A New Method of Synthesis of Some 2-Aryl and 2-Heterocyclic Benzimidazole, Benzoxazole and Benzothiazole Derivatives

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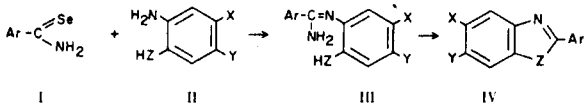
A new one-step facile method for the synthesis of some benzimidazole, benzoxazole and benzothiazole derivatives is described. The method involves the action of aromatic and heterocyclic selenoamides on some *o*-phenylenediamine, *o*-aminophenol and *o*-aminothiophenol and their derivatives.

J. Heterocyclic Chem., 16, 13 (1979).

As a result of the continuing interest in the chemistry of the benzimidazole, benzoxazole and benzothiazole nucleus, we have studied the action of non-substituted aromatic and heterocyclic selenoamide on 1,2-diamines, aminophenoles or aminomercaptans. In a previous paper (1), we reported the synthesis of 2-alkyl benzimidazole, benzoxazole and benzothiazole derivatives prepared by the action of aliphatic selenonesters on reagents possessing two adjacent nucleophilic sites (NH_2 ,OH,SH).

We now wish to report the synthesis of some 2-aryl benzimidazole, benzoxazole and benzothiazole derivatives. Our study has shown that reactions of aromatic and heterocyclic selenoamides with 1,2-dinucleophilic reagents in refluxing toluene or pyridine proceed in complete analogy with the behaviour of aliphatic selenonesters. On the basis of previous experience (1), initial interaction between the selenocarbonyl group I and amino group of II would be expected to result in elimination of hydrogen selenide and formation of a substituted amidine III as an intermediate. It then appears that this is followed by action of the second nucleophilic groups (NH_2, OH, SH), to the NH_2-group of III and consequently elimination of ammonia. A five-membered, heterocyclic ring (IV) is thus formed; the reaction path is shown in the Scheme.

Scheme



I II III IV

Ar = Benzene derivatives or heterocyclic rings.

X = H, Cl, CH_3 Y = H, CH_3 Z = NH, O, S

The reaction of selenoamides with two adjacent nucleophilic reagents provides a simple and satisfactory method for preparation of 2-aryl and 2-heterocyclic benzimidazole, benzoxazole and benzothiazole derivatives.

The physical properties of the above mentioned compounds are listed in Table I and their nmr and mass spectral data in Table II.

EXPERIMENTAL

Melting points were determined on a Kofler hotbench and on a Maquenne block apparatus. H-Nmr spectra were determined with a Varian EM-360 instrument (TMS as the internal standard). Mass spectra were taken on a Varian Mat CH7A Mass spectrometer. Microanalytical samples were analysed by Service Central de Microanalyses (C.N.R.S.), 2, rue Henry-Dunant, 94320 Thiais, France and Dornis & Kolbe Mikroanalytisches Laboratorium, Hohenweg 17, West Germany.

Aromatic and heterocyclic selenoamides were prepared from the corresponding nitriles (2). The starting *o*-phenylenediamines, *o*-aminophenol and *o*-aminothiophenol and their derivatives were used as purchased.

Method A. General Procedure for the Synthesis of 2-Aryl and 2-Heterocyclic Benzimidazole and Benzoxazole Derivatives.

To a solution of *o*-phenylenediamine (1.08 g., 0.01 mole) in toluene was added a solution of benzoselenoamide (1.84 g., 0.01 mole) in toluene. After heating under reflux for 3 hours, the reaction mixture was cooled and filtered. The crude product was recrystallized from toluene (1.35 g., 70%), m.p. 295° (1, see Table I).

In the case of the experiments that were carried out in pyridine, the reaction mixture was cooled and the elemental selenium was removed by filtration. The filtrate was poured into cold water and the product was collected by filtration or extracted with ether. After drying over sodium sulfate, the ether was removed in a rotary evaporator.

Method B. General Procedure for the Synthesis of 2-Aryl and 2-Heterocyclic Benzothiazole Derivatives.

o-Aminothiophenol (1.25 g., 0.01 mole) dissolved in anhydrous pyridine was added to a solution of 1.84 g. (0.01 mole) of the benzoselenoamide in anhydrous pyridine. The solution was heated under reflux for 14 hours. The reaction mixture was cooled and elemental selenium was removed by filtration. The solution was poured into cold water and extracted with ether. After drying over sodium sulfate, the ether was removed and the residue was purified by column chromatography through aluminium oxide type 5016 A (basic), using benzene/petroleum ether 4:6. Recrystallization from ethanol/water gave 1.1 g. (50%) of 2-phenylbenzothiazole (21, see Table I), m.p. 114°.

