Synthesis of (Thio)substituted -1,3-Butadienes and -Butenynes

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Abstract: In this study, 2H-1,1,3,4,4-pentachloro-1,3-butadiene (1) was reacted with different thiols (2-methyl-2-propanethiol 2a, benzyl mercaptan 2b, 4-tert-butylbenzenethiol 2c, 4-nitrothiophenol 2d) in ethanol in the presence of NaOH to afford mono-thio-substituted-1,3-butadienes and mono- and tris-thio-substituted-1-buten-3-ynes. Among them, (4-tert-butylphenyl)(1,3,4,4-tetrachlorobuta-1,3-dienyl)sulfane (4c) exhibited two isomers of mono products. Moreover, the reaction of compound (1) with 2-hydroxythiophenol (2e) in dimethylformamide in the presence of triethylamine took place the formation of OH-protected butadiene structure 2-((Z)-1,3,4,4-tetrachlorobuta-1,3-dietylthio)phenol (4e) and ring-closed butadiene structure (E)-2-(2,3,3-trichloroallylidene)benzo[d][1,3]oxathiole (6), together and with two isomers of each. Their structures identified on the basis of GC-MS(+EI) analysis with different retention times (RT). Characterization of the synthesized compounds was done using several methods, mass spectrometry (GC-MS(+EI)), 1H-, 13C-, APT- NMR, FTIR and elemental analysis.

Keywords: Thioethers, 1-buten-3-ynes, 1,3-butadienes, GC-MS, thiols.

Submitted: March 07, 2019. Accepted: April 11, 2019.

Cite this: Kacmaz A. Synthesis of (Thio)substituted -1,3-Butadienes and -Butenynes. JOTCSA. 2019;6(2):201-6.

DOI: https://dx.doi.org/10.18596/jotcsa.536853.

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INTRODUCTION

Organosulfur compounds are widely found in natural products (1) and play a major role in many biological systems (2). In this field of organosulfur chemistry, thioether moieties are essential fragments of many biologically active compounds (3, 4). For example, α-fluorinated thioethers are valuable compounds for modern agrochemicals (5). Also, there is a US patent (6) that discloses some thio derivatives of haloalkylpolyenes and their biological, specifically fungicidal, activities. Additionally, compounds with high sulfur content constitute an important class of materials chemistry, supramolecular chemistry, and polymer chemistry (7). In this respect, synthesis of a lot of organosulfur compounds are going on.

Also, polyhalo-1,3-butadienes and conjugated en-ynes are valuable precursor for various synthetic applications (8, 9). In addition, sulfonyle-substituted-1,3-butadienes and allenyl sulfones are used as the starting materials some reactions (Diels-Alder, Michael additions, etc.) (9-11).

Reactions of polyhalo-dienes and –butenes with thiols or amines have been previously reported by Ibis and co-workers and Roedig and coworkers (12-26). Yoshimatsu et al. reported the preparation of 2-sulfonyl-1-buten-3-ynes and their reactions with nucleophiles (9).

It is reported by our laboratory, that the reaction between 1 and different thiols under mild conditions results the formation of thio-substituted 1,3-butadienes/butenynes (12-14). Among them, in 2010 (19) and 2016 (20), we reported that some mono-, bis-, tris- and tetrakis- substituted butenynes, butadienes or buta-1,2,3-trienes and their halogenation (iodination/bromination) and oxidation of some butadienes to their corresponding sulfoxides or sulfones. In these studies, in order to product mono-, bis-, tris- or tetrakis-substituted thioethers, having butadiene or butyne skeleton, we used different reactant ratio and...
different reaction medium (DMF/triethylamine, EtOH/NaOH etc.) via nucleophilic reactions.

Taking into account the above mentioned facts, it is reported herein the synthesis and structural characterization of some butenyes or 1,3-butadienes, which having thioether skeleton.

MATERIAL AND METHODS

Infrared spectra (IR) were recorded on a Perkin Elmer Spectrum One FTIR instrument. GC-MS spectra, equipped with an Electron Impact (EI) source, were recorded on a Thermo Finnigan Trace DSQ system using He as carrier gas. 1H NMR, 13C NMR spectra in CDCl3 were recorded on a Varian Unity Inova spectrometer, with tetramethylsilane (TMS) as standard. Elemental analyses were performed on a Thermo FinniganFlash EA 1112 Series Elemental Analyzer. UV-vis spectra were taken from Perkin Elmer Lambda 35 UV-Vis spectrophotometer.

