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All isomers of the monomethylnaphtho[2,1-*b*]thiophenes were synthesized by photocyclization of 2-styrylthiophenes which were either prepared by the Wadsworth-Emmons reaction or by the condensation of 2-lithiothiophene with the corresponding carbonyl compounds.

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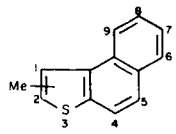
Previously we reported the synthesis of all of the monomethylbenzo[*b*]naphtho[2,1-*d*]thiophenes (2), the monomethylbenzo[*b*]naphtho[1,2-*d*]thiophenes (3) and the monomethylbenzo[*b*]naphtho[2,3-*d*]thiophenes (4) in order to determine the mutagenic and/or carcinogenic activities and in order to positively identify these substances occurring in coal-derived products and shale oils (5,6,7,8). The present paper describes the synthesis of the monomethylnaphtho[2,1-*b*]thiophenes (**2**, **4**, **5**, **6**, **7**, **8**, **9**) by the photocyclization of the corresponding 2-styrylthiophenes.

In a previous paper, we reported the photocyclization of 2-styrylbenzo[*b*]thiophene to give the corresponding benzo[*b*]naphtho[1,2-*d*]thiophene. This approach was applied to the synthesis of 6-, 7-, 8- and 9-methylnaphtho-[2,1-*b*]thiophenes. Diethyl 2-thenylphosphonate (**9**) reacted with *o*- (**10a**), *m*- (**10b**) or *p*-methylbenzaldehyde (**10c**) in dimethyl sulfoxide and sodium hydride to give 2-(*o*-methylstyryl)thiophene (**11a**, 75% yield), 2-(*m*-methylstyryl)thiophene (**11b**, 83% yield) and 2-(*p*-methylstyryl)thiophene (**11c**, 58% yield), respectively. Similarly, **11b** and **11c** were also obtained in good yield (**11b** in 83% and **11c** in 78%) from 2-thiophenecarboxaldehyde (**13**), upon reaction with diethyl *m*-methylbenzylphosphonate (**12a**) and diethyl *p*-methylbenzylphosphonate (**12b**), respectively.



