lactones<sup>2</sup> and ketones<sup>3</sup>. While dithiane anions serve as acyl anion equivalents, their vinylogs, ketene dithioacetal anions, have the potential of functioning as  $\beta$ -propionate anion equivalents ( $\gamma$ -substitution) or  $\alpha,\beta$ -unsaturated acyl anion equivalents<sup>4</sup> ( $\alpha$ -substitution). We report in this Letter our results concerning the conjugate addition of these anions to several  $\alpha,\beta$ -unsaturated ketones.

Deprotonation of 2-ethylidene-1,3-dithiane(1)<sup>5</sup> is readily achieved with lithium diisopropylamide (LDA) (-15°C, THF, 0.5h) while 2-isopropylidene-1,3-dithiane(2) is 54% deprotonated (LDA, THF, -15° to -5°C, 0.75h) under similar conditions. Deprotonation of 2 to the extent of 82% could be achieved using LDA-HMPA (3 equiv)-THF for 0.5 h at 0°C. The degree of deprotonation was determined by GC-MS of the D<sub>2</sub>O quenched anions, which provided 2-deuterio-2-isopropylidene-1,3-dithiane (82%) and undeuterated starting material 2 (18%).

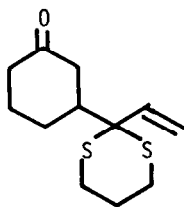
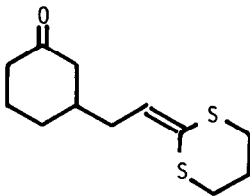
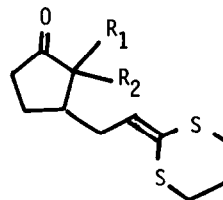
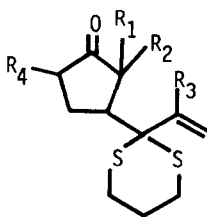
The conjugate additions were effected at -78°C followed by warming to 25°C and eventual protonation or alkylation of the resultant enolates. The regioselectivity of the reaction of these lithium anions in THF and/or THF-HMPA or their cuprous salts in THF with cyclohexenone (3), cyclopentenone(4), and 2-methylcyclopentenone (5) is outlined in the Table.

Table<sup>a</sup>

<u>Entry</u>	<u>Ketene-Dithioacetal</u>	<u>Enone</u>	<u>Rxn Conditions</u>	<u>Products (rel %)</u>	<u>Distilled Yield %</u>
1	1	3	LDA, THF	<u>7</u> (71) <u>6</u> (20) <u>1,2</u> (9)	68
2	1	3	LDA, THF CuI <sup>+</sup> (MeO) <sub>3</sub> P	<u>6</u> (98) <u>7</u> (2)	67
3	1	5	LDA, THF	<u>8a</u> (60) <u>9a</u> (16) <u>1,2</u> (24)	82
4	1	5	LDA, THF CuI <sup>+</sup> (MeO) <sub>3</sub> P	<u>9a</u> (98) <u>8a</u> (2)	54
5	1	5	LDA, THF HMPA	<u>9a</u> (100)	66
6	1	4	LDA, THF	<u>8b</u> (70) <u>9b</u> (26) <u>1,2</u> (4)	44
7	1	5	1) LDA, THF, HMPA 2) CH <sub>3</sub> I	<u>9c</u> (89) <u>9d</u> (6) <u>9a</u> (5)	70
8	2	5	LDA, THF HMPA	<u>9e</u> (100)	71
9	2	5	1) LDA, THF, HMPA 2) CH <sub>2</sub> =CHCH <sub>2</sub> Br	<u>9f</u> (90) <u>9g</u> (10)	68
10	1	5	1) LDA, THF, HMPA 2) CH <sub>2</sub> =CH-CH <sub>2</sub> Br	<u>9h</u> (90) <u>9i</u> (6) <u>9a</u> (4)	67

a) all new compounds were identified by elemental analysis, NMR, GC-MS and IR.

