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Communication

Synthesis of 4-Arylselanylpyrazoles Through Cyclocondensation Reaction Using Glycerol as Solvent

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We describe here a simple method to synthesize 4-arylselanylpyrazoles by reaction of α-arylselanyl-1,3-diketones with arylhydrazines using glycerol as solvent at 60 °C under N_2 atmosphere. This is a direct cyclocondensation reaction performed with α-arylselanyl-1,3-diketones and arylhydrazines bearing electron-withdrawing and electron-donating groups affording the corresponding 4-arylselanylpyrazoles in moderate to good yields.

Keywords: green chemistry, glycerol, pyrazole, heterocycle, organoselenium compound

Introduction

Pyrazoles represent a significant class of heterocyclic compounds used widely in agrochemical and especially pharmaceutical industry.[1] This class of biologically active nitrogen compounds exhibit a number of important pharmacology properties, such as antibacterial, antiobesity, antitumor, antileukemic, anti-inflammatory and analgesic.[2] For example, substituted pyrazoles constitute the core structures of important commercial drugs, such as Celecoxib,[3] Metamizole,[4] Zaleplon,[5] Sildenafil[6] and Fipronil[7] (Figure 1).

The synthesis of these heterocyclic compounds can be achieved by several different methods. Generally pyrazoles could be synthesized by reaction of 1,3-dicarbonyl compounds with hydrazines,[8] 1,3-dipolar cycloadition employing alkenes or alkynes,[9] reaction of unsaturated aldehydes or ketones with hydrazines,[10] the functionalization of unsubstituted pyrazoles,[11] among others.[12] Therefore, the search for a practical reaction system for the synthesis of substituted pyrazoles in terms of mild reaction conditions and economic viability, continues to attract the interest of synthetic organic chemists.

In this sense, the development of methodologies employing recyclable and environmentally friendly solvents has gained much interest recently, because of the extensive use of solvents in almost all of the chemical and pharmaceutical industries, and of the predicted disappearance of fossil oil.[13] With the increase in biodiesel production and consequently, the market saturation of glycerol, in the last years, this side product of biodiesel production emerged as an alternative for the replacement of conventional solvents.[14]

The use of glycerol as a sustainable solvent for green chemistry was recently reported,[14] particularly for the synthesis of organoselenium compounds.[15] Organoselenium compounds are attractive molecules due to their selective reactions[16] and are often linked to interesting biological activities.[17] Among organoselenium compounds, those containing nitrogen heterocycles in their structure are of special interest and this class of molecules has shown a range of pharmacological properties.[17,18] However, there are few reports on the preparation of selanyl-substituted pyrazoles and as example, bis(3*R*,5*R'*-1*H*-pyrazol-4-yl) selenides were synthesized in high yields by reaction between 3- and 3,5-substituted pyrazoles with selenium dioxide.[19] Consequently, the search for new and efficient methods for the synthesis of nitrogen-functionalized organoselenium compounds, more specifically selanyl-substituted pyrazoles, remains a challenge in organic chemistry.

In view of the explained above, we report here our contribution to the application of glycerol as solvent in the synthesis of selanyl-substituted heterocycles. The present methodology describes a simple method to synthesize a range of 4-arylselanylpyrazoles by reaction

