A Novel Route to Alkenoyl- and Cinnamoylketene Dithioacetals

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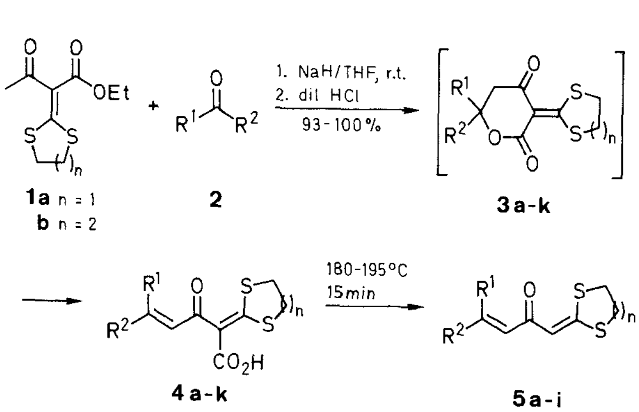
2-Acetyl(ethoxycarbonyl)methylene-1,3-dithietane and -dithiane (**1**) were condensed with various aldehydes or ketones to afford high yields of the corresponding substituted 2-(1-carboxy-2-oxo-3-butenylidene)-1,3-dithietanes and -dithianes **4**, which upon heating decarboxylated smoothly to give the title compounds in high yield.

Recently we reported an improved method for the preparation of acylketene dithioacetals **1** and its conversion to thiolane protected β-ketoaldehydes.[1] In our on-going efforts to use acylketene dithioacetals as versatile precursors we have discovered a new method for the preparation of various enoylketene dithioacetals. We had originally attempted to condense **1** with various aldehydes or ketones to obtain condensation products similar to those of Thuiller.[2]

In recent work, Junjappa and co-workers have reported[3-5] the preparation of various alkenoyl- and cinnamoylketene dithioacetals which involved the direct aldol condensation of acylketene dithioacetals with aromatic aldehydes and the 1,4-addition of a Grignard reagent to a (3-amino-2-alkenoyl)ketene dithioacetal. They also described the synthetic utility of the title compounds.

In this report, we describe a novel route for preparing various alkenoyl- and cinnamoylketene dithioacetals **5** by utilizing the aforementioned, easily prepared acyl(ethoxycarbonyl)ketene dithioacetals **1**[1] (Scheme **A**).

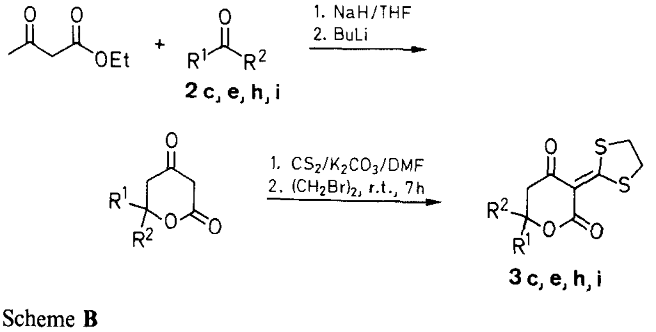


3, 5	n	R^1	R^2	3, 5	n	R^1	R^2
a	1	4-ClC_6H_4	H	g	2	Ph	Ph
b	1	2-ClC_6H_4	H	h	1	*t*-Bu	H
c	1	4-MeOC_6H_4	H	i	1	*t*-Bu	Me
d	2	4-MeOC_6H_4	H	j	1	$n\text{-C}_6H_{11}$	H
e	1	Ph	Me	k	1	$-(CH_2)_5-$	

Scheme **A**

Interestingly, at room temperature, deprotonation of 2-acetyl(ethoxycarbonyl)methylene-1,3-dithietane and -dithiane (**1**) by sodium hydride and addition of carbonyl compounds **2** afforded substituted 2-(1-carboxy-2-oxo-3-butenylidene)-1,3-dithietanes and -dithianes **4** (see Table 1) in high yields instead of the expected, direct condensation product 1-(2-alkenoyl)-1-carboethoxyketene dithioacetals. The overall outcome of the reaction was an aldol condensation and an ester hydrolysis.