General Procedure for the Synthesis of Thioethers (3a, 3b, 3c, 3d, 4b, 4c, 4d and 5a)

Synthesis of thioethers (3a, 3b, 3c, 3d, 4b, 4c, 4d and 5a) were carried out by the reaction of 1 (8.8 mmol) with equimolar amount of different thiol (2-methyl-2-propanethiol 2a, benzyl mercaptoan 2b, 4-tert-butylenzenethiol 2c, 4-nitrothiophenol 2d) in ethanol (20 mL) with NaOH. After the progress/completion of the reaction was monitored by thin layer chromatography (TLC), the resulting mixture was extracted with chloroform and water. The organic phase was dried by adding anhydrous Na2SO4 and evaporated under vacuum. The crude product was purified by column chromatography with n-hexane over silica gel to yield products. The physical and spectral data of the products are as follows.

Synthesis of tert-butyl(3,4,4-trichlorobut-3-en-1-ynyl)sulfane (3a) and 1,1,4,4-tetramethyl(3-tert-pentylthio)-2-chlorobut-1-en-3-yne (5a)

Compounds 3a and 5a were synthesized according to general procedure:

3a: Known compound (27, 28): Spectral data were in agreement with literature values. Yield (36%), MS (EI, 70 ev) m/z (%): 242.0 (M+, 6), 244.0 (6), 186.0 (12), 188 (12), 114.9 (15), 57.0 (100), 41.0 (48), 29.1 (36); Anal.Calcd. for C8H8Cl2S (243.58): C, 39.45; H, 3.72; S, 13.16. Found: C, 39.43; H, 3.70; S, 13.14.

5a: Light yellow oil, Yield (5%), Rf (n-hexane): 0.3; IR spectrum, v, cm⁻¹: 2134 (C≡C), 2962, 2921, 2861, 1456, 1260, 799; 1H NMR spectrum, δ ppm: 1.39 (s, CH3), 1.42 (s, CH3); APT NMR spectrum, δ ppm: 93.72, 89.92 (C=C), 133.89, 126.58 (C=CH2), 50.00, 49.09, 48.16 (C-CH3), 30.47, 30.45, 30.30, 30.27, 30.24, 29.80, 29.77, 29.61, 29.58 (CH3); MS (EI, 70 ev) m/z (%): 350.2 (M+, 6), 352.2 (2.5), 238.1 (10), 240.1 (5), 182.0 (54), 57.1 (100), 146.0 (9); Anal.Calcd. for C15H12Cl2S (351.03): C, 54.74; H, 7.75; S, 27.40. Found: C, 54.72; H, 7.72; S, 27.42.

Synthesis of benzylic(3,4,4-trichlorobut-3-en-1-ynyl)sulfane (3b) and benzylic(1,3,4,4-tetrachlorobut-1,3-diynyl)sulfane (4b)

Compounds 3b and 4b were synthesized according to general procedure:

3b: Yellow oil, Yield (40%), Rf (n-hexane): 0.5; IR spectrum, v, cm⁻¹: 2151 (C≡C), 3063, 3031, 1459, 1454, 958; 1H NMR spectrum, δ ppm: 4.05 (s, CH2benzyl, 2H), 7.3-7.4 (m, CH3benzy) 1H; 13C NMR spectrum, δ ppm: 138.08, 129.33, 129.27, 128.99, 128.89, 128.36, 113.08 (CH3benzyl, C=Cbenzyl), 87.88, 92.47 (C=C), 40.83 (CH2benzy); MS (EI, 70 ev) m/z (%): 278.1 (M+, 31), 241.1 (100), 206.1 (74), 115.0 (77); Anal. Calcd. for C12H10ClS (277.6): C, 47.59; H, 2.54; S, 11.55. Found: C, 47.57; H, 2.52; S, 11.53.