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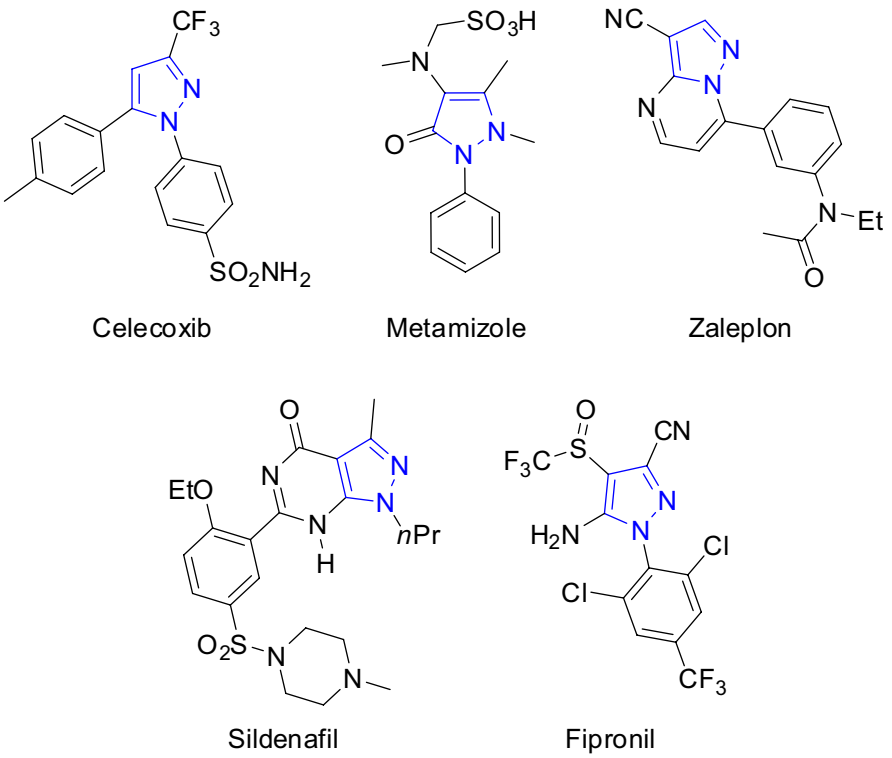
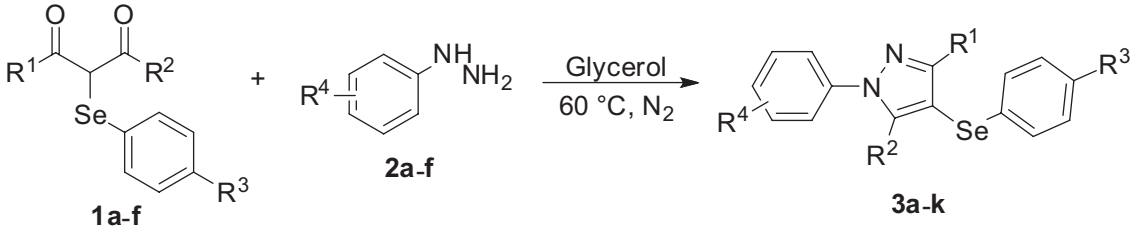


Figure 1. Drugs containing pyrazole moiety in their structure.



Scheme 1. General scheme of the reaction.

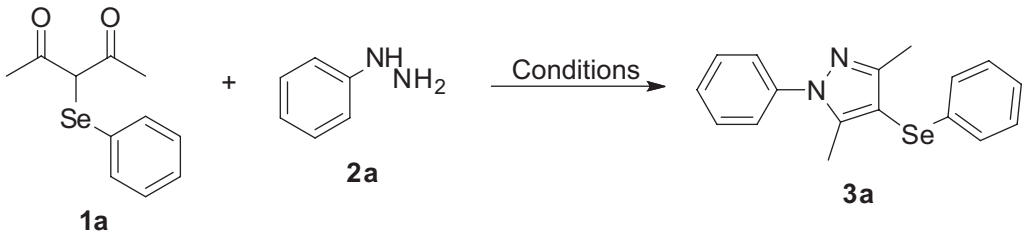
of α-arylselanyl-1,3-diketones with arylhydrazines using glycerol as solvent (Scheme 1).

Results and Discussion

Initially, we chose α-phenylselanylacetylacetone **1a** and phenylhydrazine **2a** as model substrates to establish the best conditions for this reaction and some experiments, including solvent tests, stoichiometry and temperature were performed to synthesize 3,5-dimethyl-1-phenyl-4-(phenylselanyl)-1*H*-pyrazole **3a** (Table 1). The starting material **1a**, which exists predominantly in enolic form (ratio of keto:enol = 1:9), was synthesized according protocol described by Sonoda and co-workers.[20]

