SELENA AND THIADIAZOLE FUSED POLYCYCLICPOLYTHIA COMPOUNDS - PART-III

D. Bhaskar Reddy*, A. Balaiah, V. Padmavathi & A. Padmaja
Department of Chemistry, Sri Venkateswara University, Tirupati - 517 502, India

Abstract: The selena and thiadiazole rings have been fused on 1/2-thiachroman-4-ones **1** & **2**, 4,9/4, 10-dithiahexahydrophenanthren-1-ones **9** & **10**, D-homo-6, 11/7, 11-dithia-1,3,5(10), 8,13(14)-gonapentaen-18a-ones **17** & **18** through their semicarbazones by reaction with selenium dioxide and thionyl chloride, respectively. The new compounds are characterized by thier IR and ^{1}H NMR data.

Introduction

In the chase for new and novel heterocycles capable of performing a variety of functions, steroid analogs have been identified as unique and interesting compounds. Polycyclicpolythia compounds which are analogous to thiasteroids exhibit a variety of chemotherapeutic properties (1-3). In continuation of our interest in polycyclicpolythia compounds (4,5), it was thought to develop selena/thiadiazole rings on the latter so that the resulting compounds would not only consists of sulfur but also nitrogen and/or selenium in the fused ring systems. Indeed, reports about selenium containing heterocycles which are biologically potent are relatively less (6-8). Therefore, the present study aims at the development of hitherto unknown selena and thiadiazole fused polycyclicpolythia compounds.

Results & Discussion

The α-ketomethylene group present in thiachroman-4-one **1** and 2-thiachroman-4-one **2** has been exploited to develop selena and thiadiazole rings. Treatment of **1** and **2** with semicarbazide hydrochloride gave the corresponding semicarbazones, **3** and **4**. The latter on reaction with selenium dioxide in acetic acid undergoes oxidative cyclization (6,7) to 1-thiadihydronaphthalen [3,4-*d*]1',2',3'-selenadiazole **5** and 2-thiadihydronaphthalen [3,4-*d*]-1',2',3'-selenadiazole **6**. When **3** and **4** subjected to Hurd-Mori reaction process with thionyl chloride in dichloromethane (9) furnished 1-thiadihydronaphthalen [3,4-*d*]1',2',3'-