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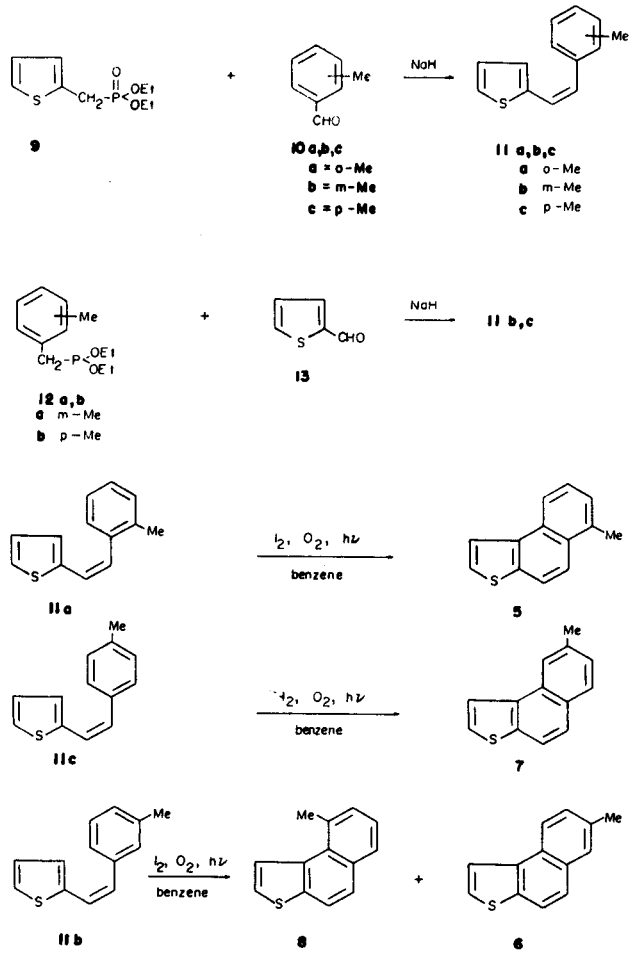
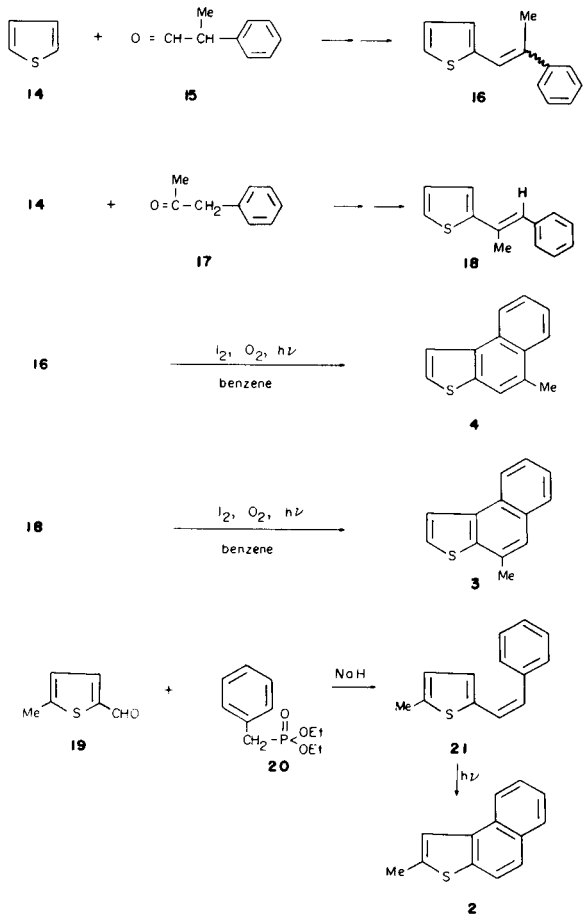


Photocyclization of **11a** and **11c** was carried out in dry benzene in the presence of iodine and air to give the corresponding 6-methyl- and 8-methylnaphtho[2,1-*b*]thiophene (**5** and **7**) each in yields of 40%. The *m*-methylstyryl compound **11b** gave two products *via* photocyclization, namely, 7-methyl- (**6**) and 9-methylnaphtho[2,1-*b*]thiophene (**8**) which were separable by chromatography on a basic alumina column using *n*-pentane and benzene as the eluents. This is consistent with the report of Carruthers and Stewart (9) who did not separate the isomers. The structural assignment between the 7-methyl and 9-methyl derivatives are based upon the nmr spectra. In **8** the methyl signal (δ 3.11) is more deshielded than the methyl signal in **6** (δ 2.53) due to the ring current effect.

The synthesis of compounds with a methyl group at the α- or β-position of the corresponding styryl compounds was carried out by applying the condensation of 2-lithio-



benzo[*b*]thiophene and the carbonyl compound. The reaction of thiophene (**14**) with *n*-butyllithium gave the lithio derivative which reacted with 2-phenylpropionaldehyde (**15**) to give the styryl compound **16** in 66% yield. Compound **18** was also obtained in 68% yield from the lithio derivative of **14** and phenylacetone (**17**). The photocyclization of **16** and **18** in benzene with iodine and oxygen gave 5-methylnaphtho[2,1-*b*]thiophene (**4**) in 56% yield and 4-methylnaphtho[2,1-*b*]thiophene (**3**) in 38% yield. Compound **16** is a mixture of *E* and *Z* isomers, both of which can be photocyclized because of the photochemically initiated equilibrium between *E* and *Z* isomers. Compound **18** is the *E* isomer. These conclusions are based upon the nmr spectra detailed in the experimental.