Thus, a mixture of α-phenylselanylacetylacetone **1a** (0.5 mmol) and phenylhydrazine **2a** (0.5 mmol) in glycerol (1.0 mL) was stirred at room temperature under air atmosphere for 5 h. Under these reaction conditions, the product **3a** was obtained only in 35% yield and a slight decomposition of the starting material during the reaction time was observed (Table 1, entry 1). Aiming to improve the yield of product **3a** a mixture of compound **1a** and phenylhydrazine **2a** in glycerol was reacted in open atmosphere at 60 and 90 °C. Interestingly, when we carried out the reaction at 60 °C, the desired product **3a** was obtained in 70% yield after 4 h (Table 1, entry 2). However, when the temperature of reaction was increased to 90 °C, the desired product **3a** was formed in 55% and a great decomposition of starting material **1a** was observed after 1.5 h (Table 1, entry 3). An increase in the yield was obtained when the reaction was performed at 60 °C under N_2 atmosphere (Table 1, entry 4). Unfortunately, when the reaction was carried out at room temperature under N_2 atmosphere, it yielded the product **3a** in 40% (Table 1, entry 5). Gratefully, when the reaction was performed at 60 °C under N_2 atmosphere using a little excess of

Table 1. Reaction conditions optimization[a]



entry	**1a** / mmol	Solvent	Temperature / °C	time[b] / h	Yield[c] / %
1	0.5	Glycerol	r.t.	5.0	35
2	0.5	Glycerol	60	4.0	70
3	0.5	Glycerol	90	1.5	55
4	0.5	Glycerol	60	3.0	75[d]
5	0.5	Glycerol	r.t.	5.5	40[d]
6	0.6	Glycerol	60	3.0	82[d]
7	0.6	PEG-400	60	5.0	27[d]
8	0.6	H_2O	60	5.0	53[d]
9	0.6	EtOH	60	5.0	77[d]
10	0.6	–	60	5.0	45[d]

[a]Reactions were performed using α-phenylselanylacetylacetone **1a**, phenylhydrazine **2a** (0.5 mmol) and 1.0 mL of solvent; [b]during this time, a slight decomposition of the starting material **1a** in diphenyl diselenide and 2,4-pentanedione was observed. Traces of 3,5-dimethyl-1-phenyl-1*H*-pyrazole were observed as by-product; [c]yields are given for isolated product **3a**; [d]reactions were performed under N_2 atmosphere. PEG: polyethylene glycol; r.t.: room temperature.

substrate **1a** (0.6 mmol), the corresponding product **3a** was obtained in 82% after 3.0 h (Table 1, entry 6). Regarding the influence of the solvent on the reaction, a range of environmentally friendly solvents were tested on the same protocol described above and the desired product **3a** was obtained in lower yields compared with the reaction performed in glycerol (Table 1, entries 6 *vs.* 7-9). Finally, the reaction was performed without solvent at 60 °C and product **3a** was obtained in 45% yield (Table 1, entry 10). In this reaction without solvent we observed the decomposition of the starting material **1a** after 5 h at 60 °C.

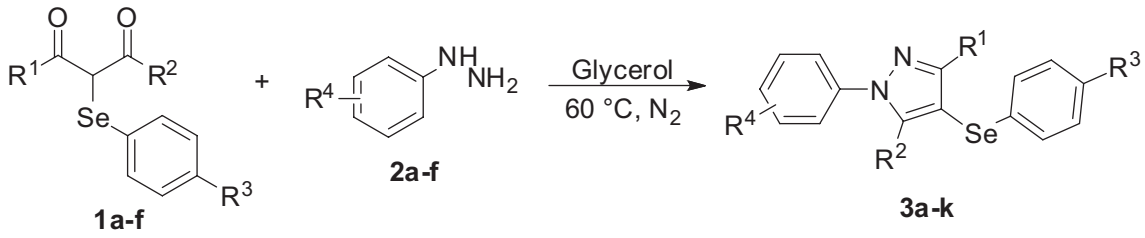
In fact, and according to our observations, during the whole time in all reactions the starting material **1a** suffers decomposition. This result is not surprising since this starting material can undergo a C–Se bond cleavage prompted by temperature or exposure to light.[21] The formation of 3,5-dimethyl-1-phenyl-1*H*-pyrazole as by-product could be explained by the cyclocondensation of 2,4-pentanedione with phenylhydrazine **2a** in the reaction media.

