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REACTIONS OF ELEMENTAL SULFUR AND SELENIUM WITH SOME ACETYLENIC COMPOUNDS. FORMATION OF THIOPHENES AND SELENOPHENES

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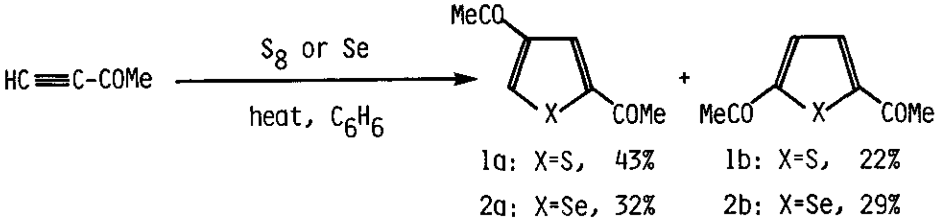
Abstract — The reaction of 3-butyn-2-one with elemental sulfur at 205-215 °C in benzene in a stainless autoclave afforded 2,4- and 2,5-diacetylthiophenes in 43% and 22% yields, respectively. Under similar conditions, the reaction with elemental selenium gave 2,4- and 2,5-diacetylselenophenes in 32% and 29% yields, respectively. Diphenylacetylene reacted with sulfur and selenium to produce tetraphenylthiophene (78%) and tetraphenylselenophene (38%), respectively. The reaction of di(2-thienyl)acetylene with sulfur provided tetra(2-thienyl)thiophene in 57% yield. The reaction of dimethyl acetylenedicarboxylate with sulfur in the presence of diphenylacetylene afforded 2,3-bis(methoxycarbonyl)-4,5-diphenylthiophene (29%) and tetrakis(methoxycarbonyl)thiophene (15%). On the basis of these results, the mechanism for the formation of thiophenes and selenophenes is disccused.

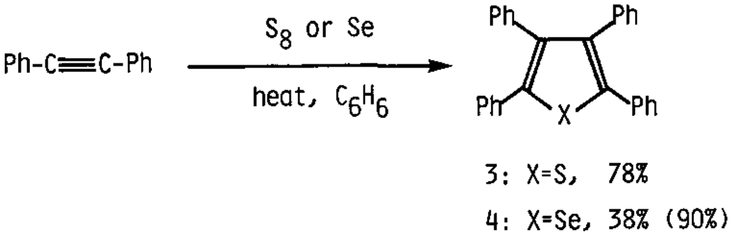
As early as 1895 Michael reported the preparation of 2,3,4,5-tetrakis(methoxycarbonyl)thiophene by reaction of elemental sulfur with dimethyl acetylenedicarboxylate (DMAD).[1] One of the earliest sources of thiophene involved passing acetylene through molten sulfur or over iron pyrites.[2] Thereafter, however, chemistry on reactions of sulfur with acetylenic compounds has not much developed.[3-7] Reactions of elemental selenium with acetylenes have scarcely been studied.[4,5] In our continuing interest in reactions of elemental sulfur and selenium with reactive organic compounds,[8,9] we have previously reported the reactions of elemental sulfur and selenium with acetylenic compounds including DMAD, methyl propiolate, and benzyne.[10] Herein we report further results on reactions of sulfur and selenium with acetylenes.

We have previously reported that methyl propiolate reacts with elemental sulfur at 205-215 °C for 14 h in benzene in a stainless autoclave to afford 2,4- and 2,5-bis(methoxycarbonyl)thiophenes in 41% and 19% yields, respectively.[10] Under similar conditions, the reaction with selenium gave 2,4- and 2,5-bis(methoxycarbonyl)selenophenes in 45% and 30% yields, respectively.[10] We have now investigated the reaction of sulfur and selenium with 3-butyn-2-one. A mixture of elemental sulfur and excess 3-butyn-2-one (ca. 5 equiv) in benzene was heated at 205-215 °C for 14 h in a stainless autoclave. Chromatographic workup of the mixture gave 2,4- and 2,5-diacetylthiophenes

