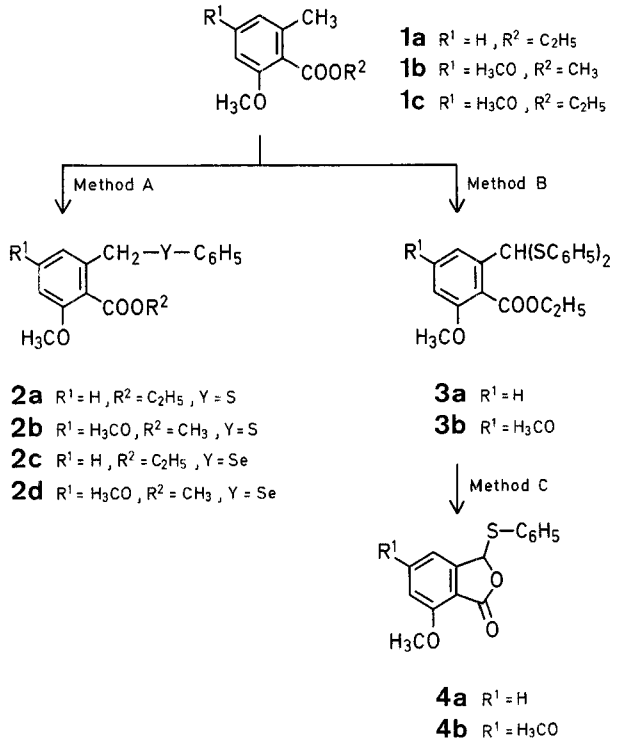
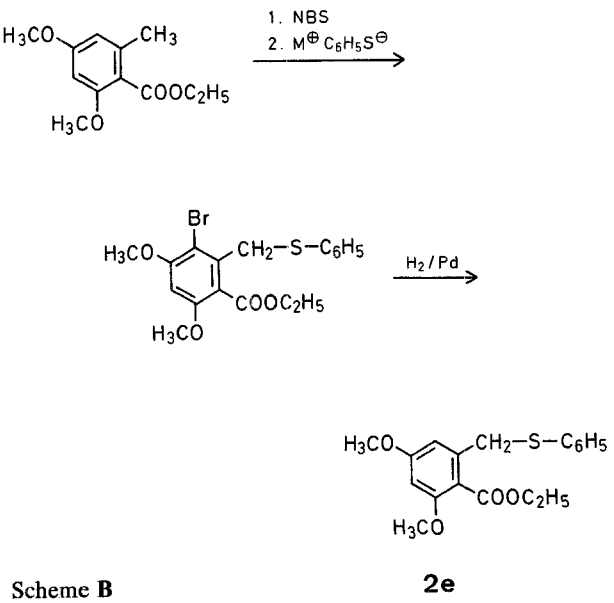


Method A: 1. lithium diisopropylamide (1 equiv); 2. diphenyl disulfide (1.1 equiv) or diphenyl diselenide (1.1 equiv)
Method B: 1. lithium diisopropylamide (3 equiv); 2. diphenyl disulfide (2.2 equiv)
Method C: trifluoroacetic acid/water

Scheme A

Successful *mono*thiophenylation and *mono*selenophenylation of *ortho*-toluates **1a, b** was cleanly accomplished by their addition to an equivalent of lithium diisopropylamide at −78 °C in tetrahydrofuran followed by immediate inverse addition of 1.1 equivalent of diphenyl disulfide or diphenyl diselenide (Table), producing **2a, b** or **2c, d**, respectively.

Treatment of **1a** and **1c** with 3 equivalents of lithium diisopropylamide and 2.2 equiv of diphenyl disulfide in tetrahy-



Scheme B

ortho-Toluate Carbanion Chemistry: Sulfenylation and Selenation

Frank M. HAUSER*[1], Richard P. RHEE, Subbarao PRASANNA

Department of Chemistry and Biochemical Sciences, Oregon Graduate Center, Beaverton, Oregon 97006, U.S.A.

Steven M. WEINREB[2], John H. DODD

Department of Chemistry, Pennsylvania State University, University Park, Pennsylvania 16802, U.S.A.

A number of groups have recently demonstrated the use of compounds such as **2** and **4** for construction of linear polycyclic aromatic compounds[3-9]. However, the syntheses described to date for these types of compounds have generally been somewhat long and inefficient. We report here a new and improved method of preparation of such intermediates via direct lithiation of the aromatic methyl group of several substituted toluates followed by either sulfenylation or selenation of the generated carbanion (Scheme A)[9,10].

