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FUNCTIONALIZED CYCLOPENTANES VIA RADICAL CYCLIZATIONS USING THIOCARBONATE DERIVATIVES AS INITIATORS AND TERMINATORS

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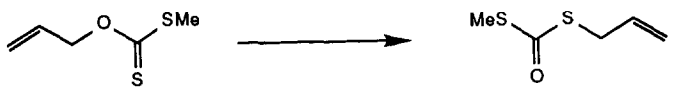
Abstract: A radical-based cyclization is described that employs xanthates or cyclic thionocarbonates as initiators and allylic dithiocarbonates or allylic thiocarbamates as terminators.

The practicality of free radical reactions to serve as a means of forming carbon-carbon bonds has been amply demonstrated over the past decade.[1] One of the goals of this area of synthetic chemistry is to design free radical cyclization reactions that provide highly functionalized products. In this Letter we report the use of two known reactions of sulfur compounds to realize this goal.

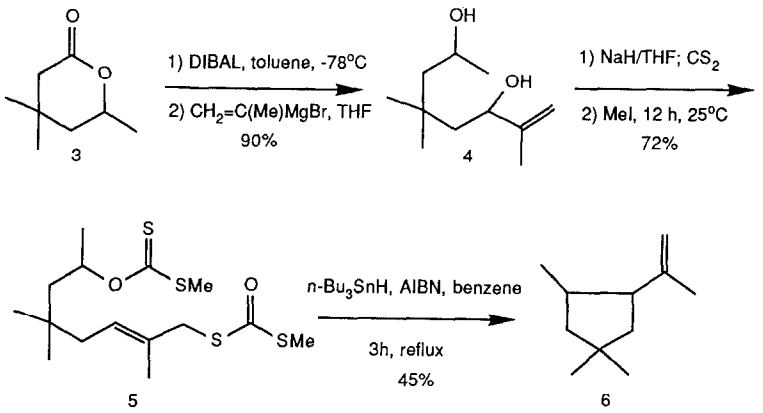
In 1909, Oddo and del Rosso[2] unknowingly observed the prototypical [3,3]-sigmatropic rearrangement of allyl S-methyl xanthate **1** to allyl S-methyl dithiocarbonate **2**. In the interim,



1 2

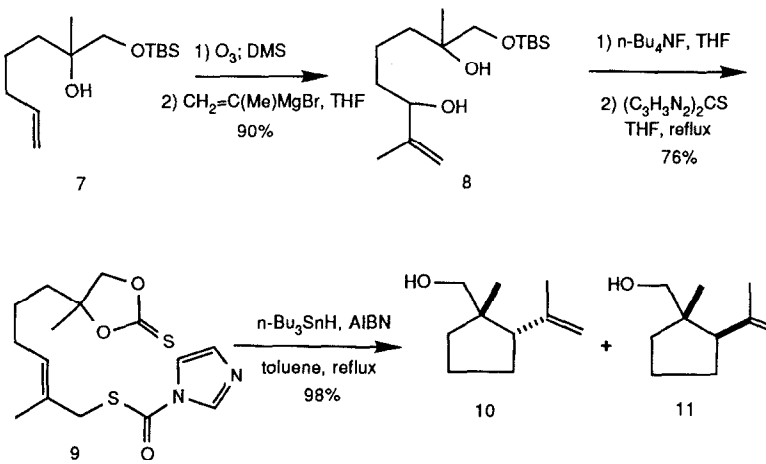
Harano,[3] Nakai[4] and Ueno[5] have studied the mechanism of the rearrangement and have applied the reaction synthetically. Secondly, Barton's now classic procedure for the free radical deoxygenation of alcohols can employ xanthates or thionocarbamates (thiocarbonyl imidazolides).[6] In the context of a more elaborate synthetic problem, we considered that these seemingly unrelated reactions of thiocarbonates could become willing partners in a useful free radical-based cyclization reaction.