(1a and 1b) in 43% and 22% yields, respectively, and a small amount of 1,3,5-triacetylbenzene. Under similar conditions, the reaction with selenium also gave 2,4- and 2,5-diacetylselenophenes (2a and 2b) in 32% and 29% yields, respectively, and a small amount of 1,3,5-triacetylbenzene. These results show that 3-butyn-2-one is comparable with methyl propiolate in reactivity toward sulfur and selenium, though less reactive than DMAD. The yields and isomer ratios are also comparable with those obtained by reactions with methyl propiolate.[10]

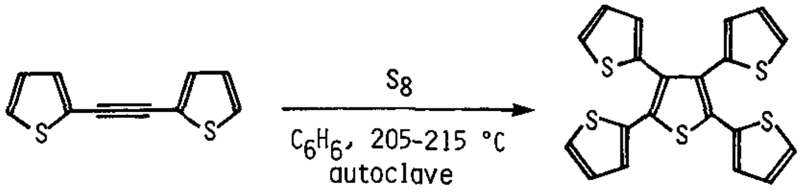


The reaction of diphenylacetylene with sulfur was sluggish in refluxing o-dichlorobenzene. Thus a mixture of sulfur and diphenylacetylene (2 equiv) in o-dichlorobenzene was refluxed for 45 h to obtain 2,3,4,5-tetraphenylthiophene (3) in 68% yield with 12% recovery of diphenylacetylene. When the reaction was conducted in benzene at 200-210 °C for 14 h using an autoclave, the yield of 3 was improved to 78%. The reaction with elemental selenium under the same conditions gave 2,3,4,5-tetraphenylselenophene (4) only in 5% yield with 87% recovery of the starting acetylene. When the reaction was carried out at 225-230 °C for 14 h, 4 was obtained in 38% yield (or 90% yield based on consumed diphenylacetylene). Accordingly, the reaction of diphenylacetylene with sulfur and selenium provides a very simple one-pot method for the preparation of 3 and 4 since all of the starting materials are commercially available at reasonable prices.



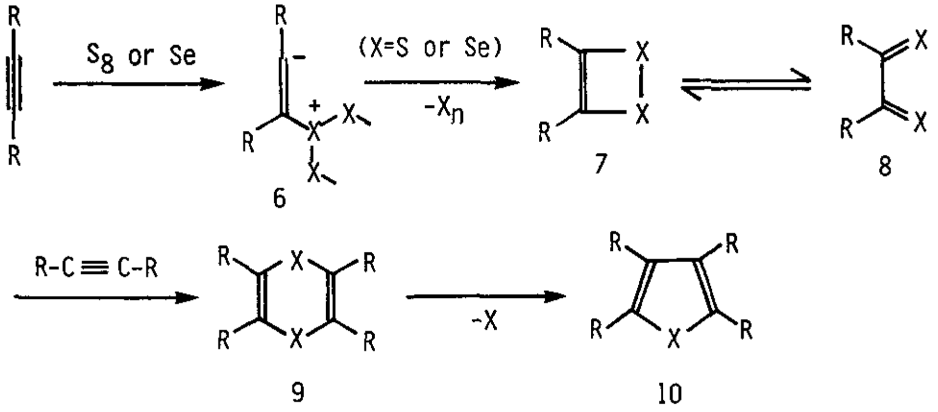
Currently we are interested in the preparation, bioactivities, and physicochemical properties of oligothiophenes.[11,12] In this connection we have applied the above reaction to the preparation of structurally interesting 2,3,4,5-tetra(2-thienyl)thiophene (5). Heating di(2-thienyl)acetylene

(2 equiv) with sulfur in benzene at 205-215 °C for 14 h cleanly afforded the expected thiophene 5 in 57% yield.