The synthesis of 1-methylnaphtho[2,1-*b*]thiophene (**1**) has already been prepared by our group (10) using the Wadsworth-Emmons reaction followed by photocyclization. In a similar manner, the reaction of 5-methyl-2-thiophenecarboxaldehyde (**19**) gave the corresponding styryl compound **21** which was irradiated in benzene with iodine and oxygen to give the desired 2-methylnaphtho[2,1-*b*]-thiophene (**2**) in 30% yield.

EXPERIMENTAL

Melting points were determined on a Thomas Hoover melting point apparatus and are uncorrected. The ^{1}H-nmr spectra were obtained on a Varian EM 360A spectrometer in the solvents indicated. Chemical shifts are reported in δ units. Mass spectra were obtained on a Hewlett-Packard model 5980A mass spectrometer. Elemental analyses were performed by MHW Laboratories, Phoenix, Arizona.

Method a).

2-(*m*-Methylstyryl)thiophene (**11b**).

Sodium hydride (50%, 1.5 g, 30 mmoles) in 100 ml of dry dimethyl sulfoxide, 4.68 g (20 mmoles) of diethyl 2-thenylphosphonate was added dropwise with stirring. After the addition, the solution was stirred at room temperature for 20 minutes. To the above pale yellow solution was added dropwise 2.4 g (20 mmoles) of *o*-tolualdehyde. The solution was stirred at room temperature for 2 hours. A large excess of water was added and the mixture was extracted with benzene. The benzene layer was dried over sodium sulfate and evaporated at reduced pressure to give a crude product which was chromatographed on a silica gel column using hexane as the eluent, giving 3.3 g (83%) of pale yellow crystals, mp 80°.

Method b).

Sodium hydride (50%, 1.5 g, 31 mmoles) was placed in 100 ml of dry dimethyl sulfoxide. The slurry was cooled to 20° and 4.48 g (20 mmoles) of diethyl *m*-methylbenzylphosphonate was added dropwise with stirring. To the above yellow solution, 2.24 g (20 mmoles) of 2-thiophenecarboxaldehyde (**13**) was added dropwise at room temperature and stirred for 2 additional hours. A large excess of water was added and the resulting precipitate was collected by filtration and recrystallized from methanol to give 3.3 g (83%) of colorless crystals, mp 80° (lit 80° (9)); nmr (deuteriochloroform): 2.37 (s, CH_3, 3H), 6.84-7.33 (m, aromatic and ethenyl-H, 9H); ms: m/e 200 (M^+, 100), 185 (67), 184 (58), 199 (28).

2-(*o*-Methylstyryl)thiophene (**11a**).

This compound was synthesized from **9** (2.34 g, 10 mmoles) and *o*-tolualdehyde (**10a**) (1.20 g, 10 mmoles) in a manner similar to the preparation of **11b** (method a) and was obtained as a pale yellow oil (lit 120°/0.5 mm Hg (9)) in 75% yield; nmr (deuteriochloroform): 2.31 (s, CH_3, 3H), 6.46-7.50 (m, aromatic-H and ethenyl-H, 9H); ms: m/e 200 (M^+, 100), 189 (55), 184 (37), 167 (25).

2-(*p*-Methylstyryl)thiophene (**11c**).

This compound was synthesized from **9** and **10c** as well as from **12b** and **13** by the following two methods. Methods a and b are similar to the method used for the preparation of **11b**. The yields by method a (from **9** and **10c**) and b (from **12b** and **13**) were 58% and 78%, respectively. This product was recrystallized from methanol to give colorless crystals, mp 116 (lit (9) 115-116°); nmr (deuteriochloroform): 2.31 (s, CH_3, 3H), 6.87-7.30 (m, aromatic and ethenyl-H, 9H); ms: m/e 200 (M^+, 100), 199 (28), 185 (67), 184 (58).

6-Methylnaphtho[2,1-*b*]thiophene (**5**).

