Selenium Heterocycles. XVI. 1,2,3-Selenadiazolyl Derivatives of Polycyclic Aromatic Compounds and Steroids (1)

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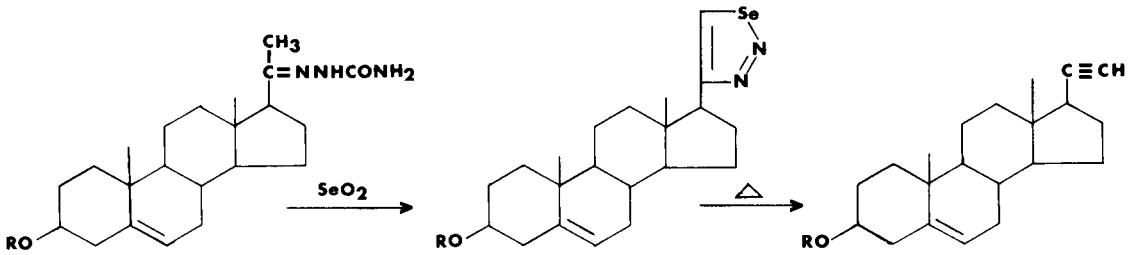
Semicarbazones of α-methylene ketones or aldehydes are known to afford 1,2,3-selenadiazoles when reacted with selenium dioxide (2-6). 1,2,3-Selenadiazoles are thermaly unstable and afford the corresponding acetylene compounds (3-6) or 1,4-diselenine derivatives if they are fused with cycloalkanes having less than eight carbon atoms in their rings (5).

As many pharmacologically active steroids contain the 17-α-ethynyl moiety, it was of interest to study the application of the above reaction to readily available 17-β-acetylsteroids. Also, several representative acetyl aromatic polycyclic compounds and 3,4-dihydro-6-methoxy-1(2*H*)naphthalenone were transformed to their corresponding 1,2,3-selenadiazolyl derivatives for pharmacological studies.

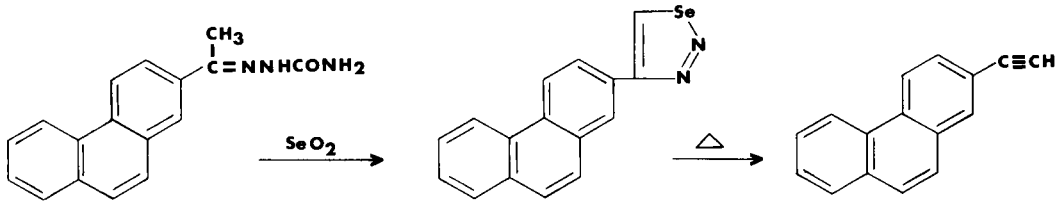
The simplest 1,2,3-selenadiazole derivative prepared in this work was 4-β-naphthyl-1,2,3-selenadiazoles (**1**). β-Acetylnaphthalene semicarbazone gave 80 per cent of 4-β-naphthyl-1,2,3-selenadiazole. However, in the case of the α-isomer, the semicarbazone was transformed into the starting ketone. Similarly 9-acetylanthracene gave only the starting 9-acetylanthracene. Good yields of 1,2,3-selenadiazoles (**4a,b**) were obtained from 3-β-hydroxypregn-5-en-20-one semicarbazone (**3a**) and its 3β-acetate derivative (**3b**), which in turn were pyrolysed to afford the corresponding 17β-ethynyl derivatives (**5a.b**) (Scheme I).

Methyl-2-phenanthryl ketone semicarbazone (**6**) and selenium dioxide afforded a good yield of 4-[phenanthren-2-yl]-1,2,3-selenadiazole (**7**), which on mild pyro-



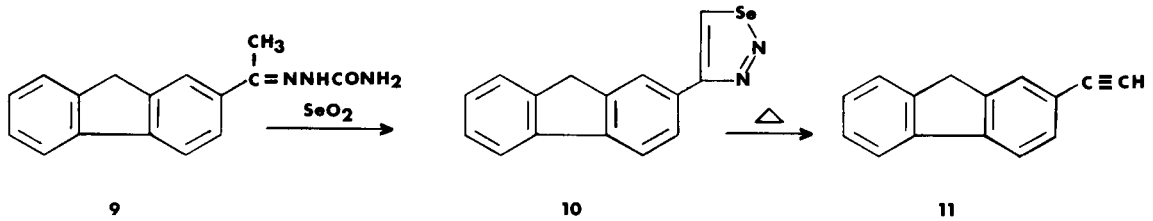
3(a,b) 4(a,b) 5(a,b)

