

Iodine-mediated Synthesis of 4-Selanylpyrazoles

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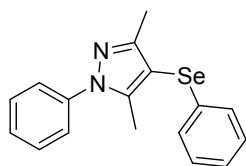
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Experimental

A typical procedure for the preparation of 4-selenylpyrazoles:

3,5-Dimethyl-1-phenyl-1*H*-pyrazole **1a** (0.24 mmol), diphenyl diselenide **2a** (0.1 mmol) and I₂ (0.1 mmol) were added successively to 1,2-dichloroethane (2 mL). The mixture was vigorously stirred at r. t. for 6 h. Upon completion, the reaction was quenched by addition of sat. aq. Na₂S₂O₃ (2 mL) and H₂O (5 mL), respectively. The mixture was extracted with CH₂Cl₂ (3×5 mL) and the combined organic phase was dried over anhydrous Na₂SO₄, filtered, and concentrated under reduced pressure. The residue was then purified on a silica gel plate (10:1 petroleum ether-ethyl acetate) to furnish products **3a** 51 mg (78%).

3,5-Dimethyl-1-phenyl-4-(phenylselanyl)-1*H*-pyrazole (**3a**)



White solid; mp 76–77°C (Lit.¹ 67–69°C).

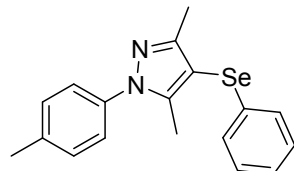
¹H NMR (500 MHz, CDCl₃) δ (ppm): 7.52–7.47 (m, 4H), 7.43–7.39 (m, 1H), 7.25–7.15 (m, 5H), 2.40 (s, 3H), 2.35 (s, 3H).

¹³C NMR (125 MHz, CDCl₃) δ (ppm): 153.34, 144.15, 139.93, 133.03, 129.21, 129.19, 128.40, 127.84, 125.82, 124.84, 102.91, 13.02, 12.54.

IR (film) 3050, 2925, 1595, 1574, 1502, 1476, 1379, 1021, 765, 738, 694 cm⁻¹.

MS (ESI): *m/z* (%) 329 [(M+H)⁺, 100].

3,5-Dimethyl-4-(phenylselanyl)-1-(*p*-tolyl)-1*H*-pyrazole (**3b**)



White solid; mp 65–67°C.

¹H NMR (500 MHz, CDCl₃) δ (ppm): 7.36 (d, *J* = 10.0 Hz, 2H), 7.29 (d, *J* = 10.0 Hz, 2H), 7.24–7.19 (m, 4H), 7.19–7.12 (m, 1H), 2.43 (s, 3H), 2.37 (s, 3H), 2.34 (s, 3H).

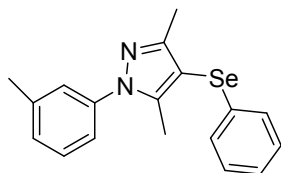
¹³C NMR (125 MHz, CDCl₃) δ (ppm): 153.05, 144.08, 137.77, 137.75, 133.08, 129.68, 129.14, 128.32, 125.73, 124.71, 102.19, 21.13, 12.96, 12.40.

IR (film) 3040, 2921, 1576, 1518, 1475, 1412, 1383, 1088, 1064, 1019, 825, 737, 691 cm^{-1} .

MS (ESI): m/z (%) 343 [(M+H)⁺, 100].

HRMS: calcd for $\text{C}_{18}\text{H}_{19}\text{N}_2\text{Se}$ [M+H]⁺ 343.0713, found 343.0699.

3,5-Dimethyl-4-(phenylselanyl)-1-(*m*-tolyl)-1*H*-pyrazole (3c)



Yellow oil¹.

