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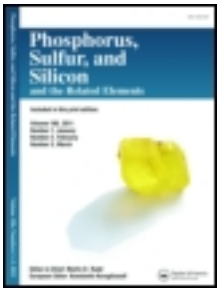

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Synthesis and Pesticidal Properties of Thio and Seleno Analogs of Some Common Urea Herbicides

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Synthesis and Pesticidal Properties of Thio and Seleno Analogs of Some Common Urea Herbicides

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Thio and seleno analogs of fenuron, isoproturon, chlorotoluron, metoxuron, monuron, and diuron were synthesized from the corresponding aryl amines. Their reaction with thiophosgene leads to isothiocyanates. Aryl amines were also converted (via isocyanides) to isoselenocyanates. The reaction of both isothio- and isoselenocyanates with dimethylamine affords the corresponding thio and seleno analogs of the above-mentioned urea herbicides. Herbicidal activity of the synthesized compounds was slightly lower than the activity of the parent urea herbicides. The thio and seleno analogs as well as the parent ureas showed good fungicidal activity at a concentration of 200 ppm against selected fungi.

Keywords Isocyanides; isoselenocyanates; isothiocyanates; selenoureas; thioureas; urea herbicides

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INTRODUCTION

Thio- and selenoureas exhibit a wide scope of biological activity. The importance of thioureas as biologically active compounds (pesticides, bactericides) has been known for a long time, as summarized in a recent review.[1] Pesticidal activities of thioureas have been described,[2–6] and their fungicidal properties have been recently reviewed.[7] Both thioureas and selenoureas are effective superoxide radical scavengers.[8] Selenoureas act as effective antioxidants and show low toxicity for some human cells.[9] *N*, *N*-Unsubstituted selenourea derivatives are tyrosinase inhibitors.[10] The relationship of thione/thiol and selone/selenol tautomerism in *N*, *N*-disubstituted cyclic thio- and selenoureas to their inhibition capacity of peroxidase-catalyzed reactions was demonstrated.[11]

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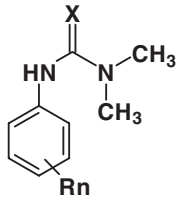

R_n	Urea herbicide, X = O
H	Fenuron
4-*i*-C_3H_7	Isoproturon
3-Cl, 4-CH_3	Chlorotoluron
3-Cl, 4-CH_3O	Metoxuron
4-Cl	Monuron
3,4-Cl_2	Diuron

FIGURE 1 1,1-Dimethyl-3-aryl ureas—parent urea herbicides described in this article.

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Isothio- and isoselenocyanates are the most useful intermediates for the synthesis of thio- and selenoureas, respectively. The chemistry of isothio- and isoselenocyanates has been recently reviewed.[12] The application of isoselenocyanates as useful precursors for selenium-containing heterocycles has been recently reviewed independently by Heimgartner et al.[13] and Garud et al.[14] In our previous articles, we proposed a 4-isoselenocyanate-2,2,6,6-tetramethylpiperidin-1-oxyl as an isoselenocyanate bearing a nitroxyl moiety.[15,16]

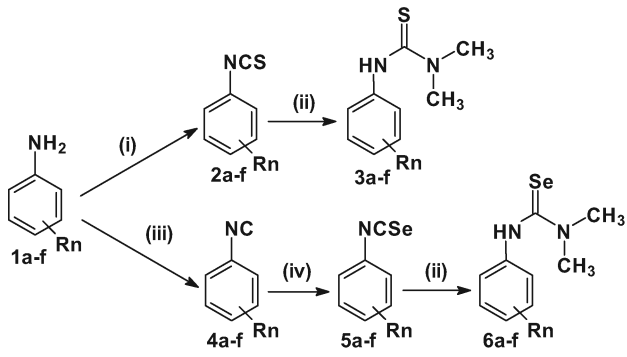
1,1-Dimethyl-3-aryl ureas such as fenuron, isoproturon, chlorotoluron, metoxuron, monuron, and diuron (Figure 1) are known as urea herbicides.[17–19]

With the exception of **3d** (R_n = 3-Cl, 4-CH_3O, X = S), the thio analogs of the urea herbicides in Figure 1 are known compounds: **3a** (R_n = H, X = S),[20,21] **3b** (R_n = 4-*i*-C_3H_7, X = S),[22] **3c** (R_n = 3-Cl, 4-CH_3, X = S),[6] **3e** (R_n = 4-Cl, X = S),[20,21] **3f** (R_n = 3,4-Cl_2, X = S).[2,22] In particular, **3a** and **3e** have been widely described and are commercially available (Aldrich, Rare Chemicals). To the best of our knowledge, the corresponding seleno analogs have not been described to date, except **6a** (R_n = H, X = Se).[23–25] As far as we know, a direct comparison of the pesticidal properties of $ArNHC(X)N(CH_3)_2$ (X = O, S, Se) has not been reported to date.

Herein we present the synthesis and pesticidal activity of thio and seleno analogs of the above-mentioned herbicides (Figure 1, X = S, Se).

RESULTS AND DISCUSSION

The synthesis of the thio and seleno derivatives of fenuron, isoproturon, chlorotoluron, metoxuron, monuron, and diuron is presented in Scheme 1. The yields of the synthesized derivatives **2–6**, as well as their physicochemical and spectral data, are presented in Tables I–V.



SCHEME 1 (i) $CSCl_2$, NEt_3, benzene; (ii) $HN(CH_3)_2$, benzene; (iii) $CHCl_3$/NaOH, PTC; (iv) Se, $CHCl_3$.

Appropriate aniline derivatives **1a–f** were converted to the corresponding isothiocyanates **2a–f** using thiophosgene[26] in the presence of triethylamine as a catalyst, as described previously.[27] Compounds **2a–f** were isolated by means of vacuum distillation and column chromatography, as well as crystallization, and were obtained in 19–73% yield (Table I).