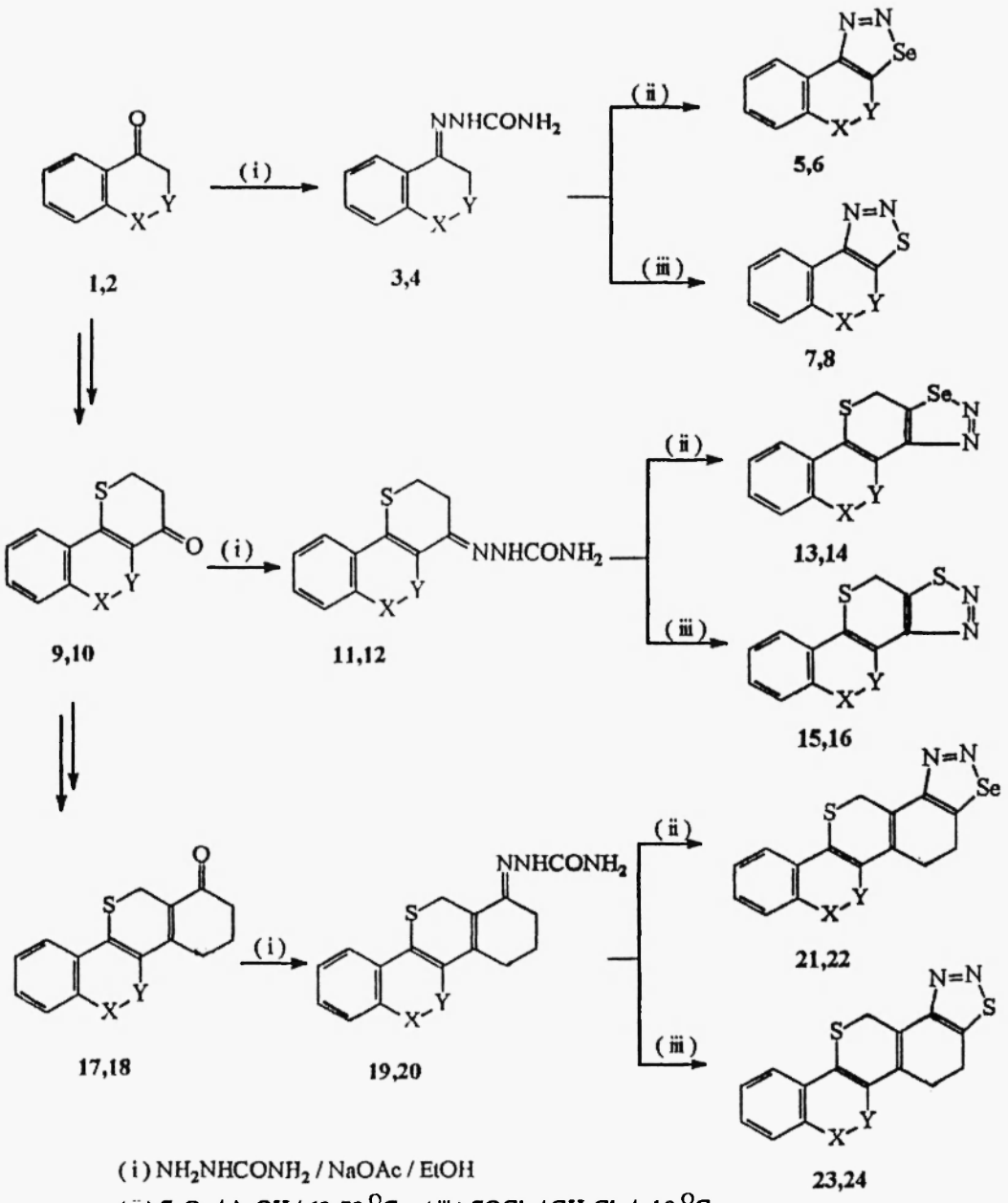
thiadiazole 7 (10) and 2-thiadihydronaphthalen [3,4-*d*]1',2',3'-thiadiazole 8. On the other hand, condensation of 1 and 2 with β-mercaptopropanoic acid followed by cyclodehydration with phosphorus pentoxide furnished 4,9-dithiahexahydrophenanthren-1-one 9 and 4,10-dithiahexahydrophenanthren-1-one 10, respectively (4). The selena and thiadiazole rings have been developed on the latter by oxidative cyclization with selenium dioxide and Hurd-Mori reaction with thionyl chloride via their semicarbazones 11 & 12. Thus 4,9-dithiatetrahydrophenanthren [1,2-*d*] 1',2',3'-selena/ thiadiazole 13 & 15 and 4,10-dithiatetrahydrophenanthren[1,2-*d*] 1',2',3'-selena/thiadiazole 14 & 16 have been prepared. Besides this, D-homo-6,11-dithia-1,3,5(10),8,13(14)-gonapentaen-18a-one 17 and D-homo-7,11-dithia-1,3,5(10),8,13(14)-gonapentaen-18a-one 18 have been obtained by the reaction of 9 and 10 with γ-chlorobutyric acid followed by cyclodehydration with phosphorus pentoxide (4). The selena and thiadiazole rings have been developed on 17 and 18 by adopting the above methodology so as to get D-homo-6,11-dithia-1,3,5(10),8,13(14)-gonapentaen [18,18a-*d*]1', 2', 3'-selena/thiadiazole (21 & 23) and D-homo-7,11-dithia-1,3,5(10),8,13(14)-gonapentaen[18,18a-*d*]1',2',3'-selena thiadiazole (22 & 24), a new class of polycyclicpolythia selena/thiadiazoles (Scheme). All the compounds were obtained in relatively good yields (62 -78%) and were chromatographically pure.

Experimental

Melting points were determined on a Mel-Temp apparatus which are uncorrected. The IR spectra in KBr pellets were recorded on a Perkin-Elmer 993 infrared spectrometer (ν in cm^{-1}), ^1H NMR spectra were run in $CDCl_3$ on 90 or 200 MHz on Perkin-Elmer instrument with TMS as an internal standard (chemical shifts in δ, ppm).