The lithium anion of 2-ethylidene-1,3-dithiane shows regioselectivity (entries 1, 3, 6) for 1,4- $\gamma$  substitution. The  $\gamma/\alpha$  ratio of the 1,2 products has not been determined. A significant reversal of selectivity is observed by using 3 equiv. of HMPA (entries 5 and 8) or the cuprous salt of the anion (entries 2 and 4), generated by addition of CuI<sup>+</sup>(MeO)<sub>3</sub>P to the lithium anion, providing the 1,4- $\alpha$  product as the dominant isomer. When the conjugate addition of entry 2 was conducted at -78°C for 0.25 h and then quenched with methanol at -78°C, the 1,4- $\alpha$  product was obtained along with unreacted cyclohexenone, indicating, in this

678 a,  $R_1 = \text{CH}_3$ ,  $R_2 = \text{H}$ b,  $R_1 = R_2 = \text{H}$ 9 a,  $R_1 = \text{CH}_3$ ,  $R_{2-4} = \text{H}$ b,  $R_{1-4} = \text{H}$ c,  $R_1 = R_2 = \text{CH}_3$ ,  $R_3 = R_4 = \text{H}$ d,  $R_1 = R_2 = R_4 = \text{CH}_3$ ,  $R_3 = \text{H}$ e,  $R_1 = R_3 = \text{CH}_3$ ,  $R_2 = R_4 = \text{H}$ f,  $R_1 = R_3 = \text{CH}_3$ ,  $R_2 = R_4 = \text{C}_3\text{H}_5$ ,  $R_4 = \text{H}$ g,  $R_1 = R_3 = \text{CH}_3$ ,  $R_2 = R_4 = \text{C}_3\text{H}_5$ h,  $R_1 = \text{CH}_3$ ,  $R_2 = \text{C}_3\text{H}_5$ ,  $R_3 = R_4 = \text{H}$ i,  $R_1 = \text{CH}_3$ ,  $R_2 = R_4 = \text{C}_3\text{H}_5$ ,  $R_3 = \text{H}$ 

instance, that the 1,4 product does not arise upon warming to 25°C.

The enolates generated in the conjugate additions can be regioselectively alkylated using methyl iodide (entry 9) or allyl bromide (entries 10 and 11). The allylated products 9f and 9h are homogeneous substances and are assumed to have the bulky dithianyl group trans to the allyl residue<sup>6</sup>.

A typical experimental procedure (entry 7) is as follows: To a solution of 0.77 mmole of LDA in 3.0 mL of dry THF at -20°C (N<sub>2</sub>) was added a solution of 114 mg (0.77 mmol) of 1 in 1.0 mL of THF and the mixture was stirred at -20° to -10°C for 0.5 h. To the deep red solution at -10°C was added 0.4 mL (2.3 mmol) of HMPA and the mixture was cooled to -78°C (alternatively, 1.5 equivalents of a solution of cuprous iodide-trimethylphosphite complex in THF solution was added to the deep red solution at -78°C and stirred for 0.5 h forming a yellow suspension). A solution of 75 mg (0.77 mmol) of 2-methylcyclopentenone (5) in 1 mL of THF was added at -78°C. The mixture was warmed to 0°C over 1 h, stirred at 0°C for an additional 0.5 h, then cooled to -78°C, and 0.07 mL (1.2 mmol) of neat methyl iodide was added.

The reaction mixture was allowed to warm to 25°C over 3 h and stirred at 25°C for 13 h. The mixture was taken up in hexane and washed successively with water and saturated brine. After drying ( $\text{MgSO}_4$ ) of the hexane solution and concentration in vacuo, the crude reaction product was distilled (Kugelrohr, 110°C, 0.02 mm) to afford 155 mg of a pale yellow liquid which contained 89% 9c (70% yield), 5% 9a and 6% 9d, as determined by vpc analysis (1.5% OV-101, 160°C). The vpc collected materials had the following spectral properties: 9c: ( $\text{CCl}_4$ , 270 MHz)  $\delta$  1.00 (3H, s), 1.21 (3H, s), 1.72-2.37 (6H, m), 2.50-2.63 (1H, m), 2.79-2.84 (4H, m), 5.42 (1H, dd,  $J_{\text{cis}} = 10.2$  Hz,  $J_{\text{gem}} = 1.5$  Hz), 5.50 (1H, dd,  $J_{\text{trans}} = 17.2$  Hz,  $J_{\text{gem}} = 1.5$  Hz), and 5.88 (1H, dd,  $J_{\text{trans}} = 1.72$  Hz,  $J_{\text{cis}} = 10.2$  Hz); ir ( $\text{CCl}_4$ ) 1745(s) and 1625(w)  $\text{cm}^{-1}$ ; mass spectrum (70 eV) m/e (rel int) 256 (54,  $\text{M}^+$ ), 145 (100), 106 (33), and 71 (37).

Anal. Calcd for  $\text{C}_{13}\text{H}_{20}\text{OS}_2$ : C, 60.89; H, 7.86. Found: C, 60.97; H, 7.78.

9d: mass spectrum (70 eV) m/e (rel int) 270 (15,  $\text{M}^+$ ), 256 (23), 145 (100), 106 (34), and 71 (22).

9a: identical in all respects to the major component obtained in entry 5.

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