SYNTHESIS OF SUBSTITUTED β-(2-SELENIENYL)-ETHYLAMINES

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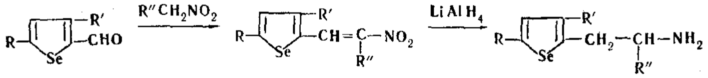
Substituted β-(2-selenienyl)ethylamines were synthesized by the reduction of the corresponding α,β-unsaturated nitro compounds. 2-(ω-Nitrovinyl)selenophene was alkoxylated and aminated.

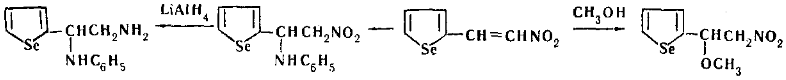
In searching for new neuro- and psychotropic agents we have accomplished the synthesis of substituted β-(2-selenienyl)ethylamines, whose structures recall that of phenamine.

For this, we condensed the isomeric 3- and 5-methyl-2-formylselenophenes with nitromethane and nitroethane in the presence of basic compounds. The α,β-unsaturated nitro compounds thus formed (Table 1) were reduced with lithium aluminum hydride:



The best yields of α,β-unsaturated nitro compounds were obtained when n-butylamine or ammonium acetate was used as the condensing agent.

2-(ω-Nitrovinyl)selenophene was alkoxylated and aminated at its activated double bond (addition of methanol and aniline, respectively). The nitroamine obtained was reduced with lithium aluminum hydride to the corresponding 2-(2-amino-1-phenylaminoethyl)selenophene:



The constants, yields, and elementary analyses of the amines and their hydrochlorides are presented in Table 2.

The results of pharmacological tests on animals indicated that the hydrochlorides of the above amines have central sympathomimetic properties and considerably lower toxicity than the preparations with similar action currently used in medical practice.

EXPERIMENTAL

1-(5-Methyl-2-selenienyl)-2-nitroethylene (I). A solution of 1.43 g of sodium hydroxide in 4.5 ml of water was added to a solution of 6 g (0.03 mole) of 5-methyl-2-formylselenophene [1] and 2.1 g (0.03 mole) of nitromethane in 7 ml of methanol at 10-15 deg. The mixture was stirred at 10-15 deg for 30 min; 50 ml of water was added; and the resulting mixture was poured with stirring into a mixture of 5 ml of hydrochloric acid (sp. gr. 1.19), 5 ml of water, and 20 g of ice. The resulting precipitate was washed with ice water to give 2 g (27%) of product.

1-(2-Selenienyl)-2-nitropropene. A solution of 10 g (0.06 mole) of 2-formylselenophene [2], 10 g (0.13 mole) of nitroethane, and 2.5 g of ammonium acetate in 30 ml of glacial acetic acid was refluxed with stirring for 2 h. The mixture was cooled and poured into a mixture of 10 ml of water and 20 g of ice. The resulting precipitate was washed with ice water to give 5.2 g (38%) of yellow crystals with mp 61 deg (from methanol).

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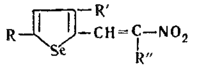
TABLE 1

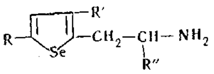


R	R′	R″	mp*	Empirical formula	Found, %		Calculated, %		Yield, % †			
					C	H	C	H	A	B	C	D
H	CH_3	H	67	$C_7H_7NO_2Se$	38,9 39,5	3,1 3,6	38,9	3,3	10 20	10 20	31	10
CH_3	H	H	83	$C_7H_7NO_2Se$	38,9	3,6	38,9	3,3	23 27	50	20	40 50
H	H	CH_3	61	$C_7H_7NO_2Se$	39,2 39,0	3,6 3,6	38,9	3,3	3,5	24	38	32
H	CH_3	CH_3	95	$C_8H_9NO_2Se$	42,1 41,9	4,2 4,4	41,8	3,9	3,0	—	31	60
CH_3	H	CH_3	106	$C_8H_9NO_2Se$	42,2 42,1	4,2 4,2	41,8	3,9	2,8	—	54	40

* From methanol.

† In the presence of aqueous sodium hydroxide (A), in the presence of alcoholic sodium hydroxide (B), in the presence of ammonium acetate (C), and in the presence of n-butylamine (D).

