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Preparation of Benzo[b]thiophenes by Pd(0)-Catalyzed Intramolecular Cyclization of Allyl (and Propargyl) *o*-Iodophenyl Sulfides.

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Abstract.- Benzo[b]thiophenes are prepared by intramolecular Pd(0)-catalyzed Heck reaction of allyl *o*-iodophenyl sulfides Pd(0)-Catalyzed intramolecular cyclization of *o*-iodophenyl propargyl sulfide in the presence of a hydride donor gives 3-methylene-2,3-dihydrobenzo[b]thiophene, which reacts with several enophiles in ene type reactions. However, allyl (and propargyl) aryl sulfides react with palladium(II) chloride to afford polymeric $[PdCl(SAr)]_2$

INTRODUCTION

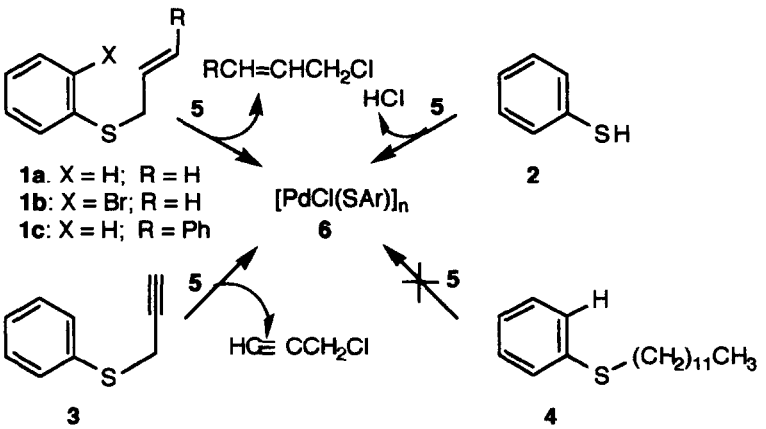
Pd(0)-Catalyzed intramolecular cyclization of allyl (and propargyl) *o*-halogenophenyl ethers and amines is a well established method for the preparation of benzo[b]furans[1] and indoles.[2] Intramolecular cyclization of appropriate ethers and amines can also be induced by tin hydrides,[3] samarium(II) iodide,[4] Co(I) species,[5] and Zr species.[6] A related method is the Pd(0)-catalyzed intermolecular reaction of *o*-halogenophenols and of *o*-halogenoanilines with alkynes which affords benzo[b]furans[7] and indoles.[8] In sharp contrast with the Pd-catalyzed preparation of benzofurans and indoles, application of these methodologies to the synthesis of benzo[b]thiophenes seems to be unexplored.[9,10]The pronounced thiophilicity of transition metals could be the origin of such a gap in the chemical literature. However, we and others have recently shown that unprotected sulfur nucleophiles are compatible with Pd(0) in Pd(0)-catalyzed allylation of nucleophiles (Tsuji-Trost reaction).[11] Moreover, some benzo[b]thiophene derivatives are potent antifungal agents[12] and one of them, sertaconazole, is presently in the market.[13] On the other hand, Pd(II)-catalyzed S- to N- Claisen rearrangement of S-allylthioimidates[14] and alkyl allyl N-aryldithiocarbonimidates[15] have been described.

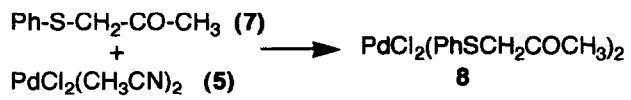
RESULTS

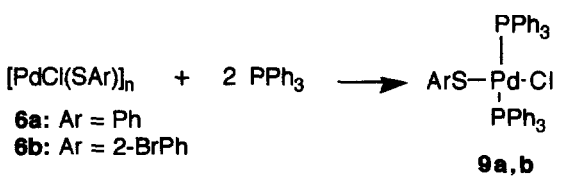
With all the above in mind we decided to explore the Pd(0)-catalyzed cyclizations of allyl aryl sulfides and aryl propargyl sulfides. In palladium(0) organic chemistry Pd(II) species are frequently added to the reaction medium; they are reduced *in situ* to Pd(0) species which are the actual catalysts. In addition we wanted to test the feasibility of a Pd(II)-mediated S- to C- Claisen rearrangement. Therefore, we initially explored the behaviour of allyl aryl sulfides, **1**, in the presence of a Pd(II) compound i.e. bis(acetonitrile)dichloropalladium(II), **5** (Scheme I).

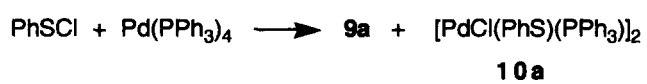
When sulfide **1a** was treated in hot THF with stoichiometric amounts of **5**, a red wine coloured solid material precipitated. This very insoluble material was identified as the polymeric palladium complex **6a**, that had been prepared by a different method.[16] Thus, treatment of **6a** as previously described[16] with excess molten triphenylphosphine gave a violet mononuclear complex with a mp consistent with that reported for *trans*-

chloro(phenylthio)bis(triphenylphosphine)palladium(II), **9a**.[16] Polymer **6a** was very difficult to purify, as was the mononuclear complex **9a**. However, an X-ray diffraction study confirmed structure **9a**. Full details will be published elsewhere. Similar results were obtained with sulfide **1b** leading to **6b** and **9b**.The other presumed product formed in the reactions of **1a,b** with **5** is allyl chloride which was not detected due to its volatility. However, sulfide **1c** reacted with **5** to afford **6a** and cinnamyl chloride that was isolated and characterized. Polymer **6a** was more simply prepared by reaction of benzenethiol, **2**, with **5**. Mononuclear complex **9a** was also formed albeit in low yield from benzenesulfenyl chloride and tetrakis(triphenylphosphine)palladium(0), the main product of this reaction being the dinuclear complex **10a**.[16] Treatment of phenyl propargyl sulfide, **3**, with **5** also produced **6a**, but no reaction was observed when dodecyl phenyl sulfide, **4**, was heated in THF in the presence of **5**. Therefore, the unsaturation present in the aliphatic chain of **1** and **3** is a requisite for the formation of **6**. Finally, 1-(phenylthio)propanone, **7**, a precursor for 3-methylbenzo[b]thiophene preparation, also reacts with **5** to give a complex, **8**, with retention of the aliphatic chain.