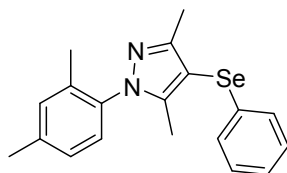
¹H NMR (500 MHz, CDCl_3) δ (ppm): 7.40–7.33 (m, 2H), 7.28–7.20 (m, 6H), 7.19–7.15 (m, 1H), 2.44 (s, 3H), 2.39 (s, 3H), 2.35 (s, 3H).

¹³C NMR (125 MHz, CDCl_3) δ (ppm): 153.14, 144.08, 139.79, 139.34, 133.03, 129.15, 128.82, 128.59, 128.33, 125.75, 125.56, 121.76, 102.39, 21.37, 12.97, 12.48.

IR (film) 3054, 2923, 2854, 1610, 1529, 1497, 1437, 1379, 1091, 1046, 1021, 999, 787, 735, 693 cm^{-1} .

MS (ESI): m/z (%) 343 [(M+H)⁺, 100].

3,5-Dimethyl-1-(2,4-dimethylphenyl)-4-(phenylselanyl)-1*H*-pyrazole (3d)



White solid; mp 56-57°C.

¹H NMR (500 MHz, CDCl_3) δ (ppm): 7.25–7.14 (m, 7H), 7.13–7.07 (m, 1H), 2.40 (s, 3H), 2.34 (s, 3H), 2.13 (s, 3H), 2.05 (s, 3H).

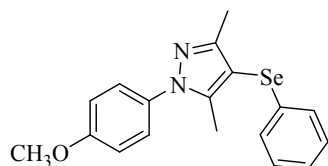
¹³C NMR (125 MHz, CDCl_3) δ (ppm): 152.67, 145.45, 139.48, 135.88, 135.60, 133.18, 131.65, 129.18, 128.18, 127.50, 127.35, 125.72, 100.70, 21.21, 17.19, 12.97, 11.37.

IR (film) 3064, 2922, 2853, 1576, 1511, 1474, 1436, 1024, 834, 740, 692 cm^{-1} .

MS (ESI): m/z (%) 357 [(M+H)⁺, 100].

HRMS: calcd for $\text{C}_{19}\text{H}_{21}\text{N}_2\text{Se}$ [M+H]⁺ 357.0870, found 357.0845.

3,5-Dimethyl-1-(4-methoxyphenyl)-4-(phenylselanyl)-1*H*-pyrazole (3e)



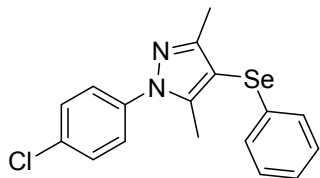
White oil².

¹H NMR (500 MHz, CDCl_3) δ (ppm): 7.41–7.35 (m, 4H), 7.25–7.15 (m, 2H), 7.02–6.97 (m, 3H), 3.87 (s, 3H), 2.34 (s, 3H), 2.33 (s, 3H).

¹³C NMR (125 MHz, CDCl_3) δ (ppm): 159.14, 152.91, 144.20, 133.10, 133.04,

129.13, 128.33, 126.36, 125.73, 114.25, 101.87, 55.57, 12.93, 12.24.
IR (film) 3066, 2923, 2852, 1578, 1522, 1475, 1411, 1249, 1024, 832, 732, 689 cm^{-1} .
MS (ESI): m/z (%) 359 [(M+H)⁺, 100].

1-(4-Chlorophenyl)-3,5-dimethyl-4-(phenylselanyl)-1H-pyrazole (3f)



Brown solid; mp 72-73°C.

¹H NMR (500 MHz, CDCl₃) δ (ppm): 7.47 (d, J = 10.0 Hz, 2H), 7.44 (d, J = 10.0 Hz, 2H), 7.25–7.12 (m, 5H), 2.40 (s, 3H), 2.34 (s, 3H).

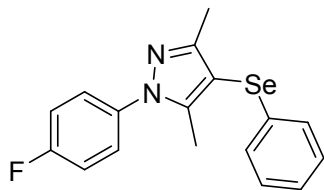
¹³C NMR (125 MHz, CDCl₃) δ (ppm): 153.62, 144.09, 138.37, 133.49, 132.73, 129.19, 128.48, 125.90, 125.86, 103.23, 12.95, 12.53.

