Facile Synthesis and Diels–Alder Reactions of 2,6-Divinyl-1,4-dithiin

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Abstract: A new and facile synthetic pathway to 2,6-divinyl-1,4-dithiin, involving easily available precursors is reported. The utility of the title compound as a reactive diene in Diels–Alder reactions was demonstrated in the synthesis of various thianthrene derivatives.

Key words: alkynes, allenes, 2,6-divinyl-1,4-dithiin, Diels–Alder reactions, regioselectivity

1,4-Dithiins have attracted a special interest because of their structural and electronic properties and of the wide variety of synthetic transformations they undergo.1–3 Their utility in advanced materials is well known.4–6

The most common method for preparation of 1,4-dithiins involves elimination reactions of appropriately substituted dithiane analogues. Thus, the parent compound was obtained by vapor phase dealkoxylation of 2,5-dialkoxy-1,4-dithianes over alumina at an elevated temperature.7 Another general approach is based on cycloadditions of either four- and two-atom fragments, or a five-atom fragment and a one-atom unit. Addition of sodium sulfide to dialkynyl sulfide, which occurs readily in DMF–methanol, demonstrates this kind of approach.8

Recently, we have reported the preparation of the first divinyl-1,4-dithiin.9 Thus, 2,6-divinyl-1,4-dithiin has been isolated from the reaction of 1,4-bis(4-bromo-but-2-ynyloxy)benzene (I) with an excess of alumina supported sodium sulfide in boiling tetrahydrofuran. The surprising formation of 2,6-divinyl-1,4-dithiin (4) has been presumed to take place via cyclic sulfide 2 that undergoes a base catalyzed rearrangement to the corresponding diallelyl sulfide 3, followed by nucleophilic attack of disulfide anion on the resulting allene and fragmentation (Scheme 1).

Subsequent investigations on the chemical behavior of cyclic sulfur bridged di- and tetrapropargylic compounds such as 5 and 6 (Figure 1),9,10 showed that 2,6-divinyl-1,4-dithiin can also be obtained by treatment of the above with an excess of sodium sulfide nonahydrate in dimethyl sulfoxide.

However, these approaches are of limited utility as synthetic pathways, in view of the considerable difficulties and moderate yields for the preparation of cyclic di- and tetrapropargylic sulfides.9,10 Despite of the above difficulties, formation of 2,6-divinyl-1,4-dithiin from isolated cy-
clic sulfides such as 5 and 6 sustain our presumption that it is formed via rearrangement of bis-propargylic sulfide units to the corresponding diallenyl sulfides (Scheme 1). Furthermore, it seems that the good leaving group abilities of dianions derived from catechol, resorcinol or hydroquinone, play an important role as driving force in the formation of 4.

We now wish to report here a new method for the synthesis of 2,6-divinyl-1,4-dithiin (4) and Diels–Alder reactions of this compound with various dienophiles.

Based on the above findings, we have designed a new and short synthetic pathway for 2,6-divinyl-1,4-dithiin, which involves easily available precursors. Thus, 1-bromo-4-phenyloxy-2-butyne (7) reacts easily with an equimolar amount of sodium sulfide nonahydrate affording the corresponding bis-propargylic sulfide 8. In the presence of an excess of sodium sulfide nonahydrate in dimethyl sulfoxide this acyclic sulfide provides 2,6-divinyl-1,4-dithiin (4) in 75% yield (Scheme 2). Moreover, the reaction of 1-bromo-4-phenyloxy-2-butyne with 2.5 equivalents of sodium sulfide nonahydrate in dimethyl sulfoxide affords dithiin 4 in 65% isolated yield (Scheme 2). These transformations fully sustain the proposed mechanism for the formation of 2,6-divinyl-1,4-dithiin (4) from cyclic or acyclic bis-propargylic sulfides.

1,4-Dithiins, especially those with electron-withdrawing substituents, can react as dienophiles in [2+4]-cycloadditions with suitable dienes. Although the synthesis of 2-vinyl-1,4-dithiin has been reported many years ago, no references for Diels–Alder reactions of this compound can be found. So, we decided to investigate the possible modes of reactivity of 4 in [2+4]-cycloaddition reactions and have found that dithiin 4 is a rather reactive diene. Thus, while heating of 2,6-divinyl-1,4-dithiin with cyclopentadiene results in full recovery of starting materials, the reaction with various olefinic dienophiles takes place after 2 hours in refluxing benzene solution with high yields.

Tetracyanoethylene reacts with 2,6-divinyl-1,4-dithiin with the formation of a mixture of two isomers 9a and 9b in a ratio of 1:1 (Scheme 3). Based on NMR data, symmetrical structures are obtained for both, however, we are unable to distinguish the two isomers.

2,6-Divinyl-1,4-dithiin reacts with dimethyl acetylenedicarboxylate in a similar manner to tetracyanoethylene. However, in this case reaction is completed in about 72 hours and the 1H NMR spectrum of the crude reaction product shows that a mixture of three products has been formed. Along with the expected tetramethyl 3,7,9a,10a-tetrahydrothianthrene-1,2,8,9-tetracarboxylate isomers 10a,b (Scheme 4), a small amount (10%) of a compound with a 1,2,4-substituted aromatic pattern appears.
Attempts to separate 10a,b by chromatography on silica gel failed. Under any set of conditions (flash chromatography, PTLC) 10a,b were obtained as a mixture, which contains ca. 60% of primary product. Surprisingly, larger amounts of the aromatic by-product were isolated in pure form. The presence of a 1,2,4-substituted aromatic pattern for this compound indicates that 10a,b undergo aromatization with elimination of hydrogen sulfide (Scheme 5). Indeed, the spectral data fit the structure of 3,4,4′-thiobis(dimethyl phthalate) (11), a known compound that has been prepared by an alternative procedure. Although this kind of aromatization usually takes place under basic conditions it is obvious that in this case it is catalyzed by silica.