A solution of 0.5 g (2.5 mmoles) of **11a** and 0.05 g of iodine in 360 ml of dry benzene was irradiated for 4 hours with a 450 Watt Hanovia medium pressure mercury lamp. During the course of the reaction, a slow stream of air was passed through the solution. The solvent was evaporated *in vacuo* and the residue was purified by chromatography on a neutral alumina column using hexane as the eluent giving 0.20 g (40%) of colorless crystals. This product was recrystallized from methanol to give colorless needles, mp 120° (lit (9) 120-122°); nmr (deuteriochloroform): 2.32 (s, 6-CH_3, 3H), 6.97-7.90 (m, aromatic-H, 7H); ms: m/e 198 (M^+, 100), 197 (51), 190 (18), 184 (21), 165 (11). The picrate gave orange-red needles, mp 142° (lit (9) mp 140-142°).

8-Methylnaphtho[2,1-*b*]thiophene (**7**).

This compound was synthesized from 1 g (5 mmoles) of **11c** and 0.1 g of iodine in a manner similar to the preparation of **5** and was obtained as colorless crystals in 40% yield. This compound was recrystallized from methanol to give colorless needles, mp 66° (lit (9) 65-66°); nmr (deuteriochloroform): 2.56 (s, 8-CH_3, 3H), 7.29 (bd, J = 9 Hz, 7-H, 1H), 7.50 (d, J = 5 Hz, 2-H, 1H), 7.70 (d, J = 2 Hz, 4-H, 5-H, 2H), 7.80 (d, J = 9 Hz, 6-H, 1H), 7.92 (d, J = 5 Hz, 1-H, 1H), 8.07 (bd, 9-H, 1H); ms: m/e 198 (M^+, 100), 197 (45), 165 (18), 153 (15), 152 (16). The picrate gave orange-red needles, mp 135° (lit (8) 135-136°).

8-Methylnaphtho[2,1-*b*]thiophene (**7**).

This compound was synthesized from 1 g (5 mmoles) of **11c** and 0.1 g of iodine in a manner similar to the preparation of **5** and was obtained as colorless crystals in 40% yield. This compound was recrystallized from methanol to give colorless needles, mp 66° (lit (9) 65-66°); nmr (deuteriochloroform): 2.56 (s, 8-CH_3, 3H), 7.29 (bd, J = 9 Hz, 7-H, 1H), 7.50 (d, J = 5 Hz, 2-H, 1H), 7.70 (d, J = 2 Hz, 4-H, 5-H, 2H), 7.80 (d, J = 9 Hz, 6-H, 1H), 7.92 (d, J = 5 Hz, 1-H, 1H), 8.07 (bd, 9-H, 1H); ms: m/e 198 (M^+, 100), 197 (45), 165 (18), 153 (15), 152 (16). The picrate gave orange-red needles, mp 135° (lit (8) 135-136°).

7-Methylnaphtho[2,1-*b*]thiophene (**6**) and 9-Methylnaphtho[2,1-*b*]thiophene (**8**).

A solution of 1 g (5 mmoles) of **11b** and 0.1 g of iodine in 360 ml of dry benzene was irradiated in a manner similar to that described for the synthesis of **5**. After evaporation of the solvent, the residue was chromatographed on a silica gel column using hexane as the eluent, giving 0.5 g of colorless crystals. The nmr (deuteriochloroform) of this product exhibited two methyl signals at 2.45 and 2.91 ppm (1:1) due to methyl protons in the 1 and 3 positions of naphtho[2,1-*b*]thiophene. These products were again chromatographed on a basic alumina column (Aldrich 19944-3) using *n*-pentane and benzene as the eluent.

Compound **8**.

This compound eluted first with *n*-pentane and was obtained in 20% yield (0.2 g), mp 77°. This product was recrystallized from methanol to give colorless needles, mp 77° (lit (9) 76-77°); nmr (deuteriochloroform): 3.11 (s, 9-CH_3, 3H), 7.32-7.93 (m, aromatic-H, 6H), 8.25 (d, J = 5 Hz, 1-H, 1H); ms: m/e 198 (M^+, 100), 197 (40), 165 (41), 153 (17), 152 (18). The picrate gave orange-red needles, mp 152° (lit (9) 157°).

Compound **6**.

