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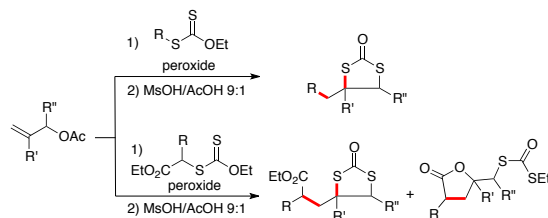
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A Convergent Approach to 1,3-Dithiolan-2-ones and an Unexpected Synthesis of Lactones

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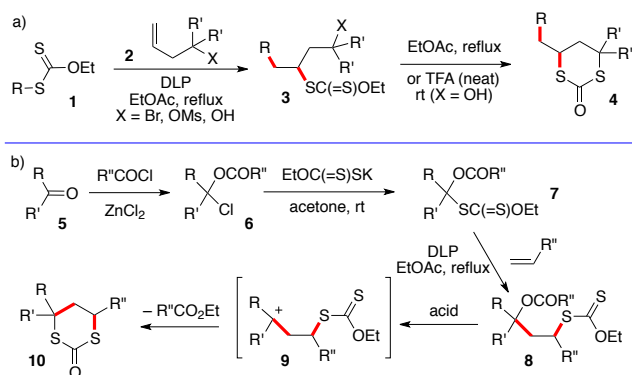
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ABSTRACT: A convergent route to 1,3-dithiolan-2-ones based on the radical addition of xanthates to allylic acetates is described. The process is modular, uses inexpensive starting materials and reagents, and is atom economical, since both sulfur atoms of the xanthate end up in the products. With adducts derived from xanthates bearing an ester group, an unexpected transformation leading to lactones was uncovered.

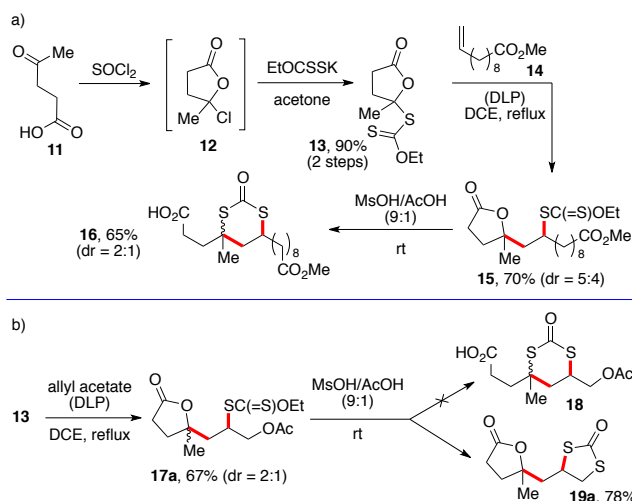
We developed convenient routes to dithianone **4** based on the radical addition of xanthates **1** to alkenes of general structure **2**, where X is a leaving group such as a bromide or a sulfonate (Scheme 1a).¹ The addition leads to adducts **3** which undergoes concomitant ionic ring-closure with ultimate elimination of EtX. It is therefore sufficient to simply keep heating the reaction mixture to complete the process without the need to isolate intermediate adduct **3**. To complement this one-pot procedure, we conceived of an alternative approach whereby the xanthate would bear the latent leaving group, thus allowing the use of a broader variety of alkene partners.² It is based on the availability of xanthates of type **7** derived from ketones **5** through the geminal acetoxy chlorides **6** (Scheme 1b).^{3,4} The radical addition would then lead to adducts **8** possessing a tertiary acetate and therefore capable, under the action of a strong acid, of generating a tertiary cation **9** that would be captured internally by the neighboring xanthate to give finally 1,3-dithianones **10**.