Preparation of semicarbazones of thiachroman-4-one 3, 2-thiachroman-4-one 4, 4,9-dithiahexahydrophenanthren-1-one 11, 4,10-dithiahexahydrophenanthren-1-one 12, D-homo 6,11-dithia-1,3,5(10),8,13(14)-gonapentaen-17a-one 19 and D-homo-7,11-dithia-1,3,5(10), 8,13(14)-gonapentaen-18a-one 20

A mixture of 1/2/9/10/17/18 (0.005 mole), semicarbazide hydrochloride (0.001 mole) sodium acetate (0.002 mole) in ethanol (40 ml) was refluxed for 2-3h on a steam-



(i) $NH_2NHCONH_2$ / NaOAc / EtOH

(ii) SeO_2 / AcOH / 60-70 °C , (iii) $SOCl_2$ / CH_2Cl_2 / -10 °C

1,3,5,7,9,11,13,15,17,19,21,23 : X = S ; Y = CH_2

2,4,6,8,10,12,14,16,18,20,22,24 : X = CH_2 ; Y = S

SCHEME

bath and cooled. The separated solid was filtered, washed with water and recrystallized from ethanol to get pure **3/4/11/12/19/20**. **3**: Yield 84%, m.p. 156-57°C; **4**: Yield 81%, m.p. 165-66°C; **11**: Yield 80%, m.p. 205-08°C; **12**: Yield 76%,m.p.197-99°C; **19**: Yield 72%, m.p. >300°C; **20**: Yield 75%, m.p. >300°C.

Preparation of 1-thiadihydronaphthalen [3,4-*d*] 1',2',3'-selenadiazole 5, 2-thiadihydronaphthalen [3,4-*d*] 1',2',3'-selenadiazole 6, 4,9-dithiatetrahydrophenanthren-[1,2-*d*]1',2',3'-selenadiazole 13, 4-10-dithiatetrahydrophenanthren [1,2-*d*] 1',2',3'-selenadiazole 14, D-homo-6,11-dithia-1,3,5(10),8,13(14)-gonapentaen[18,18a-*d*] 1',2',3'-selenadiazole 21, D-homo-7,11-dithia-1,3,5(10),8,13(14)-gonapentaen[18,18a-*d*] 1',2',3'-selenadiazole 22.

The semicarbazone **3/4/11/12/19/20** (0.0005) mole was treated with selenium dioxide powder (0.0005) mole in glacial acetic acid (20 ml) and the mixture was gently heated (60-70°) with stirring unitl the evolution of gas ceased. Then the reaction mixture was cooled, filtered and poured onto crushed ice, to get a solid product. It was filtered, dried and recrystallized from pet. ether (60-80°C) to afford a pure compound. **5**: Yield 66%, m.p. 98-100°C (Found C, 42.53; H, 2.51, $C_9H_6N_2SSe$ requires C, 42.70, H, 2.39%); IR : 1450 (N=N) cm^{-1}, ^1H NMR: δ 4.28 (s, 2H, CH_2), 6.85-7.02 (m, 4H, Ar-H). **6**: Yield 62%, m.p. 95-97° C (Found C, 42.57; H, 2.28, $C_9H_6N_2SSe$ requires C,42.70; H, 2.39%); IR: 1445 (N=N) cm^{-1}; ^1H NMR: δ 4.25 (s, 2H, CH_2), 6.91-7.05 (m, 4H,Ar-H). **13**: Yield 69%, m.p. 123-25°C (Found C, 44.80; H, 2.36, $C_{12}H_8N_2S_2Se$ requires C, 44.58; H 2.49%); IR: 1448 (N=N) cm^{-1}, ^1H NMR: δ 4.18 (s, 2H, S-CH_2 - C-Se), 4.28 (s, 2H, CH_2), 7.02-7.14 (m, 2H, Ar-H). **14**: Yield 65% m.p. 131-33°C (Found C, 44.77; H, 2.65 $C_{12}H_8N_2S_2Se$ requires C, 44.58: H, 2. 49%); IR: 1452 (N=N) cm^{-1}; ^1H NMR: δ 4.21 (s, 2H, S-CH_2-C-Se), 4.29 (s, 2H, CH_2), 7.05-7.15 (m, 4H, Ar-H). **21**: Yield 60%, m.p. 143-45°C (Found C, 50.94; H, 3.30, $C_{16}H_{12}N_2S_2Se$ requires C, 51.20, H, 3. 22%); IR: 1438 (N=N) cm^{-1}, ^1H NMR: δ 2.98-3.12 (m, 4H, $2CH_2$), 4.24 (s, 2H, S-CH_2-C=C), 4.30 (s, 2H, Ar-S-CH_2-C=C), 7.00-7.12 (m, 4H, Ar-H). **22**: Yield 64%, m.p. 137-39°C (Found C,