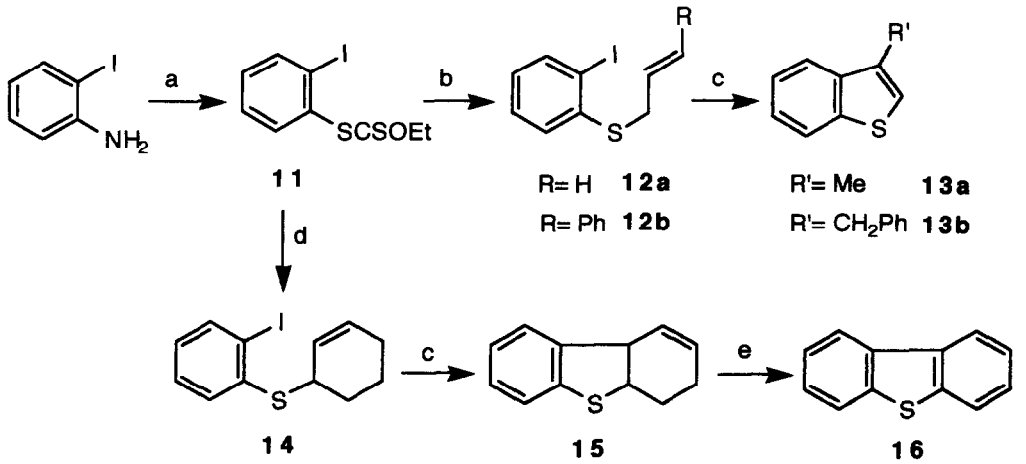




SCHEME I

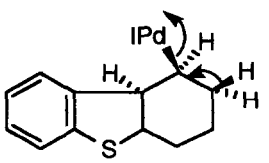
Once the behaviour of allyl aryl and of aryl propargyl sulfides in front of palladium(II) chloride was sufficiently understood, we turned our attention to Pd(0)-catalyzed cyclizations that had been previously used successfully for indole preparations. In particular we focused on the Heck reaction[2b,e,f] and on the tandem cyclization-hydride ion capture process.[2d,h] In all the experiments discussed below Pd was introduced directly in the form of Pd(0).

The results of the intramolecular Heck reaction as applied to benzo[b]thiophene preparation are shown in Scheme II. *o*-Iodosulfides **12a,b** were prepared from the commercially available *o*-iodoaniline. Treatment of both **12a** and **12b** under conventional Heck conditions using tetrakis(triphenylphosphine)palladium(0) as catalyst in the presence of triethylamine produced 3-substituted benzo[b]thiophenes **13a,b** in 70 and 35% isolated yields respectively. Similarly, iodosulfide **14** was prepared from 3-bromocyclohexene and intermediate **11**. Heck cyclization of **14** afforded a mixture of alkenes in which **15** was predominant. The crude mixture was directly aromatized to dibenzothiophene **16** with dichlorodicyanoquinone in refluxing dioxane. Compound **15** arises from *cis* HPdI elimination from the postulated intermediate **17**, formed by Pd(0) insertion into the C-I bond followed by *cis* addition of the C-PdI moiety to the allylic double bond.[17]



a.- i) $NaNO_2$, HCl, 0°C ii) KSCSOEt; b.- i) KOH/EtOH ii) R-CH=CH-CH_2-X;
c.- cat. $Pd(PPh_3)_4$, NEt_3, CH_3CN, Δ ; d.- i) KOH/EtOH ii) 2-cyclohexenyl bromide
e.- 2,3-dichloro-5,6-dicyanoquinone, dioxane, Δ

SCHEME II



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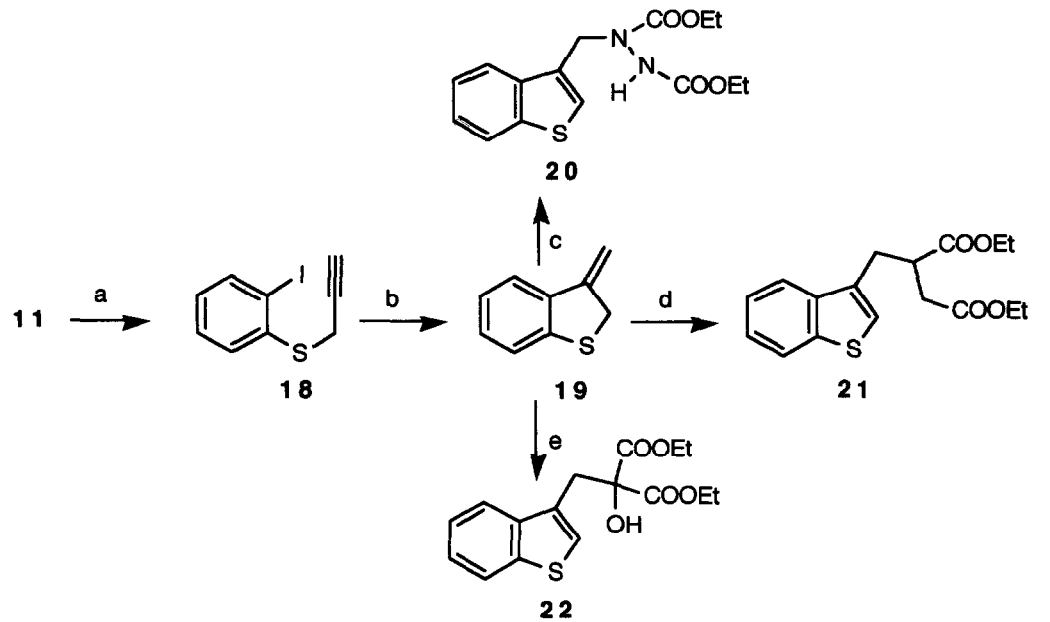
The second approach to Pd(0)-catalyzed preparation of benzo[b]thiophenes, the tandem cyclization-hydride ion capture process is shown in Scheme III.