Amines **1a–f** were converted to the corresponding isocyanides **4a–f** in the isonitrile reaction.[28–34] Compounds **4a–f** were isolated by means of vacuum distillation as well as column chromatography and were obtained in 32–66% yields (Table III).

Direct selenation of isocyanides **4a–f** with gray selenium[35] affords the corresponding isoselenocyanates **5a–f** in analogy to a previously described procedure.[15,16] Compounds **5a–f** were isolated by means of column chromatography and were obtained in 21–91% yield (Table IV). This is in contrast to a report in the literature,[36] where the authors claim that isoselenocyanates cannot be purified chromatographically. Some isoselenocyanates were isolated by means of vacuum distillation, but in these cases, the yields were significantly lower.

Isothio- and isoselenocyanates (**2a–f** and **5a–f**, respectively) were converted to the thio- and selenoureas **3a–f** and **6a–f**, respectively, using dmethylamine in benzene solution as described previously.[16,37]

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TABLE I Aryl Isothiocyanates 2: Yields, Physicochemical and Spectroscopic Data

	R_n	Yield [%] (isolation and purification)	b.p. [°C/mm Hg], m.p. [°C]	MS (EI, 70 eV, m/z, int. [%])	^{1}H NMR (200 MHz, $CDCl_3$)	^{13}C NMR (50 MHz, $CDCl_3$)	IR (ν, cm^{-1})[a]
2a	H	65 (distillation)	b.p. 53/0.6 (68-70/1)[38]	135 (M, 100), 77 (59), 51 (20)	7.1-7.4 (m, 5H, C_6H_5) [b]	125.6, 127.5, 129.4, 131.2 [b]	(film) 2084 (NCS), 1592, 1490, 749, 684 [b]
2b	4-*i*-C_3H_7	45 (distillation)	b.p. 123-130/5 (252/760)[41]	177 (77, M), 162 (100, M-CH_3), 128 (36), 104 (15), 77 (9)	1.23 [d, J = 7.0 Hz, 6H, $(CH_3)_2CH$], 2.90 [septet, J = 7.0 Hz, 1H, $(CH_3)_2CH$)], 7.17 (m, 4H, C_6H_4)	23.8 [$(CH_3)_2CH$], 33.9 [$(CH_3)_2CH$], 125.6, 127.5, 128.6, 148.4	(film) 2960, 2111 (NCS), 1506, 831
2c	3-Cl, 4-CH_3	68 (chromatography, hexane) 22 (distillation)	b.p. 98-100/1 (98-110/3.5)[42]	185 (40), 183 (100, M), 149 (32), 148 (69), 125 (8), 104 (6), 90 (4), 89 (8), 76 (5), 75 (5), 63 (14), 51 (6), 50 (6)	2.35 (s, 3H, CH_3), 7.01 (dd, J = 2.1 Hz, 8.1 Hz, 1H, arom-H), 7.14-7.24 (m, 2H, arom-H) [c]	20.0 (CH_3), 124.1, 126.3, 130.1, 131.7, 135.1, 135.9	(film) 2103 (NCS), 1602, 1560, 1487, 1051, 812
2d	3-Cl, 4-CH_3O	64 (crystallization, benzene or hexane)	m.p. 86-87 (89)[41]	201 (36), 199 (100, M), 186 (37), 184 (100), 158 (23), 156 (60), 63 (20)	3.90 (s, 3H, OCH_3), 6.87 (d, J = 8.8 Hz, 1H, arom-H), 7.11 (dd, J = 2.4 Hz, 8.8 Hz, 1H, arom-H), 7.27 (d, J = 2.4 Hz, 1H, arom-H) [c]	56.4 (OCH_3), 112.3, 123.2, 124.2, 125.1, 127.5, 135.8, 154.3	2111 (NCS), 1494, 1439, 1303, 1265, 1063, 870, 809

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TABLE I Aryl Isothiocyanates 2: Yields, Physicochemical and Spectroscopic Data *(Continued)*

	R_n	Yield [%] (isolation and purification)	b.p. [°C/mm Hg], m.p. [°C]	MS (EI, 70 eV, m/z, int. [%])	^{1}H NMR (200 MHz, $CDCl_3$)	^{13}C NMR (50 MHz, $CDCl_3$)	IR (ν, cm^{-1})[a]
2e	4-Cl	73 (crystallization, hexane)	m.p. 44-45 (42-44)[44]	171 (35), 169 (M, 100), 113 (10), 111 (30), 85 (5), 75 (21), 50 (8)	7.23 (m, 4H, arom-H) [d]	127.0, 130.0, 133.1, 136.9 [e,f]	2184 (NCS), 2138, 2099 (NCS), 1483, 1091, 826 [e]
2f	3,4-Cl_2	19 (chromatography, HA9)	m.p. 75-79 (60-61)[46]	207 (13.5), 205 (68), 203 (100, M), 168 (10), 147 (17), 145 (26), 111 (6), 109 (18), 75 (11), 74 (15)	7.07 (dd, $J = 2.5$ Hz, 8.5 Hz, 1H, arom-H), 7.33 (d, $J = 2.5$ Hz, 1H, arom-H), 7.42 (d, $J = 8.5$ Hz, 1H, arom-H) [f]	124.9, 127.4, 131.2, 131.5, 133.5, 154.9	(film) 2089, 2034 (NCS), 1586, 1468, 1126, 1034, 813 [g]

[a] KBr unless otherwise stated.
[b]–[g] Spectroscopic data are consistent with: [b] ref. [39,40]; [c] ref. [43]; [d] ref. [39,43]; [e] ref. [39]; [f] ref. [40,45]; [g] ref. [47].