57% 5

The previously proposed mechanism by us for the formation of thiophenes and selenophenes is as follows.[10] 1,2-Dithietes (1,2-diselenetes) 7 are first formed via initial formation of betaines 6 by electrophilic attack of acetylenes on sulfur and selenium. Tautomerization of 7 to 8 and the Diels-Alder reaction of 8 with acetylenes give 1,4-dithiins (1,4-diselenins) 9, which would afford the final products 10 with thermal extrusion of sulfur (selenium). An alternative mechanism involving thiirene intermediate 11, however, also seems possible. Evidence supporting for the 1,2-dithietes (1,2-diselenetes) mechanism stems from the following observations. a) Krebs et al. isolated the corresponding 1,2-dithietes by treatment of 3,3,6,6-tetramethyl-1-thia-4-cycloheptyne and its S-dioxide with elemental sulfur.[6] b) The reaction of methyl propiolate with di-N-morpholino disulfide, which proceeds via a thiirene intermediate (trapped by carbon disulfide to give a 1,3-dithiole-2-thione derivative), afforded 2,5-bis(methoxycarbonyl)thiophene exclusively,[13]



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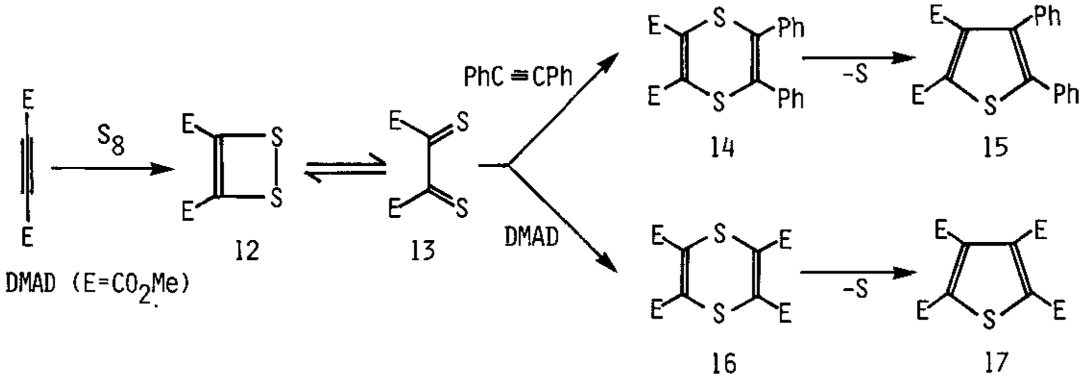
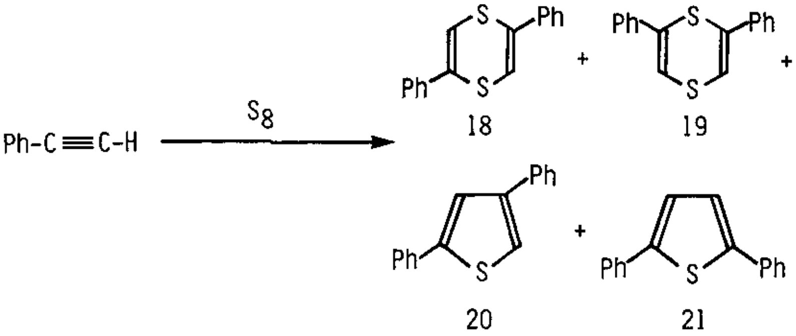
while in the present case the reaction of methyl propiolate with sulfur affords both 2,4- and 2,5-bis(methoxycarbonyl)thiophenes in a comparable yield.[10] c) We obtained thianthrene and selenanthrene by reactions of benzyne with sulfur and selenium.