TABLE 2



R	R′	R″	bp (mm)	n_D, (°C)	Yield, %	Hydrochloride					
						mp	empirical formula	found, %		calculated, %	
								C	H	C	H
H	CH_3	H	99 (5—6)	1,5765 (20)	84	158	$C_7H_{11}NSe \cdot HCl$	37,5 37,7	5,5 5,5	37,4	5,4
CH_3	H	H	97 (5—6)	1,5710 (21)	64	191	$C_7H_{11}NSe \cdot HCl$	37,6 37,6	5,9 5,1	37,4	5,4
H	H	CH_3	79 (3)	1,5635 (25)	78	157	$C_7H_{11}NSe \cdot HCl$	37,5 37,6	5,7 5,6	37,4	5,4
H	CH_3	CH_3	99 (5—6)	1,5628 (20)	78	169	$C_8H_{13}NSe \cdot HCl$	39,7 39,9	6,0 6,2	40,3	5,9
CH_3	H	CH_3	96 (5—6)	1,5540 (20)	69	140	$C_8H_{13}NSe \cdot HCl$	39,6 39,8	5,8 6,0	40,3	5,9

1-(3-Methyl-2-selenienyl)-2-nitropropene. A solution of 4.35 g (0.025 mole) of 3-methyl-2-formylselenophene [3], 1.9 g (0.04 mole) of nitroethane, and 0.12 g of n-butylamine in 4 ml of absolute ethanol was refluxed for 8 h; cooled with ice; and the resulting precipitate was suction-filtered to give 3.42 g (60%) of product.

2-(5-Methyl-2-selenienyl)ethylamine. A solution of 5.6 g (0.025 mole) of I in 110 ml of absolute ether was added with stirring to 4.25 g (0.15 mole) of lithium aluminum hydride in 95 ml of absolute ether. The mixture was refluxed for 2 h, cooled, and carefully decomposed with 30 ml of water. The ether solution was decanted, and the residue was stirred twice with fresh portions of ether (50-70 ml each). The combined ether solutions were dried with potassium carbonate and vacuum-distilled under nitrogen to give 3.2 g (64%) of a product with bp 97 deg (5 mm) and n_D^{21} 1.5710. The hydrochloride was obtained in quantitative yield with mp 191 deg by passing dry hydrogen chloride through an absolute-ether solution of the amine.

2-(2-Nitro-1-methoxyethyl)selenophene. 2-(ω-Nitrovinyl)selenophene [4] [8.23 g (0.04 mole)] was dissolved with heating in 30 ml of methanol, the solution was cooled with ice, and 36.7 ml of a solution of sodium methoxide (from 2.5 g of sodium and 60 ml of methanol) was added. A strong stream of carbon dioxide was passed through the solution for 15-20 min, 150 ml of water was added, and carbon dioxide was again passed through the mixture for 15-20 min. The mixture was extracted with ether, and the extract was washed with water and dried with calcium chloride. Vacuum distillation gave 3.5 g (37%) of a viscous yellow oil with bp 123 deg (3 mm), $n_D^{26.5}$ 1.5525, and d_4^{20} 1.5392. Found %: C 36.0, 36.1; H 3.8, 3.7. $C_7H_9NO_3Se$. Calc. %: C 35.9; H 3.9.

2-(2-Nitro-1-phenylaminoethyl)selenophene (II). A mixture of 6.87 g (0.034 mole) of 2-(ω-nitrovinyl)-selenophene and 3.16 g (0.034 mole) of aniline was allowed to stand at 20 deg with periodic stirring for 5 h. The reaction product was recrystallized from methanol to give 6.2 g (62%) of a product with mp 60-61 deg (from benzene–petroleum ether). Found %: C 49.1, 49.1; H 3.8, 4.1. $C_{12}H_{12}N_2O_2Se$. Calc. %: C 48.8; H 4.1.

2-(2-Amino-1-phenylaminoethyl)selenophene. A solution of 5.9 g (0.02 mole) of II in 110 ml of absolute ether was added in 2 h to 3.8 g (0.1 mole) of lithium aluminum hydride in 100 ml of absolute ether. The mixture was refluxed for 2 h, cooled, and carefully decomposed with 31 ml of water. The precipitate was extracted with ether, and the extract was dried with potassium carbonate and vacuum-distilled under nitrogen to give 3.7 g (75%) of a viscous, yellow oil with bp 203-205 deg (17 mm). The monohydrochloride had mp 186-188 deg (dec., from alcohol). Found %: C 48.1, 48.1; H 5.2, 5.4. $C_{12}H_{14}N_2Se$. Calc. %: C 47.7; H 5.3.

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