4b: Yellow oil, Yield (7%), Rf (n-hexane): 0.6; IR spectrum, v, cm⁻¹: 3064, 3030, 2926, 2853, 1602, 1567, 1495, 1454, 942; 1H NMR spectrum, δ ppm: 4.18 (s, CH2benzy, 2H), 6.48 (s, 1H, >C=CH), 7.3-7.4 (m, CH3benzy, 5H); 13C NMR spectrum, δ ppm: 136.40, 129.22, 129.13, 128.92, 127.90, 126.98, 126.29, 126.27, 124.51, 122.19, 40.84; MS (EI, 70 ev) m/z (%): 314.1 (M+, 15), 186.0 (100); Anal. Calcd. for C12H10ClS (314.06): C, 42.07; H, 2.57; S, 10.21. Found: C, 42.05; H, 2.55; S, 10.23.

Synthesis of (4-tert-butyphenyl)(3,4,4-trichlorobut-3-en-1-ynyl)sulfane (3c) and (4-tert-butyphenyl)(1,3,4,tetrachlorobut-1,3-diynyl)sulfane (4c, isomer mixture)

Compound 3c and 4c were synthesized according to general procedure:

3c: Known compound (26, 29). Spectral data were in agreement with literature values. Rf (n-hexane): 0.9; APT NMR spectrum, δ ppm: 89.96, 89.46 (C=C), 113.07, 126.59 (C=C), 151.21, 127.41 (C=C), 127.24, 126.92 (CH3benzyl), 31.44 (CH3), 34.85 (C-CH3); MS (EI, 70 ev) m/z (%): 320.2 (M+, 45), 322.2 (16), 303.1 (100), 117.1 (42), 233.2 (11); Anal. Calcd. for C16H13Cl2S (319.68): C, 52.60; H, 4.10; S, 10.03. Found: C, 52.58; H, 4.12; S, 10.01.

4c, isomer mixture: Light yellow oil, Yield (50%), Rf (n-hexane): 0.8; IR spectrum, v, cm⁻¹: 2962, 2905, 2869, 1594, 1570, 1489, 1263, 823; 1H NMR, δ ppm: 6.14 (s, 1H, >C=CH), 6.48 (s, 1H, >C=CH), 7.37 (s, 4H, Ar-H), 7.32 (s, 4H, Ar-H), 1.26 (s, 3H, Me), 1.257 (s, 3H, Me), 1.253 (s, 3H, Me), 1.249 (s, 3H, Me), 1.243 (s, 3H, Me), 1.23 (s, 3H, Me); APT NMR, δ ppm: 152.24, 154.16, 136.71, 137.05, 132.67, 132.62, 132.56, 132.53, 126.19, 125.91, 125.82, 125.77, 125.71, 125.68, 125.29, 124.52, 124.50, 123.49, 119.49, 119.36; 33.83, 30.25, 30.22, 30.20, 30.17, 30.14 (Ctert, CH3). MS (EI, 70 ev) m/z (%): 356.1 (M+, 58), 341.1 (100).
Synthesis of (3,4,4-trichlorobut-3-ynyl)(4-nitrophenyl)sulfane (3d) and (1,3,4,4-tetrachlorobuta-1,3-dienyl)(4-nitrophenyl)sulfane (4d)

Compounds 3d and 4d were synthesized according to general procedure:
3d: Known compound (25). Spectral data were in agreement with literature values. Yield (18%), R\(_f\) (CHCl\(_3\)): 0.4; APT NMR, \(\delta_{C, ppm}: 91.65, 83.95 (C≡C), 145.85, 139.44, 128.46, 111.31, 125.32, 125.30, 123.55, 123.56; MS (El, 70 e\(^{-}\)) \(m/z\) (%): 309.1 (M\(^+\), 53), 226.1 (100), 227.1 (21), 191.1 (29), 156.1 (32), 115.0 (43). Anal.Calcd. for C\(_{10}H_4Cl_3NO_2S (308.57)\) C, 38.92; H, 1.31; S, 10.39. Found: C, 38.90; H, 1.29; S, 10.37.