REFERENCES AND NOTES

(1) V. I. Cohen and S. Pourabass, *J. Heterocyclic Chem.*, 14, 1321 (1977).

(2) V. I. Cohen, *Synthesis*, (1978) in press.

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Table I

Physical Properties of 2-Aryl and 2-Hetaryl Benzimidazole, Benzoxazole and Benzothiazole Derivatives

No.	Ar	X	Y	Z	Reaction Solvent	Time of reflux (hours)	Crystallization Solvent	M.p. °C	Yield %	Formula	Analyses (%) Calculated/Found C	H	N	S
1	C_6H_5	H	H	NH	Pyridine of Toluene	2 5	Toluene	295	70	$C_{13}H_{10}N_2$	80.43 80.11	5.15 5.19	14.42 14.17	
2	4-$CH_3C_6H_4$	H	H	NH	Toluene	3	Anisole	285	60	$C_{14}H_{12}N_2$	80.78 80.75	5.77 5.96	13.45 13.48	
3	4-$CH_3OC_6H_4$	H	H	NH	Toluene	20	Toluene	229	75	$C_{14}H_{12}N_2O$	75.02 75.06	5.35 5.38	12.49 12.44	
4	4-ClC_6H_4	H	H	NH	Pyridine	4	Ethanol/water	303	55	$C_{13}H_9ClN_2$	68.30 68.36	3.94 3.98	12.25 12.23	
5	C_6H_5	CH_3	H	NH	Pyridine or Toluene	2 3	Toluene/ Petroleum ether	250	60	$C_{14}H_{12}N_2$	80.78 80.57	5.77 5.98	13.45 13.25	
6	4-ClC_6H_4	CH_3	H	NH	Toluene	13	Toluene	224	65	$C_{14}H_{11}ClN_2$	69.31 69.37	4.53 4.60	11.54 11.71	
7	C_6H_5	Cl	H	NH	Pyridine	20	Benzene/ Petroleum ether	212	81	$C_{13}H_9ClN_2$	68.30 68.25	3.94 4.08	12.25 12.27	
8	4-$CH_3C_6H_4$	Cl	H	NH	Pyridine	20	Xylene	240	50	$C_{14}H_{11}ClN_2$	69.31 69.39	4.53 4.58	11.54 11.56	
9	4-$CH_3C_6H_4$	CH_3	CH_3	NH	Pyridine	8	Ethanol	244	73	$C_{16}H_{16}N_2$	81.37 81.50	6.78 6.76	11.85 11.83	
10	2-Thienyl	H	H	NH	Toluene	15	Anisole	305	60	$C_{11}H_8N_2S$	66.00 65.73	4.00 4.10	13.99 13.76	16.02 16.01
11	2-Pyridyl	H	H	NH	Pyridine	13	Toluene	225	77	$C_{r2}H_9N_2$	73.85 73.97	4.61 4.72	21.53 21.42	
12	2-Thienyl	CH_3	H	NH	Pyridine or Toluene	4 10	Xylene	260	60	$C_{12}H_{10}N_2S$	67.29 67.25	4.67 4.73	13.07 13.00	14.97 14.99
13	2-Thienyl	Cl	H	NH	Pyridine	20	Benzene	228	50	$C_{11}H_7ClN_2S$	56.31 56.30	2.98 3.08	11.93 12.00	13.66 13.56
14	2-Pyridyl	CH_3	CH_3	NH	Toluene	105	Toluene	195	45	$C_{14}H_{13}N_3$	75.35 75.43	5.83 5.95	18.82 18.85	
15	C_6H_5	H	H	O	Pyridine	17	Ethanol/water	102	65	$C_{13}H_9NO$	80.01 79.96	4.61 4.73	7.17 7.18	
16	4-$CH_3C_6H_4$	H	H	O	Pyridine	17	Ethanol	114.5	50	$C_{14}H_{11}NO$	80.40 80.44	5.26 5.33	6.69 6.76	
17	4-$CH_3OC_6H_4$	H	H	O	Pyridine	8	Ethanol/water	105	40	$C_{14}H_{11}NO_2$	74.68 74.30	4.89 5.20	6.22 6.62	
18	4-ClC_6H_4	H	H	O	Pyridine	8	Ethanol/water	148	70	$C_{13}H_8ClNO$	68.01 67.98	3.48 3.56	6.10 6.12	
19	2-Thienyl	H	H	O	Pyridine	22	Ethanol/water	108	70	$C_{11}H_7NOS$	65.67 65.71	3.48 3.57	6.96 7.07	15.94 15.80