We now therefore examined trapping of α-dithione (α-diselone) intermediates **8** by the Diels-Alder reaction. DMAD reacts with sulfur in refluxing *o*-dichlorobenzene to give 2,3,4,5-tetrakis-(methoxycarbonyl)thiophene (**17**),[10] while the reaction of diphenylacetylene with sulfur under the same conditions is sluggish as already described. Thus, if the proposed mechanism is operative, 2,3-bis(methoxycarbonyl)-4,5-diphenylthiophene (**15**) should be formed by the reaction of DMAD with sulfur in the presence of diphenylacetylene; the 1,2-dithiete **12** is first formed from DMAD and sulfur, tautomerizes to **13**, and then reacts with diphenylacetylene to give the 1,4-dithiin **14**, which finally affords **15** with elimination of sulfur. Actually the reaction of DMAD (1 equiv) with sulfur in the presence of diphenylacetylene (2 equiv) in refluxing *o*-dichlorobenzene for 5 h afforded **15** in 29% yield along with **17** in 15% yield. The fact that tetraphenylthiophene **3** is not formed indicates that sulfur first reacts with DMAD. This result adds another supporting evidence for the proposed mechanism, although the mechanism involving thiirene intermediates cannot be excluded completely.



It was reported that phenylacetylene reacts with sulfur at 140 °C with evolution of hydrogen sulfide to give 2,4-diphenylthiophene (**20**) as the sole product.[4] This reaction is of interest in that it gives only the 2,4-isomer and also occurs under milder conditions than those applied DMAD, methyl propiolate, 3-butyn-2-one, and diphenylacetylene. We reinvestigated this reaction and found that it is more complex than that previously reported. A mixture of sulfur and phenylacetylene (2 equiv) was gradually heated without solvent, and when the temperature reached about 125 °C, a vigorous reaction occurred with evolution of gas, which ceased in a few minutes. Chromatographic workup of the mixture gave a 2:1 mixture of 2,5- and 2,6-diphenyl-1,4-dithiins

(**18** and **19**, 16%), 2,4-diphenylthiophene (**20**, 15%) contaminated with a trace amount of 2,5-diphenylthiophene (**21**), and a small amount of 1,3,5-triphenylbenzene. The reaction carried out in refluxing chlorobenzene similarly afforded a 2:1 mixture of **18** and **19** in 18% yield and **20** (contaminated with **21**) in 9% yield. The mechanism of this reaction is not so simple and apparently differs from that of our reactions.



EXPERIMENTAL

Reaction of Sulfur with 3-Butyn-2-one. A mixture of 449 mg (14 mg-atoms) of sulfur and 4.70 g (69 mmol) of 3-butyn-2-one in 100 ml of benzene was heated at 205-215 °C for 14 h in a stainless autoclave. The resulting brown mixture was evaporated to leave 3.5 g of the brown semisolid, which was subjected to column chromatography (Merck silica gel 40, 70-230 Mesh, 80 g). Elution with methylene chloride gave 2,5-diacetylthiophene (**1b**), 2,4-diacetylthiophene (**1a**), and 1,3,5-triacetylbenzene in this order. Separation of **1a** and **1b** and of **1a** and triacetylbenzene was, however, incomplete. The mixture part was rechromatographed using a mixture of ether and hexane (3:2) as eluent. Finally, 1.00 g (43%) of **1a**, 0.51 g (22%) of **1b**, and 0.17 g of triacetylbenzene were obtained. **1a**: mp 78.5-79 °C (lit.,[14] mp 76.5-78 °C); ^{1}H-nmr (CDCl$_3$) δ 2.58 (3H, s, Me), 2.62 (3H, s, Me), 8.08 (1H, d, $J \approx 1$ Hz, ring), 8.12 (1H, d, $J \approx 1$ Hz, ring). **1b**: mp 171.5-172.5 °C (lit.,[15] mp 172-173 °C); ^{1}H-nmr (CDCl$_3$) δ 2.56 (6H, s, Me), 7.58 (2H, s, ring). 1,3,5-Triacetylbenzene: mp 155-157 °C [mp of the commercial product (Aldrich), 160-162 °C].

