Single Step Synthesis of Norbornan-2-one Dithioacetals from Cyclopent-2-en-1-one Dithioacetals and Dienophiles

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2-(2-Mercaptoethylthio)cyclopenta-1,3-dienes are thermally generated *in situ* from cyclopent-2-en-1-one dithioacetals under neutral conditions and intercepted with dienophiles ultimately to give norbornan-2-one dithioacetals.

Recently, we demonstrated that cyclopent-2-en-1-one ethylene acetal **1a** is capable of undergoing ring cleavage to afford the cyclopenta-1,3-dienol ether **2a**, which in turn is trapped by dienophiles to give norbornan-2-one ethylene acetals **4a** in good yields.[1] This reaction should be synthetically valuable, since the transformation is purely a thermal process and hence it can be conducted under strictly neutral conditions. However there is a small drawback in that certain cyclopent-2-en-1-one acetals cannot be prepared directly from the corresponding carbonyl compounds.[2] In this context, it is desirable to extend the reaction to dithioacetals **1** (X = S), since they are readily accessible in the direct dithioacetalization of cyclopent-2-en-1-ones, at least when C-3 is substituted. In fact, we found that the reactions similar to those of the oxygen analogue took place smoothly, although a slightly higher temperature was required.

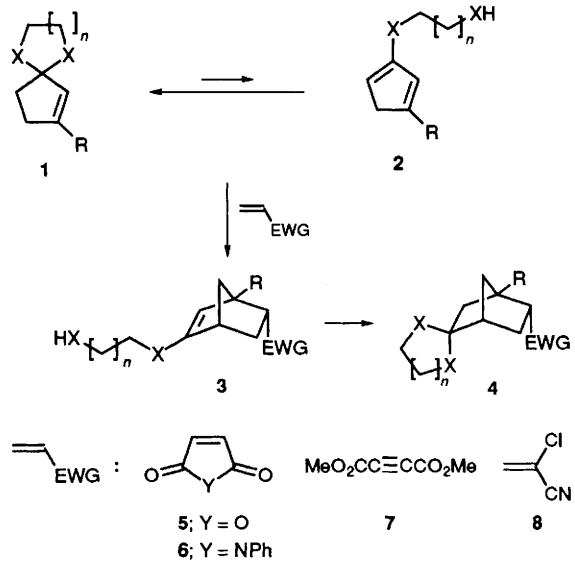
The reaction of **1b** with typical dienophiles **5–8** proceeded smoothly and cleanly in acetonitrile at 120 °C to afford the corresponding adducts in good yield. Various functionalized norbornan-2-one dithioacetals were synthesized similarly in a one-step process. The results are summarized in Table 1. Structural assignment of the adducts was primarily based on their 500 MHz ^{1}H NMR spectra including decoupling experiments. Unexpectedly, 1,3-dithiane **1c** is more reactive than 1,3-dithiolane **1b**, for reasons that are not clear at present. It is noteworthy that the addition of **7** to bicyclic derivatives **16** and **19** gave **18** and **21**, respectively, as a single stereoisomer. Their stereochemistry was unambiguously assigned by the absence (H^a–H^b in **18**) and the presence (H^c–H^d, J = 3 Hz, in **21**) of long-range coupling in these norbornene systems.

Table 1 Reactions of dithioacetals with dienophiles[a]

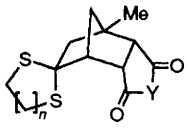
Dithioacetal	Dienophile	*t*/h	Adduct	Yield[b] (%) (*endo*:*exo*)
1b	**5**	5	**9**	97 (62:38)
	6	20	**10**	81 (87:13)
	7	9	**12**	78 (—)
	8[c]	24	**14**	83 (79:21)[d]
1c	**5**	3	**11**	90 (67:33)
	7	4	**13**	76 (—)
	8[c]	20	**15**	83 (66:34)[d]
16	**7**	18	**18**	68 (—)
19	**7**	18	**21**	69 (—)

[a] Reactions were carried out in acetonitrile (3 ml) using the dithioacetal (1 mmol) and 1.7 equiv. of the dienophile at 120 °C (in a sealed tube). [b] Isolated yield based on amount of dithioacetal used. Conversion of dithioacetal was almost complete. [c] 2,6-Dimethylpyridine (25 mol%) was added. [d] Ratio of two stereoisomers.

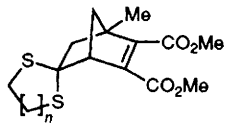
The formation of the adducts **4** (X = S) is best accounted for in terms of the Diels–Alder reaction of **2** (X = S), generated *in situ* from **1** (X = S) by 1,2-elimination, with dienophiles, followed by recyclization in the primary adduct **3** (X = S) to **4** (X = S) as in the case of oxygen analogue[1] (Scheme 1; EWG = electron-withdrawing group). The observed *endo*-selectivity and regioselectivity are also consistent with the intermediacy of **2** (X = S). The exclusive formation of the *exo*-H^b product **18** may be explained in terms of the preferential protonation of the vinyl sulfide double bond in the intermediate **17** from the *exo*-face upon recyclization. The exclusive formation of **21** is consistent with the π-facial selectivity expected for **20**, to which **7** approaches from the sterically less hindered face, *i.e.* *syn* to the angular hydrogen H^c.



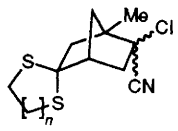
Scheme 1



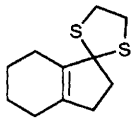
9; n = 1, Y = O
10; n = 1, Y = NPh
11; n = 2, Y = O



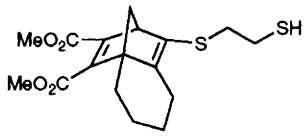
12; n = 1
13; n = 2



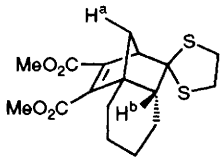
14; n = 1
15; n = 2



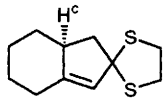
16



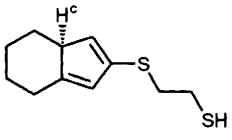
17



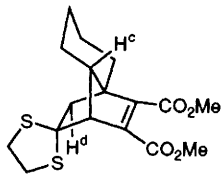
18



19



20



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The present method has several synthetic advantages. It is noteworthy, for example, that the reaction was not complicated by double bond scrambling in the cyclopentadiene intermediates **2** (X = S). Since the starting dithioacetals are readily accessible *via* direct dithioacetalization of the corresponding carbonyl compounds,[3] the reaction with dithioacetals has an advantage over that of the oxygen analogues. Furthermore, the dithioacetal group, which can serve as a useful intermediate in a variety of functional group transformations,[4] is introduced directly into the product.

The results obtained here suggest that cyclic dithioacetals may tend to isomerize to the ring-opened vinyl sulfide form reversibly and that these processes can be exploited synthetically. Although much attention has been paid to the chemistry of dithioacetals,[5] such a thermal equilibration has, to our knowledge, not previously been pointed out.

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