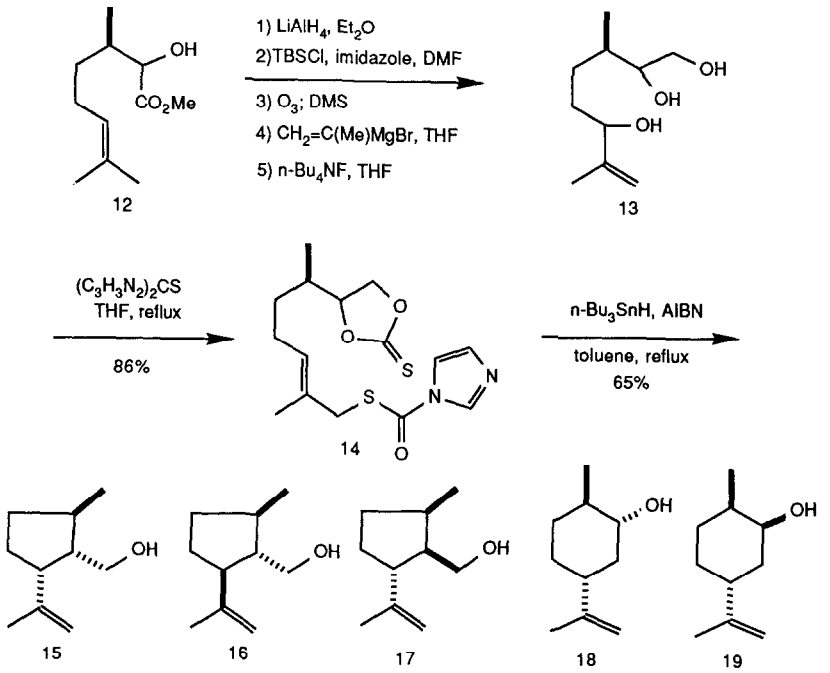
Diol **4**[7] was readily prepared from the known lactone **3**[8]. An attempt to prepare the bis-xanthate of the diol gave directly the allylic dithiocarbonate **5**. The Barton mechanism for the deoxygenation invokes attack of the carbon-sulfur double bond at sulfur by the tri-n-butylstannyl



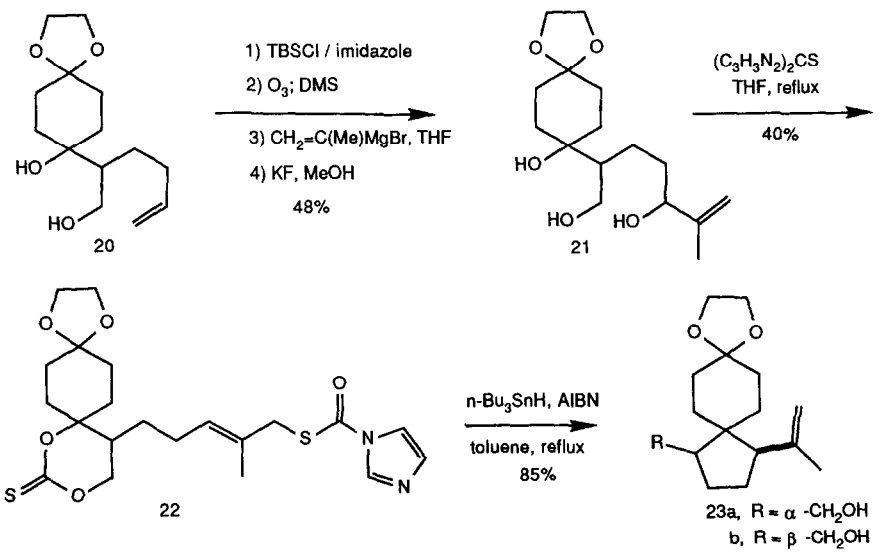
radical.[6,9] Accordingly, the xanthate can act as the radical initiator and the allylic dithiocarbonate as the terminator. In the event, the reaction gave a 5:1 (cis:trans) mixture of olefins **6**.[10] The ^{1}H NMR spectrum of the cis isomer displayed the vinyl hydrogens as distinct signals, while the trans isomer's vinyl hydrogens appeared as a singlet.[11]

To increase the functionality at the initiator end of a chain, the cyclic thionocarbonate-allylic thiocarbamate **9** was prepared.[12] Not unexpectedly, radical generation occurred at the tertiary site to give a nearly equal mixture of the two hydroxyolefins **10** and **11**. The stereoisomer bearing the higher field methyl singlet in its ^{1}H NMR spectrum (δ 0.92 vs. 1.22) was assigned to structure **11**.[13] Neither six-membered ring products from formation of a primary radical, nor olefinic products formed by radical-initiated elimination of the diol functionality could be detected.[14]





On the contrary,[15] when methyl α-hydroxycitronellate **12**[16] was converted to the cyclic thionocarbonate-allylic dithiocarbamate **14**, a mixture of 5- to 6-membered ring cyclization products was isolated in a 4:1 ratio. The cyclopentanes were identified as **15**, **16** and **17**, formed in a ratio of 57:37:6.[17] The two major components derived from the secondary radical have a trans relationship



between the methyl and the hydroxymethyl indicating a preference for an equatorial methyl group on the tether during cyclization. Dihydrocarveol **18** and neodihydrocarveol **19**, identified as the $NaBH_4$ reduction of *trans*-dihydrocarvone, were formed in a 3:1 ratio.

Finally, the 1,3-thionocarbonate **22** underwent exclusive spirocyclization via the tertiary radical to give a 2:1 mixture of alcohols **23a** and **23b**. Oxidation (Swern), epimerization (MeONa/MeOH) and reduction ($NaBH_4$) gave a 12:1 mixture of **23a/23b**. The stereochemistry was assigned in analogy with epimerizations conducted upon intermediates in syntheses of cedrene.[18]

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