when a third member named furoguaiacidin was isolated (as the diethyl ether) by Majumder and Bhattacharyya[2] from the same source, these were the only known examples of lignans possessing the furan heterocycle system.

We now report a short synthesis of 2,5-bis(4-ethoxy-3-methoxyphenyl)-4-methoxymethyl-3-methylfuran (**3**), the structure proposed for furoguaiacidin diethyl ether. Alkylation of ethyl 4-ethoxy-3-methoxybenzoylacetate (**4**) with α-bromo-4-ethoxy-3-methoxypropiophenone (**5**) using sodium hydride gave the diketo ester (**6**) which, without isolation, was converted to the required furan, ethyl 2,5-bis(4-ethoxy-3-methoxyphenyl)-3-methylfuran-4-carboxylate (**7**). Reduction of this ester with lithium aluminum hydride gave the alcohol (**8**) which on alkylation with methyl iodide–sodium hydride in dimethoxyethane gave the product, furoguaiacidin diethyl ether (**3**) with physical constants (mp, nmr, ir, uv) in excellent agreement with those reported.

Experimental Section

Nmr spectra were measured in deuteriochloroform solution with tetramethylsilane as internal standard.

Ethyl 4-Ethoxy-3-methoxybenzoylacetate (4). A previously described procedure[3] was modified by using sodium hydride instead of sodium ethoxide and reducing the reaction time from 60 hr to 30 min: nmr δ 1.23 (t, 3 H, $J = 7$ Hz, $-CO_2CH_2CH_3$), 1.47 (t, 3 H, $J = 7$ Hz, $ArOCH_2CH_3$), 3.87 (s, 3 H, OCH_3), 3.90 (s, 2 H, CH_2), 4.13 (q, 2 H, $J = 7$ Hz, $ArOCH_2CH_3$), 4.17 (q, 2 H, $J = 7$ Hz, $-CO_2CH_2CH_3$), 6.75–7.57 (m, 3 H, ArH).

α-Bromo-4-ethoxy-3-methoxypropiophenone (5) was crystallized from methanol and had mp 72–73° (lit.[4] 76–77°); nmr δ 1.47 (t, 3 H, $J = 7$ Hz, $ArOCH_2CH_3$), 1.85 (d, 3 H, $J = 6.5$ Hz, CH_3CHBr), 3.88 (s, 3 H, OCH_3), 4.16 (q, 2 H, $J = 7$ Hz, $ArOCH_2CH_3$), 5.29 (q, 1 H, $J = 6.5$ Hz, $CH_3CHBrCO$), 6.78–7.62 (m, 3 H, ArH).

Ethyl 2,5-Bis(4-ethoxy-3-methoxyphenyl)-3-methylfuran-4-carboxylate (7). Sodium hydride (122 mg, 57% oil dispersion) was added with stirring to absolute ethanol (50 ml) under nitrogen, followed by a solution of the keto ester **4** (770 mg) in the same solvent (25 ml). This mixture was stirred for 15–20 min, and a solution of the bromo ketone **5** (830 mg) in ethanol (25 ml) was added dropwise. The flask was then stoppered and stirred at room temperature for 3 days. Hydrogen chloride gas was bubbled through the reaction mixture for 20 min at 0°, then the resulting dark solution refluxed for 1 hr, poured into water (300 ml), and extracted with chloroform. Removal of the solvent and crystallization of the dark residue from methanol gave the furan ester (**7**) as pale yellow prisms (550 mg): mp 113–115°; nmr δ 1.32 (t, 3 H, $J = 7$ Hz, $-CO_2CH_2CH_3$), 1.47 (t, 6 H, $J = 7$ Hz, $ArOCH_2CH_3$), 2.38 (s, 3 H, CH_3), 3.92 (s, 6 H, OCH_3), 4.14 (q, 4H, $J = 7$ Hz, $ArOCH_2CH_3$), 4.33 (q, 2 H, $J = 7$ Hz, $-CO_2CH_2CH_3$), 6.83–7.57 (m, 6 H, ArH).

Anal. Calcd for $C_{26}H_{30}O_7$: C, 68.70; H, 6.65. Found: C, 68.80; H, 6.68.

