A New Synthetic Route to 3,4-Bridged 1,6,6a λ^4 -Trithiapentalenes

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Abstract: A new synthetic route to 3,4-bridged 1,6,6a λ^4 -trithiapentalenes is developed based on reactions of cyclic ketones with Bredereck's reagent followed by thiolation of keto dienamines with phosphorus pentasulfide or Lawesson's reagent.

Key words: $1,6,6a\lambda^4$ -Trithiapentalenes, Bredereck's reagent, phosphorus pentasulfide, Lawesson's reagent

1,6,6a λ^4 -Trithiapentalenes **1** possess a unique trisulfurcontaining bicyclic ring system. These compounds may exist as a mixture of degenerate valency tautomers that rapidly interconvert between the symmetrical formula 1 and 1,2-dithiol-3-ylidene thiones 2.1 The average length of the S-S bond (2.34 Å) found in $1,6,6a\lambda^4$ -trithiapentalenes is distinctly longer than that of a single covalent S-S bond (2.08 Å).^{1a} Between late 1950's and early 1980's, the structure and chemical property of $1,6,6a\lambda^4$ -trithiapentalenes were the subject of many studies and discussion. There are several synthetic pathways to $1,6,6a\lambda^4$ -trithiapentalenes 1 in the literature.² However, the synthetic scope for 3,4-bridged derivatives **1a** is limited, only a few carbon bridged compounds have been made by thiolating 1,3,5-triketones or dithiolium salts.³ In a research project related to the evaluation of biological activities of 3,4bridged trithiapentalenes, we explored other synthetic opportunities and discovered a new chemistry as shown in Scheme 2. Various commercially available cyclic ketones can be converted to the corresponding trithiapentalenes within two steps by this reaction process.



Scheme 1

Table 1



The new method is very straightforward. Thus, heating of a cyclic ketone with 3 to 4 equivs. of bis-dimethylamino*t*-butoxymethane (Bredereck's Reagent)⁴ at 80-110 °C for 2-4 hours gives the keto dienamine **3** in 90-95% yield. At the key step of thiolation, refluxing of **3** with 1–1.5 equivs. of Lawesson's reagent leads to the formation of the 3,4-bridged-1,6,6a λ^4 -trithiapentalene **4**. After flash column chromatgraphy purification of the final product, the yield for this two-step reaction ranges from 22% to 49% (Table 1).⁵ Similar yields have been obtained by using P₂S₅ as the alternative thiolating reagent.



Scheme 2

Many 3,4-bridged 1,6,6 $a\lambda^4$ -trithiapentalenes have been prepared by this protocol. The scope of this reaction is demonstrated by using a broad range of substituted cyclic or heterocyclic ketones as starting material. The bridged ring size can be varied from five to seven. In addition to alkyl and aryl groups, substituents such as ester, ketal, and cyano groups are tolerated. This method is also applied to the synthesis of bistrithiapentalene 21. Further extension to acyclic ketones in the preparation of $1,6,6a\lambda^4$ -trithiapentalenes 22-24 is also achieved. The structure of compound 10 is confirmed by an X-ray diffraction study (Figure 1). It is noteworthy to mention that compound 10 is found to be symmetrical by ¹H and ¹³C NMR analysis at room temperature. However, X-ray structure of this compound indicated that the two S-S bonds in compound 10 are not of equal length; one S-S bond distance is 2.409 Å, while the other one is 2.264 Å.



Figure 1 X-Ray Structure of Compound 10

General procedure for the synthesis of 3,4-bridged 1,6,6a λ^4 -trithiapentalenes. Preparation of **10**: A mixture of 1.74 g (10 mmol) of 4-phenylcyclohexanone and 8 mL (38 mmol, 3.8 equivs) of bisdimethylamino-*t*-butoxymethane (Bredereck's Reagent) was heated neat at 110 °C for 4 h. The reaction mixture was cooled to room temperature and water was added. After extraction with ethyl acetate, the combined organic layers were washed with NaHCO₃ (aq.) and brine, dried over MgSO₄, and concentrated in vacuo. The resulting crude product was triturated with *n*-BuCl/hexanes to give 2.70 g (95%) of keto dienamine as a brown solid (mp 158.1-158.7 °C). To a solution of 0.85 g (3.0 mmol) of this keto dienamine in 10 mL of dry benzene was added 1.20 g (3.0 mmol) of Lawesson's reagent. The mixture was heated to reflux for 1.5 h. The cooled reaction mixture was filtered. The filtrate was extracted with ethyl acetate. The combined organic layers were washed with 5% NaOH (aq) and brine, dried over MgSO₄, and concentrated in vacuo. The crude product was purified by column chromatography on silica gel (elution with 20:1, hexanes:ethyl acetate) to give 340 mg (41%) of **10** as a brown solid, mp 106.9-108.4 °C. ¹H NMR (CDCl₃) δ 3.05-3.35 (m, 5H), 7.23-7.40 (m, 5H), 8.85 (s, 2H). ¹³C NMR (CDCl₃) δ 3.56 (t, 2C), 38.1 (d), 125.4 (d), 125.5 (d, 2C), 127.3 (d, 2C), 138.1 (s, 2C), 142.4 (s), 156.4 (d, 2C), 169.5 (s). IR (neat) 1406 (s) cm⁻¹. MS *m/e* (rel. intensity) 277 (M⁺+1, 100).

In summary, we have developed a general synthetic protacol which provides easy access to various 3,4-bridged-1,6,6a λ^4 -trithiapentalenes. The synthetic utility of phosphorus pentasulfide and Lawesson's reagent has been extended.

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References and Notes

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- (5) Keto dienamine 3 can be consumed by reacting with 1-1.5 equivs. of Lawesson's reagent. Low isolation yield is probably related to the photoinstability of the product during flash column chromatography, see ref. 2b.

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