a.- i) KOH/EtOH ii) HCl iii) K_2CO_3, acetone iv) propargyl bromide;

b.- cat. $Pd(PPh_3)_4$, HCOOH/piperidine, CH_3CN, Δ;

c.- DEAD, toluene, Δ; d.- diethyl fumarate, toluene, Δ; e.- diethyl oxomalonate, toluene, Δ

SCHEME III

o-Iodophenyl propargyl sulfide, **18**, was treated with catalytic tetrakis(triphenylphosphine)palladium(0) in the presence of a hydride donor, i.e. formate anion. 3-Methylene-2,3-dihydrobenzo[b]thiophene, **19**, was isolated. Compound **19** was not very stable and showed propensity to isomerize to the fully aromatic 3-methylbenzo[b]thiophene in the presence of protic acids or upon chromatography. However, it reacts in ene type reactions[18] with diethyl azodicarboxylate, diethyl fumarate and diethyl oxomalonate to afford diethyl 1-((benzo[*b*]thien-3-yl)methyl)hydrazine-1,2-dicarboxylate, **20**, diethyl 2-((benzo[*b*]thien-3-yl)methyl)succinate, **21**, and diethyl 2-((benzo[*b*]thien-3-yl)methyl)-2-hydroxymalonate, **22**, respectively. The crude reaction mixture containing **19** was treated with the enophiles without further purification. However, piperidine should be eliminated, otherwise products from Michael type addition of piperidine to the enophile can be obtained.

In summary, we have shown that Pd(0)-catalyzed intramolecular cyclizations can be used for the preparation of benzo[b]thiophenes.

EXPERIMENTAL

Allyl phenyl sulfide, **1a**. (General method).

A mixture of benzenethiol (16.97 g, 154 mmol), allyl bromide (18.52 g, 150 mmol), potassium carbonate (24.86 g, 180 mmol) and acetone (150 mL) was refluxed under argon for 15 h. The cooled mixture was filtered and the filtrate was evaporated. The residue was partitioned between diethyl ether and water, the organic phase was dried and evaporated to afford **1a** (17.94 g, 80%); bp 40C/1mmHg (Lit.[19] bp 114C/23.5 mmHg); ^{1}H-NMR ($CDCl_3$): 3.6 (dt, J = 7.0 and 1.2 Hz, 2H), 5.0-5.3 (m, 2H), 5.9 (ddt, J = 17.0, 10.0 and 7.0 Hz, 1H), 7.1-7.5 (m, 5H); ^{13}C-NMR ($CDCl_3$): 36.8, 117.1, 125.8, 128.4, 129.5, 133.4, 135.9.

Sulfides **3** and **4** were prepared as for **1a**.

Propargyl phenyl sulfide, **3**.

This compound was obtained from propargyl bromide. It had bp 70-75°C (oven temperature)/1 mm Hg (Lit.[20] bp 104-110C/10mmHg); ^{1}H-NMR ($CDCl_3$): 2.2 (t, J = 2.7 Hz, 1H), 3.6 (d, J = 2.7 Hz, 2H), 7.1-7.5 (m, 5H).

Dodecyl phenyl sulfide, **4**.

This compound was obtained from dodecyl bromide. It had mp 29-31C (Lit.[19] mp 33-34C); ^{1}H-NMR ($CDCl_3$): 0.8-1.9 (m, 23H), 2.95 (t, J = 7.4 Hz, 2H), 7.1-7.6 (m, 5H).

Cinnamyl phenyl sulfide, **1c**.

Benzenethiol (4.40 g, 40 mmol) in THF (10 mL) was added over washed sodium hydride (1.92 g of 50% dispersion in mineral oil, 40 mmol) in anhydrous THF (10 mL). The mixture was stirred at room temperature under argon until bubbling of hydrogen ceased. This mixture was then added to a solution of cinnamyl acetate (7.05 g, 40 mmol), bis(dibenzylideneacetone)palladium (0) (0.23 g, 0.4 mmol) and triphenylphosphine (1.05 g, 4 mmol) in anhydrous THF (15 ml). The mixture was stirred under argon at room temperature for 19 h and finally it was partitioned between dichloromethane and water. The organic layer was dried and evaporated to afford a redish solid which upon washing with hexane afforded a solid that was recrystallised from hexane. Sulfide **1c** (5.2 g, 60%) had mp 73-76C (Lit.[21] mp 78.5C); IR (KBr): 963 cm^{-1}; ^{1}H-NMR($CDCl_3$): 3.6 (d, J = 5.0 Hz, 2H), 5.8-6.5 (m, 2H), 6.9-7.7 (m, 10H).

Allyl 2-bromophenyl sulfide, **1b**. (General procedure).