IR (film) 3064, 2924, 2853, 1577, 1527, 1501, 1475, 1404, 1381, 1087, 1011, 835, 739, 689 cm^{-1} .

MS (ESI): m/z (%) 363 [(M+H)⁺, 15].

HRMS: calcd for C₁₇H₁₆ClN₂Se [M+H]⁺ 363.0167, found 363.0161.

3,5-Dimethyl-1-(4-fluorophenyl)-4-(phenylselanyl)-1H-pyrazole (3g)



Yellow oil.

¹H NMR (500 MHz, CDCl₃) δ (ppm): 7.48–7.43 (m, 2H), 7.25–7.16 (m, 7H), 2.37 (s, 3H), 2.34 (s, 3H).

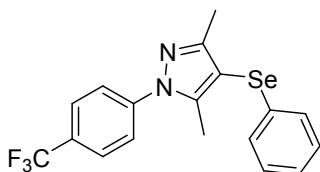
¹³C NMR (125 MHz, CDCl₃) δ (ppm): 162.89, 160.91, 153.33, 144.25, 135.90, 132.77, 129.19, 128.46, 126.72 (d, J = 8.8 Hz), 125.88, 116.08 (d, J = 22.5 Hz), 102.76, 12.91, 12.36.

IR (film) 3069, 2925, 2853, 1577, 1515, 1476, 1410, 1382, 1225, 1154, 1090, 1019, 841, 736, 690 cm^{-1} .

MS (ESI): m/z (%) 347 [(M+H)⁺, 100].

HRMS: calcd for C₁₇H₁₆FN₂Se [M+H]⁺ 347.0463, found 347.0421.

3,5-Dimethyl-4-(phenylselanyl)-1-(4-trifluoromethylphenyl)-1H-pyrazole (3h)

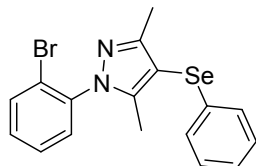


Yellow solid; mp 70-74°C.

¹H NMR (500 MHz, CDCl₃) δ (ppm): 7.77 (d, J = 10.0 Hz, 2H), 7.66 (d, J = 10.0 Hz,

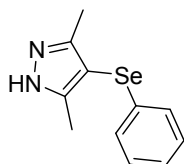
2H), 7.63–7.56 (m, 1H), 7.25–7.16 (m, 4H), 2.47 (s, 3H), 2.35 (s, 3H).
 ^{13}C NMR (125 MHz, CDCl_3) δ (ppm): 154.14, 144.24, 142.57, 132.52, 129.26, 128.64, 126.42, 126.03, 124.46, 104.25, 13.05, 12.86.
 IR (film) 3071, 2927, 2854, 1617, 1525, 1476, 1409, 1326, 1167, 1126, 1068, 1016, 846, 738, 691 cm^{-1} .
 MS (ESI): m/z (%) 397 [(M+H) $^+$, 100].
 HRMS: calcd for $\text{C}_{18}\text{H}_{16}\text{F}_3\text{N}_2\text{Se}$ [M+H] $^+$ 397.0431, found 397.0412.

1-(2-Bromophenyl)-3,5-dimethyl-4-(phenylselanyl)-1H-pyrazole (3i)



