

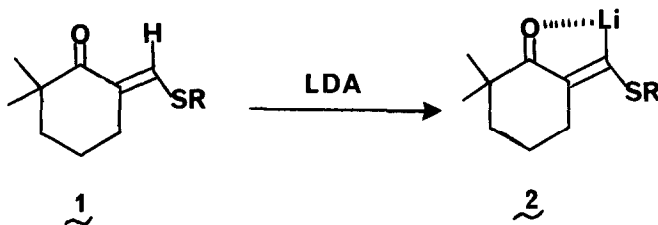
DEPROTONATION STUDIES IN  $\alpha$ -OXOKETENE DITHIOACETALS. I.<sup>1</sup>

J. P. Marino\* and J. L. Kostusyk

Department of Chemistry, University of Michigan,  
Ann Arbor, Michigan 48109

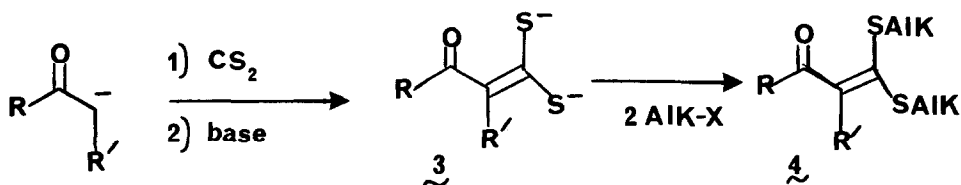
Deprotonations of  $\alpha$ -benzoyl ketene dithiomethylacetals with LDA/HMPA resulted in kinetic deprotonations at three different sites depending on the other  $\alpha$ -substituents.

A variety of synthetic approaches have recently been reported for the preparation of substituted ketene dithioacetals<sup>2</sup> and  $\alpha$ -oxoketene dithioacetals.<sup>3</sup> With few exceptions,<sup>3c</sup> the synthetic methods described to date have involved ketene dithioacetals which are devoid of other carbanion-stabilizing groups. We have been interested in synthetic applications of functionalized vinyl and allyl carbanions stabilized by sulfur. Recently we reported<sup>4</sup> that deprotonation of the  $\alpha$ -thiomethylene cyclohexanone derivative 1 yields the oxo-stabilized vinyl lithium species 2 rather than a sulfur-stabilized allyl lithium species. The regioselective deprotonation of unsaturated systems containing  $\alpha$  or  $\beta$  heteroatoms has only recently become a synthetically useful process.<sup>5</sup>



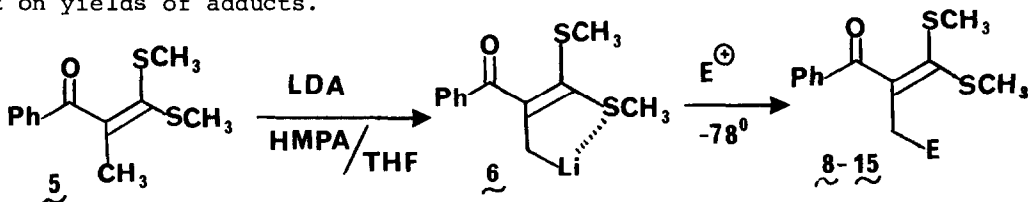
In this and the accompanying communication we wish to report our results for some deprotonation reactions of  $\alpha$ -oxoketene dithioacetals of general structure 4. We chose to study these compounds in order to avoid vinyl anion formation, as in 1, and to direct allyl anion generation in systems which contain strong complexing and electron-withdrawing moieties cross-conjugated with allyl anions.

The  $\alpha$ -oxoketene dithioacetals can be readily prepared<sup>3b</sup> by the condensation of the corresponding enolates with carbon disulfide, followed by alkylation of the intermediate dithiolate species 3. This general synthetic approach is applicable not only to enolates of ketones but also enolates of



esters and amides. The condensation product of propiophenone, 5, served as a convenient starting point for our allyl anion. Trapping of the allyl anion 6 with various electrophiles could only be accomplished if the deprotonation was affected with LDA and three equivalents of hexamethylphosphorotriamide (HPMA)<sup>6</sup> in THF (10% HMPA by volume).

