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Enethiol Assisted [3,4] and [3,5] Sigmatropic Rearrangements During Thionation of 2,3-Diaroylbicyclo[2.2.1]hepta-5-enes with Boron Sulfide

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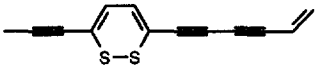
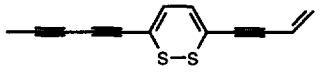
Abstract: Thionation reaction of 2,3-diaroylbicyclo[2.2.1]hepta-5-enes using *in situ* generated B_2S_3 (bis-trialkyltin sulfide or bis-trimethylsilyl sulfide reacted with BCl_3 in toluene) gave [3,4] and [3,5] sigmatropic rearrangement products.

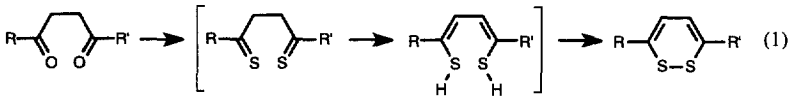
Sulfur containing natural products 3-(hexa-1,3-diyn-4-enyl)-6-(1-propynyl)-1,2-dithiacyclohexa-3,5-diene (thiarubrine A, **1**), 6-(buta-1-yn-3-enyl)-3-(1,3-pentadienyl)-1,2-dithiacyclohexa-3,5-diene (thiarubrine B, **2**), and other 1,2-dithiins isolated from *Aspilia mossambicensis* and *Chaenantis* spp. show significant bioactivity.[1-15] Recently, the total syntheses of thiarubrines A and B have been completed by Block[14] and Koreeda.[15] In order to evaluate the influence of substituents on the bioactivity of the 1,2-dithiin ring system in structure activity relationship (SAR) studies, development of synthetic procedures for the preparation of a wide variety of substituted 1,2-dithiins is important.[1-15] Although the formation of thiophenes is a consideration,[1] one possible route to 1,2-dithiins is the reaction of 1,4-dicarbonyl compounds with thionation reagents (eq 1),[16-19] to generate dienedithiols in a favorable conformation for subsequent cyclization under mild experimental conditions at low temperatures. Another possible approach envisioned that will hinder the formation of thiophene from the dienedithiols intermediate, thus giving dithiin, was the introduction of a strained ring system on the 2,3-position of the diketone moiety (eq 2).



Thiarubrine A, **1**



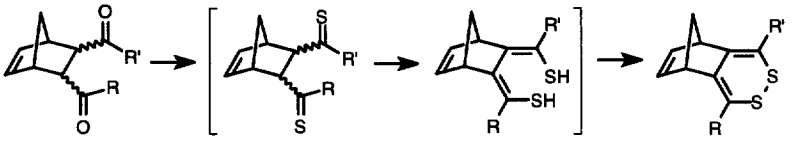
Thiarubrine B, **2**



(1)

endo,exo-2,3-Diaroylbicyclo[2.2.1]hepta-5-ene (**3**) and *endo,endo*-2,3-diaroylbicyclo[2.2.1]hepta-5-ene (**6**) were prepared by the Diels-Alder reaction of cyclopentadiene and *trans*-1,4-diaryl-2-butene-1,4-dione and *cis*-

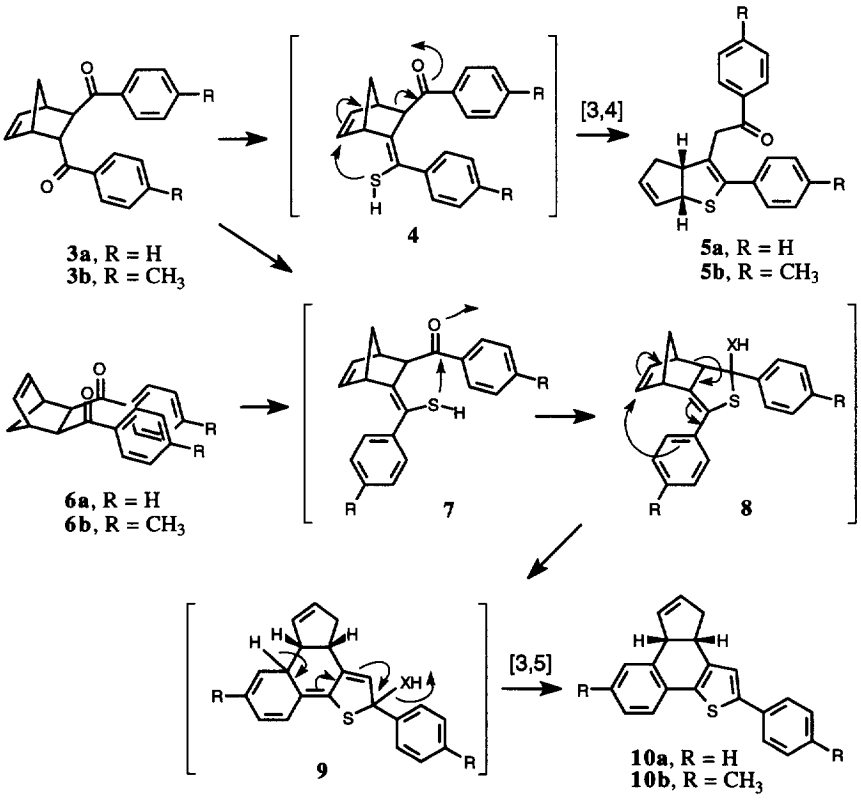
1,4-diaryl-2-butene-1,4-dione, respectively.[20-22] The (*E*)-diketones were prepared by the Friedel-Crafts acylation of benzene or toluene with fumaryl chloride.[20,21] The (*Z*)-diketones were prepared by photochemical isomerization of the (*E*)-diketones.[20-22]