In an optimized reaction, α-phenylselanylacetylacetone **1a** (0.6 mmol) and phenylhydrazine **2a** (0.5 mmol) were dissolved in glycerol (1.0 mL). The reaction mixture was stirred for 3 h at 60 °C under nitrogen atmosphere, affording 3,5-dimethyl-1-phenyl-4-(phenylselanyl)-1*H*-pyrazole **3a** in 82% yield. It is important to mention that this cyclocondensation occurs without the presence of any catalyst. This result is in agreement with previous reports in literature in which electrophilic activation of carbonyl compounds in glycerol-promoted reactions allows eliminating the use of acidic catalysts.[22]

In order to demonstrate the efficiency of this reaction, we explored the generality of our method extending the conditions to other differently substituted α-arylselanyl-1,3-diketones **1a**-**f** and different arylhydrazines **2a**-**f**, and the results are summarized in Table 2. The results disclosed in Table 2 reveal that the reaction worked well with a range of substituted arylhydrazines **2** containing electron-donating groups (EDG) and electron-withdrawing groups (EWG) at the aromatic ring, affording moderate to good yields of the desired 4-arylselanylpyrazoles **3**. Our results reveal that the reactions are not sensitive to the electronic effect of the aromatic ring in the arylhydrazine. Therefore, a comparison between entries 1-5 *vs.* 6, in which arylhydrazines with EDG and EWG were used, displays similar yields for the obtained products (Table 2, entries 1-6).

In addition, the possibility of performing the reaction with other α-arylselanyl-1,3-diketones **1b**-**f** was investigated. These α-arylselanyl-1,3-diketones **1b**-**f** were also synthesized according to Sonoda and co-workers.[20] Phenylhydrazine **2a** was efficiently cyclocondensed with a range of α-arylselanyl-1,3-diketones, affording the respective 4-arylselanylpyrazoles **3** in acceptable yields

Table 2. Generality in the synthesis of 4-arylselanylpyrazoles[a]



1a-f **2a-f** **3a-k**

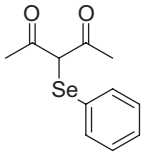
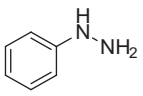
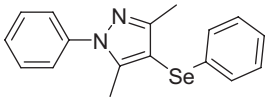
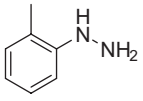
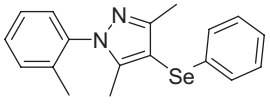
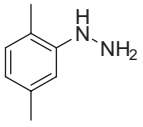
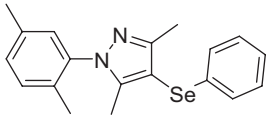
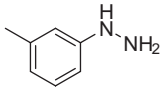
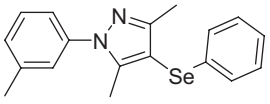
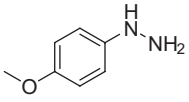
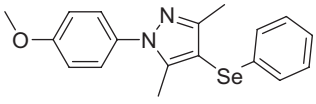
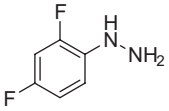
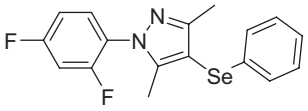
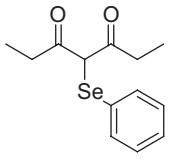
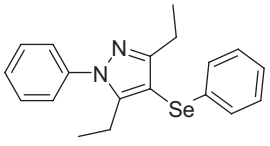
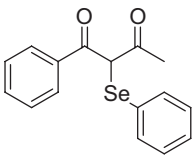
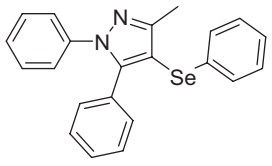
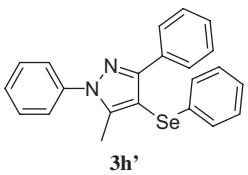
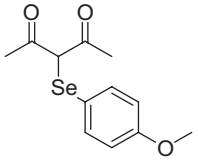
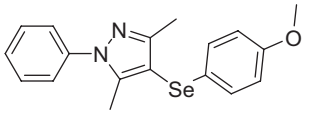
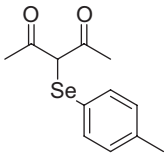
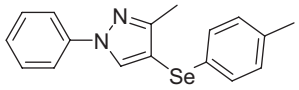
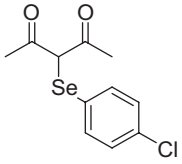
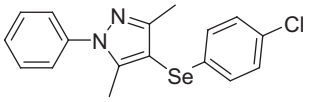
entry	α-Arylselanyl-1,3-diketone	Arylhydrazine	time[b] / h	Product	Yield[c] / %
1	 **1a**	 **2a**	3.0	 **3a**	82
2	**1a**	 **2b**	4.0	 **3b**	79
3	**1a**	 **2c**	4.5	 **3c**	81
4	**1a**	 **2d**	3.0	 **3d**	84
5	**1a**	 **2e**	3.5	 **3e**	77
6	**1a**	 **2f**	3.5	 **3f**	73
7	 **1b**	**2a**	2.5	 **3g**	87
8	 **1c**	**2a**	5.0	 **3h**  **3h'**	76[d]

