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SYNTHESIS OF 4-(2-HYDROXYARYL)-5-METHYL-1,3-DITHIOL-2-THIONES

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Abstract: The synthesis of 4-(2-hydroxyaryl)-5-methyl-1,3-dithiol-2-thiones has been accomplished by the reaction of the corresponding 4-(2-hydroxyaryl)-5-methyl-1,3-dithiol-2-ylium perchlorates with sodium sulfide nonahydrate in ethanol at room temperature. The newly obtained derivatives were characterized by NMR and MS spectrometry and IR spectroscopy.

***Keywords*:** Dithiocarbamates; Dithiolium salts; 1,3-Dithiol-2-thiones; Trithiones

Introduction

The discovery of highly conductive organic charge transfer complexes which are formed from tetrathiafulvalenes derivatives and the acceptor tetracyano-*p*-quinodimethane has prompted interest in the discovery of new electron donors and acceptors which exhibit similar conductivity.[1-4] In general, charge-transfer[5-15] or push-pull[16-20] compounds have significant applications in the field of conducting materials. For these reasons heterocyclic compounds - especially those containing sulfur and nitrogen - represent an important resource for the material chemistry[21-24] and also for medicinal chemistry.[25-29] Important precursors for tetrathiafulvalenes are the 1,3-dithiol-2-thione derivatives.[30]

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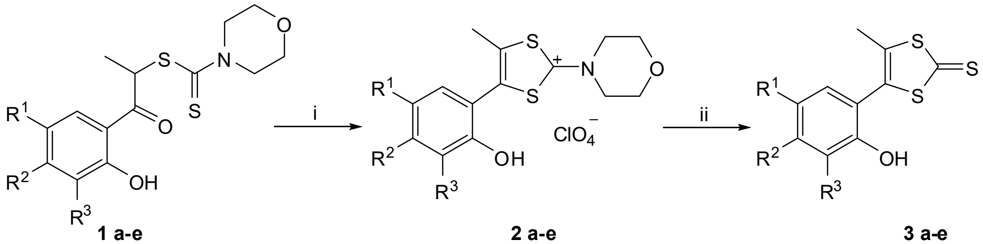
This paper reports the synthesis of novel 4-(2-hydroxyaryl)-5-methyl-1,3-dithiol-2-thione derivatives from the corresponding 1,3-dithiolium salts, via mesoionic compounds by the nucleophilic attack of sulfide anion at the C(2) position of the 1,3-dithiolium ring.

Results and Discussion

Following a reported experimental procedure,[30] the synthesis of the 1,3-dithiol-2-thiones has been accomplished in two consecutive reactions as described in Scheme 1. In a first step, 1,3-dithiolium perchlorates **2a-e** were obtained by heterocyclization of 1-(2-hydroxyaryl)-1-oxapropan-2-yl-morpholine-4-carbodithioates **1** under acidic conditions.[5-9] Compounds **1** were synthesized by the reaction of the corresponding phenacyl bromides with morpholinium morpholine-4-carbodithioate according to a reported procedure.[5] The latter are readily available from the reaction of morpholine with carbon disulfide.[31]



i. H_2SO_4 / AcOH 1:3 (v/v), 80 °C, 10 min, $HClO_4$ 70%
ii. $Na_2S \cdot 9H_2O$, EtOH, rt

Scheme 1. Synthesis of 4-(2-hydroxyaryl)-5-methyl-1,3-dithiol-2-thiones.

1, 2, 3	**a**	**b**	**c**	**d**	**e**
R^1	Br	Br	Br	Me	I
R^2	H	H	Me	H	H
R^3	H	Br	H	Br	I

The treatment of 1,3-dithiolium salts **2** with an excess of sodium sulfide nonahydrate in ethanol at room temperature afforded the corresponding 1,3-dithiole-2-thiones **3a–e** (Scheme 1). These compounds have been isolated as yellow products in good yields. The reaction mechanism involve the conversion of 1,3-dithiolium perchlorates **2** to the corresponding mesoionic phenolates under the basic condition provided by exccess sodium sulfide. Subsequently, the nucleophilic atack of sulfide anion to the C(2) atom of 1,3-dithiolium ring followed by the elimination of morpholine leads to the target 1,3-dithiole-2-thiones **3**.

The structure of 1,3-dithiole-2-thiones **3** has been proved by analytical and spectral data. The ^{1}H NMR spectra indicate the disappearance of the signals from the aliphatic area corresponding to the morpholine moietie. ^{13}C NMR spectra indicate the appearance of a new signal at ca. 208-211 ppm attributed to the thiocarbonyl group.

Experimental

General remarks: Melting points were obtained on a KSPI melting-point meter and are uncorrected. IR spectra were recorded on a Bruker Tensor 27 instrument. NMR spectra were recorded on a Bruker 400 MHz spectrometer. Chemical shifts are reported in ppm downfield from TMS. Mass spectra were recorded on a Thermo Scientific ISQ LT instrument.

General procedure for 4-(2-hydroxyaryl)-5-methyl-1,3-dithiol-2-thiones 3a–e:

To a suspension of 4-(2-hydroxyaryl)-5-methyl-2-(morpholin-4-yl)-1,3-dithiolium perchlorate (**2a–e**) (5 mmol) in EtOH (96%, 50 mL), $Na_2S \cdot 9H_2O$ (15 mmol) was added. The reaction mixture was stirred at room temperature until a homogeneous solution was obtained (ca. 2 h) and then poured into water (100 mL) and acidified with 1 N HCl solution to pH = 1.