Scheme I



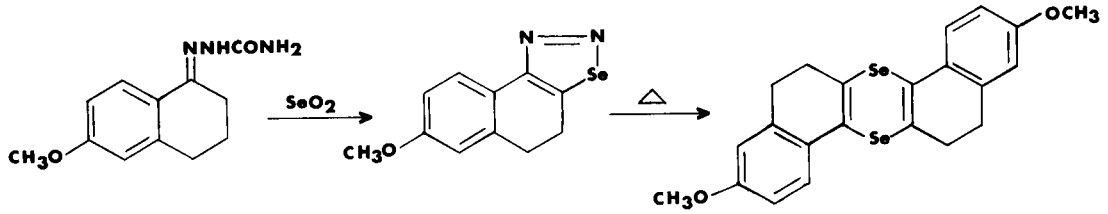
6 7 8

Scheme II



9 10 11

Scheme III



12 13 14

Scheme IV

lysis afforded a high yield of 2-ethynylphenanthrene (**8**) (Scheme II).

Methyl-2-fluorenyl ketone semicarbazone (**9**) underwent the same reaction (Scheme III).

3,4-Dihydro-6-methoxy-1(2*H*)naphthalenone semicarbazone (**12**) was reacted with selenium dioxide leading to the formation of 7-methoxy-4,5-dihydronaphtho[1,2-*d*]-1,2,3-selenadiazole (**13**) which afforded 3,10-dimethoxy-5,6,12,13,tetrahydrodinaphtho[2,1-*b*][1,2-*c*]-7,14-diselenine (**14**) (Scheme IV).

The elucidation of the structure of the 1,4-diselenine product was based on elemental analysis, nmr and mass spectroscopy; the 5,6,12,13-methylene groups appeared as a multiplet centered at δ = 2.76. It had a molecular ion of m/e 474, with abundant ions $(M-79)^+$ and $(M-158)^+$ resulting from the concurrent elimination of one and two selenium atoms, respectively.

Decomposition of 1,2,3-selenadiazoles is an exothermic reaction and excess heat brought about the formation of disubstituted selenophenes by subsequent interaction of the resulting selenium and acetylene derivatives (7). To prevent this side reaction, the selenadiazoles were diluted with a ten fold excess of clean dry sand and decomposition was achieved preferably under mild pressure. The compounds prepared are summarized in Table I.

EXPERIMENTAL

Melting points were determined on a Kofler hot stage microscope and are uncorrected. Uv spectra were measured using a Varian-Tektron 635 spectrophotometer. Ir spectra (potassium bromide disks) were recorded on a Leitz model III spectrograph. Nmr spectra were obtained with a Varian A60A instrument using TMS as the internal standard and mass spectra were determined on a Varian Mat 111 instrument.

4-β-Naphthyl-1,2,3-selenadiazole (**1**).

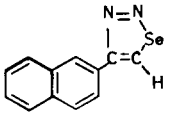
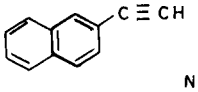
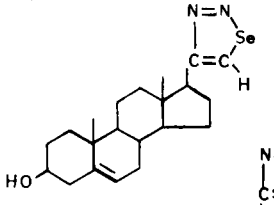
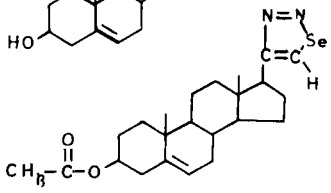
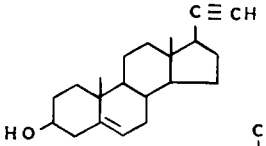
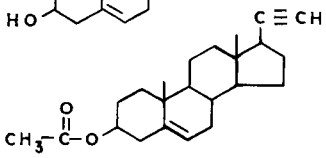
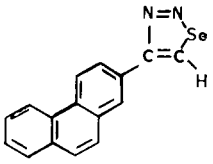
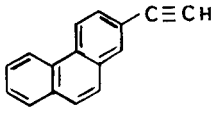
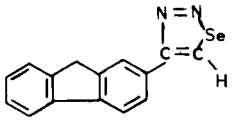
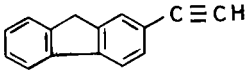
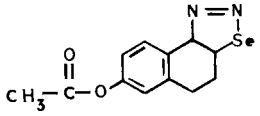
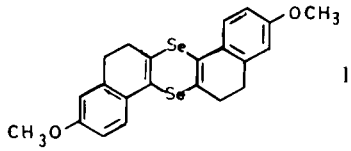
A mixture of 4.45 g. (0.02 mole) of β-acetylnaphthalene semicarbazone and 2.2 g. (0.02 mole) of selenium dioxide in 30 ml. of glacial acetic acid was stirred and warmed until gas evolution ceased. The reaction mixture was filtered, diluted with 200 ml. of cold water and extracted 3 times with a total 60 ml. of chloroform. The organic layer was neutralized with concentrated sodium bicarbonate solution and charcoaled. After evaporation of the solvent under reduced pressure, the residue was crystallized from aqueous ethanol to give 4.14 g. (80%) of white needles, m.p. 110°; molecular weight m/e 259 with the abundant ion at m/e 152 corresponding to 2-naphthylacethylene (**2**).