This compound eluted last with benzene and was obtained in a yield of 20% (0.2 g). This compound was recrystallized from methanol to give colorless needles, mp 98° (lit (9) 98°); nmr (deuteriochloroform): 2.53 (s, 7-CH_3, 3H), 7.32-7.56 (m, 2-H, 6-H, 8-H, 3H), 7.68 (s, 4-H, 5-H, 2H), 7.83 (d, J = 8 Hz, 8-H, 1H), 7.93 (d, J = 5 Hz, 1-H, 1H), 8.21 (d, J = 8 Hz, 9-H, 1H); ms: m/e 198 (M^+, 100), 197 (50), 105 (10). The picrate gave orange-red needles, mp 133° (lit (9) 132-133°).

2-(β-Methylstyryl)thiophene (**16**).

Thiophene (**14**) (8.4 g, 0.1 mole) in 200 ml of dry ether was placed in a 500 ml three-necked flask with an addition funnel, thermometer and drying tube on an inlet for dry nitrogen. This solution was then cooled to −70° in an acetone dry-ice bath and *n*-butyllithium (54 ml) was added dropwise. After the addition, the mixture was stirred for one hour at −20 to −10° and for 2 hours at room temperature. The mixture was then cooled to −70° and 2-phenylpropionaldehyde (13.4 g, 0.1 mole) in 50 ml of dry ether was added dropwise. After the addition, the solution was allowed to warm to 25° and was stirred for an additional 4 hours.

The ether solution was poured into 250 ml of 10% hydrochloric acid solution and the mixture was extracted with 2 × 100 ml portions of chloroform. The chloroform layer was dried over sodium sulfate. The chloroform was removed *in vacuo* to give a pale yellow oil; nmr (deuteriochloroform): 2.46 (bs, OH, 1H), 3.09 (m, —C*H*—CH_3, 1H), 4.92 (d, J = 7 Hz, =CH—OH, 1H), 6.65-7.00 (m, 2-H, 3-H, 4-H, 3H), 7.19 (s, phenyl-H, 5H).

A mixture of the above crude alcohol and 200 ml of concentrated hydrochloric acid solution was refluxed for 1.5 hours and then the reaction mixture was extracted with benzene. The benzene layer was dried over sodium sulfate and the benzene was evaporated to give a brown oil. This crude product was purified by chromatography on a silica gel column using hexane as the eluent, giving 13.2 g (66%) of a pale yellow oil. An analytical sample was again chromatographed on an alumina column using hexane as the eluent to give a pale yellow oil; nmr (deuteriochloroform): 2.15 (s, CH_3, 2/3 × 3H), 2.38 (s, CH_3, 1/3 × 3H), 7.52-7.13 (m, 3, 4, 5 and ethenyl-H, 4H), 7.31 and 7.35 (s, phenyl-H, 5H); ms: m/e 200 (M^+, 100), 199 (28), 185 (60), 184 (37).

Anal. Calcd. for $C_{13}H_{12}S$: C, 77.95; H, 6.04; S, 16.01. Found: C, 77.87; H, 6.01; S, 16.21.

The above product is a mixture of the *E* and *Z* isomers as shown by the two methyl singlets in the nmr spectra.

5-Methylnaphtho[2,1-*b*]thiophene (**4**).

This compound was synthesized from 1 g (5 mmoles) of **16** and 0.1 g of iodine in a manner similar to the preparation of **4** and was obtained as colorless needles in 56% yield. An analytical sample was recrystallized from methanol to give colorless needles, mp 79°; nmr (deuteriochloroform): 2.61 (s, 5-CH_3, 3H), 7.09-7.50 (m, 1-H, 6-H, 2H), 8.01-8.19 (m, 9-H, 1H); ms: m/e 198 (M^+, 100), 197 (80), 152 (10).

Anal. Calcd. for $C_{13}H_{10}S$: C, 78.75; H, 5.08; S, 16.17. Found: C, 78.83; H, 5.04; S, 16.24.