A solution of sodium nitrite (7.04 g, 102 mmol) in water (17 mL) was added during 45 min to an ice-cooled solution of 2-bromoaniline (17.20 g, 100 mmol) in 35% aqueous HCl (16.7 mL, 190 mmol) containing ice (20 g). On he other hand potassium ethylxanthate was prepared by strongly stirring for 2.5 h a mixture of potassium hydroxide (7.96 g, 120 mmol), ethanol (13.4 mL), water (25 mL) and carbon disulfide (13.32 g, 175 mmol). The first solution of *o*-bromobenzenediazonium salt was added slowly to the second mixture heated at 50-55°C. After the addition the mixture was stirred at 50-55°C for 30 min, then it was cooled and partitioned with dichloromethane. The organic layer was dried and evaporated to afford 23.6 g of an oil ((2-bromophenyl)ethylxanthate) which was refluxed for 10 h with potassium hydroxide (30 g, 455 mmol) in absolute ethanol (50 mL). The mixture was cooled and neutralized with 35% HCl, then it was extracted with dichloromethane. The organic layer was dried and evaporated to afford crude 2-bromobenzenethiol (16.6 g) which was used immediately without further purification. 2-Bromobenzenethiol had ^{1}H-NMR ($CDCl_3$): 4.0 (s, 1H), 6.9-7.8 (m, 4H); ^{13}C-NMR ($CDCl_3$): 121.2, 127.2, 127.9, 128.1, 132.9, 136.2. A mixture of crude 2-bromobenzenethiol (16.0 g, 84 mmol), allyl bromide (10.3 g, 84 mmol), potassium carbonate (15.68 g, 114 mmol) and acetone was refluxed under argon for 15 h. The mixture was filtered and the filtrate was evaporated. The residue was partitioned between water and diethyl ether. The organic layer was dried and evaporated to afford **1b** (8.9 g, 56% after distillation); bp.75-77C/0.05-0.1 mmHg; IR (film): 987 and 922 cm^{-1}; ^{1}H-NMR ($CDCl_3$): 3.65 (d, J =7.0 Hz, 2H), 5.1-5.5 (m, 2H), 6.0 (ddt, J = 16.6, 10.0 and 7.0 Hz, 1H), 7.0-7.8 (m, 4H); ^{13}C-NMR ($CDCl_3$): 36.2, 118.2, 124.0, 126.8, 127.5, 129.1, 132.6, 132.9, 137.4; MS(m/e): 230(31), 228(M, 34), 149(89), 134(40), 116(64), 115(25), 109(28), 108(100), 69(32), 41(81). Anal. Calcd. for C_9H_9BrS: C, 47.38; H, 3.53; S, 14.05; Br, 35.03. Found: C, 47.35; H, 3.96; S, 13.92; Br, 34.99.

Treatment of **1a** with a stoichiometric amount of $PdCl_2(CH_3CN)_2$, **5**.

A stirred mixture of **1a** (0.750 g, 5.0 mmol), **5** (1.297 g, 5.0 mmol) and THF (12 mL) was placed under argon in a sealed tube and heated progressively from 25° to 120°C for about 15 h. A red-wine precipitate appears above 70°C. This solid was filtered, washed with hexane, dried in vacuum and identified as the polymeric complex **6a**[16] (1.115 g, 81%). Mp>270C (dec.); IR(KBr): 1438, 738, 683, 478 cm^{-1}; far IR (CsI): 300, 290, 260, 247 cm^{-1} (bridged Pd-Cl).

Treatment of **1b** with a stoichiometric amount of **5**.

A stirred mixture of **1b** (0.458 g, 2.0 mmol), **5** (0.519 g, 2.0 mmol) and THF (12 mL) was placed in a sealed tube and heated under argon at 120°C for 15 h. The red solid formed was filtered, washed with pentane, dried in vacuum and identified as **6b** (0.600 g, 91%). Mp > 210C (dec.); IR(KBr): 1442, 1422, 1018, 747, 440 cm^{-1}; far IR (CsI): 295, 290, 253 (bridged Pd-Cl).

Treatment of **1c** with a stoichiometric amount of **5**.

A stirred mixture of **1c** (0.500 g, 2.2 mmol), **5** (0.573 g, 2.2 mmol) and THF (12 mL) was placed in a sealed tube and heated under argon at 120°C for 12 h. The red-wine solid formed was filtered, washed with hexane, dried in vacuum and identified as **6a**[16] (0.474 g, 85%). The filtrate was evaporated to afford cinnamyl chloride (0.249 g, 74%).

Treatment of benzenethiol, **2**, with a stoichiometric amount of **5**.

A stirred mixture of **2** (0.331 g, 0.3 mL, 3.0 mmol), **5** (0.778 g, 3.0 mmol) and THF (15 mL) was left at rt under argon for 4 h. The red-wine solid formed was filtered, washed with water, ethanol and diethyl ether and dried in vacuum to yield **6a**[16] (0.726 g, 96%).

Treatment of **3** with a stoichiometric amount of **5**.

A stirred mixture of **3** (0.593 g, 4.0 mmol), **5** (1.038 g, 4.0 mmol) and THF (12 mL) was placed in a sealed tube under argon and heated at 120°C for 5 h. The red-wine solid formed was filtered, washed with THF and dried in vacuum to yield **6a**[16] (1.00 g, 100%).

Treatment of 1-(phenylthio)propanone, **7**, with a stoichiometric amount of **5**.

A mixture of **7** (0.499 g, 3.0 mmol), **5** (0.778 g, 3.0 mmol) and THF (12 mL) was refluxed under argon for 45 min (GLC monitoring). The precipitate formed was filtered, washed with dichloromethane and diethyl ether and dried in vacuum to yield bis(1-phenylthio-2-propanone)dichloropalladium(II), **8**, which was recrystallised from $CHCl_3/CH_3CN$/hexane (0.215 g, 28% yield from **7**). Mp 182-84C; IR(KBr): 1710, 1472, 1444, 1360, 1282, 1149, 1001, 755, 692, 573, 488 cm^{-1}; ^1H-NMR ($CDCl_3$): 2.15 (s, 3H), 4.12 (s, 2H), 7.34 (m, 3H), 7.82 (m, 2H). Anal. Calcd. for $C_{18}H_{20}Cl_2O_2PdS_2$: C, 42.40; H, 3.95; Cl, 13.90; S, 12.57. Found: C, 41.70; H, 3.90; Cl, 13.90; S, 11.75.

