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1,3,4-Thiadiazolines by a 1,5-Dipolar Ring Reconstruction of Mesoionic (2,3-Diphenyltetrazolio)thio Ylides

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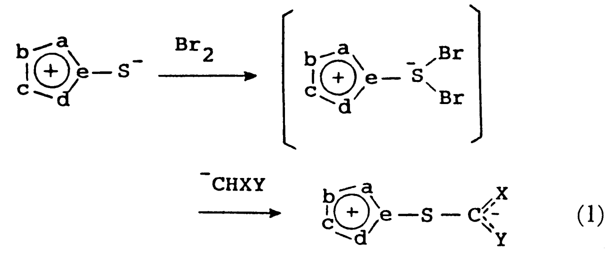
Synopsis. 4-Phenyl-2-phenylazo-2,3-dihydro-1,3,4-thiadiazoles were synthesized from 2,3-diphenyltetrazolium-5-thiolate by two methods. The formation of the thiadiazolines is rationalized by 1,5-dipolar ring closure of the intermediate mesoionic (tetrazolio)thio ylides.

We have recently reported[1] the synthesis of mesoionic thiocarbonyl ylides by the treatment of mesoionic thiolates with bromine followed by the reaction of the conjugate anions of active methylene compounds (Eq. 1). Now, we have examined the reaction of the bromine adduct of 2,3-diphenyltetrazolium-5-thiolate (**1**) with various conjugate anions of active methylene compounds and found that several anions gave thiadiazoline derivatives **2** exclusively, instead of the expected thiocarbonyl ylides. Furthermore, same thiadiazoline derivatives were also obtained from the reaction of **1** with the diazo compounds of active methylene compounds.



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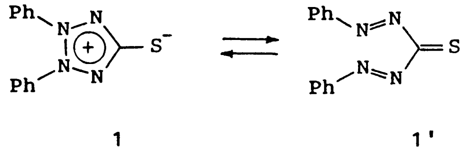
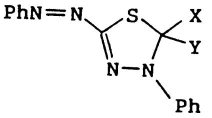
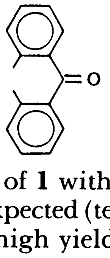


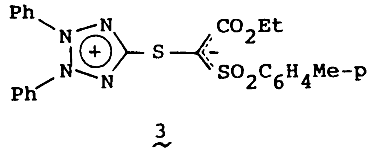
1 **1'**



2a: $X=Y=CO_2Et$
b: $X=CO_2Et$, $Y=CN$
c: $X=CO_2Et$, $Y=COMe$
d: X,Y=



The reaction of the bromine adduct of **1** with ethyl sodio-*p*-tolylsulfonylacetate gave the expected (tetrazolio)thio ylide **3** as stable crystals in a high yield. On the other hand, the reaction with diethyl sodiomalonate led to the exclusive formation of 5,5-bis(ethoxycarbonyl)-4-phenyl-2-phenylazo-2,3-dihydro-1,3,4-thiadiazole (**2a**) as deep red crystals in 94% yield, and the corresponding (tetrazolio)thio ylide was not obtained at all. The structure of **2a** was deduced from its analytical and spectral properties. The ^{13}C NMR spectrum showed two sets of phenyl signals and the absorptions of the thiadiazoline ring carbons at δ 83.0 and 154.6 ppm. Its ^{1}H NMR revealed the nonequivalency of the two ethoxycarbonyl groups. An intense absorption at 470 nm in the electronic spectrum is consistent with the presence of a phenylazo chromophore. Similar reactions with the sodium salt of ethyl cyanoacetate or ethyl acetoacetate gave the respective thiadiazolines **2b** and **2c** in good yields.



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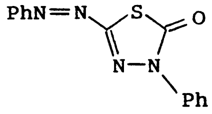
The thiadiazolines **2a** and **2c** were also prepared by refluxing of the thiolate **1** in chloroform with the diazo derivatives of diethyl malonate and ethyl acetoacetate, respectively.[2] A new thiadiazoline **2d** having a spiro-structure was synthesized by the reaction of **1** with 10-diazo-9-anthrone.