Table I (Continued)

No.	Ar	X	Y	Z	Reaction Solvent	Time of reflux (hours)	Crystallization Solvent	M.p. °C	Yield %	Formula	Analyses (%) Calculated/Found C	H	N	S
20	2-Pyridyl	H	H	O	Pyridine	20	Ethanol/water	108	85	$C_{12}H_8N_2O$	73.49	4.08	14.28	
											74.06	4.30	13.84	
21	C_6H_5	H	H	S	Pyridine	14	Ethanol/water	114	50	$C_{13}H_9NS$	73.93	4.26	6.63	15.18
											73.91	4.10	6.58	15.44
22	4-$CH_3C_6H_4$	H	H	S	Pyridine	19	Ethanol/water	83	52	$C_{14}H_{11}NS$	74.66	4.88	6.22	14.24
											74.64	4.90	6.27	14.22
23	4-$CH_3OC_6H_4$	H	H	S	Pyridine	20	Ethanol	202	40	$C_{14}H_{11}NOS$	69.71	4.56	5.80	13.29
											69.76	4.60	5.76	13.13
24	4-ClC_6H_4	H	H	S	Pyridine	20	Ethanol	116.5	50	$C_{13}H_8ClNS$	63.56	3.26	5.70	13.05
											63.65	3.24	5.67	13.10
25	2-Thienyl	H	H	S	Pyridine	14	Ethanol/water	98	63	$C_{11}H_7NS_2$	60.82	3.22	6.44	29.52
											60.77	3.30	6.58	29.77
26	2-Pyridyl	H	H	S	Pyridine	14	Ethanol/water	132	50	$C_{12}H_8N_2S$	67.92	3.77	13.20	15.11
											67.64	4.04	12.98	15.09

Table II

Chemical Shifts and Mass Spectral Data of 2-Aryl and 2-Hetaryl Benzimidazole, Benzoxazole and Benzothiazole Derivatives