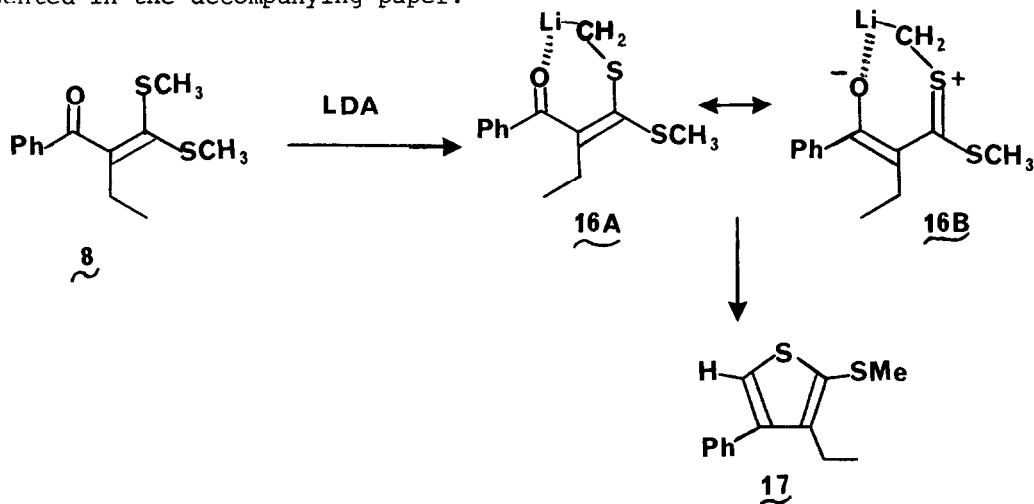
All of the products (8-15)<sup>7</sup> from the quenching of anion 6 were isolated by column chromatography along with considerable amounts of starting material 5. The combined yield of adduct and 5 for each experiment usually exceeded 90%. The low yields of 11, 12 and 13 are probably a result of the anion 6 deprotonating the highly acidic hydrogens of the electrophile, while the products 14 and 15 contain acidic hydrogens which may be removed by 6. Increasing the number of equivalents of LDA did not have any significant effect on yields of adducts.



E <sup>+</sup>	Adduct (% Yield)	E <sup>+</sup>	Adduct (% Yield)
MeI	<u>8</u> 70%	Mesityl Oxide <sup>8</sup>	<u>12</u> 40%
DCl	<u>9</u> 90%	BrCH <sub>2</sub> CO <sub>2</sub> Et	<u>13</u> 35%
PhCHO	<u>10</u> 65%	PhCO <sub>2</sub> CH <sub>3</sub>	<u>14</u> 42%
PhCOCH <sub>3</sub>	<u>11</u> 25%	Me-S-S-Me	<u>15</u> 50%

The regioselectivity observed for the reactions of anion 6 with electrophiles can easily be rationalized by steric factors. A more informative system for the test of regioselectivity is the methylated product 8. Treatment of 8 with LDA and HMPA at -78° followed by an excess of methyl iodide yielded no methylated products. Instead, the kinetic site of deprotonation was the S-methyl group which is cis to the carbonyl oxygen. Furthermore,

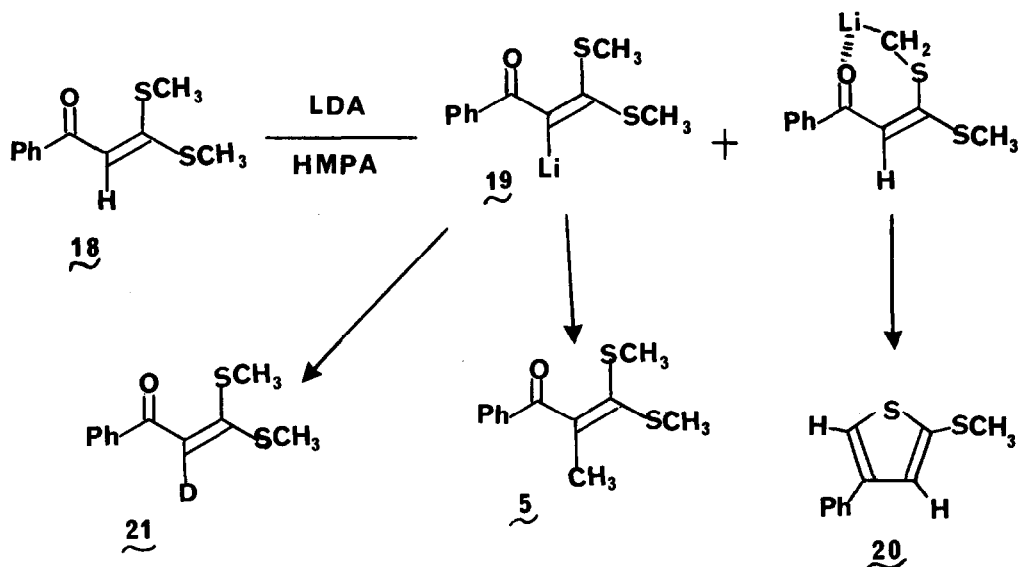
the intermediate lithio species 16 could not be trapped with methyl iodide or deuterium chloride, since it smoothly cyclized to the thiophene 17. Details of this process as a general route to 2-mercaptothiophenes are presented in the accompanying paper.



