Synthesis of some Benzimidazole, Benzoxazole and Benzothiazole Derivatives. Action of Aliphatic Selenonesters on some *o*-Phenylenediamine, *o*-Aminophenol and *o*-Aminothiophenol and their Derivatives

Victor Israel Cohen and Soraya Pourabass

Organic Chemistry Laboratory, Sciences Faculty, Ferdowsi University, Mashhad, Iran

Received June 6, 1977

Aliphatic selenonesters react with *o*-phenylenediamine, *o*-aminophenol and *o*-aminothiophenol and their derivatives to form benzimidazole, benzoxazole and benzothiazole derivatives, respectively. The mass and nmr spectra of the mentioned compounds were studied.

J. Heterocyclic Chem., 14, 1321 (1977)

A continuation of the study of the new method of synthesizing imidazole, oxazole and thiazole derivatives has led to the discovery of still another method of synthesizing benzimidazole, benzoxazole and benzothiazole derivatives. Treatment of *o*-phenylenediamine, *o*-aminophenol and *o*-aminothiophenol and their derivatives with aliphatic selenonesters in ethanol afford in all cases studied benzimidazole, benzoxazole and benzothiazole derivatives. The essential reactions are the following:

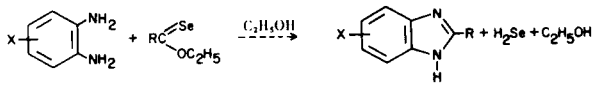
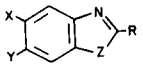


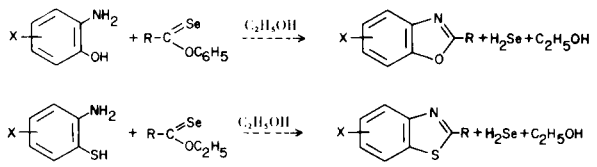
Table I

Chemical Shifts Data of Benzimidazole, Benzoxazole and Benzothiazole Derivatives



Compound No.	X	Y	Z	R		Nmr (a)
1	H	H	NH	CH_3	DMSO-d6	2.45 (3H, s); 7.10 (2H, m); 7.38 (2H, m)
2	H	H	NH	$(CH_3)_2CH$	DMSO-d6	1.35 (6H, d); 3.10 (1H, m); 7.12 (2H, m); 7.43 (2H, m)
3	H	H	NH	$CH_3(CH_2)_4$	DMSO-d6	0.85 (3H, t); 2.55 (6H, m); 2.80 (2H, t); 7.12 (2H, m); 7.40 (2H, m)
4	Cl	H	NH	$CH_3(CH_2)_2$	DMSO-d6	0.92 (3H, t); 1.80 (2H, m); 2.78 (2H, t); 7.02 (1H, d); 7.18 (1H, d); 7.50 (1H, m)
5	Cl	H	NH	$CH_3(CH_2)_4$	DMSO-d6	0.85 (3H, t); 1.50 (6H, m); 2.75 (2H, m); 6.97 (1H, d); 7.14 (1H, d); 7.42 (1H, m)
6	CH_3	H	NH	CH_3CH_2	DMSO-d6	1.30 (3H, t); 2.40 (3H, s); 2.85 (2H, q); 6.90 (1H, d); 7.35 (2H, d)
7	CH_3	H	NH	$CH_3(CH_2)_2$	DMSO-d6	0.90 (3H, t); 1.80 (2H, m); 2.38 (3H, s); 2.78 (2H, t); 6.92 (1H, d); 7.38 (2H, d)
8	CH_3	CH_3	NH	$(CH_3)_2CH$	DMSO-d6	1.35 (6H, d); 2.30 (6H, s); 3.12 (1H, m); 7.22 (2H, s)
9	H	H	O	CH_3CH_2	Carbon tetrachloride	1.40 (3H, t); 2.88 (2H, q); 7.23 (2H, m); 7.55 (2H, m)
10	H	H	O	$CH_3(CH_2)_2$	Carbon tetrachloride	1.03 (3H, t); 1.90 (2H, m); 2.92 (2H, t); 7.20 (2H, m); 7.55 (2H, m)
11	H	H	O	$CH_3(CH_2)_3$	Carbon tetrachloride	0.95 (2H, t); 1.40 (2H, m); 1.80 (2H, m); 2.85 (2H, t); 7.25 (2H, m); 7.55 (2H, m)
12	Cl	H	O	$CH_3(CH_2)_2$	Carbon tetrachloride	1.00 (3H, t); 1.87 (2H, m); 2.85 (2H, t); 7.28 (2H, m); 7.60 (1H, s)
13	Cl	H	O	$(CH_3)_2CH$	Carbon tetrachloride	1.45 (6H, d); 3.17 (1H, m); 7.20 (2H, m); 7.60 (1H, s)
14	H	H	S	$CH_3(CH_2)_2$	Carbon tetrachloride	1.00 (3H, t); 1.82 (2H, m); 2.96 (2H, t); 7.25 (2H, m); 7.80 (2H, m)
15	H	H	S	$(CH_3)_2CH$	Carbon tetrachloride	1.42 (6H, d); 3.30 (1H, m); 7.25 (2H, m); 7.80 (2H, m)
16	H	H	S	$CH_3(CH_2)_3$	Carbon tetrachloride	0.90 (3H, t); 1.60 (4H, m); 3.00 (2H, t); 7.25 (2H, m); 7.80 (2H, m)
17	H	H	S	$CH_3(CH_2)_4$	Carbon tetrachloride	0.92 (3H, t); 1.42 (2H, m); 1.83 (4H, m); 3.04 (2H, t); 7.28 (2H, m); 7.82 (2H, m)