Table 2. Generality in the synthesis of 4-arylselanylpyrazoles[a] (cont.)

entry	α-Arylselanyl-1,3-diketone	Arylhydrazine	time[b] / h	Product	Yield[c] / %
9	 **1d**	**2a**	3.0	 **3i**	68
10	 **1e**	**2a**	3.0	 **3j**	79
11	 **1f**	**2a**	3.0	 **3k**	72

[a]Reactions were performed using α-arylselanyl-1,3-diketones **1a-f** (0.6 mmol), arylhydrazines **2a-f** (0.5 mmol) in glycerol (1.0 mL) at 60 °C under N_2 atmosphere; [b]during this time, a slight decomposition of starting materials **1a-f** in diaryl diselenides and 1,3-diketones was observed. Traces of 3,5-disubstituted 1-aryl-1*H*-pyrazoles without arylselenium moiety were observed as by-product; [c]yields are given for isolated 4-arylselanylpyrazoles; [d]a mixture of regioisomers in a ratio **3h/3h'** (96:4) were obtained and determined by ^{1}H NMR.

(Table 2, entries 7-11). α-Arylselanyl-1,3-diketones **1b** and **1c** furnished the corresponding selanylpyrazoles **3g** and **3h** in 87 and 76% yield, respectively (Table 2, entries 7 and 8). In the reaction carried out with the unsymmetrical substrate **1c**, the formation of traces of regioisomer **3h'** was observed (Table 2, entry 8). We believe that the conjugative effect of aromatic ring in substrate **1c**, that stabilizes the enol-tautomer, can selectively contribute to increase the regioselectivity of this cyclization towards the formation of product **3h**. Besides, α-arylselanyl-1,3-diketones **1d-f** derived from substituted diaryl diselenides containing substituents such as OMe, Me and Cl furnished good yields of desired selanylpyrazoles **3i-k** (Table 2, entries 9-11).

Conclusions

In summary, we developed a simple method to synthesize a range of 4-arylselanylpyrazoles by reaction of α-arylselanyl-1,3-diketones with arylhydrazines using glycerol as solvent. Cyclocondensations of α-arylselanyl-1,3-diketones with arylhydrazines were performed using glycerol as solvent at 60 °C under N_2 atmosphere and establishing a route to obtain 4-arylselanylpyrazoles containing electron-withdrawing and electron-donating groups in moderate to good yields. The toxicological and pharmacological evaluations of the synthesized arylselanylpyrazoles are under study in our laboratories.

Experimental

General remarks

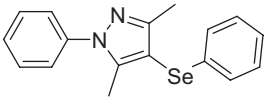
The reactions were monitored by thin-layer chromatography (TLC) carried out on Merck silica gel (60 F_{254}) by using UV light as visualizing agent and 5% vanillin in 10% H_2SO_4 and heat as developing agents. Baker silica gel (particle size 0.040-0.063 mm) was used for flash chromatography. Proton nuclear magnetic resonance (^{1}H NMR) spectra were obtained at 300 MHz on a Varian Gemini NMR and at 400 MHz on Bruker DPX 400 spectrometers. Spectra were recorded in $CDCl_3$ solutions. Chemical shifts are reported in ppm, referenced to tetramethylsilane (TMS) as the external reference. Coupling constants (*J*) are reported in Hertz. Carbon-13 nuclear magnetic resonance (^{13}C NMR) spectra were obtained at 75 MHz on a Varian Gemini NMR and at 100 MHz on Bruker DPX 400 spectrometers. Chemical shifts are reported in ppm, referenced to the solvent peak of $CDCl_3$. Low-resolution mass spectra (MS) were obtained with a Shimadzu GC-MS-QP2010 mass spectrometer.