4,α-Naphthyl-1,2,3-selenadiazole, 4-[phenanthren-2-yl]-1,2,3-selenadiazole (7) and 4-[fluoren-2-yl]-1,2,3-selenadiazole (10) reported in Table I, were prepared similarly (Table I).

7-Methoxy-4,5-dihydronaphtho[2,1-*d*]-1,2,3-selenadiazole (**13**).

3,4-Dihydro-6-methoxy-1-(2*H*)naphthalenone semicarbazone (**12**) (8) (6.99 g., 0.03 mole) was dissolved in 70 ml. of hot glacial acetic acid. To the hot stirred solution 3.3 g. (0.03 mole) of selenium dioxide was added and the reaction mixture was gently refluxed until gas evolution ceased. The hot solution was filtered and diluted with 200 ml. of water. The precipitate was filtered and crystallized from aqueous ethanol to give 5.9 g. (75%) of the desired 1,2,3-selenadiazole derivative, m.p. 108-112°; uv max (methanol): 255, 263 and 333 nm; nmr (deuteriochloroform): δ 3.70 (q, CH_2, 4H), 4.10 (s, CH_3, 3H), 7.13-8.57 (m, aromatic, 3H); ir ν max: 3328, 1617, 1493, 1380, 1248, 1165, 1031, 918

Table I

Compound No.		M.p., °C	Yield %	Formula	C% Calcd.	C% Found	H% Calcd.	H% Found
1		110	80	$C_{12}H_8N_2Se$	55.60	55.58	3.09	3.16
2		36 (a)	60	$C_{12}H_8$	94.74	94.84	5.26	5.29
4a		156	12	$C_{21}H_{30}N_2OSe$	62.22	62.37	7.41	7.38
4b		160	47	$C_{23}H_{32}N_2O_2Se$	61.88	61.97	7.17	7.32
5a		150 (b)	34	$C_{21}H_{30}O$	84.56	84.63	10.07	10.00
5b		153	17	$C_{23}H_{32}O_2$	82.63	82.69	9.58	9.53
7		160	55	$C_{16}H_{10}N_2Se$	62.14	62.10	3.24	3.20
8		74	35	$C_{16}H_{10}$	95.05	95.25	4.95	4.88
10		150	16	$C_{15}H_{10}N_2Se$	60.61	60.59	3.37	3.32
11		83 (c)	4	$C_{15}H_{10}$	94.73	94.70	5.26	5.22
13		98	75	$C_{11}H_{10}N_2OSe$	49.81	49.79	3.77	3.70
14		168	11	$C_{22}H_{20}O_2Se_2$	55.70	55.79	4.22	4.40

(a) Ref. (9) gives m.p. 36°. (b) Ref. (10) gives m.p. 166-168.5°. (c) Ref. (11) gives m.p. 85.5°.

845 and 827 cm^{-1}.

4-[3β-Hydroxypregn-5-en-17-yl]-1,2,3-selenadiazole (**4a**) and its acetate (**4b**) reported in Table I were prepared similarly (Table I).

General Procedure for the Preparation of Acetylenes.

Five to 10 g. of the appropriate 1,2,3-selenadiazoles were mixed with 10 times their weight of clean dry sand and gradually heated in an oil bath to 180° under reduced pressure (50-100 mm Hg), extracted with chloroform, filtered through a short coloumn of silica gel and charcoal layers (Table I).

3,10-Dimethoxy-5,6,12,13-tetrahydro-dinaphto[2,1-*b*][1,2-*e*]-7,14-diselenine (**14**).

7-Methoxy-4,5-dihydronaphtho[1,2-*d*]-1,2,3-selenadiazole (**13**) (2.65 g., 0.01 mole) was diluted with 26 g. of clean dry sand and treated as described above for the preparation of acetylenes. After evaporation of chloroform, the residue was crystallized from ethanol to give 0.2 g. (10.5%) m.p. 168°; uv max (methanol): 283 nm; ir ν max: 3195, 1610, 1680, 1460, 1216, 1130, 1058, 1039, 863 and 798 cm^{-1}.

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