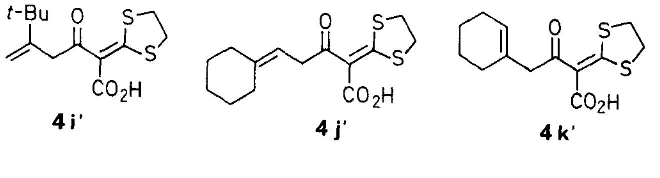
As an acidic workup (5% HCl) had been performed, we speculated that simple condensation, followed by hydrolysis during acidic workup, might have afforded the 1-(2-alkenoyl)-1-carboxyketene dithioacetals **4**. However, the presence of **4** was detected in the reaction mixture by TLC before the acidic workup. Thus, it was surmised that hydrolysis had occurred via the intermediate lactone **3** (see Table 3). Cleavage of **3** could have occurred due to the presence of sodium ethoxide generated during cyclocondensation or the presence of excess sodium hydride. To determine the actual mechanism, the lactones, **3c, e, h, i**, were prepared by a different route[1,6] (Scheme **B**) and then subjected to acidic workup conditions (excess 1 N HCl).



Scheme **B**

The lactones **3c, e, h, i** were inert not only to the acidic workup condition but also to sodium hydride in tetrahydrofuran. In contrast, treatment of lactones **3c, e,h, i** with sodium ethoxide in tetrahydrofuran gave quantitative amounts of the corresponding acids, **4c, e, h, i**. Additional evidence to support the proposed mechanism was gained when lactone **3e** was isolated from a mixture of condensation product **4e**. However we were not able to isolate **4e** from this mixture due to the instability of the compound.[7]

For lactones **3i, 3j** and **3k**, where competitive β-elimination is possible, the deconjugated products, **4i′**, **4j′** and **4k′** were isolated almost exclusively.



It was interesting to note that decarboxylation of **4i′** gave conjugated product **5i**[8] exclusively, while **4j′** and **4k′** gave only deconjugated products, **5j′** and **5k′**.[9] In either case decarboxylation occurred smoothly at 180–195 °C to give the corresponding conjugated and deconjugated alkenoylketene dithioacetals.

Table 1. Compounds **4** Prepared

Product	Yield[a] (%)	mp (°C)[b] (dec)	Molecular Formula[c]	IR (KBr)[d] ν(cm^{-1})	^{1}H-NMR (DMSO-d_6/TMS)[e] δ, J(Hz)	MS (70 eV)[f] m/z (%)
4a	96	173–173.5	$C_{14}H_{11}ClO_3S_2$ (326.8)	3000, 1650, 1630, 1570, 1480, 1420	3.36–3.46 (m, 4H), 7.31–7.70 (m, 6H), 13.03 (br s, 1H)	326 (M^+, 18), 282 ($M^+ - CO_2$, 35)
4b	93	177–180	$C_{14}H_{11}ClO_3S_2$ (326.8)	2800, 1630, 1590, 1430, 1280	3.37–3.51 (m, 4H), 7.37–7.84 (m, 6H), 13.13 (br s, 1H)	326 (M^+, 25), 282 ($M^+ - CO_2$, 17)
4c	94	181–183	$C_{15}H_{14}O_4S_2$ (322.4)	2940, 1650, 1620, 1580, 1520, 1430	3.35–3.55 (m, 4H), 3.80 (s, 3H), 6.98 (d, 2H, J = 8.8), 7.16 (d, 1H, J = 15.7), 7.50 (d, 1H, J = 15.7), 7.61 (d, 2H, J = 8.8), 13.02 (br s, 1H)	322 (M^+, 24), 278 ($M^+ - CO_2$, 9)
4d	93	154	$C_{16}H_{16}O_4S_2$ (336.4)	2900, 1640, 1590, 1540, 1280	2.09–2.19 (m, 2H), 2.95 (m, 4H), 3.81 (s, 3H), 6.83 (d, 1H, J = 15.8), 6.97 (d, 2H, J = 8.8), 7.45 (d, 1H, J = 15.8), 7.64 (d, 2H, J = 8.8), 12.90 (br s, 1H)	292 ($M^+ - CO_2$, 92)
4f	98	114–116	$C_{20}H_{16}O_3S_2$ (368.5)	2800, 1620, 1590, 1500, 1420	3.27–3.36 (m, 4H), 6.84 (s, 1H), 7.07–7.37 (m, 10H), 12.81 (br s, 1H)	324 ($M^+ - CO_2$, 24)
4g	98	143–145	$C_{21}H_{18}O_3S_2$ (382.5)	3000, 1630, 1600, 1450, 1260	2.05–2.14 (m, 2H), 2.83–2.87 (m, 4H), 6.66 (s, 1H), 7.09–7.38 (m, 10H), 12.72 (br s, 1H)	338 ($M^+ - CO_2$, 30)
4h[g]	100 (crude)	177–179	$C_{12}H_{16}O_3S_2$ (272.4)	2950, 1670, 1640, 1420, 1240	1.13 (s, 9H), 3.43 (s, 4H), 6.68 (d, 1H, J = 16.0), 7.03 (d, 1H, J = 16.0), 10.72 (br s, 1H)	272 (M^+, 24), 228 ($M^+ - CO_2$, 25)
4i'[h]	95 (crude)	160–162	$C_{13}H_{18}O_3S_2$ (286.4)	2950, 1630, 1430, 1400, 1280	1.07 (s, 9H), 3.32 (s, 4H), 3.50 (s, 2H), 4.55 (s, 1H), 4.90 (s, 1H), 11.53 (br s, 1H)	286 (M^+, 3), 242 ($M^+ - CO_2$, 10)
4j'	90	141–142	$C_{14}H_{18}O_3S_2$ (298.4)	2900, 1660, 1610, 1430, 1270	1.0–2.5 (m, 10H), 3.38 (s, 4H), 3.65 (d, 2H, J = 7.0), 5.33 (t, 1H, J = 7.0), 11.62 (br s, 1H)	298 (M^+, 4), 254 ($M^+ - CO_2$, 1)
4k'	96	127–128	$C_{13}H_{16}O_3S_2$ (284.4)	2900, 1620, 1420, 1280	1.6–2.28 (m, 8H), 3.32–3.39 (m, 4H), 3.54 (m, 2H), 5.38 (m, 1H), 13.07 (br s, 1H)	284 (M^+, 6), 240 ($M^+ - CO_2$, 4)