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TABLE II Aryl Thioureas 3: Yields, Physicochemical and Spectroscopic Data

	R_n	Yield [%]	m.p. [°C]	MS (EI, 70 eV, m/z, int [%])	^{1}H NMR (200 MHz) [a]	^{13}C NMR (50 MHz) [a]	IR (ν, cm^{-1}, KBr)
3a	H	91	.128-130 (132[21], 133[20])	180 (100, M), 147 (17), 136 (12), 135 (12), 88 (93), 77 (21), 71 (30), 51 (10), 44 (21) [b]	3.27 (s, 6H, $N(CH_3)_2$), 7.1-7.4 (m, 5H, C_6H_5)[c]	41.6 [$N(CH_3)_2$], 125.2, 125.6, 128.8, 140.0, 182.2 (C=S) [d]	3320, 1592, 1534, 1496, 1375, 1322, 1305, 1144, 711[e]
3b	4-*i*-C_3H_7	83	125-127	222 (67, M), 189 (24), 179 (6), 177 (9), 162 (21), 159 (9), 152 (40), 137 (24), 128 (13), 88 (100)	1.24 [d, J = 7.2 Hz, 6H, $(CH_3)_2CH$], 2.90 [septet, J = 7.2 Hz, 1H, $(CH_3)_2CH$)], 3.31 [s, 6H, $N(CH_3)_2$], 7.19 (s, 4H, arom-H)	24.0 [$(CH_3)_2CH$], 33.6 [$(CH_3)_2CH$], 41.4 [$N(CH_3)_2$], 125.0, 126.8, 137.4, 146.3, 182.4 (C=S)	3286, 2955, 1591, 1538, 1374, 1325, 1260, 1142, 833, 739, 699
3c	3-Cl, 4-CH_3	74	164 (164.5-166)[6]	230 (15), 228 (41, M), 197 (4), 195 (13), 183 (17), 168 (5), 158 (8), 148 (13), 88 (100), 73 (7), 71 (26), 44 (21)	2.34 (s, 3H, CH_3), 3.34 (s, 6H, $N(CH_3)_2$), 6.99 (s, 1H, NH), 7.09 (dd, J = 2.1 Hz, 8.2 Hz, 1H, arom-H), 7.19 (d, J = 8.2 Hz, 1H, arom-H), 7.25 (d, J = 2.1 Hz, 1H, arom-H)	19.4 (CH_3), 41.4 ($N(CH_3)_2$), 124.2, 126.0, 130.6, 133.3, 133.8, 138.6, 181.8 (C=S)	3280, 1580, 1538, 1495, 1327

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TABLE II Aryl Thioureas 3: Yields, Physicochemical and Spectroscopic Data *(Continued)*

	R_n	Yield [%]	m.p. [°C]	MS (EI, 70 eV, m/z, int [%])	^{1}H NMR (200 MHz) [a]	^{13}C NMR (50 MHz) [a]	IR (ν, cm^{-1}, KBr)
3d	3-Cl, 4-CH_3O	81	165-167	246 (9), 244 (23, M), 213 (4), 211 (10), 201 (11), 199 (29), 186 (12), 184 (33), 176 (10.5), 174 (29), 158 (10), 156 (28), 88 (100), 73 (13), 71 (15), 63 (16), 44 (21.5), 42 (13)	in (CD_3OD): 3.33 (s, 6H, $N(CH_3)_2$), 3.91 (s, 3H, OCH_3), 7.00 (d, J = 8.5 Hz, 1H, arom-H), 7.15 (dd, J = 2.4 Hz, 8.5 Hz, 1H, arom-H), 7.31 (d, J = 2.4 Hz, 1H, arom-H)	in (CD_3OD): 41.6 ($N(CH_3)_2$), 56.9 (OCH_3), 112.9, 122.7, 127.7, 130.1, 135.7, 154.6, 181.9 (C=S)	3209, 1539, 1506, 1327, 1235, 1139, 1063
3e	4-Cl	91	149 – 151 (151[21], 152[20], 150-151.5[49])	216 (14), 214 (40, M), 183 (4), 181 (11), 171 (33), 169 (90), 113 (15), 111 (45), 88 (100), 75 (36), 71 (37), 51 (8), 50 (16), 44 (37) [f]	3.34 (s, 6H, $N(CH_3)_2$), 7.26 (m, 4H, arom-H) [f]	41.4 ($N(CH_3)_2$), 126.9, 128.6, 130.9, 138.4, 181.6 (C=S)	3284, 1589, 1541, 1492, 1324

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3f	3,4-Cl_2	92	164-166 (166.5)[2]	250 (19), 248 (28, M), 217 (6), 215 (9), 205 (24), 203 (35), 147 (9), 145 (14), 111 (5), 109 (14), 88 (100), 71 (26), 44 (22), 42 (13)	3.35 (s, 6H, $N(CH_3)_2$), 7.03 (bs, NH), 7.18 (dd, $J = 2.3$ Hz, 8.5 Hz, 1H, arom-H), 7.39 (d, $J = 8.5$ Hz, 1H, arom-H), 7.42 (d, $J = 2.3$ Hz, 1H, arom-H)	41.7 ($N(CH_3)_2$), 124.7, 126.8, 129.4, 130.4, 132.6, 139.4, 182.1 (C=S)	3194, 1542, 1476, 1314

[a] $CDCl_3$ unless otherwise stated.

[b] MS data are consistent with ref.[1] except the literature value for m/z 180 (M, 59)[1].

[c] ^1H NMR data are consistent with those in ref.[1], two separate CH_3 signals (3.26 and 3.30) are detected in ref.[48].

[d] ^{13}C NMR data are consistent with those in ref.[48] two separate CH_3 signals (41.39 and 41.47) are detected in ref[1].

[e] IR are consistent with those in ref.[1,48].

[f] Spectroscopic data are consistent with those in ref.[49].

