RING EXPANSION OF SPIROCYCLIC DITHIOKETALS *VIA* 1,3-SULFUR MIGRATION BY THE MITSUNOBU REACTION

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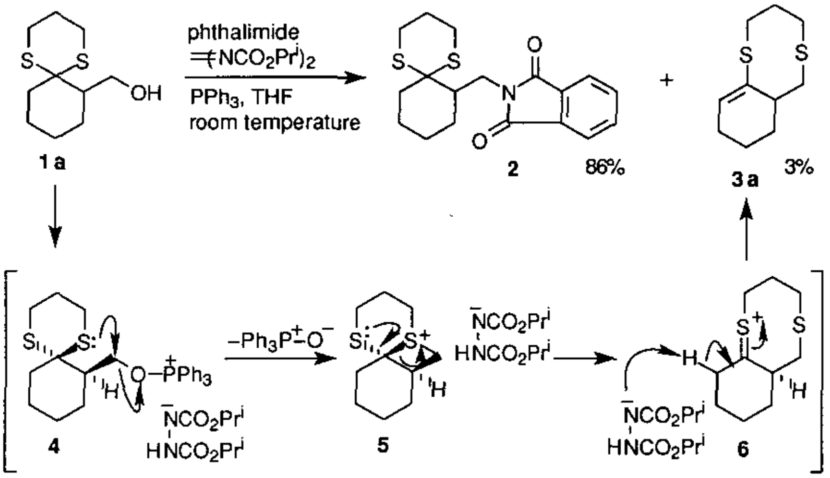
Abstract —— *Treatment of the spirocyclic dithioketals of some β-hydroxy* ketone derivatives with diisopropyl azodicarboxylate and triphenylphosphine furnished the ring-expanded products *via* 1,3-sulfur migration.

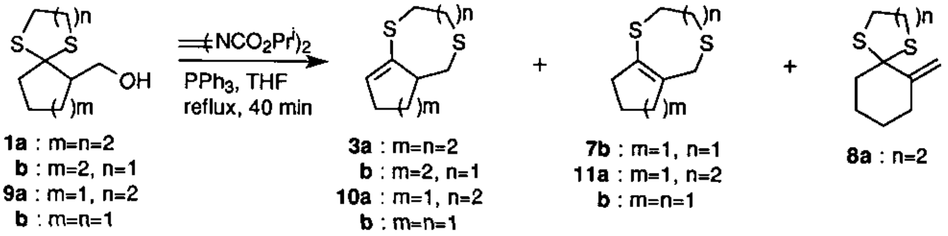
In relation to our ongoing synthetic study, we carried out displacement reaction of the hydroxy group of a dithioacetal (**1a**) of a β-hydroxy ketone by phthalimide by employing the Mitsunobu reaction.[1] The reaction afforded the expected *N*-substituted imide (**2**) in 86% and a trace (~3%) of the olefinic product (**3a**). The dehydration is rather common side-reaction encountered in the Mitsunobu reaction,[1b] however, **3a** was not the simple dehydration product but the ring expanded product involving 1,3-sulfur atom migration.[2~5] This may be reasoned by the preferential participation of the internal sulfur atom in the initially generated phosphonium intermediate (**4**) to form the sulfonium salt (**5**) which in turn collapsed to the sulfenium salt (**6**) to give the ring-expanded product (**3a**) (**Scheme 1**).



Scheme 1

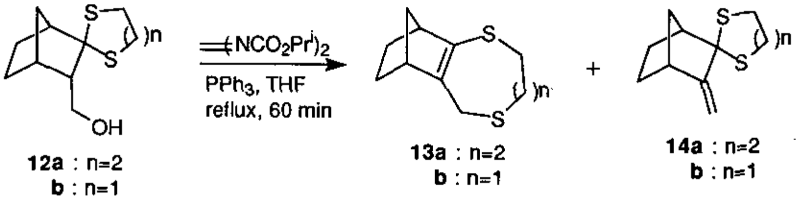
Since this indicates us that **3a** should be formed exclusively in the absence of phthalimide, we synthesized a series of substrates having five or six membered spirocyclic ketal functionality and subjected to the Mitsunobu conditions without addition of the nucleophile to develop a convenient route to 1,3-disulfur heterocycles.

Thus, when the cyclohexanedithiane (**1a**) was refluxed with diisopropyl azodicarboxylate (6 equiv.) and triphenylphosphine (4 equiv.) in THF for 40 min, a 4:1 mixture of the ring-expanded products (**3a**) and (**7b**) accompanied by a trace of the simple dehydration product (**8a**) was generated in 60% total yield. On the same treatment, the dithiolane analogue (**1b**) furnished a mixture of two ring-expanded products (**3b** and **7b**), and the dehydration product (**8b**) in ratio of 1:5:5 in 85% total yield. Similarly, the cyclopentanedithiane (**9a**) afforded a 2:1 mixture of the ring-expanded products (**10a** and **11a**), and the cyclopentanedithiolane (**9b**) afforded a 1:5 mixture of **10b** and **11b** in total yields of 93 and 70%, respectively (**Scheme 2**).



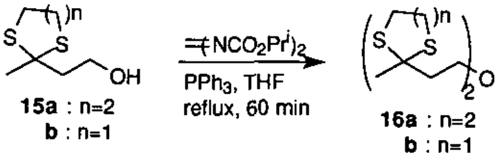
Scheme 2

The same rearrangement also occurred more facilely with the substrates having bicyclo[2.2.1]heptane system. Thus, the dithiane (**12a**) afforded a 8:1 mixture of the ring-expanded product (**13a**) and the dehydration product (**14a**) in 90% total yield. Similarly, a 8:1 mixture of the expanded product (**13b**) and the dehydration product (**14b**) was obtained in 80% total yield from the dithiolane (**12b**) (**Scheme 3**).



Scheme 3

Very interestingly, the reaction did not occur in the same way with the linear thioketals (**15a** and **b**), which furnished the symmetric ethers (**16a** and **b**), in yields of 15 and 6%, respectively, under the same conditions (**Scheme 4**).



Scheme 4

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