(a) Chemical shifts are expressed in δ scale using internal TMS as the standard.



The Ladenburg ring closure, using *o*-diamines and acides (1-6), or nitriles (7) to form benzimidazoles, *etc.*, was extended to the aldehydes (8-10). In the course of our investigations we have discovered a facile potentially one-step process in which *o*-phenylenediamine and its derivatives are converted to 2-alkylbenzimidazoles and related compounds upon treatment with alkyl selenonesters in organic solvents (methanol or ethanol) at room temperature.

The formation of benzoxazoles from *o*-aminophenols has been effected by use of acid anhydrides (11,12), amides (13,14), nitriles (7), acyl chlorides (15), imino esters (16), and *ortho*-esters (17). In the present study it was found that the treatment of *o*-aminophenol and its derivatives with alkyl selenonesters afforded benzoxazole derivatives.

It was found that formation of the thiazole ring occured by interaction of 2-aminobenzenthiol with orthoesters (17) and amides (18). Treatment of 2-aminothiophenol with the selenonesters in ethanol provide benzthiazoles derivatives.

The nmr and mass spectral fragmentation of the aforementioned compounds are listed in Tables I and II.

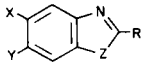
Table II

Mass Spectral Data of Benzimidazole, Benzoxazole and Benzothiazole Derivatives

Compound No.	MS, m/e (%)	Molecular Formula (m/e)
1	39 (8); 52 (8); 63 (13); 64 (10); 65 (9); 66 (8); 90 (8); 92 (8); 104 (6); 131 (55); 132 (100)	$C_8H_8N_2$ (132)
2	39 (12); 51 (8); 52 (9); 63 (8); 65 (11); 78 (26); 118 (7); 119 (6); 132 (5); 145 (100); 146 (12); 159 (26); 160 (46)	$C_{10}H_{12}N_2$ (160)
3	77 (9); 131 (16); 132 (100); 133 (10); 145 (49); 146 (18); 159 (13); 188 (24)	$C_{12}H_{16}N_2$ (188)
4	63 (25); 166 (16); 167 (100); 169 (33); 180 (40); 182 (13); 194 (32); 196 (11)	$C_{10}H_{11}ClN_2$ (194-196)
5	63 (8); 165 (16); 166 (100); 167 (16); 168 (33); 179 (53); 180 (19); 181 (19); 193 (13); 222 (19); 224 (6)	$C_{12}H_{15}ClN_2$ (222-224)
6	51 (10); 77 (14); 79 (16); 145 (32); 159 (100); 160 (72)	$C_{10}H_{12}N_2$ (160)
7	39 (7); 51 (8); 77 (10); 78 (7); 91 (5); 104 (5); 131 (5); 144 (6); 145 (28); 146 (100); 159 (22); 173 (15); 174 (31)	$C_{11}H_{14}N_2$ (174)
8	39 (7); 41 (5); 79 (12); 91 (5); 171 (7); 173 (100); 174 (13); 187 (26); 188 (53)	$C_{12}H_{16}N_2$ (188)
9	38 (9); 39 (11); 58 (19); 59 (14); 66 (7); 91 (9); 104 (6); 132 (16); 146 (100); 147 (64)	C_9H_9NO (147)
10	63 (13); 132 (15); 133 (100); 146 (29); 161 (28)	$C_{10}H_{11}NO$ (161)