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TABLE III Aryl Isocyanides 4: Yields, Physicochemical and Spectroscopic Data

	R_n	Yield [%] (isolation and purification)	b.p. [°C/mm Hg], m.p. [°C]	MS (EI, 70 eV, m/z, int [%])	^{1}H NMR (200 MHz, $CDCl_3$)	^{13}C NMR (50 MHz, $CDCl_3$)	IR (ν, cm^{-1}) [a]
4a	H	66 (chromatography, hexane) 30% (distillation)	b.p. 68-69.5/22, 35-38/0.7 (43-44/1.5[50], 64/22[51])	103 (M, 100), 77(35), 76 (49), 51 (18), 50 (17) [b]	7.35 (m, 5H, C_6H_5) [b]	126.2, 126.4, 129.2, 129.3, 164.1 (NC) [b]	(film) 2126 (NC), 1588, 1486, 1455, 754, 684, 513[b]
4b	4-*i*-C_3H_7	33 (distillation)	b.p. 60-61/0.6, 55-56/0.6	145 (31, M), 130 (100, M-CH_3), 104 (17), 103 (53), 77 (18)	1.23 [d, $J = 7.0$ Hz, 6H, $(CH_3)_2CH$], 2.92 [septet, $J = 7.0$ Hz, 1H, $(CH_3)_2CH$)], 7.24 (m, 4H, C_6H_4)	23.7 [$(CH_3)_2CH$], 34.0 [$(CH_3)_2CH$], 126.3, 127.4, 129.3, 150.5, 163.4 (NC)	(film): 2963, 2124 (NC), 1508, 837, 550
4c	3-Cl, 4-CH_3	36 (distillation) 27 (chromatography, hexane)	b.p. 65-70/0.6	153 (12), 151 (38), 116 (100), 89 (27), 63 (12), 40 (10)	2.39 (s, 3H, CH_3), 7.17 (dd, $J = 1.7$ Hz, 8.1 Hz, 1H, arom-H), 7.25 (d, $J = 8.1$ Hz, 1H, arom-H), 7.36 (d, $J = 1.7$ Hz, 1H, arom-H)	20.1 (CH_3), 124.7, 126.9, 131.6, 135.0, 138.3, 165.1 (NC)	(film) 2126 (NC), 1487, 1053, 876, 816, 731

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4d	3-Cl, 4-CH_3O	32 (chromatography, HA9)	m.p. 77-79	169 (30), 167 (91, M), 154 (23), 152 (69), 126 (33), 124 (100)	3.93 (s, 3H, OCH_3), 6.90 (d, $J = 8.8$ Hz, 1H, arom-H), 7.28 (dd, $J = 2.4$ Hz, 8.8 Hz, 1H, arom-H), 7.42 (d, $J =$ 2.4 Hz, 1H, arom-H)	56.5 (OCH_3), 111.9, 119.6, 123.1, 126.1, 128.2, 155.8, 164.1 (NC)	2128 (NC), 1598, 1498, 1439, 1278, 1064, 1018, 869, 818
4e	4-Cl	40 (crystallization, hexane, then chromatography, HA9)	m.p. 71-73.5 (73-75)[52]	139 (32), 138 (8), 137 (100, M), 102 (56), 75 (21), 51 (19), 50 (30)[b]	7.26-7.41 (m, 4H, arom-H)[b]	122.7, 127.8, 129.9, 135.6, 165.7 (NC)[b]	2126 (NC), 1650, 1486, 1405, 1091, 1017, 830, 512[b]
4f	3,4-Cl_2	53 (crystallization, hexane)	m.p. 50-53 (32-33)[53]	175 (10), 173 (65), 171 (100, M), 138 (14), 136 (41), 100 (38), 75 (17), 74 (20), 50 (19)	7.24 (dd, $J = 2.2$ Hz, 8.6 Hz, 1H, arom-H), 7.48 (d, $J =$ 8.6 Hz, 1H, arom-H), 7.49 (d, $J = 2.2$ Hz, 1H, arom-H)	125.8, 128.4, 131.4, 133.8, 134.4, 155.5, 167.2 (NC)	3095, 2133 (NC), 1465

[a] KBr unless otherwise stated.
[b] Spectroscopic data are consistent with those reported in ref.[52].

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TABLE IV Aryl Isoselenocyanates 5: Yields, Physicochemical and Spectroscopic Data

	R_n	Yield [%] (isolation and purification)	b.p. [°C/mm Hg], m.p. [°C]	MS (EI, 70 eV, m/z, int [%])	^{1}H NMR (200 MHz, $CDCl_3$)	^{13}C NMR (50 MHz, $CDCl_3$)	IR (ν, cm^{-1}) [a]
5a	H	91 (chromatography, HA9 or hexane)		185 (18), 183 (100, M), 181 (49), 103 (28), 77 (77), 51 (30), 50 (14)	7.22-7.42 (m, 5H, C_6H_5)[b]	126.0, 128.1, 129.6 [b]	(film) 2116, 2040 (NCSe), 1589, 1487, 749, 683
5b	4-*i*-C_3H_7	90 (chromatography, HA9) 77 (distillation)	b.p. 102-102.5/0.5	227 (18), 226 (11), 225 (97, M), 223 (48), 222 (17), 221 (18), 212 (17), 211 (10), 210 (98, M-CH_3), 208 (48), 207 (17), 206 (19), 145 (6), 130 (31), 129 (10), 128 (19), 104 (100), 103 (21), 91 (6), 77 (21), 51 (9), 41 (5), 39 (7)	1.23 [d, J = 7.0 Hz, 6H, $(CH_3)_2CH$], 2.91 [septet, J = 7.0 Hz, 1H, $(CH_3)_2CH$)], 7.21 (s, 4H, C_6H_4)	23.7 [$(CH_3)_2CH$], 33.9 [$(CH_3)_2CH$], 126.0, 127.6, 129.4, 149.4	(film) 2959, 2122 (NCSe), 1504, 831
5c	3-Cl, 4-CH_3	63 (chromatography, HA9)		233 (43), 231 (100, M), 229 (48), 228 (20), 227 (18), 196 (23), 194 (14), 151 (15), 150 (10), 127 (18), 125 (56), 116 (37), 99 (11), 89 (40), 63 (22)	2.37 (s, 3H, CH_3), 7.09 (dd, J = 2.0 Hz, 8.2 Hz, 1H, arom-H), 7.22 (d, J = 8.2 Hz, 1H, arom-H), 7.30 (d, J = 2.0 Hz, 1H, arom-H)	20.0 (CH_3), 124.2, 126.5, 128.2, 131.6, 135.0, 136.7	2160, 2119 (NCSe), 1484, 1050, 863, 813