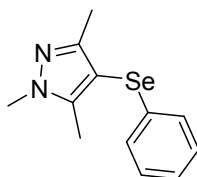
Yellow oil.
 ^1H NMR (500 MHz, CDCl_3) δ (ppm): 7.76–7.72 (m, 1H), 7.48–7.46 (m, 2H), 7.40–7.36 (m, 1H), 7.28 (s, 1H), 7.23–7.20 (m, 3H), 7.17 (dd, J = 6.3, 2.3 Hz, 1H), 2.35 (s, 3H), 2.19 (s, 3H).
 ^{13}C NMR (125 MHz, CDCl_3) δ (ppm): 153.47, 146.10, 138.87, 133.46, 132.99, 130.97, 129.84, 129.18, 128.41, 128.10, 125.72, 122.50, 101.39, 12.98, 11.50.
 IR (film) 3059, 2924, 2853, 1577, 1532, 1496, 1438, 1380, 1063, 1023, 782, 760, 736, 691 cm^{-1} .
 MS (ESI): m/z (%) 407 [(M+H) $^+$, 7].
 HRMS: calcd for $\text{C}_{17}\text{H}_{16}\text{BrN}_2\text{Se}$ [M+H] $^+$ 406.9662, found 406.9651.

3,5-Dimethyl-4-(phenylselanyl)-1H-pyrazole (3k)



Yellow oil; (Lit. 1 91–93°C).
 ^1H NMR (500 MHz, CDCl_3) δ (ppm): 7.22–7.10 (m, 5H), 6.23 (br s, 1H), 2.35 (s, 6H).
 ^{13}C NMR (125 MHz, CDCl_3) δ (ppm): 149.29, 132.62, 129.18, 128.40, 125.89, 100.32, 11.90.
 IR (film) 3183, 3072, 2924, 2853, 1578, 1477, 1438, 1298, 1022, 735, 690 cm^{-1} .
 MS (ESI): m/z (%) 253 [(M+H) $^+$, 100].

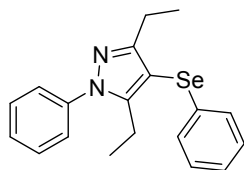
4-(Phenylselanyl)-1,3,5-trimethyl-1H-pyrazole (3l)



Yellow oil.

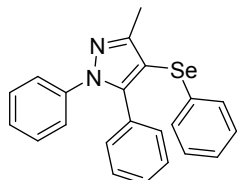
^1H NMR (500 MHz, CDCl_3) δ (ppm): 7.22–7.10 (m, 5H), 3.83 (s, 3H), 2.31 (s, 3H), 2.25 (s, 3H).
 ^{13}C NMR (125 MHz, CDCl_3) δ (ppm): 151.76, 143.84, 133.41, 129.04, 128.14, 128.09, 125.56, 100.13, 36.68, 12.77, 10.95.
 IR (film) 3056, 2924, 2854, 1577, 1528, 1476, 1438, 1381, 1067, 1022, 910, 734, 691, 666 cm^{-1} .
 MS (ESI): m/z (%) 267 [(M+H) $^+$, 100].
 HRMS: calcd for $\text{C}_{12}\text{H}_{15}\text{N}_2\text{Se}$ [M+H] $^+$ 267.0400, found 297.0388.

3,5-Diethyl-1-phenyl-4-(phenylselanyl)-1H-pyrazole (3m)



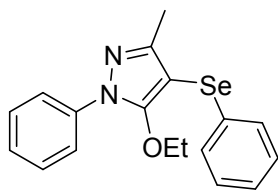
Red solid; mp 53–54°C (Lit.¹ orange oil).
 ^1H NMR (500 MHz, CDCl_3) δ (ppm): 7.52–7.47 (m, 4H), 7.46–7.42 (m, 1H), 7.25–7.19 (m, 4H), 7.18–7.14 (m, 1H), 2.80 (q, $J = 7.5$ Hz, 2H), 2.73 (q, $J = 7.6$ Hz, 2H), 1.24 (t, $J = 7.6$ Hz, 3H), 1.02 (t, $J = 7.5$ Hz, 3H).
 ^{13}C NMR (125 MHz, CDCl_3) δ (ppm): 158.34, 149.84, 140.04, 133.68, 129.19, 129.07, 128.13, 125.63, 125.45, 100.39, 20.90, 19.22, 13.93, 13.75.
 IR (film) 3068, 2971, 2929, 2853, 1597, 1578, 1503, 1476, 1437, 1389, 1069, 1040, 1022, 770, 735, 692 cm^{-1} .
 MS (ESI): m/z (%) 357 [(M+H) $^+$, 100].