2,5-Bis(4-ethoxy-3-methoxyphenyl)-4-hydroxymethyl-3-methylfuran (8). A solution of the ester **7** (149 mg) in ether (15 ml) was added with stirring to lithium aluminum hydride (*ca.* 0.5 g) in ether (30 ml) at 0° under nitrogen. The mixture was allowed to reach room temperature on standing overnight, then decomposed by addition of ethyl acetate, then water until coagulation occurred. The solution was decanted, dried ($MgSO_4$), and evaporated to yield the alcohol **8**, crystallized from methanol as colorless needles: mp 147–148°; nmr δ 1.45 (t, 6 H, $J = 7$ Hz, $ArOCH_2CH_3$), 2.03 (br s, 1 H, -OH), 2.25 (s, 3 H, CH_3), 3.88 (s, 6 H, OCH_3), 4.09 (q, 6 H, $J = 7$ Hz, $ArOCH_2CH_3$), 4.62 (s, 2 H, CH_2OH), 6.80–7.52 (m, 6 H, ArH).

Anal. Calcd for $C_{24}H_{28}O_6$: C, 69.88; H, 6.84. Found: C, 69.80; H, 6.90.

Furoguaiacidin Diethyl Ether (3). To a stirred solution of the alcohol **8** (547 mg) in dry 1,2-dimethoxyethane (25 ml) was added methyl iodide (10 drops) and sodium hydride (*ca.* 10 mg, 57% oil dispersion) under nitrogen. More methyl iodide (25 drops) was then added and the mixture stirred overnight at room temperature. Removal of the solvent under reduced pressure gave a yellow-green crystalline residue, which was dissolved in chloroform, washed with water, and dried. Removal of the colored impurity was effected by preparative tlc (silica gel, Merck PF 254+366) using benzene–acetone (9:1) to give furoguaiacidin diethyl ether (**3**) as colorless prisms (290 mg) from methanol: mp 133.5–135° (lit.[2] mp 135°); $\lambda(C_2H_5OH)$ 258 nm (log 4.47) and 324 (4.16); nmr δ 1.45 (t, 4 H, $J = 7$ Hz, $ArOCH_2CH_3$), 2.27 (s, 3 H, CH_3), 3.45 (s, 3 H, $-CH_2OCH_3$), 3.92 (s, 6 H, $ArOCH_3$), 4.12 (q, 4 H, $J = 7$ Hz, $ArOCH_2CH_3$), 4.40 (s, 2 H, CH_2OCH_3), and 6.83–7.37 (m, 6 H, ArH).

Acknowledgment. This investigation was supported by a research grant (GM 19566) from the National Institutes of General Medical Sciences, U.S. Public Health Service.

Registry No.—**3**, 52465-56-2; **4**, 53293-05-3; **5**, 721-42-6; **7**, 53293-06-4; **8**, 53293-07-5.

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Anomalous Reaction of Selenium and Carbon Disulfide with Sodium Acetylide. Synthesis of Selenium Analogs of 1,3-Dithiole-2-thione[1]

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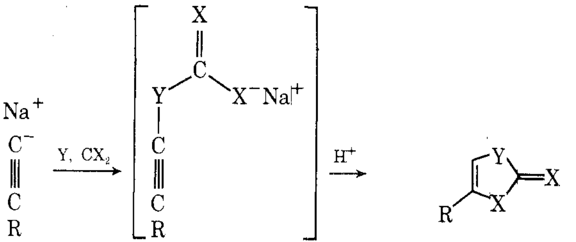
In 1964, Mayer and Gebhardt[2] reported a simple one-step synthesis of 1,3-dithiole-2-thione (**1**) which involved the addition of sulfur and carbon disulfide to sodium acetylide (eq 1). This procedure was subsequently extended with the preparation of 5-phenyl-1,3-thiaselenole-2-thione (**2**).[3] We report here the anomalous reaction that occurs in the attempt to prepare the parent compound of **2** by this method.