4d: Yellow, R\(_f\) (n-hexane): 0.2, Yield (35 %); IR spectrum, \(\nu, \text{cm}^{-1}\): 3055, 1599, 1579, 1345, 1265, 739; \(^1\)H NMR, \(\delta, \text{ppm}: 6.78 (s, 1H, >C=CH), 8.14 (d, 2H, Ar-H, J= 6.6), 7.46 (d, 2H, Ar-H, J= 6.8); \(^{13}\)C NMR spectrum, \(\delta_{C, ppm}: \) 146.30, 139.31, 132.94, 129.82, 129.43, 123.41, 123.24; MS (El, 70 e\(^{-}\)) \(m/z\) (%): 345.1 (M\(^+\), 47), 343.1 (35), 347.1 (24), 273.1 (100), 192.1 (57), 308.1 (53), 227.1 (21); Anal.Calcd. for C\(_{10}H_5Cl_4NO_2S (345.03)\) C, 34.81; H, 1.46; S, 9.27. Found: C, 34.78; H, 1.43; S, 9.27.

Synthesis of 2-((Z)-1,3,4,4-tetrachlorobuta-1,3-dienylthio)phenol (4e) and (E)-2-(2,3,3-trichloroallylidene)benzo[d][1,3]oxathiole (6) (isomer mixtures)

Synthesis of 4e and 6 were carried out by the reaction of 1 (6.6 mmol) with 2-mercaptophenol 2e (26.5 mmol) in DMF (20 mL) with Et\(_3\)N (2.5 mL) at room temperature. After the progress/completion of the reaction was monitored by TLC, the resulting mixture was extracted with chloroform and water. The organic phase was dried by adding anhydrous Na\(_2\)SO\(_4\) and evaporated under reduced pressure. The crude product was purified by column chromatography with n-hexane over silica gel to give products 4e and 6 butadiene mixtures with their isomers.

4e and 6 with their isomer mixture: Dark yellow oil, Yield (30%), R\(_f\) (3CH\(_2\)Cl/1 n-hexane): 0.6; IR spectrum, \(\nu, \text{cm}^{-1}\): 3456 (-OH), 1471, 1575 (C=CH\(_3\)) cm\(^{-1}\); \(^1\)H NMR, \(\delta, \text{ppm}: 7.40 (d, 3H, Ar-H, J= 6.35 Hz), 7.35 (d, H, Ar-H, J= 7.32 Hz), 7.26 (t, 4H, Ar-H, J= 6.8Hz), 6.95 (d, 4H, Ar-H, J= 7.32Hz), 6.85 (t, 4H, Ar-H, J= 7.08Hz), 6.51 (s, 2H, >C=CH), 6.24 (s, H, >C=CH), 6.17 (s, H, >C=CH), 5.90-6.12 (s, broad, 2H, -OH); \(^{13}\)C NMR spectrum, \(\delta_{C, ppm}: \) 156.59, 135.64, 135.51, 135.45, 135.33, 132.66, 132.42, 132.29, 131.93, 128.63, 125.39, 123.52, 123.19, 122.24, 121.76, 121.72, 121.67, 116.81, 116.37, 116.24, 116.16; MS (El, 70 e\(^{-}\)) \(m/z\) (%): 280.1 (6) and 316.1 (4e): (C\(_{10}H_5Cl_3OS; 279.57 for compd. 6), (C\(_{10}H_6Cl_4OS; 316.03 for compound 4e).

RESULTS AND DISCUSSION

Reaction of 1 with some thiols 2a-e in ethanol (with NaOH) or DMF (with triethylamine) at room temperature gave the thioethers (3a-d, 4b-e, 5a, 6) (Scheme 1). Also, compounds 4c, 4e and 6 were obtained as isomeric mixtures, their structures were especially identified with GC-MS (+EI) analyses (different retention times of isomers).
The reaction of 1 with equivalent 2-methyl-2-propanethiol 2a in EtOH/NaOH at room temperature provided the mono-(thio)substituted-1-buten-3-yne 3a (27, 28) and tris-(thio)substituted-1-buten-3-yne 5a. In the IR spectra of 5a, the characteristic absorption of acetylenic bond (C≡C, 2134 cm⁻¹) appeared in the expected range. Also, the ¹³C NMR signals for this compound 5a δ 93.72, 89.92 corresponded to the acetylenic group (C≡C).