[a] Yield of isolated product.
[b] Uncorrected. Measured with a Thomas-Hoover melting point apparatus.
[c] Accurate mass determined (±0.002 mass units).
[d] Recorded on a Shimadzu IR-435 spectrophotometer.
[e] Recorded on Bruker AM-300 spectrometer and Jeol PMX 60 SI spectrometer.
[f] Obtained on a Shimadzu QP 1000 spectrometer.
[g] Completely transformed into **3h** after 6 months.
[h] Structure was confirmed by ^{13}C-NMR using DEPT method.

Table 2. Compounds **5** Prepared

Product	Yield[a] (%)	mp (°C)[b]	Molecular Formula[c]	IR (KBr)[d] ν(cm^{-1})	^{1}H-NMR ($CDCl_3$/TMS)[e] δ, J(Hz)	MS (70 eV)[f] m/z (%)
5a	99	171–180	$C_{13}H_{11}ClOS_2$ (282.8)	1630, 1580, 1490, 1400	3.43 (m, 4H), 6.80 (d, 1H, J = 16.0), 6.93 (s, 1H), 7.20–7.80 (m, 5H)	282 (M^+, 90)
5b	93	117–119	$C_{13}H_{11}ClOS_2$ (282.8)	1640, 1580, 1480, 1420	3.40 (m, 4H), 6.70 (d, 1H, J = 16.0), 6.85 (s, 1H), 7.00–7.73 (m, 4H), 7.97 (d, 1H, J = 16.0)	282 (M^+, 28)
5c	95	108–110	$C_{14}H_{14}O_2S_2$ (278.4)	1640, 1560, 1480	3.36 (m, 4H), 3.80 (s, 3H), 6.60 (d, 1H, J = 16.0), 6.78 (s, 1H), 6.84 (d, 2H, J = 8.0), 7.45 (d, 2H, J = 8.0), 7.55 (d, 1H, J = 16.0)	278 (M^+, 74)
5d	92	205–207	$C_{15}H_{16}O_2S_2$ (292.4)	1650, 1440, 1280	2.24 (m, 2H, J = 7.0), 2.98 (t, 4H, J = 7.0), 3.81 (s, 3H), 6.58 (d, 1H, J = 16.0), 6.79 (s, 1H), 6.85 (d, 2H, J = 8.0), 7.45 (d, 2H, J = 8.0), 8.02 (d, 1H, J = 16.0)	292 (M^+, 93)
5e	53	139–141	$C_{14}H_{14}OS_2$ (262.4)	1630, 1580, 1485, 1120	2.65 (s, 3H), 3.35 (m, 4H), 6.53 (s, 1H), 6.83 (s, 1H), 7.83–7.1 (m, 5H)	262 (M^+, 28)
5f	88	125–127	$C_{19}H_{16}OS_2$ (324.4)	1580, 1480, 1200	3.28 (m, 4H), 6.18 (s, 1H), 6.54 (s, 1H), 7.25 (s, 10H)	324 (M^+, 67)
5g	91	128–130	$C_{20}H_{18}OS_2$ (338.5)	1610, 1500, 1200	2.13 (m, 2H, J = 7.0), 2.85 (t, 4H, J = 7.0), 6.15 (s, 1H), 6.50 (s, 1H), 7.25 (s, 10H)	338 (M^+, 48)
5h	61	87–89	$C_{11}H_{16}OS_2$ (228.4)	2950, 1630, 1600, 1490, 1220	1.07 (s, 9H), 3.35 (m, 4H), 6.23 (d, 1H, J = 16.0), 6.83 (s, 1H), 6.97 (d, 1H, J = 16.0)	228 (M^+, 87)