Glycerol 99.5% was purchased from Synth® (Brazil) and was used without previous purification.

General procedure for the synthesis of 4-arylselanylpyrazoles

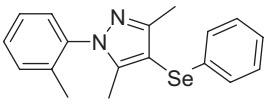
To a 5 mL round-bottomed flask containing an appropriate α-arylselanyl-1,3-diketone **1a**-**f** (0.6 mmol) and arylhydrazine **2a**-**f** (0.5 mmol) was added 1.0 mL of glycerol. The resulting solution was stirred 60 °C at N_2 atmosphere for the time indicated in Table 2. After that, the reaction mixture was received in water (20.0 mL), extracted with ethyl acetate (3 × 5.0 mL), dried over $MgSO_4$, and concentrated under vacuum. The residue was purified by column chromatography on silica gel using ethyl acetate/hexane as the eluent.

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



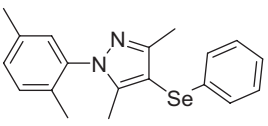
Yield 82%; orange solid; m.p. 67-69 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.44-7.46 (m, 4H), 7.32-7.39 (m, 1H), 7.17-7.19 (m, 4H), 7.10-7.14 (m, 1H), 2.36 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.05, 143.87, 139.66, 132.79, 128.98, 128.95, 128.12, 127.56, 125.58, 124.54, 102.42, 12.82, 12.32; MS (relative intensity) 330 (2), 329 (12), 328 (M^+, 12), 327 (65), 326 (8), 325 (35), 324 (13), 248 (23), 247 (29), 246 (100), 231 (7), 206 (5), 171 (3), 130 (8), 118 (34), 115 (3), 103 (5), 91 (4), 78 (9), 77 (90), 65 (5), 51 (24), 41 (3).

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



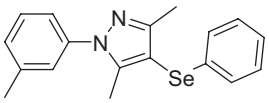
Yield 79%; yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33-7.37 (m, 2H), 7.25-7.30 (m, 2H), 7.11-7.20 (m, 5H), 2.33 (s, 3H), 2.12 (s, 3H), 2.08 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.82, 145.06, 138.65, 135.91, 133.20, 130.90, 129.28, 129.06, 127.94, 127.61, 126.58, 125.56, 100.47, 17.15, 12.91, 11.26; MS (relative intensity) 344 (12), 343 (9), 342 (M^+, 67), 341 (9), 340 (33), 339 (13), 338 (12), 325 (2), 281 (3), 262 (85), 261 (91), 246 (30), 232 (9), 221 (11), 220 (17), 207 (4), 204 (8), 185 (5), 178 (3), 169 (7), 157 (6), 144 (13), 132 (49), 128 (5), 115 (14), 106 (4), 103 (6), 92 (9), 91 (100), 89 (12), 77 (29), 65 (53), 51 (19), 41 (4).

1-(2,5-Dimethylphenyl)-3,5-dimethyl-4-(phenylselanyl)-1*H*-pyrazole (**3c**)



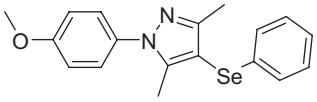
Yield 81%; yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.13-7.25 (m, 8H), 2.37 (s, 3H), 2.32 (s, 3H), 2.11 (s, 3H), 2.03 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 152.70, 145.14, 139.18, 136.14, 135.48, 133.29, 131.49, 129.05, 127.89, 127.34, 127.18, 125.52, 100.25, 21.13, 17.07, 12.92, 11.26; MS (relative intensity) 358 (19), 357 (21), 356 (M^+, 100), 355 (15), 354 (50), 352 (20), 341 (9), 339 (4), 276 (29), 275 (62), 261 (58), 260 (25), 246 (8), 234 (12), 222 (17), 220 (10), 198 (8), 184 (30), 169 (7), 159 (22), 157 (15), 146 (20), 131 (16), 115 (17), 105 (28), 103 (26), 91 (31), 79 (38), 77 (64), 65 (15), 51 (14), 41 (4).