Mono(thio)substituted-1-buten-3-yne compound 3b obtained from the reaction of 1 and benzyl mercaptan 2b, besides mono(thio)-substituted product 4b was obtained in this reaction. Compound 3b revealed characteristic signals at δ(ppm) 87.88, 92.47 due to acetylenic carbons (in ¹³C NMR), and signals at δ 4.05 ppm due to benzyl protons and δ 7.3-7.4 ppm aromatic protons, together, in the ¹H NMR spectra. The other compound 4b exhibited the formation of butadiene skeleton: as evidence, the presence of singlet butadiene proton signal (>C=CH, δ 6.48 ppm) in the ¹H NMR spectrum and by the disappearance of acetylenic carbons (C≡C) at about δ 80-90 ppm in the ¹³C NMR spectrum. Also, compounds 3b and 4b showed a molecular ion peak (M⁺), 278.0 (3b) and 314.1 (4b), which were agreement with the molecular formulas.

Reaction of the 1 with 4-tert-butylbenzenethiol 2c afforded compound 3c (26, 29) and two isomers mixture of compound 4c. Compound's presence was detected by gas chromatography via their different retention times and same molecular mass (m/z = 356.1). In addition, proton-NMR spectrum of 4c the apperance of two vinyl protons at δ = 6.14 and 6.48 ppm supported to formation of two isomers.

When 1 was reacted with 2d, compounds 3d (ref 25) and 4d were obtained. The ¹H NMR spectra of 4d exhibit its characteristic signals at δ 8.14, 7.46 ppm due to aromatic protons and δ 6.78 ppm due to butadiene proton (>C=CH). Also, compounds 3d (M⁺+, 309.1) and 4d (M⁺, 345.1) showed molecular ion peaks, as expected.

The reaction of 1 with 2-hydroxythiophenol 2e in DMF with triethylamine gave a mixture of two butadiene compounds (4e and 6), each of them having two isomers. This mixture could not be separated with column chromatography. However, especially, these butadienes and their isomers were separated and characterized by GC-MS method. Furthermore, while 4e had OH protected structure, compound 6 was obtained by the ring formation. The GC-MS chromatogram for 4e and 6 is shown in Figure 1. It can be seen that the compound 6 with two isomers is evident at 8.21 min, together with the peak at 8.37 min. Each isomer of 6 has the same molecular ion peak of m/z 280.1. (Fig. 2 (a) and (b)) and same mass fragmentation pattern. Also, literature survey showed that similar ring formation between 2-nitro-1,1,3,4,4-pentachloro-1,3-butadiene and 2-hydroxythiophenol 2e in room temperature, with 45% yield (15).

The compound 4e also contains two isomers with the retention time of (RT) 8.63 min and 8.78 min. Each isomers of 4e has the same molecular ion peak of m/z 316.1 (Figure 2 (c) and (d)) and same mass fragmentation pattern. Compound 4e had mono(4-hydroxyphenylthio)substituted-1,3-butadiene structure. Moreover, there was a reaction in the literature that tetrakis(4-hydroxyphenylthio)-substituted-1,3-butadiene was synthesized from 1,1,3,3,4,4-hexachlorobutene and 2-hydroxythiophenol 2e in the presence of triethylamine (30).

Furthermore, in the ¹H NMR spectrum of butadiene mixtures and their isomers (4e and 6), the typical absorptions were observed such as OH signals at δ 5.90-6.12 ppm (broad), butadiene's proton signals (>C=CH), at δ 6.51, 6.24, 6.17 ppm and aromatic ring signals at δ 6.8-7.46 ppm region, which provide additional supporting evidence for their characterization.

![Figure 1. GC-MS (+EI) chromatogram of butadiene structures (4e and 6) with their isomers.](image-url)
**CONCLUSION**

Thioether moieties revealed pronounced biological value such as fungicidal properties. In this study, thio-substituted 1,3-butadienes and butenynes were obtained from the reactions between thiols and compound 1 in EtOH or DMF at room temperature. Also, some isomers were identified on the basis of GC-MS(+EI) analysis with different retention times (RT). The structures of S- substituted compounds were elucidated by elemental analyses, (GC-MS(+EI)), IR, $^1$H, $^{13}$C or APT NMR spectroscopies.

**ACKNOWLEDGMENTS**

This study was funded by Istanbul University with the project number (NP-42986). I thank the Research Fund of Istanbul University – Cerrahpasa for financial help.

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