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5d	3-Cl, 4-CH_3O	33 (chromatography, HA9)	m.p. 112-113	249 (43), 247 (100, M), 245 (47), 244 (15), 243 (17), 234 (39), 232 (91), 230 (43), 229 (13), 228 (15), 206 (18), 204 (41), 202 (9), 201 (6), 200 (7), 169 (8), 167 (19), 154 (6), 152 (17), 126 (18), 124 (42), 63 (32)	3.92 (s, 3H, OCH_3), 6.88 (d, $J = 8.8$ Hz, 1H, arom-H), 7.19 (dd, $J = 2.4$ Hz, 8.8 Hz, 1H, arom-H), 7.33 (d, $J = 2.4$ Hz, 1H, arom-H)	56.5 (OCH_3), 112.2, 122.6, 123.2, 125.6, 127.9, 154.9	2136, 2110 (NCSe), 1494, 1437, 1263, 1060, 1018, 869, 809, 703
5e	4-Cl	59 (chromatography, hexane)	m.p. 70.5-71.5 (68-70)[55]	219 (43), 217 (M, 100), 215 (47), 214 (15), 213 (17), 139 (25), 137 (75), 113 (18), 111 (55), 102 (20), 75 (61), 51 (14), 50 (31)	7.29 (m, 4H, arom-H) [b]	127.3, 129.9, 133.8 [b]	2148 (NCSe), 1484, 1404, 1087, 1013, 850, 825
5f	3,4-Cl_2	21 (chromatography, hexane)	m.p. 38-39	255 (16), 253 (64), 251 (100, M), 249 (45), 173 (54), 171 (86), 147 (24), 145 (37), 136 (13), 109 (37), 100 (17), 75 (24), 74 (29)	7.14 (dd, $J = 2.4$ Hz, 8.6 Hz, 1H, arom-H), 7.40 (d, $J = 2.4$ Hz, 1H, arom-H), 7.44 (d, $J = 8.6$ Hz, 1H, arom-H)	125.5, 128.0, 129.4, 131.4, 132.6, 133.9	2961, 2150 (NCSe), 2107 (NCSe), 1581, 1465, 1259, 1094, 1030, 862, 808, 715

[a] KBr unless otherwise stated.
[b] Spectroscopic data are consistent with those reported in ref.[54].

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TABLE V Aryl Selenoureas 6: Yields, Physicochemical and Spectroscopic Data

	R_n	Yield [%]	m.p. [°C]	MS (EI, 70 eV, m/z, int [%])	^{1}H NMR (200 MHz) [a]	^{13}C NMR (50 MHz) [a]	IR (ν, cm^{-1}, KBr)
6a	H	54	104-105 (108-110)[23,24]	230 (18), 228 (100, M), 226 (49), 147 (87), 136 (14), 132 (19), 91 (11), 77 (20), 71 (14) [b]	3.30 (s, 6H, $N(CH_3)_2$), 7.0-7.4 (m, 5H, C_6H_5), 7.55 (s, 1H, NH)	43.5 ($N(CH_3)_2$), 125.7, 126.2, 128.9, 140.5, 181.9 (C=Se)	3299, 1592, 1539, 1496, 1380, 1316, 1305, 755, 693 [c]
6b	4-*i*-C_3H_7	82	142-146	272 (10), 271 (7), 270 (52, M), 268 (26), 267 (10), 266 (10), 227 (5), 225 (5), 210 (5), 189 (100), 159 (15), 136 (14), 134 (7), 133 (9), 104 (8), 91 (7), 78 (4), 77 (6), 71 (17), 44 (7)	1.24 [d, J = 6.8 Hz, 6H, $(CH_3)_2CH$], 2.90 [septet, J = 6.8 Hz, 1H, $(CH_3)_2CH$)], 3.33 [s, 6H, $N(CH_3)_2$], 7.17 (m, 4H, C_6H_4)	23.9 [$(CH_3)_2CH$], 33.6 [$(CH_3)_2CH$], 43.4 [$N(CH_3)_2$], 125.4, 126. 9, 138.0, 146.8, 182.0 (C=Se)	3434, 3250, 2957, 1540, 1375, 1320, 829
6c	3-Cl, 4-CH_3	31	142-144	278 (26), 276 (60, M), 274 (29), 273 (11), 272 (10), 233 (11), 231 (25), 229 (12), 228 (6), 227 (5), 197 (33), 195 (100), 180 (22), 139 (16), 136 (35), 125 (23), 89 (23), 71 (42), 63 (13), 44 (42)	2.35 (s, 3H, CH_3), 3.38 (s, 6H, $N(CH_3)_2$), 7.06 (dd, J = 2.0 Hz, 8.0 Hz, 1H, arom-H), 7.15 – 7.25 (m, 2H, arom-H)	19.7 (CH_3), 43.3 ($N(CH_3)_2$), 124.7, 126.4, 130.8, 134.0, 134.0, 139.1, 181.8 (C=Se)	3172, 1542, 1325, 1127, 1048