Scheme 1. Convergent Routes to 1,3-Dithian-2-ones



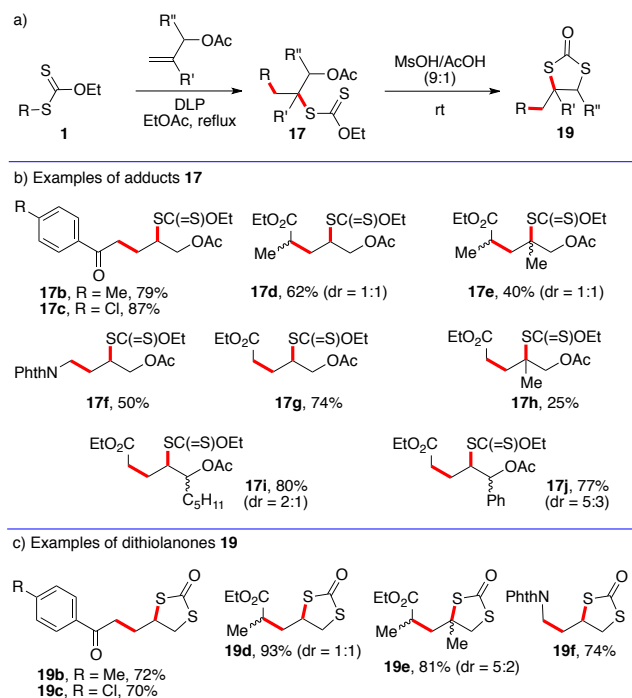
We earlier illustrated this strategy on one example involving the addition of xanthate **13** derived from levulinic acid **11** to methyl 10-undecenoate **14** leading to adduct **15** (Scheme 2a).¹ Treatment with a 9:1 mixture of methanesulfonic acid (MsOH) and acetic acid furnished the expected dithianone **16**. It is worth emphasizing again that this synthesis is not only convergent and atom economical, but all the carbon atoms in the main chain of dithianone **16** are derived from the biomass. Levulinic acid **11** is produced from lignocellulosic waste,⁵ and methyl 10-undecenoate **14** is derived from castor oil.⁶ However, when we attempted to extend this reaction to allyl acetate adduct **17a**, no 1,3-dithian-2-one **18** was observed. Instead, we isolated 1,3-dithiolan-2-one **19a** in good yield (Scheme 2b). The displacement of the primary acetate is clearly faster than the opening of the tertiary lactone, even though under acidic conditions the latter would lead to a more stable tertiary cation. The process therefore appears to have more of an S_N2 than an S_N1 character.

Scheme 2. Unexpected Route to 1,3-Dithiolan-2-ones



This observation opened a simple route to 1,3-dithiolan-2-ones **19** through the two-step sequence displayed in Scheme 3a. First, addition of xanthates **1** to various allyl acetates to give the corresponding adducts **17** followed next by exposure to MsOH/acetic acid to induce ring closure to the desired 1,3-dithiolan-2-ones **19**. Adducts **17b-j**, prepared uneventfully according to the first step, are collected in Scheme 3b. Treatment of the first five, **17b-f**, furnished indeed the expected 1,3-dithiolan-2-ones **19b-f** (Scheme 3c). Thus, by an appropriate choice of the alkene partner, both 1,3-dithian-2-ones **4** and 1,3-dithiolan-2-ones **19** can be prepared in just two steps, often accomplished in a one-pot operation. They correspond to conveniently protected forms of 1,3- and 1,2-dithiols.

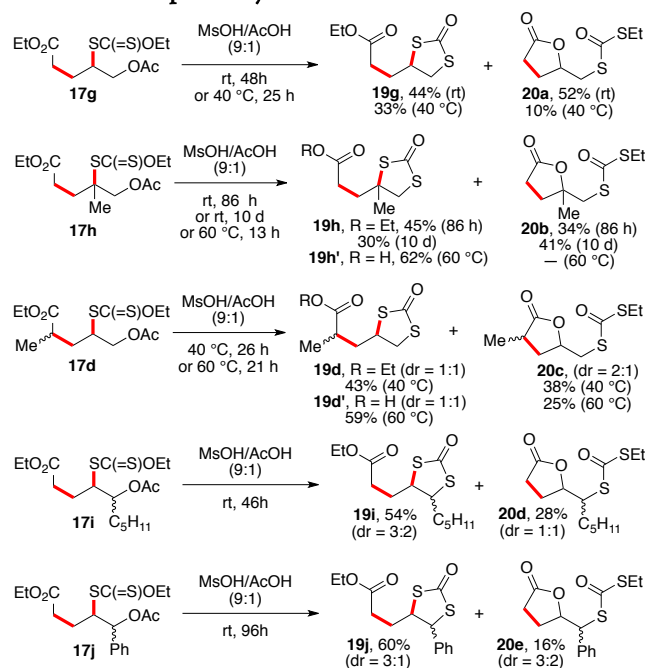
Scheme 3. Examples of 1,3-Dithiolan-2-ones