Treatment of **6a** with excess triphenylphosphine. Formation of **9a**.

Polymer **6a** (0.250 g, 1.0 mmol) was portionwise added to molten (79-81°C) triphenylphosphine (0.787 g, 3.0 mmol). The mixture was stirred for 10 min and cooled. Excess triphenylphosphine was eliminated by washing with hexane. The violet solid was *trans*-chloro(phenylthio)bis(triphenylphosphine)palladium(II)[16], **9a** (0.583 g, 75%). Mp 171-73C (from THF /hexane) (Lit.[16] mp 170C); IR(KBr): 1479, 1434, 1095, 742, 692, 518 cm^{-1}; far IR (CsI): 314 cm^{-1} (terminal Pd-Cl).

Treatment of **6b** with excess triphenylphosphine. Formation of **9b**.

Complex **9b** was obtained from **6b** in 78% yield as for **9a**. Mp 149-51C; IR(KBr): 1480, 1433, 1118, 744, 693, 541, 514 cm^{-1}; far IR (CsI): 327 cm^{-1} (terminal Pd-Cl). Anal. Calcd. for $C_{42}H_{34}BrClP_2PdS$: C, 59.04; H, 4.01; Br, 9.35; Cl, 4.15; S, 3.75. Found: C, 60.04; H, 4.12; Br, 9.41; Cl, 3.72; S, 3.10.

Reaction of benzenesulfenyl chloride with *tetrakis*(triphenylphosphine)palladium (0).

A mixture of benzenesulfenyl chloride (0.304 g, 2.0 mmol), *tetrakis*(triphenylphosphine)palladium(0) (2.311 g, 2.0 mmol) and THF (15 mL) was refluxed under argon for one hour. The reaction mixture was cooled and the yellow solid formed was filtered, washed with hexane, dried in vacuum and identified as **10a**[16] (0.830 g, 80%). Mp 228-230C (Lit.[16] mp 257C); IR(KBr): 1575, 1481, 1435, 1187, 999, 741, 707, 693, 526, 510 cm^{-1}; far IR (CsI): 360, 320, 312 cm^{-1} (terminal Pd-Cl). When hexane was added to the filtrate a violet solid precipitated which was identified as **9a** (0.200 g, 13%).

Sulfides **12a-b** and **14** were prepared from 2-iodoaniline as for **1b**.

Allyl 2-iodophenyl sulfide, **12a**.

This compound was prepared from 2-iodoaniline and allyl bromide. It had bp 100-110C (oven temperature)/0.1-0.2 mmHg; ^1H-NMR ($CDCl_3$): 3.55 (d, J = 6.7 Hz, 2H), 5.1-5.3 (m, 2H), 5.85 (ddt, J = 17.1, 10.1 and 6.7, 1H), 6.8-7.9 (m, 4H).

Cinnamyl 2-iodophenyl sulfide, **12b**.

This compound was prepared from 2-iodoaniline and cinnamyl chloride. Mp 69-70C; ^1H-NMR ($CDCl_3$): 3.69 (dd, J = 7.0 and 1.1 Hz, 2H), 6.22 (dt, J = 15.7 and 7.0 Hz, 1H), 6.46 (d, J = 15.7 Hz, 1H), 6.8 (ddd, J = 8.0, 7.7 and 2.5 Hz, 1H), 7.13-7.32 (m, 7H), 7.77 (dd, J = 7.7 and 1.1 Hz, 1H). Anal. Calcd. for $C_{15}H_{13}IS$: C, 51.15; H, 3.72; S, 9.10. Found: C, 51.06; H, 3.78; S, 8.94.

2-Cyclohexenyl 2-iodophenyl sulfide, **14**.

This compound was prepared from 2-iodoaniline and 3-bromocyclohexene (NBS bromination of cyclohexene). It had bp 175-180C (oven temperature)/0.1 mmHg; ^{1}H-NMR ($CDCl_3$): 1.5-2.1 (m, 6H), 3.85 (m, 1H), 5.7-5.9 (m, 2H), 6.86 (dt, J = 8.0 and 1.6 Hz, 1H), 7.28 (dt, J = 8.0 and 1.3, 1H), 7.37 (dd, J = 8.0 and 1.5 Hz, 1H), 7.82 (dd, J = 8.0 and 1.3, 1H). Anal. Calcd. for $C_{12}H_{13}IS$: C, 45.58; H, 4.14; S, 10.14. Found: C, 45.60; H, 4.12; S, 10.09.

3-Methylbenzo[*b*]thiophene, **13a**.

A degassed mixture of **12a** (3.088 g, 11.0 mmol), *tetrakis*(triphenylphosphine)palladium(0) (0.700 g, 0.55 mmol), triethylamine (1.67 g, 16.5 mmol) and anhydrous acetonitrile (100 mL) was placed in a sealed tube and heated under argon at 140°C for 15 h (GLC monitoring). After cooling, the mixture was filtered, the filtrate was evaporated and the residue was partitioned between dichloromethane and water. The organic layer was dried with anhydrous sodium sulfate and the solvent evaporated. A digestion of the resulting oil in hexane allowed the separation of insoluble triphenylphosphine oxide. Evaporation of the hexane layer and microdistillation of the residue afforded **13a** (1.137 g, 70%). Bp 65-70C (oven temperature)/0.3-0.5 mmHg (Lit[22] bp 106-10C/12 mmHg); ^{1}H-NMR ($CDCl_3$): 2.40 (s, 3H), 6.96 (s, 1H), 7.23-7.37 (m, 2H), 7.64 (m, 1H), 7.80 (m, 1H).