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6d	3-Cl, 4-CH_3O	43	198-199	294 (7), 292 (15, M), 290 (9), 249 (21), 247 (48), 245 (22), 234 (23), 232 (48), 230 (22), 213 (18), 211 (48), 206 (11), 204 (27), 202 (12), 167 (25), 152 (20), 126 (21), 124 (44), 116 (32), 72 (27), 71 (17), 63 (44), 62 (22), 44 (70), 42 (100)	3.40 (s, 6H, $N(CH_3)_2$), 3.91 (s, 3H, OCH_3), 6.91 (d, $J = 8.7$ Hz, 1H, arom-H), 7.17 (dd, $J = 2.4$ Hz, 8.7 Hz, 1H, arom-H), 7.26 (d, $J = 2.4$ Hz, 1H, arom-H)	43.1 ($N(CH_3)_2$), 56.3 (OCH_3), 111.7, 122.2, 126.5, 128.7, 133.7, 153.6, 182.4 (C=Se)	3440, 1541, 1505, 1324, 1239, 1128, 1065, 1027, 801
6e	4-Cl	66	136-139	264 (21), 262 (46, M), 260 (23), 259 (8), 258 (9), 219 (12), 217 (26), 215 (13), 183 (32), 181 (100), 166 (30), 137 (25), 136 (25), 125 (17), 113 (15), 111 (28), 75 (35), 71 (32), 44 (33)	3.34 (s, 6H, $N(CH_3)_2$), 7.24 (m, 4H, arom-H), 7.45 (s, 1H, NH)	43.2 ($N(CH_3)_2$), 127.3, 128.9, 131.6, 138.9, 181.8 (C=Se)	3450, 3161, 1542, 1495, 1400, 1381, 1317, 1088, 818, 691

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TABLE V Aryl Selenoureas 6: Yields, Physicochemical and Spectroscopic Data *(Continued)*

	R_n	Yield [%]	m.p. [°C]	MS (EI, 70 eV, m/z, int [%])	^{1}H NMR (200 MHz) [a]	^{13}C NMR (50 MHz) [a]	IR (ν, cm^{-1}, KBr)
6f	3,4-Cl_2	67	170-171 (dec)	298 (19), 296 (31, M), 294 (15.5), 253 (65), 251 (99.5), 249 (42), 217 (41), 215 (63), 202 (12), 200 (17), 173 (67), 171 (100), 161 (10), 159 (13), 147 (37.5), 145 (57.5), 136 (39), 111 (19), 109 (54.5), 100 (21), 75 (40), 74 (43), 71 (34), 50 (20), 45 (41.5), 44 (92.5), 42 (26.5)	in (DMSO-d6): 3.35 (s, 6H, $N(CH_3)_2$), 7.32 (dd, $J = 2.4$ Hz, 8.7 Hz, 1H, arom-H), 7.56 (d, $J = 8.7$ Hz, 1H, arom-H), 7.61 (d, $J = 2.4$ Hz, 1H, arom-H), 9.40 (s, 1H, NH)	(DMSO-d6): 42.5 ($N(CH_3)_2$), 126.5, 126.6, 127.9, 129.5, 129.8, 142.0, 180.2 (C=Se)	1544, 1471, 1394, 1319

[a] $CDCl_3$ unless otherwise stated.
[b] According to ref.[25] the intensities of m/z 228 and 71 are inverted: 228 (20, M), 71 (100).
[c] IR spectroscopic data are consistent with those reported in ref.[23].

Compounds **3a–f** and **6a–f** were purified by means of crystallization (benzene) and were obtained in 74–92% (**3a–f**, Table II) and 31–82% (**6a–f**, Table V) yields, respectively.

The structure of all synthesized compounds was confirmed by comparison of the physicochemical data with those reported in the literature (if available) and by the set of spectroscopic data (MS, ^{1}H and ^{13}C NMR, IR) (Tables I–V): **2a**,[38–40] **2b**,[41] **2c**,[42,43] **2d**,[41,43] **2e**,[39,40,43–45] **2f**,[46,47] **3a**,[1,20,21,48] **3c**,[6] **3e**,[20,21,49] **3f**,[2] **4a**,[50–52] **4e**,[52] **4f**,[53] **5a**,[54] **5e**,[54,55] **6a**.[23–25]

It should be noted that in the ^{13}C NMR spectra, no signals were reasonably attributed to an isoselenocyanate group in **5a–f**, despite using a relaxation delay up to 5 sec. The only chemical shifts that might be attributed to an isothiocyanate group are those for **2d** (135.8 ppm) and **2e** [136.9 ppm (136.70,[40] 136.87[45])]; however the intensity of the broadened signals was very weak.

The observed problems with the detection of both isothio- and isoselenocyanate signals are consistent with the literature data. For a series of aryl isoselenocyanates, no signal for the isoselenocyanate group was detected.[54] For 4-methylphenyl isoselenocyanate, no resonance was observed for the isoselenocyanate carbon atom under a variety of experimental conditions, included extended relaxation delays of 5 sec.[56] Measurements of the ^{13}C NMR signals of an isoselenocyanate group in the series of glycosyl isoselenocyanates indicate that the ^{13}C chemical shift of the isoselenocyanate carbon atom is of low intensity and appears in the range of 144.8–146.8 ppm.[57] The ^{13}C NMR spectra of a series of 16 4-substituted phenyl isothiocyanates were recorded using a rather high concentration of 10 mol% and appropriate decoupling conditions to increase the intensity of the isothiocyanate signals. Despite using the above conditions, the signals of the isothiocyanate carbon atoms (132.13–139.99 ppm) exhibited very characteristic quadrupolar broadening and low intensity.[45] Analogously, for phenyl isothiocyanate (**2a**) enriched with ^{13}C isotope at the isothiocyanate carbon atom, only a very broad resonance at 135.95 ppm was detected and was attributed to the isothiocyanate carbon atom.[58] However, there are data in the literature where ^{13}C NMR signals of an isothiocyanate group are detected without any comments concerning the potential broadening and intensity. Such a situation is described for aliphatic isothiocyanates, 130.4–134.3 ppm,[59] and for aryl isothiocyanates with both electron-donating and electron-withdrawing substituents, 133.8 (4-methoxyphenyl isothiocyanate) and 140.3 (4-nitrophenyl isothiocyanate), respectively.[40]

