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DEALKYLATIVE DECARBOXYLATION. IV[1]. A NOVEL APPROACH TO KETENE THIOACETALS

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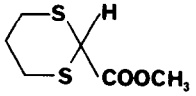
Abstract: Reaction of 2-carbomethoxy-1,3-dithiane enolate with an equimolar mixture of trimethylacetyl chloride and an aldehyde followed by dealkylative decarboxylation of the resulting pivalate yields ketene thioacetals.

Ketene thioacetals are versatile synthetic intermediates which have been employed as precursors to aldehydes and ketones (2a), carboxylic acids (2b), and cyclopropanes (2c); as substrates in Diels-Alder reactions (2d); and as Michael acceptors (2e). Preparations of ketene thioacetals include the transformation of carboxylic acid derivatives (3a), Peterson olefination (3b), Wittig (3c) and Horner-Emmons (3d) reactions, and heterolytic fragmentation (3e).

Halide-initiated dealkylative decarboxylation (4) provides a mild method for the generation of stabilized carbanions (5). Application of this procedure to suitable derivatives of 2-carbomethoxy-1,3-dithiane (6) affords an efficient route to ketene thioacetals. An important advantage of this methodology is the ability to mask, in a latent form easily expressed upon halide thermolysis, the somewhat sensitive ketene thioacetal moiety.

Thioacetal ester enolate **2** (7) failed to form an isolable adduct with aldehydes or ketones. However, dropwise addition of a 1:1 mixture of trimethylacetyl chloride and a suitable aldehyde in THF to a cold, well-stirred solution of **2** led to efficient trapping of the intermediate alkoxide as the pivaloxy ester **3**. This general reaction proceeds in quite reasonable yield (TABLE) (8).

Upon heating in dry DMF with excess anhydrous LiI, these pivalates undergo smooth fragmentation to ketene thioacetals **4**. NMR spectra of the crude reaction mixtures indicate the ketene thioacetal is the overwhelming constituent. The phenoxyacetaldehyde derivative is the only substrate which failed to fragment.



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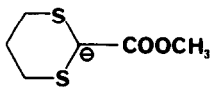

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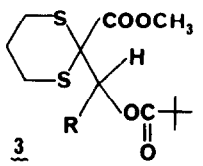

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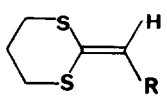
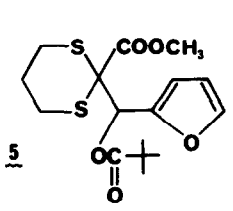


4

A direct competition experiment involving addition of a 1:1:1 mixture of 2-furaldehyde, 4-tert-butylcyclohexanone, and trimethylacetyl chloride to **2** led exclusively to **5**. Cyclohexyl adduct **6** was not observed (our estimated detection limit is 3-4%). This result suggests that high chemoselectivity in ketene thioacetal formation could be achieved in substrates possessing both aldehyde and ketone functionalities.

Systems whose potential leaving group is separated from the dithiane moiety by additional carbon atoms also have been examined. Carbocyclic products (e.g. **7**) could not be isolated from these reactions. However, attempted dealkylative decarboxylation of **8** does produce lactone **9** in high yield.



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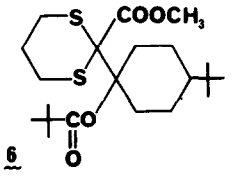

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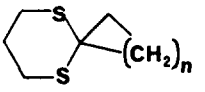

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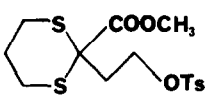

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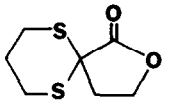


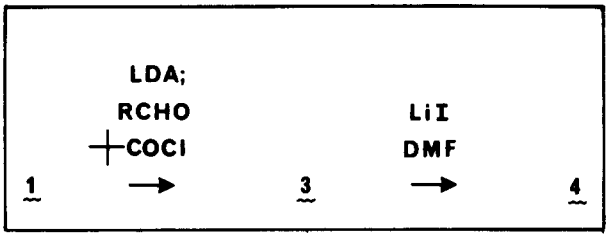
9

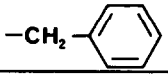
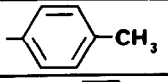
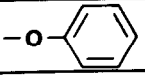
A typical enolate trapping/heterolytic fragmentation sequence is as follows:

Dithiane ester **1** (0.534 g; 3.0 mmoles) was added dropwise at -78° to a preformed solution of LDA (3.0 mmoles) in THF (25 mL). The resulting pale yellow solution was allowed to warm to -10° over 1 hour. After the enolate had been recooled to -78° a solution of pivaloyl chloride (0.362 g; 3.0 mmoles) and octyl aldehyde (0.386 g; 3.0 mmoles) in THF (10 mL) was added. The resulting mixture was stirred 2 hours at room temperature and then partitioned between ether and water. The organic layer was washed with dilute HCl, saturated bicarbonate, and saturated brine, dried, and evaporated to a yellow oil. Purification by flash chromatography afforded 0.883 g (75%) of pure pivalate.

To 0.230 g (0.59 mmoles) of the pivalate in 5 ml of DMF (freshly distilled from CaH_2 and stored over 4A molecular sieves) was added anhydrous LiI (0.400 g; 3.0 mmoles). The reaction mixture was stirred under nitrogen for 2 hours at 150°, cooled to room temperature, diluted with water, the pH adjusted to 5.0, and then extracted with ether. The organic layer was washed with water and saturated brine, dried, and evaporated to a pale brown syrup. Flash chromatography gave 0.111 g (82%) of colorless, analytically pure ketene thioacetal.

TABLE



R	3 Yield (%)	4 Yield (%)	δ PPM (vinyl H)
$-(CH_2)_6CH_3$	75	82	5.9 (t)
$-(CH_2)_8CH=CH_2$	65	70	5.9 (t)
	74	79	5.7 (d)
	40	72	6.1 (t)
$-CH=CH-CH=CHCH_3$	80	80	6.4 (d)
$-CH(CH_3)_2$	62	75	5.8 (d)
	73	68	6.7 (s)
$-CH=CH\phi$	62	78	6.4 (d)
$-CH(CH_3)\phi$	41	75	6.0 (d)
	63	78	6.9 (s)
	65	–	–

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8. All compounds described in this paper gave satisfactory analytical data.

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