1,5-Diphenyl-3-methyl-4-(phenylselanyl)-1H-pyrazole (3o)



Yellow oil¹.
 ^1H NMR (500 MHz, CDCl_3) δ (ppm): 7.55–7.48 (m, 1H), 7.43–7.36 (m, 1H), 7.35–7.25 (m, 4H), 7.25–7.15 (m, 9H), 2.41 (s, 3H).
 ^{13}C NMR (125 MHz, CDCl_3) δ (ppm): 154.02, 147.04, 139.95, 133.31, 130.19, 129.17, 128.81, 128.71, 128.61, 128.20, 127.24, 125.84, 124.85, 104.37, 103.52, 13.07.
 IR (film) 3058, 2924, 2852, 1597, 1577, 1503, 1476, 1376, 1063, 1022, 956, 765, 735, 694 cm^{-1} .
 MS (ESI): m/z (%) 391 [(M+H) $^+$, 82].

3-Ethoxy-5-methyl-1-phenyl-4-(phenylselanyl)-1H-pyrazole (3q)



White oil.

^1H NMR (500 MHz, CDCl_3) δ (ppm): 7.73 (dd, $J = 8.6, 1.2$ Hz, 2H), 7.48–7.43 (m, 2H), 7.35–7.22 (m, 5H), 7.21–7.15 (m, 1H), 4.37 (q, $J = 7.0$ Hz, 2H), 2.29 (s, 3H), 1.27 (t, $J = 5.0$ Hz 3H).

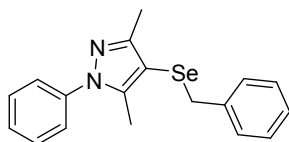
^{13}C NMR (125 MHz, CDCl_3) δ (ppm): 155.57, 153.28, 138.58, 133.37, 129.26, 128.92, 128.12, 126.66, 125.87, 122.48, 70.36, 15.33, 13.67.

IR (film) 3068, 2982, 2925, 2853, 1596, 1540, 1505, 1424, 1385, 1045, 1021, 760, 735, 691 cm^{-1} .

MS (ESI): m/z (%) 359 [(M+H) $^+$, 100].

HRMS: calcd for $\text{C}_{18}\text{H}_{19}\text{N}_2\text{OSe}$ [M+H] $^+$ 359.0663, found 359.0660.

4-(Benzylselenanyl)-3,5-dimethyl-1-phenyl-1H-pyrazole (3s)



Yellow oil.

^1H NMR (500 MHz, CDCl_3) δ (ppm): 7.50–7.44 (m, 2H), 7.40–7.33 (m, 3H), 7.23–7.19 (m, 3H), 7.03–6.97 (m, 2H), 3.73 (s, 2H), 2.28 (s, 3H), 1.89 (s, 3H).

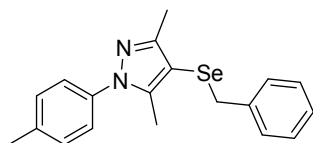
^{13}C NMR (125 MHz, CDCl_3) δ (ppm): 153.20, 144.48, 139.96, 139.25, 129.03, 128.91, 128.16, 127.61, 126.56, 124.81, 102.56, 31.69, 12.82, 11.78.

IR (film) 3060, 3027, 2925, 2853, 1597, 1527, 1503, 1453, 1411, 1380, 1087, 1021, 760, 696 cm^{-1} .

MS (ESI): m/z (%) 343 [(M+H) $^+$, 59].

HRMS: calcd for $\text{C}_{18}\text{H}_{19}\text{N}_2\text{Se}$ [M+H] $^+$ 343.0713, found 343.0101.

4-(Benzylselenanyl)-3,5-dimethyl-1-(*p*-tolyl)-1H-pyrazole (3t)



Yellow oil.