11	39 (9); 41 (7); 63 (10); 64 (9); 64 (7); 132 (8); 133 (100); 134 (10); 146 (26); 147 (7); 175 (13)	$C_{11}H_{13}NO$ (175)
12	63 (25); 166 (16); 167 (100); 168 (16); 169 (34); 180 (40); 182 (14); 195 (32); 197 (11)	$C_{10}H_{10}ClNO$ (195-197)
13	29 (20); 41 (31); 57 (57); 63 (29); 135 (14); 153 (23); 180 (100); 194 (31); 195 (67); 196 (18); 197 (22)	$C_{10}H_{10}ClNO$ (195-197)
14	45 (10); 69 (12); 108 (10); 147 (11); 148 (13); 149 (100); 162 (23); 177 (22)	$C_{10}H_{11}NS$ (177)
15	69 (14); 108 (11); 109 (16); 135 (7); 136 (7); 149 (9); 162 (100); 163 (12); 176 (21); 177 (48)	$C_{10}H_{11}NS$ (177)
16	39 (8); 41 (7); 45 (8); 69 (8); 91 (8); 93 (9); 108 (8); 109 (7); 148 (8); 149 (100); 150 (15); 162 (22); 176 (4); 191 (9)	$C_{11}H_{13}NS$ (191)
17	45 (10); 69 (9); 108 (11); 109 (8); 148 (9); 149 (100); 150 (12); 162 (35); 163 (10); 176 (11); 205 (15)	$C_{12}H_{15}NS$ (205)

Table III

Physical Properties of Benzimidazole, Benzoxazole and Benzothiazole Derivatives



Compound No.	X	Y	Z	R	Reaction Solvent	Time of contact or (reflux)	B.p. °C (mm) (M.p. °C)	Crystallization Solvent	Yield %
1	H	H	NH	CH_3	Ethanol	1 day	(175)	Benzene	83
2	H	H	NH	$(CH_3)_2CH$	Ethanol	2 days	(236)	Benzene	78
3	H	H	NH	$CH_3(CH_2)_4$	Ethanol	1 day	(164)	Benzene	92
4	Cl	H	NH	$CH_3(CH_2)_2$	Ethanol	6 days	(132)	Benzene	72
5	Cl	H	NH	$CH_3(CH_2)_4$	Ethanol	5 days	(124)	Benzene-Petroleum ether	50
6	CH_3	H	NH	CH_3CH_2	Ethanol	1 day	(168)	Benzene	94
7	CH_3	H	NH	$CH_3(CH_2)_2$	Ethanol	4 days	(152)	Benzene-Petroleum ether	86
8	CH_3	CH_3	NH	$(CH_3)_2CH$	Ethanol	3 days	(210)	Benzene-Petroleum ether	82
9	H	H	O	CH_3CH_2	Ethanol	8 days	84 (3)	---	75
10	H	H	O	$CH_3(CH_2)_2$	Ethanol	8 days	90 (7)	---	86
11	H	H	O	$CH_3(CH_2)_3$	Ethanol	8 days	87 (2)	---	60
12	Cl	H	O	$CH_3(CH_2)_2$	1-Butanol	(30 hours)	120 (3)	---	45
13	Cl	H	O	$(CH_3)_2CH$	1-Butanol	(30 hours)	110 (3)	---	30
14	H	H	S	$CH_3(CH_2)_2$	Ethanol	4 days	105 (2)	---	70
15	H	H	S	$(CH_3)CH$	Ethanol	4 days	117 (2)	---	81
16	H	H	S	$CH_3(CH_2)_3$	Ethanol	4 days	105-110 (4)	---	76
17	H	H	S	$CH_3(CH_2)_4$	Ethanol	4 days	135 (3)	---	85

EXPERIMENTAL

Melting points were determined on a Kofler hotbench apparatus. Nmr spectra were recorded on a Varian EM-360 spectrometer. Mass spectra were taken on a Varian CH7A mass spectrometer. Analyses were performed by Dornis and Kolbe Mikroanalytisches Laboratorium, Hohenweg 17, West Germany and Service Central de Microanalyse (C.N.R. S) 2, Rue Henry Dunant, 94320 Thiais, France.