Reaction of Selenium with 3-Butyn-2-one. A mixture of 789 mg (10 mg-atoms) of selenium and 3.40 g (50 mmol) of 3-butyn-2-one in 100 ml of benzene was heated at 200-210 °C for 14 h in a stainless autoclave. The resulting dark brown mixture was evaporated and the residue was treated as described above to give 0.70 g (32%) of 2,4-diacetylselenophene (**2a**), 0.62 g (29%) of 2,5-diacetylselenophene (**2b**), and a small amount of 1,3,5-triacetylbenzene.[16] **2a**: mp 99.5-100.5 °C (from hexane); ^{1}H-nmr (CDCl$_3$) δ 2.49 (3H, s, Me), 2.53 (3H, s, Me), 8.27 (1H, d, $J \approx 1.5$ Hz, ring), 8.97 (1H, d, $J \approx 1.5$ Hz, ring); ^{13}C-nmr (CDCl$_3$) δ 25.5, 26.6, 133.3, 145.6, 146.2, 151.5, 191.5, 191.9. Anal. Calcd for $C_8H_8O_2Se$: C, 44.67; H, 3.75%. Found: C, 44.37; H, 3.73%. **2b**: mp 134-135 °C (from methanol); ^{1}H-nmr (CDCl$_3$) δ 2.56 (6H, s, Me), 7.91 (2H, s, ring); ^{13}C-nmr (CDCl$_3$) 26.1, 134.5, 157.1, 191.9. Anal. Found: C, 44.62; H, 3.87%.

Reaction of Sulfur with Diphenylacetylene. a) *o-Dichlorobenzene as Solvent.* A mixture of 32 mg (1 mg-atom) of sulfur and 356 mg (2 mmol) of diphenylacetylene in 5 ml of *o*-dichlorobenzene was refluxed for 45 h. The mixture was evaporated under reduced pressure and the residue was subjected to column chromatography (Merck silica gel 60). Elution with cyclohexane gave 43 mg (12%) of diphenylacetylene and 266 mg (68%) of 2,3,4,5-tetraphenylthiophene (**3**), mp 186-187 °C (from cyclohexane) (lit.,[17] mp 184-185 °C).

b) *Benzene as Solvent in an Autoclave.* A mixture of 320 mg (10 mg-atoms) of sulfur and 3.56 g (20 mmol) of diphenylacetylene in 100 ml of benzene was heated at 200-210 °C for 14 h in an autoclave. The mixture was evaporated and the residue was recrystallized from cyclohexane to give 2.04 g (53%) of **3**, mp 186-187.5 °C. The filtrate was evaporated and the residue was purified by column chromatography to give 0.37 g (10%) of diphenylacetylene and 0.99 g (26%) of **3**.

Reaction of Selenium with Diphenylacetylene. A mixture of 0.79 g (10 mg-atoms) of selenium and 3.56 g (20 mmol) of diphenylacetylene in 100 ml of benzene was heated at 225-230 °C for 14 h in an autoclave. Unreacted selenium powder was removed from the reaction mixture by filtration and the dark red filtrate was evaporated. The residue was recrystallized from cyclohexane to give 0.60 g (14%) of 2,3,4,5-tetraphenylselenophene (**4**). The filtrate was evaporated and the residue was purified by silica gel column chromatography to give 2.09 g (58%) of diphenylacetylene and 1.06 g (24%) of **4**. The selenophene **4** recrystallized from cyclohexane does not show a clear melting point as previously described[18] and sintered at about 174-175 °C and melted completely at 184-185 °C.

When a mixture of 0.79 g (10 mg-atoms) of selenium and 3.56 g (20 mmol) of diphenylacetylene in

100 ml of benzene was heated at 200-205 °C for 14 h in an autoclave, 0.21 g (5%) of 4 was obtained with recovery of 3.12 g (87%) of diphenylacetylene.