Unlike the above, a complete stereoselective reaction has been found to take place with maleic anhydride and N-phenylmaleimide (Scheme 6).

Assuming that cycloaddition proceeds by the preferable endo-fashion, two possible stereochemistries can be envisaged for this product. Thus, the protons α to sulfur can be cis- or trans-related, but the adjacent hydrogens on the bridgeheads between the five- and six-membered rings must be cis to each other and also cis to the proximal hydrogen α to the sulfur. We do not know why only one product is obtained in this case or even which one. Possibly, the bulkier maleic moieties interfere with each other during the cycloaddition process.

In conclusion, we have developed a convenient route for the synthesis of 2,6-divinyl-1,4-dithiin involving readily available starting materials. In addition, the synthetic utility of the latter as a reactive diene in Diels–Alder reactions was demonstrated by the preparation of various thianthrene derivatives.

Melting points were obtained on a Thomas–Hoover apparatus and are uncorrected. 1H NMR and 13C NMR spectra were recorded on Bruker DPX-300 or DMX-600 spectrometer. Chemical shifts are reported in ppm downfield from TMS. IR spectra were recorded on a Nicolet 60 SXB FTIR. High resolution mass spectra were obtained on a VG-Fison AutoSpec instrument.

1-Bromo-4-phenyloxy-2-butyne was prepared according to literature procedure.

2,6-Divinyl-1,4-dithiin (4)
To a soln of 1-bromo-4-phenyloxy-2-butyne (1.12 g, 5 mmol) in dry CHCl₃ (15 mL) the corresponding dienophile (2 mmol) was added. The reaction mixture was refluxed for 2 h and then concentrated under vacuum. The residue was triturated with Et₂O to give crude reaction products as white solids. The pure products were obtained by recrystallization.

3,7,9a,10a-Tetrahydrothianthrene-1,1,2,2,8,8,9,9-octacarbonitrile 9a,9b
Prepared from 2,6-divinyl-1,4-dithiin and tetracyanoethylene and purified by fractional recrystallization from CHCl₃.

Isomer 1
Yield: 0.2 g (49%); mp 254–255 °C dec.
IR (KBr): 3441, 2977, 2934, 2256, 1637, 1439, 1250, 1122, 888, 750, 689 cm –1.
1H NMR (600 MHz, Acetone-d₆): δ = 3.63 (ddd, 1 H, J= 19.6, 2J= 2.5, 3J= 3.6 Hz, H-3), 3.98 (ddd, 1 H, J= 19.6, 2J= 5.7, 3J= 1.8 Hz, H-10a). 5.35 (ddd, 1 H, J= 2.4, 2J= 2.4, 3J= 1.8 Hz, H-10a), 6.54 (ddd, 1 H, J= 5.7, 2J= 2.5, 3J= 2.4 Hz, H-4).
13C NMR (75 MHz, Acetone-d₆): δ = 126.7 (C-4a), 126.4 (C-4b), 111.8 (CN), 110.9 (CN), 109.3 (CN), 46.2 (C-1), 45.8 (C-10a), 40.1 (C-2), 33.2 (C-3).
HRMS: m/z calcld for C₂₀H₈N₈S₂: 424.031336; found 424.030370.

Isomer 2
Yield: 0.2 g (49%); mp 301–302 °C dec.
IR (KBr): 3484, 2977, 2917, 2256, 1641, 1440, 1362, 1259, 1121, 889, 821 cm –1.
1H NMR (600 MHz, Acetone-d₆): δ = 3.63 (ddd, 1 H, J= 19.6, 2J= 2.4, 3J= 2.5, 4J= 6.2 Hz, H-3), 3.85 (ddd, 1 H, J= 19.4, 2J= 2.4, 3J= 2.4, 4J= 1.4 Hz, H-10a). 6.30 (ddd, 1 H, J= 6.2, 2J= 2.4, 3J= 1.4 Hz, H-4).

Scheme 5

Scheme 6
**Tetramethyl 3,7,9a,10a-tetrahydrothianthrene-1,2,8,9-tetra-carboxylate 10a,b**

To a solution of 2,6-divinyl-1,4-dithiin (4) (0.168 g, 1 mmol) in C₆H₆ was heated under reflux for 72 h in a closed ampule and then concentrated under vacuum. The residue was purified by chromatography on silica gel (CHCl₃–hexane, 8:1) to give 10b,a as a mixture with 4,4'-thiobis(dimethylphthalate) 11. Spectral data were extracted from this mixture.

**Compound 13**

Adduct 13 was prepared from 2,6-divinyl-1,4-dithiin, N-phenylmaleimide and recrystallized from CHCl₃.

Yield: 0.46 g (90%); mp 197–198 °C (dec.)

**References**