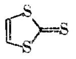
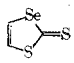
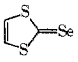
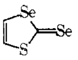
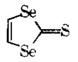
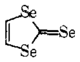


(1)

1, R = H; Y = X = S
2, R = C_6H_5; Y = Se; X = S
3, R = CH_3; Y = Se; X = S

Treatment of sodium acetylide with selenium and carbon disulfide gave, in addition to the expected product, 1,3-thiaselenole-2-thione (**4**), four other related compounds identified as **1**, 1,3-dithiole-2-selone (**5**), 1,3-thiaselenole-2-selone (**6**), and 1,3-diselenole-2-thione (**7**). In a similar reaction, sulfur and carbon diselenide reacted with sodium acetylide to give the same products as well as 1,3-diselenole-2-selone (**8**). Table I lists the relative percentages of the products formed in these two reactions. The products were easily separated by chromatography on silica gel (5% $CHCl_3$ in CCl_4). Relative to **1**, the introduction of selenium into the ring reduces the retention time on the column, while replacement of the thiocarbonyl in **1** with a selenocarbonyl increases it. In a compound such as **6**, the selenium in the carbonyl has a greater effect on the retention time than in the ring, and this material is eluted after **1**.

Table I
Relative Per Cent Composition

Reaction	Relative % composition[a]					
NaC≡CH $\xrightarrow[2.\ H^+]{1.\ Y,\ CX_2}$	 1	 4	 5	 6	 7	 8
Y = Se; X = S	22	70	5	2	1	0
Y = S; X = Se	1	1	15	25	8	50

[a] Approximate values based on amounts of material isolated after chromatography and from analysis by high-pressure liquid chromatography.

Table II
Spectroscopic Properties

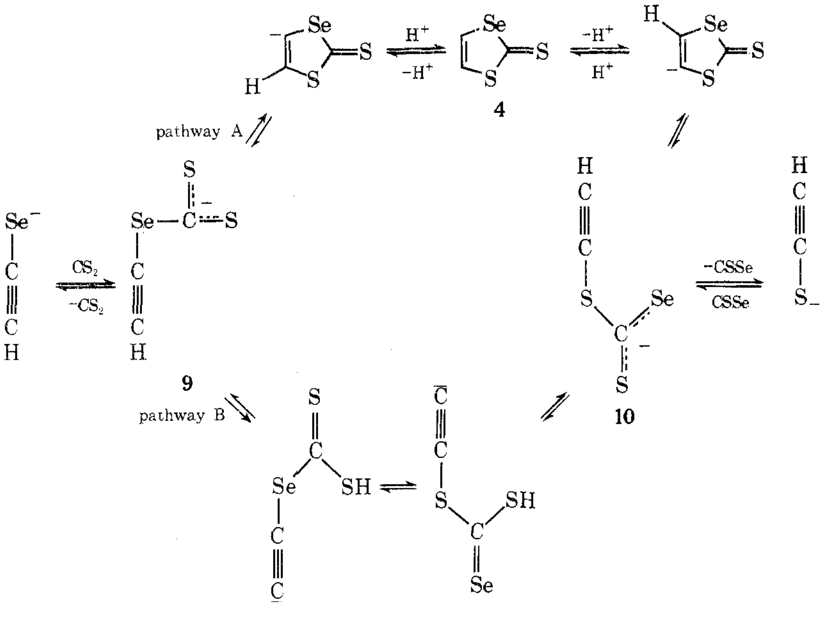
Measurement	1	4	7	5	6	8
Ir (CCl_4, cm^{-1})	1070, 1100	1060, 1095	1040, 1086	960	940	920
Nmr (δ, rel to TMS, $CDCl_3$)	7.17	7.26, 7.80 (J_{AB} = 7.5 Hz)	7.92	7.35	7.42, 8.01 (J_{AB} = 7.5 Hz)	8.10
Uv–visible, λ (ε) (hexane)	430 (100) 360 (11,000) 275 (1000) 230 (5500)	440 (100) 368 (15,500) 285 (2600) 245 (10,700)	455 (100) 377 (12,100) 290 (1850) 254 (9100)	530 (300) 402 (11,800) 295 (1000) 233 (4700)	548 (270) 410 (13,100) 305 (1500) 252 (6100)	555 (400) 413 (14,100) 318 (1200) 264 (7200)

The identification of the products in these reactions follows from their spectroscopic properties (Table II), mass spectra, and elemental analyses.[4] The ir, nmr, and uv–visible data, collected on compounds 1 and 4–8 (Table II), display remarkable additive trends for the successive introduction of selenium into **1**, which shifts the spectroscopic absorptions to lower energies. Compound 1 was identified in comparison with literature values for this material.[1,5] Compounds **7** and **8** could be prepared by independent routes: addition of selenium and carbon diselenide to sodium acetylide provided **8**, while treatment of **8** with P_4S_{10} gave **7**.