When we extended this procedure to adduct **17g**, we were surprised to find lactone **20a** alongside the expected dithiolanone **19g** (Scheme 4). Furthermore, heating to 40 °C caused a significant

decrease in the yield of both products. An indication of the cause of this decline came when we examined methallyl acetate adduct **17h**. After 86 h at room temperature, dithiolanone **19h** and lactone **20b** were isolated in 45% and 34% respectively. After 10 days at room temperature, the yield of the former dropped to 30% and the latter increased slightly to 41%, and raising the temperature to 60 °C furnished only carboxylic acid **19h'** in 62% and no lactone **20b**. A similar trend was observed with branched ester **17d**. At room temperature, only dithiolanone **19d** was formed in high yield (93%, see Scheme 3c). At 40 °C, the corresponding lactone **20c** was produced in 38% yield, while the yield of dithiolanone **19d** decreased to 43%. At 60 °C, the carboxylic acid **19d'** now dominated but a certain amount of lactone **20c** remained (25%). Presumably, steric hindrance due to the α -methyl group slows down the hydrolysis of the ester and allows the formation of lactone **20c** at the higher reaction temperatures. Finally, adducts **17i** and **17j**, furnished corresponding lactones **20d** and **20e** in modest yield, in addition to the respective dithiolanones **19i** and **19j**.

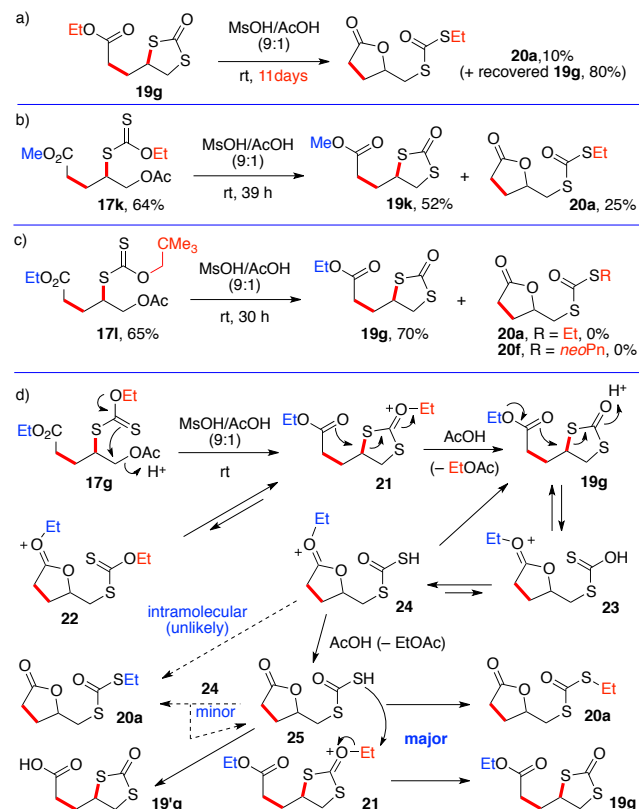
Scheme 4. Unexpected Synthesis of Lactones



Our initial mechanistic hypothesis was that lactones **20a-e** arose from the respective dithiolanones **19** and the ethyl group present on the dithiocarbonate came from the ethyl carboxylate (the Et group in red in Scheme 5a). We therefore exposed dithiolanone **19g** to the action of MsOH/AcOH for 11 days at room temperature. While the corresponding lactone **20a** was indeed produced, the yield was very low, only 10%, and the starting material was mostly recovered intact (Scheme 5a). Obviously, this pathway, if it operates at all, must be a minor one. This was confirmed by a second experiment starting with methyl ester analog **17k** which gave rise to the corresponding dithiolanones **19k** and lactone **20a** bearing an *ethyl* dithiocarbonate side chain (Scheme 5b). This ethyl group must therefore derive from the xanthate and not from the carboxylate. In a third experiment starting with the bulkier *O*-neopentyl (*neoPn*) xanthate **17l**, the reaction furnished only dithiolanones **19g**; neither the *O*-ethyl nor the *O*-neopentyl dithiocarbonate **20a** or **20f** was observed in any significant quantities, in contrast to *O*-ethyl xanthate analog **17g**,

which gave rise to 52% of *O*-ethyl dithiocarbonate **20a** (first reaction in Scheme 4).