Reaction of Sulfur with Di(2-thienyl)acetylene. A mixture of 48 mg (1.5 mg-atoms) of sulfur and 475 mg (2.5 mmol) of di(2-thienylacetylene)[19] in 100 ml of benzene was heated at 205-210 °C for 14 h in an autoclave. The mixture was evaporated and the residue was purified by silica gel column chromatography to give 14 mg (3%) of di(2-thienyl)acetylene and 291 mg (57%) of 2,3,4,5-tetra(2-thienyl)thiophene (5). 5: pale red crystals; mp 189-190 °C (from cyclohexane); ms m/z M^+ (relative intensity) 412 (100), 413 (28), 414 (25), 416 (4); uv $\lambda_{max}^{cyclohexane}$ nm (ε) 284sh (14500), 351 (14300); ^{1}H-nmr ($CDCl_3$) δ 6.8-7.3 (m); ^{13}C-nmr ($CDCl_3$) δ 126.3, 126.7, 126.9, 127.1, 129.3, 132.4, 133.3, 135.3, 135.7. Anal. Calcd for $C_{20}H_{12}S_5$: C, 58.22; H, 2.93%. Found: C, 58.38; H, 2.94%.

Reaction of Sulfur with DMAD in the Presence of Diphenylacetylene. A mixture of 160 mg (5 mg-atoms) of sulfur, 0.71 g (5 mmol) of DMAD, and 1.78 g (10 mmol) of diphenylacetylene in 40 ml of o-dichlorobenzene was refluxed for 5 h. The mixture was evaporated under reduced pressure and the residue was subjected to column chromatography (Merck silica gel 60, 60 g). Elution with cyclohexane gave first unreacted sulfur and then 1.43 g of diphenylacetylene. Elution with benzene gave 0.52 g (29%) of 2,3-bis(methoxycarbonyl)-4,5-diphenylthiophene (15). Finally elution with methylene chloride gave 0.13 g (15%) of 2,3,4,5-tetrakis(methoxycarbonyl)-thiophene (17), mp 124-125 °C (lit.,[1] mp 125-126 °C). 15: mp 105-105.5 °C (from hexane); ir (KBr) 1724, 1734 cm^{-1} (ester); ^{1}H-nmr ($CDCl_3$) δ 3.75 (3H, s, Me), 3.90 (3H, s, Me), 7.0-7.4 (10H, m, Ph). Anal. Calcd for $C_{20}H_{16}O_4S$: C, 68.16; H, 4.58; S, 9.10%. Found: C, 68.06; H, 4.37; S, 9.09%.

Reaction of Sulfur with Phenylacetylene. a) Without Solvent. A stirred mixture of 320 mg (10 mg-atoms) of sulfur and 2.04 g (20 mmol) of phenylacetylene was slowly heated under nitrogen. The mixture turned homogeneous at about 120 °C and a vigorous reaction occurred at about 125 °C with evolution of gas (probably hydrogen sulfide), which ceased in a few minutes. The resulting dark brown mixture was heated at 130-140 °C for additional 15 min. The reaction mixture was subjected to column chromatography (Merck silica gel 40, 50 g). Elution with hexane gave 0.35 g (15%) of 2,4-diphenylthiophene (20) contaminated with a trace amount of 2,5-diphenylthiophene (21); the presence of 21 in a trace amount was established by comparing this mixture with independently synthesized 20[20] and 21.[21] Further elution with hexane gave 0.22 g (16%, based on sulfur employed) of a 2:1 mixture of 2,5- and 2,6-diphenyl-1,4-dithiins (18 and 19). Structures of 18[22] and 19[23] were established by comparison with authentic samples and the ratio of 18 and 19 were determined by ^{1}H-nmr; vinyl protons of 18 appear at δ 6.72, while those of 19 δ 6.70. Finally elution with hexane gave 70 mg of 1,3,5-triphenylbenzene, mp 171-172 °C, which was identified by comparison with the commercial product (Tokyo Kasei).

b) Chlorobenzene as Solvent. A mixture of 320 mg (10 mg-atoms) of sulfur and 2.04 g (20 mmol) of phenylacetylene in 20 ml of chlorobenzene was refluxed for 5.5 h under nitrogen. The mixture was evaporated and the residue was treated as described above to give 0.21 g (9%) of 20 contaminated with a trace amount of 21 and 0.25 g (18%) of a 2:1 mixture of 18 and 19.

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