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



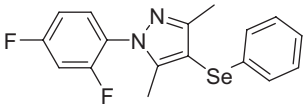
Yield 84%; yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32-7.37 (m, 2H), 7.19-7.25 (m, 7H), 2.41 (s, 3H), 2.37 (s, 3H), 2.33 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.06, 143.99, 139.68, 139.25, 132.94, 129.07, 128.74, 128.50, 128.21, 125.66, 125.45, 121.65, 102.29, 21.29, 12.89, 12.40; MS (relative intensity) 344 (15), 343 (2), 342 (M^+, 67), 340 (34), 338 (13), 263 (16), 261 (100), 246 (31), 244 (13), 232 (10), 221 (11), 220 (16), 205 (5), 169 (5), 157 (5), 143 (8), 132 (33), 130 (11), 117 (4), 115 (10), 91 (74), 77 (22), 65 (37), 51 (14), 41 (3).

1-(4-Methoxyphenyl)-3,5-dimethyl-4-(phenylselanyl)-1*H*-pyrazole (**3e**)



Yield 77%; yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36 (d, 2H, *J* 9.02 Hz), 7.11-7.19 (m, 5H), 6.97 (d, 2H, *J* 9.02 Hz), 3.84 (s, 3H), 2.32 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.00, 152.79, 144.10, 132.99, 132.89, 129.04, 128.19, 126.24, 125.62, 114.14, 101.75, 55.45, 12.85, 12.16; MS (relative intensity) 358, (38), 278 (100), 148 (33), 77 (32).

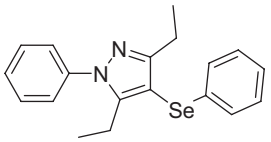
1-(2,4-Difluorophenyl)-3,5-dimethyl-4-(phenylselanyl)-1*H*-pyrazole (**3f**)



Yield 73%; yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46-7.50 (m, 1H), 7.15-7.26 (m, 5H), 7.00-7.04 (m, 2H), 2.31 (s, 3H), 2.23 (d, 3H, *J* 1.8 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.54 (dd, *J* 250.49, 11.05 Hz), 156.95 (dd, *J* 252.91, 12.53 Hz), 154.09, 146.23, 132.67, 129.92 (dd, *J* 10.02, 1.35 Hz), 129.13, 128.22, 125.76, 124.02 (dd, *J* 12.37, 4.05 Hz), 112.01 (dd, *J* 22.34, 3.89 Hz), 104.93 (dd, *J* 26.29, 23.61 Hz), 101.97, 12.93, 11.25 (d, *J* 3.64 Hz); MS (relative intensity) 366 (12), 365 (6), 364 (M^+, 59), 362 (30), 284 (99), 283 (63), 269 (7), 268 (18), 263 (9), 256 (8), 243 (11), 242 (16), 236 (4), 222

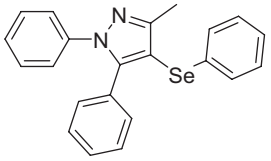
(5), 207 (8), 194 (2), 166 (6), 155 (13), 154 (100), 143 (5), 140 (7), 128 (16), 127 (28), 113 (42), 103 (9), 91 (6), 77 (32), 65 (11), 63 (3), 41 (6).

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



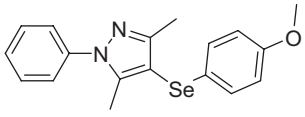
Yield 87%; orange oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44-7.48 (m, 4H), 7.35-7.40 (m, 1H), 7.15-7.21 (m, 4H), 7.10-7.13 (m, 1H), 2.78 (q, 2H, *J* 7.53, 7.55 Hz), 2.72 (q, 2H, *J* 7.57, 7.55 Hz), 1.23 (t, 3H, *J* 7.57 Hz), 0.99 (t, 3H, *J* 7.56 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.24, 149.68, 140.10, 133.63, 129.08, 128.98, 128.12, 127.99, 125.56, 125.35, 100.41, 20.84, 19.15, 13.82, 13.62; MS (relative intensity) 358 (7) 357 (8), 356 (M^+, 7), 355 (30), 353 (16), 326 (1), 276 (24), 275 (100), 260 (6), 246 (5), 231 (6), 217 (1), 204 (3), 197 (6), 183 (4), 169 (3), 155 (2), 143 (4), 132 (16), 128 (2), 117 (5), 104 (6), 91 (8), 77 (46), 65 (3), 51 (9), 41 (2).