^1H NMR (500 MHz, CDCl_3) δ (ppm): 7.28–7.18 (m, 7H), 7.03–6.97 (m, 2H), 3.72 (s, 2H), 2.41 (s, 3H), 2.27 (s, 3H), 1.87 (s, 3H).

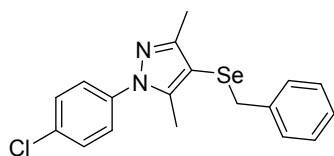
^{13}C NMR (125 MHz, CDCl_3) δ (ppm): 152.94, 144.45, 139.27, 137.56, 137.50, 129.57, 128.89, 128.14, 126.53, 124.71, 102.20, 31.69, 21.10, 12.81, 11.69.

IR (film) 3027, 2924, 2853, 1519, 1453, 1411, 1381, 1037, 1017, 823, 760, 697 cm^{-1} .

MS (ESI): m/z (%) 357 [(M+H) $^+$, 34].

HRMS: calcd for $\text{C}_{19}\text{H}_{21}\text{N}_2\text{Se}$ [M+H] $^+$ 357.0870, found 357.0857.

4-(Benzylselenenyl)-1-(4-chlorophenyl)-3,5-dimethyl-1H-pyrazole (3u)



Brown oil.

^1H NMR (500 MHz, CDCl_3) δ (ppm): 7.46–7.40 (m, 2H), 7.32–7.27 (m, 2H), 7.23–7.15 (m, 3H), 7.02–6.96 (m, 2H), 3.72 (s, 2H), 2.27 (s, 3H), 1.88 (s, 3H).

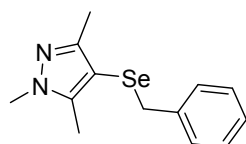
^{13}C NMR (125 MHz, CDCl_3) δ (ppm): 153.57, 144.51, 139.16, 138.49, 133.28, 129.19, 128.91, 128.15, 126.60, 125.85, 103.08, 31.68, 12.80, 11.81.

IR (film) 3060, 3027, 2926, 1597, 1528, 1450, 1406, 1379, 1092, 1012, 833, 760, 697 cm^{-1} .

MS (ESI): m/z (%) 377 [(M+H) $^+$, 58].

HRMS: calcd for $\text{C}_{18}\text{H}_{18}\text{ClN}_2\text{Se}$ [M+H] $^+$ 377.0324, found 377.0303.

4-(Benzylselenyl)-1,3,5-trimethyl-1H-pyrazole (3v)



Yellow oil.

^1H NMR (500 MHz, CDCl_3) δ (ppm): 7.20–7.17 (m, 3H), 6.99–6.95 (m, 2H), 3.71 (s, 3H), 3.65 (s, 2H), 2.15 (s, 3H), 1.89 (s, 3H).

^{13}C NMR (125 MHz, CDCl_3) δ (ppm): 151.61, 144.04, 139.43, 128.80, 128.13, 126.47, 100.44, 36.46, 31.95, 12.60, 10.32.

IR (film) 3060, 3027, 2924, 2853, 1721, 1527, 1492, 1454, 1412, 1381, 1276, 1177, 1085, 760, 697, 669 cm^{-1} .

MS (ESI): m/z (%) 281 [(M+H) $^+$, 48].

HRMS: calcd for $\text{C}_{13}\text{H}_{17}\text{N}_2\text{Se}$ [M+H] $^+$ 281.0557, found 281.0521.

References:

1. D. H. Oliveria, T. B. Aquino, J. E. R. Nascimento, G. Perin, R. G. Jacob and D. Alves, *Adv. Synth. Catal.*, 2015, **357**, 4041.
2. J. E. R. Nascimento, D. H. Oliveria, P. B. Abib, D. Alves, G. Perin and R. G. Jacob, *J. Braz. Chem. Soc.*, 2015, **26**, 1533.