3-Benzylbenzo[*b*]thiophene, **13b**.

A degassed mixture of **12b** (3.150 g, 9.0 mmol), *tetrakis*(triphenylphosphine)palladium(0) (0.520 g, 0.45 mmol), triethylamine (1.370 g, 13.5 mmol) and anhydrous acetonitrile (140 mL) was placed in a sealed tube and heated under argon at 160°C for 65 h (GLC monitoring). After cooling, the mixture was filtered and the filtrate partitioned between dichloromethane and water. The organic layer was dried and evaporated. The residue was chromatographed through silica gel. The fractions containing **13b** were microdistilled (160-165C (oven temperature)/0.1 mmHg) (Lit[23] pe 207C/14 mmHg) to give the pure compound (0.70 g, 35%) as an oil. It crystallised from isopropanol. Mp 30C; IR (film): 3065, 3030, 2903, 1497, 1462, 1437, 750, 730, 699 cm^{-1} ; ^{1}H-NMR ($CDCl_3$): 4.15 (s, 2H), 6.96 (s, 1H), 7.11-7.39 (m, 7H), 7.66 (m, 1H), 7.82 (m, 1H).

1,2,4a,9a-Tetrahydrodibenzo[*b*]thiophene, **15**, and dibenzothiophene, **16**.

A degassed mixture of **14** (1.265 g, 4.0 mmol), *tetrakis*(triphenylphosphine)palladium(0) (0.370 g, 0.32 mmol), triethylamine (1.062 g, 10.4 mmol) and anhydrous CH_3CN (50 mL) was placed in a sealed tube and heated under argon at 140-160°C for 143 h (GLC monitoring). After cooling, the mixture was filtered and the filtrate partitioned between dichloromethane and water. The organic layer was dried and evaporated. The residue was taken in benzene, excess methyl iodide added and the solution left overnight at room temperature. The formed precipitate was filtered off and the filtrate was evaporated. The residue was chromatographed through silica gel eluting with hexane. Microdistillation (105-110C (oven temperature)/0.1 mmHg) of the appropriate fractions afforded a mixture of alkenes where **15** was the major component (GLC, ^{1}H-NMR). This mixture (0.380 g) was taken in dioxane (35 mL) and treated with 2,3-dichloro-5,6-dicyanoquinone (0.908 g, 4.0 mmol) at reflux temperature for 4 h. The formed precipitate was filtered off and the filtrate evaporated. The residue was chromatographed through aluminium oxide eluting with hexane: dichloromethane 2:3 to yield **16** (0.187 g, 25% from **14**). Mp 99-102C (from i-PrOH). ^{1}H-NMR ($CDCl_3$): 7.45 (m, 4H), 7.80 (m, 2H), 8.10 (m, 2H).

2-Iodophenyl propargyl sulfide, **18**.

It was prepared from *o*-iodoaniline and propargyl bromide as for **1b**. It had bp 140C (oven temperature)/0.1 mmHg; IR (film): 3299, 2123, 1442, 1262, 1013, 741, 641 cm^{-1}; ^{1}H-NMR ($CDCl_3$): 2.2 (t, J= 2.7 Hz, 1H), 3.7 (d, J= 2.7 Hz, 2H), 6.8 (ddd, J= 7.9, 7.3 and 1.3 Hz, 1H), 7.3 (ddd, J= 7.9, 7.3 and 1.3 Hz, 1H), 7.4 (dd, J= 7.9 and 1.3 Hz, 1H), 7.8 (dd, J= 7.9 and 1.3 Hz, 1H). Anal. Calcd. for C_9H_7IS: C, 39.44; H, 2.57; S, 11.70. Found: C, 39.47; H, 2.52; S, 11.70.

3-Methylene-2,3-dihydrobenzo[*b*]thiophene, **19**.

A mixture of piperidine (1.022 g, 1.2 mL, 12 mmol), formic acid (0.414 g, 0.3 mL, 9 mmol), *tetrakis*(triphenylphosphine)palladium(0) (0.346 g, 0.3 mmol), **18** (0.822 g, 3.0 mmol) and anhydrous and degassed CH_3CN (20 mL) was refluxed under argon for 17 h (GLC monitoring). The solvent was evaporated and the residue partitioned between diethyl ether and water The organic layer was dried and evaporated. The

residue was taken in benzene, excess methyl iodide was added and the mixture left at room temperature overnight. The solid formed was filtered off and the filtrate was evaporated. A digestion of the resulting oil in pentane allowed the separation of insoluble triphenylphosphine oxide. Evaporation of the pentane layer afforded **19** and traces of **13a** (GLC). One fraction was purified by microdistillation (95-105C (oven temperature)/0.1-0.2 mmHg) and another fraction by chromatography through silica gel eluting with hexane. The total amount obtained was 0.178 g (40%). ^{1}H-NMR ($CDCl_3$): 3.98 (t, J= 2.6 Hz, 2H), 5.05 (t, J= 2.6 Hz, 1H), 5.47 (t, J= 2.6 Hz, 1H), 6.94 (m, 1H), 7.1 (m, 2H), 7.32 (dd, J= 7.0 and 1.0 Hz, 1H); MS(m/e): 149(M+1, 8), 148(M, 46), 147(M-1, 100).