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The ^{13}C NMR signal observed for the –HN–(C=X)–N (X = S, Se) moiety ($\delta = \sim$ 180 ppm) is in accordance with those reported in the literature.[56,60]

All synthesized compounds have been investigated for herbicidal and fungicidal activities involving in vitro and in vivo tests. All urea derivatives exibit herbicidal activity when applied to leaves or soil, but the activity of the thio (**3a–f**) and seleno (**6a–f**) analogs is slightly lower than the activity of the parent urea herbicides. The parent compounds as well as their thio and seleno analogs show good fungicidal activity against most fungi at a concentration of 200 ppm. In some cases, the seleno derivatives (**6a**, **6b**, **6d**) are more active than the thioureas and the parent compouds (fenuron, isoproturon, metoxuron). The herbicidal and fungicidal activity of the synthesized derivatives **3a–f** and **6a–f** is presented in Tables VI and VII.

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EXPERIMENTAL

The general protocols are analogous to those described earlier: isothiocyanates **2**,[27] thio- and selenoureas **3** and **6**,[16,37] respectively, isocyanides **4**,[32–34] and isoselenocyanates **5**.[15,16] All reagents were commercially available and were used as received without further purification. All experiments were performed in a multinecked round-bottomed flask equipped with a magnetic bar, a thermometer, a reflux condenser protected against humidity, and a dropping funnel. The formation of the products was monitored by means of TLC. TLC control and column chromatography were carried out on silica gel Merck Alurolle 5562, Alufolien 5554, and Merck 1.09385.1000 (0.040–0.063 mm, 230–400 mesh), respectively. The abbreviations for the mobile phases used throughout the text are as follows: HA9 = hexane:ethyl acetate 9:1 and BA9 = benzene:ethyl acetate 9:1. MS (EI, 70 eV, m/e, int. [%]) data were recorded using an AMD 604 mass spectrometer; IR (ν [cm^{-1}]) data were recorded using a FT/IR Jasco 420 spectrophotometer. ^1H NMR (200 MHz, δ [ppm], J [Hz], TMS) and ^{13}C NMR (50 MHz, δ [ppm], TMS) data were recorded using a Varian UNITYplus 200 spectrometer.

Isothiocyanates 2: General Procedure

A solution of thiophosgene (4.83 g, 0.042 mol, 3.2 mL) in anhydrous benzene (17 mL) was added dropwise at 10°C into an efficiently stirred solution of the amine **1** (0.04 mol) and anhydrous triethylamine (12 mL) in anhydrous benzene (85 mL). The reaction mixture was stirred for 10 min at r.t. The precipitate of triethylamine hydrochloride was

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TABLE VI Herbicidal Activity of 3a-f, 6a-f and the Parent Urea Herbicides (Weed Control %, Mean of Ten Weed Species, Upper/Lower Values = Pre-/Post-Emergence Application)

ArHNC(S) $N(CH_3)_2$	1 kg a.i./ ha	0.5 kg a.i./ ha	ArHNC(Se) $N(CH_3)_2$	1 kg a.i./ ha	0.5 kg a.i./ ha	ArHNCO $N(CH_3)_2$	1 kg a.i./ ha	0.5 kg a.i./ ha
3a	43	22	**6a**	52	26	Fenuron	92	75
	43	36		49	36		84	92
3b	70	40	**6b**	75	49	Isoproturon	100	75
	100	84		100	80		100	92
3c	14	7	**6c**	30	12	Chlorotoluron	52	30
	63	36		75	46		88	60
3d	28	7	**6d**	26	2	Metoxuron	96	92
	10	5		92	58		96	88
3e	43	18	**6e**	66	36	Monuron	94	69
	92	43		92	70		96	80
3f	30	24	**6f**	36	26	Diuron	46	38
	98	88		98	70		100	96

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TABLE VII Fungicidal Activity of 3a-f, 6a-f and the Parent Urea Herbicides (Score Index: 0-3)

ArHNC(S) $N(CH_3)_2$	*Botritis cinerea*	*Fusarium culmorum*	*Phytophthora cactorum*	*Rhizoctonia solani*	*Blumeria graminis*	ArHNC(Se) $N(CH_3)_2$	*Botritis cinerea*	*Fusarium culmorum*	*Phytophthora cactorum*	*Rhizoctonia solani*	*Blumeria graminis*	ArHNC(O) $N(CH_3)_2$	*Botritis cinerea*	*Fusarium culmorum*	*Phytophthora cactorum*	*Rhizoctonia solani*	*Blumeria graminis*
3a	0	0	0	1	0	**6a**	3	1	2	3	1	Fenuron	0	0	0	0	0
3b	3	2	3	3	3	**6b**	3	3	3	3	2	Isoproturon	2	1	3	2	—
3c	2	2	2	3	1	**6c**	3	2	3	2	1	Chlorotoluron	2	2	3	3	0
3d	1	0	1	1	0	**6d**	3	2	2	3	—	Metoxuron	2	0	2	2	—
3e	2	1	2	2	—	**6e**	3	2	2	3	—	Monuron	2	2	3	3	—
3f	1	0	0	2	2	**6f**	2	0	2	1	—	Diuron	2	2	3	3	—

Score index: 0 = 0–20% growth reduction–no effect.