Two syntheses of 4-phenyl-2-phenylazo-2,3-dihydro-1,3,4-thiadiazole derivatives from mesoionic thiolate **1** are so far reported; treatment of **1** with iron pentacarbonyl gave 1,3,4-thiadiazol-2(3*H*)-one (**4**)[3] and reaction with 2-alkylaminoindenes yielded products with the general structure **5**.[4] The formation of these products **4** and **5** is thought to occur via the acyclic valence tautomer **1′** of thiolate **1**. In our reactions, the formation of thiadiazolines **2** can also be rationalized in terms of participation of the acyclic valence tautomer **6′** of intermediate thiocarbonyl ylide **6**. The tautomer **6′** undergoes 1,5-dipolar ring closure to furnish thiadiazolines **2** (Eq. 2). The isolation of (tetrazolio)thio ylide **6** is depend upon the nature of the substituents (X and Y) on the carbanionoid carbon; only in the



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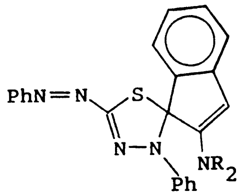

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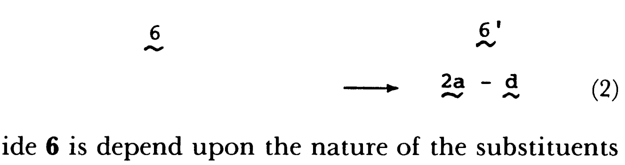

(2)

cases of strongly electron-withdrawing substituents, the ylide **6** is thought to be isolated stably.

Experimental

General. Melting points were determined on a hot-stage apparatus and are uncorrected. Infrared spectra were taken for KBr discs with a JASCO IRA-1 spectrometer. Electronic spectra were run with a Hitachi 124 spectrophotometer. ^{1}H NMR spectra were recorded on a Hitachi R-24A spectrometer (60 MHz) or on a Varian XL-200 spectrometer (200 MHz) with Me_4Si as an internal standard. ^{13}C NMR spectra were determined on a Varian XL-200 spectrometer (50 MHz). Mass spectra were recorded on a Hitachi M-52 instrument at 20 eV or on an ESCO EMD-05B at 70 eV using a direct-inlet system. Elemental analyses were performed at the Elemental Analysis Center of Kyoto University.

Synthesis of Mesoionic (Tetrazolio)thio Ylide (3). To a stirred suspension of mesoionic thiolate **1** (127 mg, 0.5 mmol) in dry dichloromethane (1.5 cm^3) was added bromine (0.030 cm^3, 0.55 mmol) and the mixture was stirred at room temperature for 10 min. The sodium salt of ethyl *p*-tolylsulfonylacetate, prepared from ethyl *p*-tolylsulfonylacetate (242 mg, 1 mmol) and an equimolar amount of sodium hydride in tetrahydrofuran (THF) (1 cm^3), was added to the bromine adduct. After 5 min, the reaction was quenched by the addition of water (1 cm^3) and ether (20 cm^3) was added. Pale yellow precipitates were filtered and washed successively with ether, water, and THF, and then dried to give ylide **3** (220 mg, 89%), mp 125 °C (MeCN); IR: 1630, 1354, 1292, 1274, 1132, 1070, 764, 686, 662 cm^{-1}; UV (MeCN): λ_{max} 231 ($\log\varepsilon$ 4.34), 258 (sh) (4.12), and 343 nm (3.21); ^{1}H NMR (60 MHz, DMSO-d_6): δ=1.00 (t, J=7 Hz, $CH_2\underline{Me}$), 2.28 (s, 3H, Me), 3.80 (q, J=7 Hz, 2H, $\underline{CH_2}Me$), 7.10 (d, J=9 Hz, 2H, aryl H), 7.70 (m, 10H, Ph), 7.75 (d, J=9 Hz, 2H, aryl H); ^{13}C NMR (DMSO-d_6): δ=14.9 ($CH_2\underline{Me}$), 21.0 (Me), 57.6 ($\underline{C}H_2Me$), 60.4 ($S-C^-$), 126.5 (ortho), 127.2 (aryl), 128.0 (aryl), 130.1 (meta), 133.3 (ipso), 133.7 (para), 139.8 ($\underline{C}$-Me), 145.0 ($C-SO_2$), 166.0 (C=O), 172.9 ($S-C^+$); Found: C, 56.38; H, 4.56; N, 10.79%. Calcd for $C_{24}H_{22}N_4S_2\cdot H_2O$: C, 56.23; H, 4.71; N, 10.93%.