5-Methyl-1,3-diphenyl-4-(phenylselanyl)-1*H*-pyrazole (**3h**)



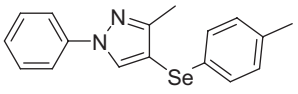
Yield 76%; yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.24-7.28 (m, 8H), 7.14-7.20 (m, 7H), 2.39 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.94, 147.00, 139.85, 133.22, 130.09, 129.90, 129.10, 128.73, 128.63, 128.49, 128.13, 127.16, 125.76, 124.76, 103.42, 13.00; MS (relative intensity) 392 (10), 391 (7), 390 (M^+, 15), 389 (58), 387 (30), 311 (22), 310 (100), 309 (99), 293 (5), 280 (7), 270 (7), 268 (12), 241 (1), 232 (9), 218 (8), 205 (6), 190 (6), 180 (21), 178 (7), 165 (16), 152 (3), 130 (5), 127 (7), 118 (4), 102 (7), 91 (6), 89 (15), 77 (93), 51 (30), 41 (2).

4-(Methoxyphenylselanyl)-3,5-dimethyl-1-phenyl-1*H*-pyrazole (**3i**)



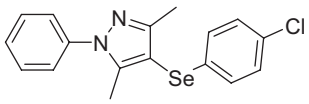
Yield 68%; red oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38-7.46 (m, 4H), 7.33-7.37 (m, 1H), 7.20 (d, 2H, *J* 8.89 Hz), 6.77 (d, 2H, *J* 8.88 Hz), 3.75 (s, 3H), 2.39 (s, 3H), 2.34 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 158.41, 152.87, 143.54, 139.81, 131.02, 129.02, 127.61, 124.67, 122.60, 114.84, 103.82, 55.21, 12.95, 12.44; MS (relative intensity) 360 (8), 359 (2), 358 (M^+, 23), 356 (11), 354 (4), 280 (2), 279 (20), 278 (100), 277 (12), 264 (7), 263 (38), 247 (2), 235 (2), 222 (4), 194 (1), 186 (1), 179 (1), 160 (1), 139 (5), 130 (3), 118 (20), 91 (2), 77 (34), 63 (3), 51 (7), 41 (3).

3,5-Dimethyl-1-phenyl-4-(*p*-tolylselanyl)-1*H*-pyrazole (**3j**)



Yield 79%; yellow solid; m.p. 85-86 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46-7.48 (m, 4H), 7.35-7.40 (m, 1H), 7.10-7.13 (m, 2H), 7.01-7.04 (m, 2H), 2.38 (s, 3H), 2.33 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.16, 143.88, 139.87, 135.67, 129.92, 129.08, 128.99, 128.74, 127.69, 124.74, 103.00, 20.91, 12.95, 12.46; MS (relative intensity) 344 (12), 343 (6), 342 (M^+, 39), 340 (22), 339 (8), 262 (100), 261 (53), 246 (19), 244 (7), 232 (7), 220 (13), 204 (5), 171 (7), 169 (5), 156 (2), 144 (8), 130 (11), 118 (46), 115 (6), 103 (7), 91 (19), 89 (7), 77 (86), 63 (6), 51 (19), 41 (4).

4-(4-Chlorophenylselanyl)-3,5-dimethyl-1-phenyl-1*H*-pyrazole (**3k**)



Yield 72%; white solid; m.p. 88-89 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46-7.48 (m, 4H), 7.38-7.41 (m, 1H), 7.10-7.19 (m, 4H), 2.37 (s, 3H), 2.32 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.07, 144.02, 139.71, 131.75, 131.20, 129.58, 129.18, 129.11, 127.82, 124.70, 102.31, 12.87, 12.38; MS (relative intensity) 364 (11), 363 (4), 362 (M^+, 17), 361 (81), 359 (42), 346 (2), 284 (31), 282 (100), 281 (73), 266 (12), 264 (6), 251 (5), 246 (37), 240 (10), 230 (4), 219 (3), 205 (10), 204 (9), 190 (2), 171 (4), 164 (5), 154 (4), 130 (9), 123 (4), 118 (56), 115 (5), 104 (4), 91 (3), 77 (91), 65 (6), 51 (20), 41 (4).

Supplementary Information

Supplementary data are available free of charge at http://jbcs.sbq.org.br as PDF file.

Acknowledgments

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