1 = 20,1–50% growth reduction–weak activity.

2 = 50,1–90% growth reduction–moderate activity.

3 = 90,1–100 % growth reduction–good activity.

filtered off and washed thoroughly with benzene (2 × 50 mL). Benzene was evaporated under reduced pressure. The residue was purified by means of vacuum distillation (**2a**–**c**), column chromatography [**2c** (hexane), **2f** (HA9)], or crystallization [**2d** (benzene or hexane)] to give isothiocyanates **2a**–**f** (Table I). If the starting amine was detected (TLC) in the filtrate (**1e** → **2e**), it was washed with 1N hydrochloric acid (100 mL) and then with a saturated sodium bicarbonate solution (50 mL). The aqueous layer was extracted with benzene (2 × 50 mL). The combined benzene layers were dried over magnesium sulphate. The drying agent was filtered off, and the solvent was evaporated under reduced pressure. The residue was purified by means of crystallization (hexane) to give **2e** (Table I).

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Isocyanides 4: General Procedure

A 50% sodium hydroxide solution (15 mL) was added to the vigorously stirred solution of the amine **1** (0.05 mol), chloroform (0.05 mol, 6.0 g, 4 mL), TEBA chloride (0.125 g), and methylene chloride (15 mL). The reaction mixture was efficiently stirred and heated at 40°C (gently refluxing) for 1–3 h (**4h**, 16 h). The progress of the reaction was thoroughly monitored by means of TLC. The reaction mixture was allowed to cool to r.t., and cold water (50–100 mL) was added. The aqueous phase was extracted with methylene chloride. The organic layer was washed with concentrated sodium bicarbonate solution and dried over magnesium sulphate. The drying agent was filtered off, and the solvent was evaporated under reduced pressure. The residue was subjected to vacuum distillation (**4a**–**c**), column chromatography [**4a**,**c** (hexane), **4d**,**e** (HA9)] or crystallization [**4e**,**f**, (hexane)] to give isocyanides **4a**–**f** (Table III).

Isoselenocyanates 5: General Procedure

A suspension of the isocyanide **4** (12 mmol) in anhydrous chloroform (16 mL) and at least a twofold molar excess of powdered gray selenium were stirred at reflux (60°C) for about 3 h (**5a**–**d**), 40 h (**5f**), or 60 h (**5e**). The time of the reaction was determined by thorough monitoring of the isoselenocyanate (**5**) formation and the decay of the amount of isocyanide by means of TLC (silica gel, HA9, BA9, visualization with UV 254 and irradiation with UV lamp for 5–10 min). The suspension was allowed to cool to r.t. and filtered through a Cellite bed. Chloroform was evaporated under reduced pressure. The residue was subjected to column chromatography: HA9 (**5a**–**d**), hexane (**5a**,**e**,**f**). In the case of

5b, the compound was also isolated and purified by means of vacuum distillation (Table IV).

Thio- and Selenoureas (3, 6): General Procedure

A solution of an excess of liquid dimethylamine (about 8 mL) in an approximately equal volume of anhydrous benzene was slowly added dropwise at about 0–5°C to the solution of the appropriate isothio- or isoselenocyanate (**2** and **5**, respectively) (6–7 mmol) in anhydrous benzene (15 mL). The stirred reaction mixture was left overnight at r.t. in the open flask (except **3e**, **6c**, **6e**, **6f**: left at r.t. for 1 h). The precipitate formed or the crystalline residue obtained after evaporation of the volatiles (**6b**: oil solidifying in a refrigerator) was thoroughly pressed on a filter, washed with benzene (2–3 mL), and crystallized from benzene (Tables II and V).

Herbicidal Bioassay, Pre- and Post-Emergence Experiments

Herbicidal activity of the thio and seleno compounds was evaluated using different weed species in pot experiments under controlled conditions. Polyethylene pots, 3.5 L capacity, were filled with 0.75 kg of soil (physicochemical characteristic: sandy clay, pH/KCl/ 6.7; organic matter 2.8%) and were wetted with water. Seeds of the 10 weed species were planted into earth (0.5 cm depth): common chickweed (*Stellaria media*), curly dock (*Rumex crispus*), ribwort (*Plantago lanceolata*), fathen (*Chenopodium album*), common poppy (*Papaver rhoeas*), black mustard (*Brassica nigra*), cleavers (*Galium aparine*), gallant soldier (*Galinsoga parviflora*), barnyard grass (*Echinochloa crus-gali*), and corn chamomile (*Anthemis arvensis*). Plants were grown to the two-leaf stage under normal glasshouse propagation conditions (temperature, 20 ± 5°C; lighting, 14 h photoperiod of daylight supplemented by lamps, 400 W). The pots were watered overhead. The test compounds were dissolved in an appropriate volume of acetone:water solution (1:3) with the addition of Tween 20 (0.05% v/v) to give the dose of 1 and 0.5 kg/ha. All treatments were applied as a pre-emergence or post-emergence spray at a volume rate of 300 L/ha using track laboratory sprayer (nozzle TeeJet60, pressure 0.2 MPa). There were three replicate pots per treatment arranged in a randomized block design. Pots after spraying were transferred to the growth chamber (temperature, day/night 20/15°C; lighting, 16 h photoperiod, white fluorescent tubes giving 200 μmol $m^{-2}s^{-2}$ PAR). A visual assessment of phytotoxicity separately for each species was made (18 days or 25 days after treatment for pre- and

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post-emergence experiments) as a percentage compared to the untreated plants. The results expressed as mean percent of phytotoxicity for 10 weed species were calculated and presented in Table VI.

In Vitro Fungicidal Bioassay

The methods for assesing fungicidal activity involving in vitro and in vivo tests were identical to those previously published.[37]

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