Scheme 5. Further Experiments and Mechanistic Hypothesis

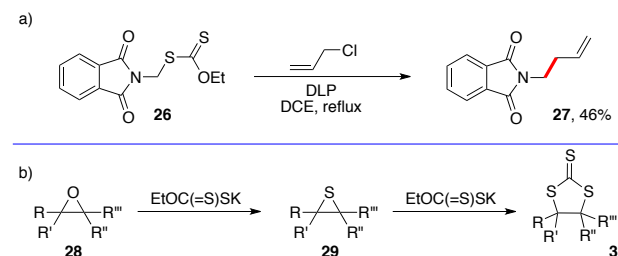


In light of the above experiments, it is possible to formulate a mechanism for this unexpected transformation (Scheme 5d). For clarity, it is outlined for the case of adduct **17g**. Acid catalyzed displacement of the acetate furnishes intermediate **21**, which can undergo a *reversible* ring opening to give derivative **22**. The equilibrium presumably favors the former, where the positive charge is stabilized by the unpaired electrons of *two* sulfur atoms. Cleavage by acetic acid leads to the observed dithiolanone **19g**; however, because of the presence of the neighboring ester group, this first product can evolve further. Protonation induces a *reversible* ring opening to provide intermediate **24**, which is slowly cleaved by acetic acid into lactone **25**. Reaction with intermediate **21** delivers final lactone **20a** as well as dithiolanone **19g**.⁷ The alkylation of lactone **25** by intermediate **24** is also possible but appears to be a minor pathway, possibly because of the lower concentration of intermediate **24** as compared to **21**. This would also explain the very slow transformation of dithiolanone **19g** into lactone **20a** (Scheme 5a). Note that in this minor path, the (blue) ethyl group derives from the ester and not the xanthate. The intramolecular conversion of intermediate **24** into lactone **20a** is unlikely on geometrical grounds. Finally, raising the temperature speeds up the acid induced opening of the lactone in compound **25** to give the free acid **19g'**, and this step eventually overtakes the alkylation step; thus, the predominant formation of **19g'** from adduct **17h** at 60 °C.

In summary, we have developed a practical route to 1,3-dithiolan-2-ones that uses inexpensive, readily available starting materials. Following the suggestion of a referee, an attempt was made to directly form 1,3-dithiolan-2-ones **19** in a manner similar to that for

1,3-dithian-2-ones **4** (Scheme 1a), by replacing allyl acetate with allyl chloride. In the event, the reaction of xanthate **26** with allyl chloride only furnished the corresponding allyl derivative **27** in 46% yield (Scheme 6a). This is not totally surprising since the radical addition-elimination on allyl halides (except fluorides) is preceded, albeit seldom used.⁸

Scheme 6. Allylation with Allyl Chloride and Synthesis of Cyclic Trithiocarbonates



1,3-dithiolan-2-ones are in fact protected 1,2-dithiols.⁹ These are valuable materials for surface modification and in polymer chemistry among various other uses.¹⁰ In this context, it is worth pointing out a little-known reaction of epoxides **28** with xanthate salts, which furnishes cyclic trithiocarbonates **30** (Scheme 6b) and these can also be considered as masked 1,2-dithiols.¹¹ The reaction proceeds via episulfides **29** that can sometimes be isolated. While this method does not involve the creation of a new carbon-carbon bond, it could be used to make cyclic 1,2-dithiol by starting with epoxides derived from cyclic alkenes. The radical and the ionic approaches are thus complementary.

ASSOCIATED CONTENT

Supporting Information

Experimental procedures, full spectroscopic data, and copies of ¹H and ¹³C NMR for all new compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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