Diethyl 1-((benzo[*b*]thien-3-yl)methyl)hydrazine-1,2-dicarboxylate, **20.**

A stirred mixture of *tetrakis*(triphenylphosphine)palladium(0) (1.15 g, 0.10 mmol), piperidine (3.41 g, 4 mL, 40 mmol), formic acid (1.38 g, 1.13 mL, 30 mL), **18** (2.996 g, 10 mmol) and anydrous and degassed CH_3CN (30 mL) was heated under argon at 70°C for 12 h (GLC monitoring). The crude mixture was filtered. A 4/9 fraction of the filtrate (which contained **19**) was evaporated and taken in toluene (40 mL). To this solution diethyl azodicarboxylate (2.93 g, 2.65 mL, 16.8 mmol) was added with a syringe and the mixture heated under argon at 80°C for 6 h (GLC monitoring). After cooling it was partitioned between diethyl ether and water, the organic layer dried with anhydrous sodium sulfate and evaporated. Flash chromatography of the resulting crude through silica gel eluting with hexane/ethyl acetate 2:1 gave **20** (0.90 g, 62% yield from **18**). Recrystallisation from chloroform/diethyl ether afforded 0.525 g (36%) of **20**. Mp 118-119C; IR(KBr): 3279, 1771, 1686 cm^{-1}; ^{1}H-NMR (d_6-DMSO) (361K): 1.10 (t, J= 7.3 Hz, 3H), 1.22 (t, J= 7.3 Hz, 3H), 4.0 (q, J= 7.3 Hz, 2H), 4.15 (q, J= 7.3 Hz, 2H), 4.83 (s, 2H), 7.37 (m, 2H), 7.58 (s, 1H), 7.86 (dd, J= 6.1 and 2.4 Hz, 1H), 7.93 (dd, J= 6.1 and 2.4 Hz, 1H), 9.0 (broad signal, 1H); MS(m/e): 322 (M, 4), 233(11), 189(4), 147(100). Anal. Calcd. for $C_{15}H_{18}N_2O_4S$: C, 55.89; H, 5.63; N, 8.69; S, 9.95. Found: C, 55.76; H, 5.79; H, 8.68; S, 9.80.

Diethyl 2-((benzo[*b*]thien-3-yl)methyl)succinate, **21.**

A stirred mixture of *tetrakis*(triphenylphosphine)palladium(0) (2.00 g, 1.7 mmol), piperidine (9.162 g, 10.6 mL, 107.6 mmol), formic acid (3.715 g, 3.0 mL, 80.7 mmol), **18** (7.37 g, 26.9 mmol) and anhydrous and degassed CH_3CN (180 mL) was heated under argon at 60-70°C for 12 h (GLC monitoring). The reaction mixture was filtered and the filtrate was evaporated. The residue was dissolved in diethyl ether and washed with water until neutrality. The organic layer was dried with anhydrous sodium sulphate and evaporated. The residue containing **19** was taken in toluene (100 mL). To a part (30 mL) of this toluene solution diethyl fumarate (2.892 g, 16.8 mmol) was added with a syringe and the solution refluxed under argon for 84 h (GLC monitoring). The crude mixture was filtered and the filtrate was evaporated. The residue was partitioned between ethyl acetate and water, the organic layer was dried with anhydrous sodium sulfate and evaporated. Flash chromatography of the residue (4.281 g) through silica gel afforded **21** (0.985 g, 35% from **18**) as an oil. Bp 190C (oven temperature)/0.1 mmHg; IR (film): 1736 cm^{-1}; ^{1}H-NMR ($CDCl_3$): 1.16 (t, J= 7.0 Hz, 3H), 1.19 (t, J= 7.0 Hz, 3H), 2.47 (dd, J= 16.8 and 5.3 Hz, 1H), 2.73 (dd, J= 16.8 and 8.2 Hz, 1H), 3.1 (dd, J= 16.3 and 10.0 Hz, 1H), 3.2 (m, 2H), 4.08 (q, J= 7.0 Hz, 2H), 4.11 (q, J= 7.0 Hz, 2H), 7.14 (s, 1H), 7.35 (m, 2H), 7.79 (dd, J= 7.3 and 2.0 Hz, 1H), 7.83 (dd, J= 7.31 and 2.0 Hz, 1H); MS(m/e): 320(M, 22), 275(9), 246(34), 173(37), 147(100), 45(25); HRMS: Calcd. for $C_{17}H_{20}O_4S$: M$^+$ 320.1082. Found: M$^+$ 320.1061.

Diethyl 2-((benzo[*b*]thien-3-yl)methyl)-2-hydroxymalonate, **22.**

To a part (30 mL) of the toluene solution containing **19** prepared above, diethyl ketomalonate (2.926 g, 16.8 mmol) was added with a syringe and the solution heated at 80°C under argon for one hour (GLC monitoring). The treatment of the crude mixture was as for **21**, compound **22** being isolated as an oil after column chromatography (1.115 g, 43% from **18**). Bp 188-190C (oven temperature)/0.1 mmHg; IR(film): 3487, 1736 cm^{-1}; ^{1}H-NMR ($CDCl_3$): 1.20 (t, J= 7.0 Hz, 6H), 3.61 (d, J= 0.7 Hz, 2H), 3.9 (broad peak, 1H), 4.17 (q, J= 7.0 Hz, 2H), 4.18 (q, J= 7.0 Hz, 2H), 7.33 (m, 3H), 7.83 (m, 2H); MS(m/e): 322(M, 9), 304(8), 249(2), 147(100); HRMS: Calcd. for $C_{16}H_{18}O_5S$: M$^+$ 322.0875. Found: M$^+$ 322.0890. Compounds **21** and **22** were contaminated by traces of the analogous benzofuran derivative. Small amounts of the corresponding aryl propargyl ether appeared in the preparation of sulfide **18**.