5i	56	oil	$C_{12}H_{18}OS_2$ (242.4)	2950, 1640, 1590, 1490, 1240	1.12 (s, 9H), 2.2 (s, 3H), 3.37 (m, 4H), 6.03 (s, 1H), 6.63 (s, 1H)	242 (M^+, 35)

Table 2. (continued)

Product	Yield[a] (%)	mp (°C)[b]	Molecular Formula[c]	IR (KBr)[d] ν (cm^{-1})	^{1}H-NMR ($CDCl_3$/TMS)[e] δ, J(Hz)	MS (70 eV)[f] m/z (%)
5j′	84	64–65	$C_{13}H_{18}OS_2$ (254.4)	2900, 1620, 1480, 1280	1.2–2.5 (m, 10H), 3.1 (d, 2H, J = 7.0), 3.33 (m, 4H), 5.57 (t, 1H, J = 7.0), 6.55 (s, 1H)	254 (M^+, 1)
5k′	98	53–55	$C_{12}H_{16}OS_2$ (240.4)	2900, 1620, 1470, 1420	1.00–2.40 (m, 8H), 2.98 (s, 2H), 3.34 (m, 4H), 5.50 (br s, 1H), 6.60 (s, 1H)	240 (M^+, 11)

[a] Yield of isolated product except **5e**, **5h**, **5i** and **5j′** of which yields were based on **1**.
[b] Uncorrected.
[c] Accurate mass determined (±0.0018 mass units).
[d] See Table 1.
[e] Recorded on a Jeol PMX 60 SI spectrometer and varian FT-80A spectrometer.
[f] See Table 1.

Table 3. Compounds **3** Prepared

Product	Yield[a] (%)	mp (°C)[b]	Molecular Formula[c]	IR (KBr)[d] ν (cm^{-1})	^{1}H-NMR ($CDCl_3$/TMS)[e] δ, J(Hz)	MS (70 eV)[f] m/z (%)
3c	65	209–210 (dec)	$C_{15}H_{14}O_4S_2$ (322.4)	1670, 1630, 1510, 1400, 1240	2.88 (dd, 1H, J = 3.3, 16.6), 3.02 (dd, 1H, J = 11.5, 16.6), 3.37–3.51 (m, 4H), 3.82 (s, 3H), 5.44 (dd, 1H, J = 3.3, 11.5), 6.92 (d, 2H, J = 6.6), 7.35 (d, 2H, J = 6.6)	322 (M^+, 23)
3e	73	235–237 (dec)	$C_{15}H_{14}O_3S_2$ (306.4)	1680, 1630, 1490, 1390, 1240	1.72 (s, 3H), 3.05 (d, 1H, J = 16.4), 3.27 (d, 1H, J = 16.4), 3.25–3.42 (m, 4H), 7.26–7.42 (m, 5H)	306 (M^+, 44)
3h	68	179–180	$C_{12}H_{16}O_3S_2$ (272.4)	1675, 1630, 1410, 1230	0.95 (s, 9H), 2.47 (dd, 1H, J = 2.4, 16.3), 2.67 (dd, 1H, J = 12.8, 16.3), 3.27–3.62 (m, 4H), 4.14 (dd, 1H, J = 2.4, 12.8)	272 (M^+, 18)
3i	82	162–164	$C_{13}H_{18}O_3S_2$ (286.4)	1670, 1640, 1420, 1240	1.06 (s, 9H), 1.34 (d, 3H, J = 1.0), 2.55 (d, 1H, J = 16.2), 2.92 (dd, 1H, J = 1.0, 16.2), 2.35–3.55 (m, 4H)	286 (M^+, 7)