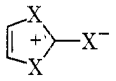
Two plausible mechanisms for the formation of the products listed in Table I are outlined in Scheme I. Pathway A involves ring closure of **9**, followed by addition and removal of H^+, and ring opening to give **10** in which a mixing of sulfur and selenium atoms has occurred. Alternately, the interconversion of **9** and **10** could be accomplished by the series of steps outlined by pathway B.[6] The formation of only one product in the case of phenyl substitution (**2**, eq 1) lends support for the two proposed mechanisms. The substituent effectively blocks the interconversion of **9** and **10**. This was further tested by treating sodium methylacetylide with selenium and carbon disulfide, which also yielded only one product, identified as 5-methyl-1,3-thiaselenole-2-thione (**3**).

Since pathway A involves removal of H^+ from the neutral ring closed product **4**, the preparation of 1 (eq 1) was carried out in the presence of **8** in order to check for the formation of mixed sulfur–selenium products. Analysis of the product mixture showed the expected presence of 1 (~95% of the product mixture), as well as **4** (~4%) and **7** (~1%). No **8** could be detected in the product mixture. While these results cannot rule out the operation of pathway B, no mixing of sulfur and selenium to give **4** and **7** would have strongly weighed against pathway A.

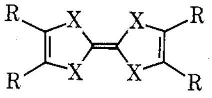
Scheme I



The reactions reported here provide an excellent opportunity to study the comparative reactivities and properties of sulfur and selenium in organic compounds. Furthermore, **1** and **4–8** are of interest as potential 6π-pseudo-aromatic systems in which each ring heteroatom contributes an electron pair as illustrated by the resonance structure **11**.[7] Synthetically, these compounds have gained attention as intermediates in the preparation of tetrathiofulvalene derivatives (**12**) which have recently been reported to form highly conducting charge-transfer salts.[8–11]



11



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Experimental Section

General. Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tenn. Molecular ion values (*m/e*) reported for compounds containing selenium are based on ^{80}Se. Some of the selenium compounds involved in the synthetic procedures described herein (*e.g.*, CSe_2 and H_2Se) are extremely toxic and difficult to control, and appropriate precautions should be exercised in handling such materials.

Reaction of Sodium Acetylide with Selenium and Carbon Disulfide. A 1-l., three-necked flask, equipped with an efficient mechanical stirrer, Dry Ice condenser, and gas inlet for acetylene was placed in a Dry Ice bath and 300 ml of ammonia added. While acetylene was being bubbled through the ammonia, 4.6 g of sodium (0.2 g-atom) was added in small portions. After the sodium had reacted, the Dry Ice bath was removed, and 200 ml of anhydrous ether and 15.8 g of powdered selenium (0.2 g-atom) were added with vigorous stirring. The ammonia was allowed to evaporate and 300 ml of acetonitrile added. Carbon disulfide (15.2 g, 0.2 mol) in 100 ml of ether was added dropwise over 1 hr. The reaction was stirred for 1 hr more, and acidified with 10% aqueous HCl. The mixture was then extracted several times with ether[12] and dried ($MgSO_4$) and the ether removed. The remaining tarry material was extracted with several portions of hot methylcyclohexane[13] from which crystallized 2.8 g of a yellow-orange solid. Column chromatography (3 ft, silica gel column, 5% $CHCl_3$ in CCl_4 eluent) on this material easily separated five products which were further purified either by recrystallization (hexane) or sublimation. Characterization of the products is based on their ir, nmr, and uv-visible spectra (see Table II), mass spectra, and elemental analyses[4] and they are the following. 1,3-Dithiole-2-thione (**1**): yellow solid; mp 49.5° (lit. 48.4°,[1] 50°[4]); *m/e* 13.4; 1,3-Thiaselenole-2-thione (**4**): yellow solid; mp 60.5°; *m/e* 182; 1,3-Dithiole-2-selone (**5**): orange solid; mp 59–60°; *m/e* 182; 1,3-Thiaselenole-2-selone (**6**): orange solid, mp 80–81°; *m/e* 230; 1,3-Diselenole-2-thione (**7**): yellow solid; mp 83–84°; *m/e* 230.