51.42; H, 3.39, $C_{16}H_{12}N_2S_2Se$ requires C, 51.20; H, 3.22%); **IR**: 1440 (N=N) cm^{-1}; ^1H NMR: δ 2.85-3.02 (m, 4H, $2CH_2$), 4.25 (s, 2H, S-CH_2-C=C), 4.34 (s, 2H, Ar-CH_2-S-C=C), 6.95-7.03 (m, 4H, Ar-H).

Preparation of 1-thiadihydronaphthalen [3,4-*d*]1',2',3'-thiadiazole 7, 2-thiadihydronaphthalen [3,4-*d*]1',2',3'-thiadiazole 8, 4,9-dithiatetrahydrophenanthren [1,2-*d*] 1',2',3'-thiadiazole 15, 4,10-dithiatetrahydrophenanthren [1,2-*d*]1',2',3'-thiadiazole 16, D-homo-6, 11-dithia-1,3,5(10), 8,13(14)-gonapentaen [18,18a-*d*]1',2',3'-thiadiazloe 23, D-homo-7, 11-dithia-1,3,5(10), 8,13(14)-gonapentaen [18,18a-*d*] 1',2',3'-thiadiazole 24.

The semicarbazone 3/4/11/12/19/20 (0.0005 mole) was added portion-wise to thionyl chloride (1.5 ml) at ice-bath temperature and later kept for 1h at room temperature. Then dichloromethane (10 ml) was added and decomposed with ice-cold sodium carbonate solution. The organic layer was separated, washed with water (10 ml, 4-5 times) and dried over anhydrous sodium sulfate. Evaporation of the solvent furnished a gummy product which was solidified by treatment with cyclohexane. It was purified by recrystallization from ethanol to get a pure compound. 7: Yield 68%, m.p. 71-73°C (lit m.p. 72-75°C). 8: Yield 70%, m.p. 106-07°C (Found C, 52. 26; H, 2.80; $C_9H_6N_2S_2$ requires C, 52.40; H, 2.93%) **IR**: 1439 (N=N) cm^{-1}, ^1H NMR; δ 4.28 (s, 2H, CH_2) 7.02-7.15 (m, 4H,Ar-H). 15: Yield 65%, m.p. 101- 02° C (Found C, 51. 89; H, 2.79, $C_{12}H_8N_2S_3$ requires C, 52.14; H, 2.91%); **IR**: 1450 (N=N) cm^{-1}; ^1H NMR: δ 4.24 (s, 2H, S-CH_2-C-S), 4.27 (s, 2H, CH_2), 6.98-7.12 (m, 4H, Ar-H). 16: Yield 68%, m.p.114-15°C (Found C, 51.93; H, 2.82, $C_{12}H_8N_2S_3$ requires C, 52.14; H, 2.91%); IR: 1452 (N=N) cm^{-1}; ^1H NMR: δ 4.25 (s, 2H, S-CH_2-C-S), 4.31 (s, 2H, CH_2), 7.02-7.13 (m, 4H, Ar-H). 23: Yield 60% m.p. 112-13°C (Found, C, 58.70, H, 3.57; $C_{16}H_{12}N_2S_3$ requires C, 58.51; H, 3.68%); IR:1440 (N=N) cm^{-1}; ^1H NMR: δ 2.89-3.05 (m, 4H, $2CH_2$), 4.28 (s, 2H, S-CH_2-C=C), 4.34 (s, 2H, Ar-S-CH_2-C=C), 6.95-7.04 (m, 4H, Ar-H). 24: Yield 64%, m.p. 107-08°C (Found C, 58.40, H, 3.82; $C_{16}H_{12}N_2S_3$ requires C, 58.51; H, 3.68%); IR: 1450 (N=N) cm^{-1}; ^1H NMR: δ

2.91-3.09 (m, 4H, $2CH_2$), 4.25 (s, 2H, S-CH_2-C=C), 4.36 (s, 2H, Ar-CH_2-S-C=C), 6.98-7.08 (m, 4H, Ar-H).

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