The resulted precipitate was filtered, washed with water, dried, and recrystallized from MeOH. Analytical data of **3a–e** are presented below.

4-(5-Bromo-2-hydroxyphenyl)-5-methyl-1,3-dithiol-2-thione **3a**: Yellow solid, 84%, m.p.=195-196 °C. ^{1}H NMR (DMSO-d_6): δ = 2.13 (3H, s, CH_3-5), 6.92 (1H_{ar}, m, H-3), 7.44 (2H_{ar}, m, H-4+H-6), 10.51 (1H, s, OH) ppm. ^{13}C NMR (DMSO-d_6): δ = 14.9, 110.5, 118.70, 118.77, 133.5, 134.0, 134.5, 139.2, 155.2, 211.5 ppm. FT-IR (ATR): ν = 3198, 1483, 1410, 1279, 832 cm^{-1}. MS (EI): *m/z* = 318 (M^+ for $C_{10}H_7{}^{79}BrOS_3$).

4-(3,5-Dibromo-2-hydroxyphenyl)-5-methyl-1,3-dithiol-2-thione **3b**: Yellow solid, 81%, m.p.=187-188 °C. ^{1}H NMR (DMSO-d_6): δ = 2.18 (3H, s, CH_3-5), 7.59 (1H, d, H-4, ^4J =2.3 Hz), 7.68 (1H, d, H-6; ^4J=2.3 Hz), 10.12 (1H, s, OH) ppm. ^{13}C NMR (DMSO-d_6): δ = 15.6, 112.1, 113.2, 117.9, 125.5, 133.1, 134.5, 137.4, 151.6, 209.9 ppm. FT-IR (ATR): ν = 3184, 1489, 1401, 1284, 811 cm^{-1}. MS (EI): *m/z* = 396 (M^+ for $C_{10}H_6{}^{79}Br_2OS_3$).

4-(5-Bromo-2-hydroxy-4-methylphenyl)-5-methyl-1,3-dithiol-2-thione **3c**:
Yellow solid, 86%, m.p.=205-206 °C. ^{1}H NMR (DMSO-d_6): δ = 2.19 (3H, s, CH_3-5), 2.25 (3H, s, CH_3), 7.00 (1H_{ar}, s, H-3), 7.51 (1H_{ar}, s, H-6), 10.50 (1H, s, OH) ppm. ^{13}C NMR (DMSO-d_6): δ = 17.8, 21.2, 114.7, 124.4, 127.4, 128.7, 129.7, 133.3, 134.5, 154.7, 208.1 ppm. FT-IR (ATR): ν = 3200, 1487, 1409, 1254, 842 cm^{-1}. MS (EI): *m/z* = 332 (M^+ for $C_{11}H_9{}^{79}BrOS_3$).

4-(3-Bromo-2-hydroxy-5-methylphenyl)-5-methyl-1,3-dithiol-2-thione **3d**:
Yellow solid, 78%, m.p.=174-175 °C. ^{1}H NMR (DMSO-d_6): δ = 2.10 (3H, s, CH_3-5), 2.27 (3H, s, CH_3), 5,87 (1H, s, OH), 6.98 (1H_{ar}, d, H-4, ^4J =2.2 Hz), 7.36 (1H, d, H-6; ^4J=2.2 Hz) ppm. ^{13}C NMR (DMSO-d_6): δ = 17.6,

21.1, 114.8, 124.1, 126.9, 128.9, 129.8, 133.4, 134.5, 154.8, 208.7 ppm. FT-IR (ATR): ν = 3188, 1495, 1412, 1284, 825 cm^{-1}. MS (EI): *m/z* = 332 (M$^+$ for $C_{11}H_9{}^{79}BrOS_3$).

4-(2-Hydroxy-3,5-diiodophenyl)-5-methyl-1,3-dithiol-2-thione **3e**: Yellow solid, 77%, m.p.=211-212 °C. ^{1}H NMR (DMSO-d_6): δ = 2.20 (3H, s, CH_3-5), 6.24 (1H, s, OH), 7.59 (1H, d, H-4, ^4J =2.0 Hz), 8.08 (1H, d, H-6, ^4J =2.0 Hz) ppm. ^{13}C NMR (DMSO-d_6): δ = 17.3, 84.0, 91.3, 119.1, 126.5, 134.1, 139.8, 148.6, 155.3, 206.0 ppm. FT-IR (ATR): ν = 3201, 1491, 1414, 1289, 814 cm^{-1}. MS (EI): *m/z* = 492 (M$^+$ for $C_{10}H_6I_2OS_3$).

Conclusions

The synthesis of valuable precursors for substituted tetrathiafulvalenes has been accomplished by the reaction of the corresponding 4-(2-hydroxyaryl)-5-methyl-1,3-dithiol-2-ylium perchlorates with sodium sulfide nonahydrate in ethanol at room temperature. The newly obtained 4-(2-hydroxyaryl)-5-methyl-1,3-dithiol-2-thiones were characterized by NMR and MS spectrometry and IR spectroscopy.

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