Reaction of Sodium Acetylide with Sulfur and Carbon Diselenide. The same experimental conditions as described above were followed. However, extreme care should be taken due to the high toxicity and foul smell of carbon diselenide.[14] On a 0.2 mol preparative scale, 1.5 g of a red solid was isolated from which were separated compounds **1** and **4–7** and also 1,3-diselenole-2-selone (**8**): red solid; mp 113.5–114°; *m/e* 278 (see Table II for ir, nmr, and uv–visible data).

Reaction of Sodium Acetylide with Selenium and Carbon Diselenide. The same experimental conditions as described above were followed to give **8** in yields varying from 10 to 25%.

Reaction of 1,3-Diselenole-2-selone (8) with P_4S_{10}. To 0.275 g of **8** (1 mmol) in 15 ml of benzene was added 1.0 g of P_4S_{10} (Pfaltz and Bauer) with stirring, and the solution was refluxed for 3 hr. Work-up consisted of filtering, adding ether, washing with $NaHCO_3$, and drying ($MgSO_4$). Evaporation of the ether gave a yellow-brown solid which was placed on a short silica gel column, and eluted with 5% $CHCl_3$ in CCl_4 to give a bright yellow solid identified as 1,3-diselenole-2-thione (**7**) in 25% yield.

Reaction of Sodium Methylacetylide with Selenium and Carbon Disulfide. The same experimental conditions as described above were followed to give, on a 0.2 mol preparative scale, 6.5 g of 5-methyl-1,3-thiaselenole-2-thione (**3**) (25% yield) as a yellow-orange solid: mp 34–35°; ir ($CDCl_3$) 1060 cm^{-1}; nmr (δ, rel to TMS, CCl_4) 2.28 (3 H, doublet), 7.20 (1 H, quartet), $J_{\text{allylic}} = 1.5$ Hz; *m/e* 196.

Reaction of Sodium Acetylide with Sulfur and Carbon Disulfide in the Presence of 8. The same experimental conditions as described above were followed on a 0.1 mol preparative scale, except that during the addition of carbon disulfide, **8** (0.1 g) was also added. High-pressure liquid chromatography revealed the presence of three products which were subsequently separated by column chromatography (5% $CHCl_3$ in CCl_4, silica gel) and identified by their ir and nmr spectra as **1** (~95% of product mixture), **4** (~4%), and **7** (~1%).

Acknowledgment. We thank D. Green for helpful discussions.

Registry No.—**1**, 930-35-8; **3**, 53555-43-4; **4**, 1120-65-6; **5**, 53555-44-5; **6**, 53555-45-6; **7**, 53555-46-7; **8**, 53555-47-8; sodium acetylide, 1066-26-8; selenium, 7782-49-2; carbon disulfide, 75-15-0; carbon diselenide, 506-80-9; sulfur, 7704-34-9; sodium methylacetylide, 10486-71-2.

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(12) Some difficulty was experienced in distinguishing the water–ether layer during the extraction step. An alternate work-up procedure has been developed by Dr. F. Wudl, Bell Laboratories, Murray Hill, N.J., which involves extraction of the acidified reaction mixture with a lighter-than-water liquid–liquid extractor, and extraction with hexane over a period of several hours.

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A Simple Synthesis of γ-Bisabolene

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To pursue our research on the biosynthesis of marine natural products, we were obliged to synthesize γ-bisabolene. Our choice of synthetic strategies was limited because we required the capability of incorporating isotopic labels during the penultimate stages of the synthesis. We explored the only previous stereoselective synthesis of γ-bisabolene[1] but could not repeat a key reaction to our satisfaction. We have therefore devised a simple synthesis of γ-bisabolene based on the Claisen rearrangement. Hexadeuterio-γ-bisabolene was also prepared by this route.

4-Methyl-3-cyclohexen-1-one (**1**), prepared from *p*-cresol by the method of Braude and Webb,[2] was treated with