The picrate was obtained as orange needles, mp 150°.

Anal. Calcd. for $C_{19}H_{13}N_3O_7S$: C, 53.40; H, 3.07; N, 9.83; S, 7.50. Found: C, 53.50; H, 3.26; N, 9.87; S, 7.63.

2-(α-Methylstyryl)thiophene (**18**).

The reaction of 4.2 g (0.5 mole) of thiophene (**14**) and 6.7 g (0.5 mole) of phenylacetone (**17**) in a manner similar to the preparation of **16** gave colorless crystals in 68% yield. An analytical sample was recrystallized from methanol to give colorless leaflets, mp 48°; nmr (deuteriochloroform): 2.25 (s, CH_3, 3H), 6.90-7.13 (m, ethenyl, 3.4 and 5-H, 5H), 7.28 (s, phenyl-H, 5H); ms: m/e 200 (M^+, 100), 199 (32), 185 (84), 184 (61), 167 (21), 165 (23).

Anal. Calcd. for $C_{13}H_{12}S$: C, 77.95; H, 6.04; S, 16.01. Found: C, 77,91; H, 6.01; S, 15.98.

4-Methylanphtho[2,1-*b*]thiophene (**3**).

This compound was synthesized by the photolysis of 1 g (5 mmoles) of **18** and 0.05 g of iodine in a manner similar to the preparation of **5** and was obtained as colorless needles in 38% yield. An analytical sample was recrystallized from methanol to give colorless needles, mp 75°; nmr (deuteriochloroform): 2.57 (s, 4-CH_3, 3H), 6.80-7.43 (m, aromatic-H, 5H), 7.81 (d, J = 5 Hz, 1-H, 1H), 8.12 (m, 9-H, 1H); ms: m/e 198 (M^+, 100), 197 (80), 165 (8).

Anal. Calcd. for $C_{13}H_{10}S$: C, 78.75; H, 5.08; S, 16.17. Found: C, 78.93; H, 5.01; S, 16.03.

The picrate was obtained as orange needles, mp 147°.

Anal. Calcd. for $C_{19}H_{13}N_3O_7S$: C, 53.40; H, 3.07; N, 9.83; S, 7.50. Found: C, 53.26; H, 3.19; N, 9.88; S, 7.68.

2-Methyl-5-styrylthiophene (**21**).

This compound was synthesized from **19** (2.5 g, 20 mmoles) and **20** (4.5 g, 20 mmoles) in a manner similar to the preparation of **16** and was obtained as colorless prisms in 15% yield. An analytical sample was recrystallized from methanol to give colorless prisms, mp 85°; nmr (deuteriochloroform): 2.39 (s, CH_3, 3H), 6.50-7.00 (m, ethenyl-H, 3- and 4-H, 4H), 7.30 (bs, phenyl-H, 5H); ms: m/e 200 (M^+, 100), 199 (43), 185 (39), 184 (39).

Anal. Calcd. for $C_{13}H_{12}S$: C, 77.95; H, 6.04; S, 16.01. Found: C, 77.93; H, 6.11; S, 16.01.

2-Methylnaphtho[2,1-*b*]thiophene (**2**).

This compound was synthesized from 0.5 g (2.5 mmoles) of **22** and 0.05

g of iodine in a manner similar to the preparation of **4** and was obtaned as colorless needles in 30% yield. An analytical sample was recrystallized from methanol to give colorless needles, mp 86° (lit (11) 88°); nmr (deuteriochloroform): 2.68 (s, 2-CH_3, 3H), 7.40-7.98 (m, aromatic-H, 6H), 8.16-8.31 (m, 9-H, 1H); ms: m/e 198 (M^+, 100), 197 (94), 165 (19), 198 (18).

The picrate was obtained as orange needles, mp 138°.

Anal. Calcd. for $C_{19}H_{13}N_3O_7S$: C, 53.40; H, 3.07; N, 9.83; S, 7.50. Found: C, 53.21; H, 3.14; N, 9.79; S, 7.32.

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