Failure to incorporate deuterium in the thiophene 17 or in recovered 8 argues against random deprotonation of the S-methyl units. It appears that the regioselective deprotonation of the S-methyl group *cis* to the carbonyl adds credibility to the concept of dipole-stabilized carbanions advanced by Beak,<sup>9</sup> i.e., structure 16B. The deprotonation alpha to sulfur as in 8 is also limited to S-methyl dithioacetals. When the S-ethyl analogue of 8 was subjected to the same base conditions, only starting material was reisolated. Thus, under these reaction conditions, neither allyl anion formation nor S-ethyl deprotonation was observed.

A further interesting development was unveiled when the acetophenone adduct 18 was subjected to the LDA/HMPA conditions. Upon quenching the reaction mixture with methyl iodide, a mixture of thiophene 20 (30%) and the methylated product 5 (35%) was obtained. A deuterium quench of a basic solution of 18 yielded both the thiophene 20 and the  $\alpha$ -deuterio ketone 21. While other mechanistic possibilities cannot be ruled out at this time, we believe that products 5 and 21 are the result of quenching the unique  $\alpha$ -keto vinyl lithium species 19. Furthermore, we have found that replacement of LDA with lithium hexamethyldisilazane (LHMDS) leads to the clean generation of anion 19 and a 90% isolated yield of 5, with no production of thiophene 20.

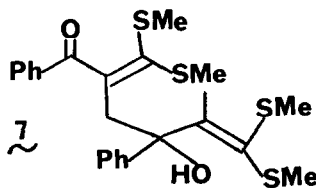
The multiple deprotonations observed for compounds 5, 8 and 18 represent significant and useful examples of regioselective anion formation as dictated by subtle structural variations. The interplay of electronic and steric



factors, as well as complexation effects, is uniquely manifested in the  $\alpha$ -oxoketene dimethylthioacetal systems. Further studies on deprotonations of functionalized vinyl sulfides are in progress.

#### References and Footnotes

1. Presented in part at the 175th ACS National Meeting, Anaheim, California, March 13-17, 1978, ORGN 23.
2. For a recent review of the chemistry of this class of compounds see: B.-T. Grobel and D. Seebach, *Synthesis*, 357 (1977) and references therein
3. (a) R. Gompper and W. Topfl, *Ber.*, **86**, 2861 (1962); (b) I. Shahok and Y. Sasson, *Tetrahedron Lett.*, 4207 (1973); (c) E. J. Corey and R. Chen, *Tetrahedron Lett.*, 3817 (1973).
4. J. P. Marino, M. Neisser and W. M. Butler, 175th ACS National Meeting, Anaheim, California, March 13-17, 1978, ORGN 22.
5. S. J. Gould and B. M. Remillard, *Tetrahedron Lett.*, 4353 (1978).
6. Without HMPA, a 50% yield of the dimer **7** was isolated. With HMPA, the deprotonation step was complete within 30 minutes at  $-78^\circ$  and the quenching step was also very fast.



7. All new compounds (**7-15**, **17**, **20**, **21**) had IR, NMR, UV, C-13 and elemental analyses ( $\pm 0.2\%$ ) consistent with the assigned structures.
8. The adduct **12** from mesityl oxide was the result of 1,2-attack by anion **6**.
9. D. B. Reitz, P. Beak, R. F. Farney and L. S. Helmick, *J. Am. Chem. Soc.*, **100**, 5428 (1978).

(Received in USA 15 March 1979)