Reaction of the Bromine Adduct of 1 with the Conjugate Bases of Active Methylene Compounds. The following reaction with diethyl sodiomalonate is representative. To a suspension of the bromine adduct of **1**, prepared as above from **1** (127 mg, 0.5 mmol) and bromine (0.030 cm^3, 0.55 mmol) in dichloromethane (1.5 cm^3), was added diethyl sodiomalonate (1.5 mmol) in THF (1 cm^3). The mixture was stirred at room temperature for 10 min. Water was added and the product was extracted with dichloromethane. The extracts were dried over anhydrous sodium sulfate and the solvent was removed. The residue was chromatographed on silica gel (eluent: dichloromethane–hexane 1 : 1) to give thiadiazoline **2a** (198 mg, 96%) as red crystals, mp 91 °C (benzene–hexane); IR: 1772, 1554, 1490, 1250, 1234, 1150, 1130, 1038, 756, 682 cm^{-1}; UV-VIS (MeCN): λ_{max} 253 ($\log\varepsilon$ 4.08), 310 (4.03), and 470 nm (4.35), ^{1}H NMR (200 MHz, $CDCl_3$): δ=1.18 (t, J=7 Hz, 6H, Me), 4.30 (q, J=7 Hz, 2H, CH_2), 4.31 (q, J=7 Hz, 2H, CH_2), 7.13—7.52 (m, 8H, Ph), 7.92 (m, 2H, Ph); ^{13}C NMR ($CDCl_3$): δ=13.7 (Me), 63.5 (CH_2), 83.0 (C^5), 117.8 (ortho), 123.4 (ortho), 124.1 (para), 128.9 (meta), 129.2 (meta), 132.1 (para), 142.1 (ipso), 151.8 (ipso), 154.6 (C^2), 165.8 (C=O); MS (20 eV): m/z (rel intensity) 412 (M^+, 6), 77 (Ph, 100); Found: C, 58.43; H, 4.80; S, 7.79%. Calcd for $C_{20}H_{20}N_4O_4S$: C, 58.24; H, 4.89; S, 7.77%.

Similarly, thiadiazolines **2b** and **2c** were synthesized and obtained as red crystals.

2b: 62% yield; mp 98 °C (MeOH); IR: 1744, 1564, 1500, 1354, 1260, 1148, 748, 680 cm^{-1}; UV-VIS (MeCN): λ_{max} 245 ($\log\varepsilon$ 4.08), 315 (4.01), and 450 nm (4.36); ^{1}H NMR (60 MHz, $CDCl_3$): δ=1.23 (t, J=7 Hz, 3H, Me), 4.34 (q, J=7 Hz, 2H, CH_2), 7.40 (m, 8H, Ph), 7.85 (m, 2H, Ph); ^{13}C NMR ($CDCl_3$): δ=13.7 (Me), 65.1 (CH_2), 71.2 (C^5), 113.2 (CN), 116.3 (ortho), 123.7 (ortho), 124.6 (para), 129.6 (meta), 129.4 (meta), 133.0 (para), 140.5 (ipso), 151.5 (ipso), 155.0 (C^2), 163.4 (C=O); MS (20 eV): m/z (rel intensity) 365 (M^+, 34), 292 ($M-CO_2Et$, 100); Found: C, 59.23; H, 4.04; N, 19.37%. Calcd for $C_{18}H_{15}N_5O_2S$: C, 59.17; H, 4.14; N, 19.16%.