0039-7881/80/0132-0072 $ 03.00

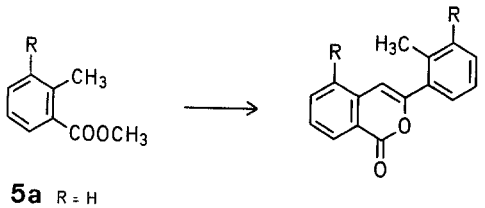
Table. Sulfenylated and selenated *ortho*-toluates

Product	Yield [%]	m.p.	Molecular[a] Formula	^{1}H-N.M.R. ($CDCl_3$) δ [ppm]
2a	87	oil	$C_{17}H_{18}O_3S$ (302.4)	1.32 (t, 3H, J=7 Hz, OCH_2CH_3); 3.77 (s, 3H, OCH_3); 4.11 (s, 2H, CH_2SAr); 4.35 (q, 2H, J=7 Hz, OCH_2CH_3); 6.79 (m, 2H, ArH); 7.21 (m, 6H, ArH)
2b	84	oil	$C_{17}H_{18}O_4S$ (318.4)	3.61 (s, 3H, OCH_3); 3.69 (s, 3H, OCH_3); 3.80 (s, 3H, OCH_3); 4.09 (s, 2H, CH_2SAr); 6.29 (s, 2H, ArH); 7.19 (m, 5H, ArH)
2c	87	oil	$C_{17}H_{18}O_3Se$ (349.3)	1.28 (t, 3H, J=7 Hz, OCH_2CH_3); 3.64 (s, 3H, OCH_3); 4.09 (s, 2H, CH_2SeAr); 4.30 (q, 2H, J=7 Hz, OCH_2CH_3); 6.51 (m, 2H, ArH); 7.14 (m, 6H, ArH)
2d	71	66.5–67.5 °C	$C_{17}H_{18}O_4Se$ (365.3)	3.71 (s, 3H, OCH_3); 3.82 (s, 3H, OCH_3); 3.89 (s, 3H, OCH_3); 4.15 (s, 2H, CH_2SeAr); 6.23 (d, 1H, J=3 Hz, ArH); 6.59 (d, 1H, J=3 Hz, ArH); 7.23–7.70 (m, 5H, ArH)
3a	83	75–76 °C	$C_{23}H_{22}O_3S_2$ (410.6)	1.17 (t, 3H, J=7 Hz, OCH_2CH_3); 3.72 (s, 3H, OCH_3); 4.15 (q, 2H, J=7 Hz, OCH_2CH_3); 5.63 [s, 1H, $CH(SAr)_2$]; 6.68 (dd, 1H, J=7 Hz, J=2 Hz, ArH); 7.0–7.35 (m, 12H, ArH)
3b	85	52–54 °C	$C_{24}H_{24}O_4S_2$ (440.6)	1.18 (t, 3H, J=7 Hz, OCH_2CH_3); 3.66 (s, 3H, OCH_3); 3.70 (s, 3H, OCH_3); 4.21 (q, 2H, J=7 Hz, OCH_2CH_3); 5.81 [s, 1H, $CH(SAr)_2$]; 6.30 (d, 1H, J=2 Hz, ArH); 6.80 (d, 1H, J=2 Hz, ArH); 7.10–7.40 (m, 12H, ArH)

[a] Satisfactory microanalytical results were obtained for all new compounds including **4a, 4b, 6a**, and **6b** (C ±0.3, H ±0.3).

drofuran smoothly afforded dithiophenylated products **3a, b** in good yields. Partial hydrolysis of **3a, b** with trifluoroacetic acid/water gave 3-thiophenylphthalides **4a, b** in 95 and 92% yields, respectively. Compound **4b** could not be prepared by the previously described method[11,12] although we have previously prepared **2e** (R^1=OCH_3, R^2=C_2H_5, Y=S) by an unpublished route (Scheme **B**).

In contrast to the well behaved nature of the anions derived from *ortho*-toluates **1a, b**, the anions derived from *ortho*-toluates **5a, b** were unstable and underwent rapid coupling to furnish isocoumarins **6a, b**. The nature and position of the aromatic substituents in various toluates clearly affect the stability of these carbanions. Based upon our limited data, we tentatively conclude that an oxygen substituent *ortho* to the ester group is necessary to decrease the carbonyl electrophilicity (by both steric and electronic effects) enough to prevent rapid coupling, thus allowing time for reaction with electrophiles[13].