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REFERENCES

1 Luo, F-T.; Schreuder, I.; Wang, R-T. *J. Org. Chem.* **1992**, *57*, 2213-2215.
2 a) Davidson, J.L.; Preston, P.N. *Adv. Heterocycl. Chem.* **1982**, *30*, 319-422.
b) Odle, R.; Blevins, B.; Ratcliff, M.; Hegedus, L.S. *J. Org. Chem.*, **1980**, *45*, 2709-2710.
c) Kasahara, A.; Izumi, T.; Murakami, S.; Yanai, H.; Takatori, M. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 927-928.
d) Burns, B.; Grigg, R.; Sridharan, V.; Worakun, T. *Tetrahedron Lett.* **1988**, *29*, 4325-4328.
e) Sundberg, R.J.; Pitts, W.J. *J. Org. Chem.* **1991**, *56*, 3048-3054.
f) Genet, J.P.; Blart, E.; Savignac, M. *Synlett* **1992**, 715-717.
g) Arcadi, A.; Cacchi, S.; Marinelli, F. *Tetrahedron Lett.* **1992**, *33*, 3915-3918.
h) Grigg, R.; Sridharan, V. *Tetrahedron Lett.* **1992**, *33*, 7965-7968.
3 Ueno, Y.; Chino, K.; Okawara, M. *Tetrahedron Lett.* **1982**, *23*, 2575-2578.
4 a) Inanaga, J.; Ujikawa, O.; Yagamuchi, M. *Tetrahedron Lett.* **1991**, *32*, 1737-1740.
b) Totleben, M.J.; Curran, D.P.; Wipf, P. *J. Org. Chem.* **1992**, *57*, 1740-1744.
c) Curran, D.P.; Totleben, M.J. *J. Am. Chem. Soc.* **1992**, *114*, 6050-6058.
5 a) Patel, V.F.; Pattenden, G. *Tetrahedron Lett.* **1987**, *28*, 1451-1454.
b) Bhandal, H.; Patel, V.F.; Pattenden, G.; Russell, J.J. *J. Chem. Soc., Perkin Trans. I*, **1990**, 2691-2701.
6 Tidwell, J.H.; Senn, D.R.; Buchwald, S.L. *J. Am. Chem. Soc.* **1991**, *113*, 4685-4686.
7 a) Kundu, N.G.; Pal, M.; Mahanty, J.S.; Dasgupta, S.K. *J. Chem. Soc., Chem. Commun.*, **1992**, 41-42.
b) Torii, S.; Xu, L.H.; Okumoto, H. *Synlett*, **1992**, 515-516.
8 Larock, R.C.; Yum, E.K. *J. Am. Chem. Soc.* **1991**, *113*, 6689-6690.
9 For reviews on benzo[b]thiophene chemistry see:
a) Iddon, B.; Scrowston, R.M. *Adv. Heterocycl. Chem.* **1970**, *11*, 177-381.
b) Scrowston, R.M. *Adv. Heterocycl. Chem.*. **1981**, *29*, 171-249.
10 For reviews in biologically active benzo[b]thiophene derivatives see:
a) Campaigne, E.; Knapp, D.R.; Neiss, E.S.; Bosin, T.R. *Adv. Drug Res.* **1970**, *5*, 1-54.
b) Bosin, T.R.; Campaigne, E.E. *Adv. Drug Res.* **1977**, *11*, 191-232.
11 a) Goux, C.; Lhoste, P.; Sinou, D.*Tetrahedron Lett.* **1992**, *33*, 8099-8102.
b) Moreno-Mañas, M.; Pleixats, R.; Villarroya, M. *Tetrahedron* **1993**, *49*, 1457-1464.
c) Arredondo, Y.; Moreno-Mañas, M.; Pleixats, R.; Villarroya, M. *Tetrahedron* **1993**, *49*, 1465-1470.
12 Raga, M.; Palacín, C.; Castelló, J.M.; Ortiz, J.A.; Cuberes, M.R.; Moreno-Mañas, M. *Eur. J. Med. Chem.* **1986**, *21*, 329-332.
13 Raga, M.M.; Moreno-Mañas, M.; Cuberes, M.R.; Palacín, C.; Castelló, J.M.; Ortiz, J.A. *Arzneim. Forsch.*. **1992**, *42(I)*, 691-694.
14 Tamarn, Y.; Kagotani, M.; Yoshida, Z. *J. Org. Chem.* **1980**, *45*, 5221-5223.
15 Garín, J.; Meléndez, E.; Merchán, F.L.; Tejero, T.; Uriel, S.; Ayestarán, J. *Synthesis* **1991**, 147-149.
16 Boschi, T.; Crociani, B.; Toniolo, L.; Belluco, U. *Inorg. Chem.* **1970**, *9*, 532-537.
17 Collman, J.P.; Hegedus, L.S.; Norton, J.R.; Finke, R.G. Principles and Applications of Organotransition Metal Chemistry, University Science Books, Mill Valley, **1987**, pp 124-126.
18 Snider, B.B. "The Prins and Carbonyl Ene Reactions" , vol. 2, pp. 527-561 and "Ene Reactions with Alkenes as Enophiles", vol. 5, pp. 1-27 in *Comprehensive Organic Synthesis* . Ed. by Trost, B.M. and Fleming, I. Pergamon Press, Oxford, **1991**.
19 Vitali, T.; Nardelli, M. *Ann. Chim. (Rome)* **1951**, *41*, 499-502.

20 Sato, K.; Miyamoto, O. *Nippon Kagaku Zasshi* **1956**, 1409-1411. C.A. 53:5112, **1957**.
21 Briscoe, P.A.; Challenger, F.; Duckworth, P.S. *J. Chem. Soc.* **1956**, 1755-1768.
22 Marshall, P.G.; Henderson, J.R.; Chapman, N.B.; Clarke, K.; Iddon, B.; James, J.W.; Hedge, M.J. (Aspro Nicholas Ltd.) *Brit. Patent.* 1174411, **1969**. C.A. 72:100493, 1970.
23 Royer, R.; Demerseman, P.; Chentin, A. *Bull. Soc. Chim. Fr.* **1961**, 1534-1542.