2c: 94% yield; mp 72 °C (hexane); IR: 1742, 1730, 1550, 1500, 1366, 1248, 1164, 1152, 774, 752, 686 cm^{-1}; UV-VIS (MeCN): λ_{max} 254 ($\log\varepsilon$ 4.06), 304 (4.02), and 477 nm (4.41); ^{1}H NMR (60 MHz, $CDCl_3$): δ=1.17 (t, J=7 Hz, 3H, $CH_2\underline{Me}$), 2.45 (s, 3H, COMe), 4.27 (q, J=7 Hz, 2H, CH_2), 7.35 (m, 8H, Ph), 7.80 (m, 2H, Ph); ^{13}C NMR ($CDCl_3$): δ=13.6 (Me), 25.5 ($CO\underline{Me}$), 63.2 ($\underline{C}H_2Me$), 86.7 (C^5), 116.5 (ortho), 123.3 (ortho), 123.7 (para), 129.0 (meta), 129.2 (meta), 132.2 (para), 141.8 (ipso), 151.7 (ipso), 153.5 (C^2), 166.5 ($\underline{C}O_2Et$), 196.0 ($\underline{C}OMe$); MS (70 eV): m/z (rel intensity) 382 (M^+, 2), 77 (Ph, 100); Found: C, 59.82; H, 4.66; N, 14.60%. Calcd for $C_{19}H_{18}N_4O_3S$: C, 59.67; H, 4.74; N, 14.65%.

Reaction of Thiolate 1 with Diazo Compounds. A solution of thiolate **1** (389 mg, 1.53 mmol) and diethyl diazomalonate[5] (549 mg, 2.95 mmol) in chloroform (12 cm^3) was heated at reflux for 24 h. The solvent was removed and the residue was column chromatographed on silica gel (eluent: chloroform) to afford red crystals of thiadiazoline **2a** (229 mg, 47%), identical with the compound obtained above. The reactions with ethyl diazoacetoacetate[5] and 10-diazo-9-anthrone[6] were similarly carried out and the corresponding thiadiazolines **2c** and **2d** were isolated in 5 and 65% yields, respectively.

2d: Mp 286 °C (benzene); IR: 1660, 1596, 1536, 1492, 1362, 1318, 1266, 1224, 1156, 930, 770, 746, 740, 710, 682 cm^{-1}; UV-VIS (MeCN): λ_{max} 253 ($\log\varepsilon$ 4.32), 279 (sh) (4.24), 302(sh) (4.11), and 476 nm (4.33); ^{1}H NMR (200 MHz, $CDCl_3$): δ=6.90—7.10 (m, 4H, aryl H), 7.50—7.70 (m, 8H, Ph and aryl H), 7.70—7.90 (m, 4H, Ph and aryl H), 8.41 (d, J=8 Hz, 2H, aryl H); ^{13}C NMR ($CDCl_3$): δ=81.1 (C^5), 116.9 (ortho), 122.9 (para), 123.3 (ortho), 127.5 (aryl CH), 127.8 (aryl CH), 129.0 (meta or aryl CH), 129.2 (meta or aryl CH), 129.4 (meta or aryl CH), 132.0 (para), 133.4 (aryl $=\overset{|}{C}-$), 134.9 (aryl CH), 140.5 (ipso or aryl $=\overset{|}{C}-$), 143.7 (ipso or aryl $=\overset{|}{C}-$), 151.9 (ipso), 154.8 (C^2), 181.8 (C=O); MS (20 eV): m/z (rel intensity) 446 (M^+, 100); Found: C, 72.62; H, 4.01; S, 7.24%. Calcd for $C_{27}H_{17}N_4OS$: C, 72.63; H, 4.06; S, 7.18%.

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