5a R = H
5b R = H_3CO

6a,b

Monothiophenylation and Monoselenophenylation; General Procedure:

ortho-Toluate **1a** or **1b** (5.0 mmol) in dry tetrahydrofuran (8 ml) is added under nitrogen to a stirred solution of lithium diisopropylamide (5.1 mmol) in tetrahydrofuran (12 ml) cooled to −78 °C. The resulting red solution is transferred via a cannula to a Dry Ice/acetone jacketed addition funnel. Slow addition of the solution to a magnetically stirred solution of either diphenyl disulfide (1.20 g, 5.5 mmol) in dry tetrahydrofuran (15 ml) cooled to −78 °C or analogously diphenyl diselenide (1.71 g, 5.5 mmol) is performed. After the addition is completed, 5% hydrochloric acid (10 ml) is added to the cold solution. The reaction mixture is added to 5% hydrochloric acid (50 ml) and diethyl ether (75 ml). After separating the layers, the organic layer is washed twice with 5% sodium hydroxide (25 ml portions), once with saturated aqueous sodium chloride, and once with water. The organic layer is dried with sodium sulfate, and evaporated at reduced pressure. The residue is chromatographed on silica (100 g, chloroform) to give either monothiophenylated products **2a** or **2b** or monoselenophenylated products **2c** or **2d**.

Isocoumarins 6a or 6b:

Attempted monothiophenylation of *ortho*-toluates **5a** and **5b** using the above conditions furnishes coupled products **6a** and **6b** in 41% and 34% yield, respectively. Yields of 67% and 59% are obtained for **6a** and **6b** when the metallated *ortho*-toluates **5a** and **5b**, initially generated at −78 °C, are allowed to warm to room temperature and no diphenyl disulfide is added.

6a: m.p. 85 °C.

^{1}H-N.M.R. (CCl_4): δ=2.40 (s, 3H, $ArCH_3$); 6.43 (s, 1H, ArCH=); 7.08–7.68 (m, 7H, ArH); 8.16 ppm (d, J=7 Hz, 1H, ArH).

6b: m.p. 119–120 °C.

^{1}H-N.M.R. ($CDCl_3$): δ=2.26 (s, 3H, $ArCH_3$); 3.78 (s, 3H, OCH_3); 3.84 (s, 3H, OCH_3); 6.80–7.50 (m, 5H, ArH); 7.86 ppm (d, J=7 Hz, 1H, ArH).

Dithiophenylation:

ortho-Toluate **1a** or **1b** (5.15 mmol) in dry tetrahydrofuran (15 ml) is added under nitrogen to a magnetically stirred solution of lithium diisopropylamide (15.45 mmol) in tetrahydrofuran (15 ml) cooled to −78 °C. To the orange red anion solution is rapidly added diphenyl disulfide (2.47 g, 11.34 mmol) in tetrahydrofuran (15 ml). After the solution has warmed to room temperature, acetic acid (10 ml), and water (30 ml) are added and the organic layer is evaporated. The precipitated oil is dissolved in ethyl acetate (75 ml) and successively washed with water (50 ml), 5% sodium hydroxide (25 ml portions), water, and brine, then dried with magnesium sulfate, and evaporated at reduced pressure. The residue is chromatographed on silica (100 g, dichloromethane) to give dithiophenylated products **3a** or **3b**.

3-Thiophenyl-1(3*H*)isobenzofuranones 4a and 4b:

Phenylthioacetal **3a** or **3b** (3 mmol) in trifluoroacetic acid (20 ml)/water (1 ml) is heated under reflux for 45 min at which time thin layer chromatographic analysis shows complete disappearance of the starting material. The reaction mixture is evaporated at reduced pressure, and the residue chromatographed on silica (50 g, dichloromethane) to give pure **4a** or **4b**.

4a: m.p. 126–127 °C.

^{1}H-N.M.R. (acetone-d_6): δ=3.90 (s, 3H, OCH_3); 6.88 (s, 1H, C_6H_5–S–CH), 7.13 (t, J=8 Hz, 1H, ArH), 7.24–7.60 (m, 6H, ArH), 7.72 ppm (t, J=8 Hz, 1H, ArH).

4b: m.p. 131–132 °C.

^{1}H-N.M.R. ($CDCl_3$): δ=3.83 (s, 3H, OCH_3); 3.85 (s, 3H, OCH_3); 6.37 (d, J=2 Hz, 1H, ArH); 6.49 (s, 1H, Ar–CH–S); 6.62 (d, J=2 Hz, 1H, ArH); 7.20–7.60 ppm (m, 4H, ArH).

The authors wish to thank the National Cancer Institute of DHEW, (CA 18141 and CA 25145) for support of this work.

Received: August 21, 1979

[1] Recipient of a Research Career Development Award, 1978–82, from the National Cancer Institute (CA 00486).

[2] A. P. Sloan Foundation Fellow, 1975–1979. Recipient of a Research Career Development Award, 1975–80, from the National Heart, Blood, Lung Institute (HL 00176).

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