No.	NMR (a)	MS: m/e (%)	Formula
1	7.20 (m, 5H); 7.45 (m, 2H); 8.18 (m, 2H)	39 (7); 51 (7); 63 (12); 64 (12); 77 (9); 90 (11); 97 (8); 104 (6); 166 (5); 167 (5); 193 (20); 194 (100)	$C_{13}H_{10}N_2$ (194)
2	2.34 (s, 3H); 7.20 (m, 4H); 7.50 (m, 2H); 8.05 (d, 2H)	103 (4); 104 (6); 207 (23); 208 (100)	$C_{14}H_{12}N_2$ (208)
3	3.85 (s, 3H); 7.05 (d, 2H); 7.20 (m, 2H); 8.15 (d, 2H)	39 (6); 63 (8); 65 (7); 77 (7); 91 (12); 92 (9); 108 (7); 112 (9); 133 (3); 181 (27); 209 (38); 224 (100)	$C_{14}H_{12}N_2O$ (224)
4	7.20 (m, 4H); 7.60 (m, 2H); 8.20 (d, 2H)	63 (7); 64 (8); 90 (7); 114 (6); 193 (12); 228 (100); 230 (33)	$C_{13}H_9ClN_2$ (228-230)
5	7.00 (m, 5H); 7.45 (m, 1H); 8.14 (m, 2H)	39 (3); 51 (8); 77 (16); 104 (24); 207 (54); 208 (100)	$C_{14}H_{12}N_2$ (208)
6	2.43 (s, 3H); 7.00 (d, 2H); 7.45 (d, 2H); 7.60 (d, 2H); 8.18 (d, 2H)	51 (7); 77 (14); 103 (12); 121 (6); 241 (47); 242 (100); 243 (31); 244 (33)	$C_{14}H_{11}ClN_2$ (242-244)
7	7.20 (m, 5H); 7.55 (m, 1H); 8.17 (m, 2H)	63 (12); 77 (8); 90 (7); 104 (5); 114 (8); 124 (5); 166 (5); 192 (7); 193 (6); 228 (100); 230 (34)	$C_{13}H_9ClN_2$ (228-230)
8	2.35 (s, 3H); 7.08 (m, 4H); 7.46 (m, 1H); 8.07 (d, 2H)	63 (7); 90 (5); 103 (7); 121 (7); 207 (9); 241 (17); 242 (100); 244 (33)	$C_{14}H_{11}ClN_2$ (242-244)
9	2.30 (s, 3H); 2.32 (s, 6H); 7.28 (d, 4H); 8.00 (d, 2H)	65 (5); 91 (10); 110 (8); 118 (16); 221 (28); 235 (37); 236 (100)	$C_{16}H_{16}N_2$ (236)
10	7.05-7.37 (m, 3H); 7.38-7.85 (m, 4H)	39 (6); 63 (7); 64 (6); 90 (4); 96 (6); 100 (7); 156 (5); 167 (4); 174 (3); 200 (100)	$C_{11}H_8N_2S$ (200)
11	7.10-8.83 (8H)	39 (4); 51 (5); 52 (4); 63 (5); 64 (6); 78 (8); 90 (4); 97 (3); 105 (4); 167 (13); 194 (17); 195 (100)	$C_{12}H_9N_3$ (195)
12	6.98-7.40 (m, 3H); 7.41-7.80 (m, 3H)	39 (4); 51 (6); 77 (11); 78 (7); 104 (8); 107 (8); 110 (6); 213 (56); 214 (100)	$C_{12}H_{10}N_2S$ (214)
13	7.05-7.40 (m, 3H); 7.41-7.92 (m, 3H)	39 (5); 63 (10); 90 (4); 96 (6); 110 (3); 117 (7); 124 (6); 172 (3); 190 (3); 199 (9); 234 (100); 236 (38)	$C_{11}H_7ClN_2S$ (234-236)
14	7.15-8.80 (6H)	39 (3); 51 (5); 65 (5); 78 (9); 91 (7); 105 (6); 208 (39); 222 (49); 223 (100)	$C_{14}H_{13}N_3$ (223)
15	7.40 (m, 5H); 7.67 (m, 2H); 8.20 (m, 2H)	38 (6); 39 (5); 51 (7); 63 (23); 64 (21); 77 (13); 83 (8); 92 (10); 97 (5); 167 (19); 195 (100)	$C_{13}H_9NO$ (195)
16	2.40 (s, 3H); 7.33 (m, 4H); 7.68 (m, 2H); 8.03 (d, 2H)	63 (7); 64 (6); 91 (9); 209 (100)	$C_{14}H_{11}NO$ (209)
17	3.87 (s, 3H); 7.12 (d, 2H); 7.40 (m, 2H); 7.78 (m, 2H); 8.15 (d, 2H)	58 (10); 59 (7); 112 (6); 127 (4); 128 (3); 182 (26); 210 (31); 225 (100)	$C_{14}H_{11}NO_2$ (225)
18	7.43 (m, 4H); 7.68 (m, 2H); 8.22 (d, 2H)	38 (3); 63 (16); 64 (16); 75 (3); 92 (8); 100 (5); 111 (3); 114 (4); 166 (5); 201 (10); 229 (100); 231 (33)	$C_{13}H_8ClNO$ (229-231)
19	7.17-7.52 (3H); 7.71 (m, 2H); 7.90 (d, 2H)	38 (5); 39 (6); 63 (14); 64 (13); 92 (6); 100 (4); 173 (10); 201 (100)	$C_{11}H_7NOS$ (201)
20	7.34-8.98 (8H)	63 (10); 64 (8); 78 (14); 196 (100)	$C_{12}H_8N_2O$ (196)
21	7.35-7.78 (6H); 8.05 (m, 2H)	69 (12); 108 (23); 211 (100)	$C_{13}H_9NS$ (211)
22	7.30 (m, 4H); 7.55 (m, 2H); 8.05 (m, 2H)	39 (3); 63 (5); 69 (10); 82 (4); 91 (4); 108 (8); 225 (100)	$C_{14}H_{11}NS$ (225)
23	3.84 (s, 3H); 7.10 (d, 4H); 7.50 (m, 2H); 8.05 (m, 2H)	45 (3); 63 (4); 69 (7); 108 (3); 120 (6); 154 (4); 198 (25); 226 (32); 241 (100)	$C_{14}H_{11}NOS$ (241)
24	7.50 (m, 4H); 7.65 (m, 2H); 8.05 (m, 2H)	58 (3); 63 (5); 69 (18); 82 (7); 108 (31); 122 (5); 210 (7); 245 (100); 247 (37)	$C_{13}H_8ClNS$ (245-247)
25	7.10-7.70 (3H); 7.90 (m, 2H); 8.10 (m, 2H)	39 (4); 45 (3); 58 (5); 63 (4); 69 (15); 82 (7); 108 (21); 173 (4); 217 (100)	$C_{11}H_7NS_2$ (217)
26	7.32-8.95 (8H)	51 (7); 57 (4); 63 (6); 69 (16); 78 (8); 82 (7); 106 (9); 108 (14); 110 (10); 186 (7); 212 (100)	$C_{12}H_8N_2S$ (212)

(a) Chemical shifts are expressed on the δ scale using TMS as the standard and deuteriodimethylsulfoxide as the solvent.