All of the aliphatic selenonesters were preapred from the corresponding iminoester (19). *o*-Phenylenediamine, *o*-aminophenol and *o*-aminothiophenol and their derivatives were purchased from commercial sources.

Preparation of Benzimidazole, Benzoxazole and Benzothiazole Derivatives.

A. The following procedure is typical for solid compounds. *o*-Phenylenediamine (1.08 g., 0.01 mole) was dissolved in 10 ml. of anhydrous ethanol and 1.51 g. (0.01 mole) of methylselenonester in 10 ml. of anhydrous ethanol was added with stirring. The mixture was allowed to stand at room temperature for 1 day, then the suspension which resulted was filtered. The filtrate was evaporated leaving 1.09 g. (83%) of product (Table III, Experiment No. 1), m.p. 175°.

B. The following procedure is typical for liquid compounds. A solution of 1.25 g. (0.01 mole) of o-aminothiophenol in 10 ml. of anhydrous ethanol was cooled in an ice bath and 1.79 g. (0.01 mole) of propylselenonester in 10 ml. of anhydrous ethanol was added with stirring. The mixture was allowed to stand at room temperature for 4 days then the suspension which resulted was filtered. Distillation of the reaction mixture gave 2-propylbenzothiazole (Table III, Experiment No. 14) (1.24 g., 70%), b.p. 105 (2 mm).

REFERENCES AND NOTES

(1) A. Ladenburg, *Ber.*, **8**, 677 (1875).

(2) M. A. Phillips, *J. Chem. Soc.*, 2393 (1928).

(3) E. C. Wagner and W. H. Millett, *Org. Synth.*, Coll. Vol. II, 65 (1943).

(4) B. A. Poral-Koshits and G. M. Kharkharova, *Zh. Obshch. Khim.*, 25, 2138 (1955).

(5) T. Momai, H. Higurashi, M. Abe and D. Mizuno, *Yakugaku Zasshi*, 78, 242 (1958).

(6) United States Borax & Chemical Corp., British Patent 1,015,937 (Cl.C 07d), Jan. 5, 1966.

(7) E. L. Halljes, Jr. and E. C. Wagner, *J. Org. Chem.*, **9**, 31 (1944).

(8) R. Weidenhagen, *Ber.*, **69B**, 2263 (1936).

(9) D. Jerchel, H. Fischer, and M. Kracht, *Ann. Chem.*, 575, 162 (1952).

(10) Monsanto Chemicals (Australia) Ltd., British Patent 1,083,201 (Cl.C.07d) Sept. 13, 1967.

(11) A. Ladenburg, *Ber.*, **9**, 1524 (1876).

(12) M. A. Phillips, *J. Soc. Chem. Ind.*, **56**, 474T (1937).

(13) St. V. Niementowski, *Ber.*, **30**, 3062 (1897).

(14) S. Skraup and M. Moser, *ibid.*, **55**, 1080 (1922).

(15) D. A. Drapkina, V. G. Brudz, V. A. Inshakova and N. I. Badaikova, *Metody Poluch. Khim. Reakt. Prep.*, **15**, 184 (1967).

(16) G. I. Braz, G. V. Myasnikova, A. Ya. Yakubovich, V. P. Bazov, I. E. Kardash and A. N. Pravednikov, *Khim. Geterotsikl. Soedin.*, **2**, 215 (1967).

(17) G. L. Jenkins, A M. Knevel and C. S. Davis, *J. Org. Chem.*, 26, 274 (1961).

(18) J. Metzger and H. Plank, *Bull. Soc. Chim. France*, **23**, 1692 (1956).

(19) V. I. Cohen, *J. Org. Chem.*, **42**, 2645 (1977).