[a] Yield of isolated product **3** based on ethyl acetoacetate.
[b] Uncorrected.
[c] Satisfactory microanalyses obtained: C ±0.44, H ±0.30.
[d] Recorded on a Shimadzu IR-435 spectrophotometer.
[e] Recorded on a Bruker AM-300 spectrometer.
[f] Obtained on a Shimadzu QP-1000 spectrometer.

The other ketene dithioacetals **4** were found to decarboxylate smoothly to give the corresponding alkenoyl- and cinnamoylketene dithioacetals **5** (see Table 2). The ^{1}H-NMR data (J = 16 Hz, for HC=CH) for **4a–d, h** and **5a–d, h** indicated that the E isomers were formed exclusively. Examination of a Dreiding model revealed that the most stable conformation of intermediate **3** has a proton being removed and the carboxylate leaving group in an antiperiplanar geometry. Therefore, an anti-elimination mechanism would explain the observation of E isomers.

2-(1-Carboxy-2-oxo-4,4-diphenyl-3-butenylidene)-1,3-dithietane (4f); Typical Procedure:
To a stirred solution of 2-acetyl(ethoxycarbonyl)methylene-1,3-dithietane (**1**; 2.32 g, 10 mmol) in dry THF (50 mL), is added NaH (0.84 g, 59% in mineral oil dispersion, 21 mmol) under a nitrogen atmosphere. After stirring for 10 min, benzophenone (**2f**; 1.89 g, 10.4 mmol) is added over 30 min period. Stirring is continued for 5 h at r.t. until no starting material is detected by TLC (hexane/EtOAc = 3:1). The reaction mixture is poured into cold 5% HCl (30 mL) and the precipitate filtered and recrystallized from EtOH to afford the desired **4f** as yellow needles; yield: 3.60 g (98%).

2-(2-Oxo-4,4-diphenyl-3-butenylidene)-1,3-dithietane (4f); Typical Procedure:
Compound **4f** (3.68 g, 10 mmol) is heated in an oil bath at 180 ~ 195 °C for 15 min until the evolution of carbon dioxide ceased. The obtained solid is recrystallized from EtOH to give **5f** as yellow needles: yield: 2.85 g (88%).

3-(1,3-Dithiet-2-ylidene)-2,4-dioxotetrahydropyran 3; General Procedure:
To a well-stirred suspension of 2,4-dioxotetrahydropyran (0.1 mol) and anhydrous K_2CO_3 (0.3 mol) in DMF (50 mL), is added CS_2 (0.15 mol) at r.t. To the reaction mixture 1,2-dibromoethane (0.12 mol) is added dropwise over 30 min. Stirring is continued 7 h at r.t. Ice-water (500 mL) is added to precipitate the yellow-colored product, which is recrystallized from EtOH to give **3** (Table 3).

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(7) The acid **4e** present in the mixture was being decarboxylated to afford **5e** during column chromatography.
(8) When **3i** prepared separately was subjected to reaction condition (2 eq NaH/THF) it was recovered intact. However when 1 equiv of abs EtOH was added to the reaction mixture, conjugated isomer of **4i** was obtained within 2 hr which upon prolonged stirring (overnight) was changed into **4i**′.
(9) While small amount (7%) of conjugated isomer of **5j** was formed after decarboxylation of **4j**′, **4k**′ did not give any corresponding conjugated isomer of **5k**.