(2)

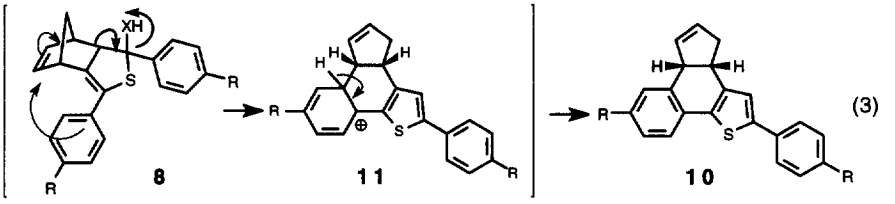
The thionation of *endo,exo*-2,3-dibenzoylbicyclo[2.2.1]hepta-5-ene using bis(tributyltin)sulfide and boron trichloride (BCl_3) as the thionating reagent, *in situ* generated B_2S_3,[16] gave 3-(2-oxo-2-phenylethyl)-2-phenyl-6,7-dihydrocyclopenta[3.2-*b*]thiophene **5a** and thiophene **10a**, while *endo,endo*-2,3-dibenzoylbicyclo[2.2.1]hepta-5-ene yielded compound **10a** as the only product. Thionation of ketone **3a** by using bis(trimethylsilyl)sulfide (hexamethyldisilthiane)/BCl_3[16,17] as the thionating agent gave products **5a** and **10a** in 36% and 26% yield, respectively, while diketone **6a** gave only the thiophene **10a** in 54% yield.

Scheme 1



The thionation of *endo,exo*-diketones **3** probably cause the formation of the enethiols **4** and **7**, respectively, owing to the presence of the labile α-proton. The orientation of the SH group of the enethiols presumably determines the pathway the rearrangement will take to yield the product **5** or **10**. The *endo,endo*-diketone **6** appears to favor the enethiol **7** in order to minimize steric effects by the neighboring aroyl group, thus, affording the thiophene **10** as the only product.

The formation of **5** can be viewed as an enethiol assisted [3,4] sigmatropic rearrangement[23-26] while the formation of **10** can be explained as a [3,5] sigmatropic rearrangement.[27,28] The release of the ring strain of the norbornene system and the formation of the thiophene ring system maybe the driving force behind these [3,4] and [3,5] sigmatropic rearrangements.[23-28] The formation of **10** also can be envisioned as a [2,3,2] sigmatropic type rearrangement resulting in a carbocation intermediate **11** through which, by a loss of proton achieving an aromatic ring, affords the product (eq 3).



The yield of rearrangement products under various thionating reagents were investigated. The results showed that bis(tricyclohexyltin)sulfide $(((C_6H_{11})_3Sn)_2)S$[16] was the best thionating reagent among the three that were tested (table 1). The compounds $(Bu_3Sn)_2S$[16] and $(TMS)_2S$[17] have offensive odors and must be handled in a hood under N_2 condition with heavy protection while $((C_6H_{11})Sn)_2S$[16] was a white crystalline high melting solid that did not require extreme care in handling. The adventage of using $(TMS)_2S$[17] was the easy workup in isolating the products.

Table 1. Yields of Rearrangement Products with Various Thionating Reagents.

1,4-diketone	thionating reagent	product yield (%)			
		5a	5b	10a	10b
3a	$(Bu_3Sn)_2S$	19		13	
	$((C_6H_{11})_3Sn)_2S$	45		20	
	$(TMS)_2S$	36		26	
3b	$(Bu_3Sn)_2S$		25		15
	$((C_6H_{11})_3Sn)_2S$		35		20
	$(TMS)_2S$		30		20
6a	$(Bu_3Sn)_2S$			21	
	$((C_6H_{11})_3Sn)_2S$			75	
	$(TMS)_2S$			58	
6b	$(Bu_3Sn)_2S$				23
	$((C_6H_{11})_3Sn)_2S$				70
	$(TMS)_2S$				54

The treatment of **3a** and **6a** with BCl_3 in toluene at rt resulted in decomposition, suggesting that oxygen is not a suitable atom to afford the [3,4] and [3,5] sigmatropic rearrangements[23-28] products under the experimental condition. The thionation condition is apparently crucial for the [3,4] and [3,5] sigmatropic rearrangements.[23-28]

The structure of the rearrangement products **5** and **10** were elucidated by HREIMS, ^1H NMR, ^{13}C NMR, DEPT, H-H COSY, and 2-D INADEQUATE (Incredible Natural Abundunce Double Quantum Transfer Experiment) NMR experiments.[29]

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29. Conditions and the aspects of the heteroatom assisted [3,4] and [3,5] sigmatropic rearrangements will be published in a full paper.

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