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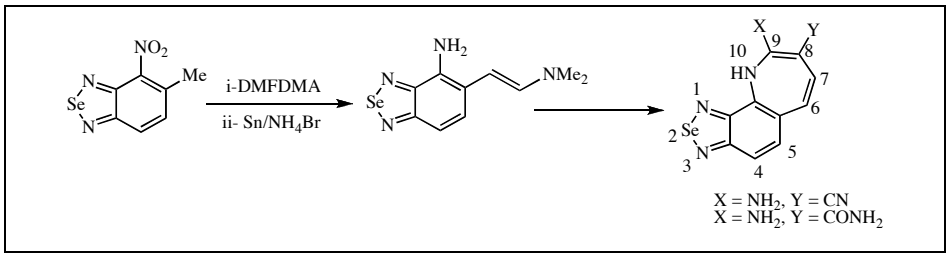

5-Methyl-4-nitro-2,1,3-benzoselenadiazole (**1**) was converted into (*E*)-5-(2-dimethylamino)vinylbenzo-[*c*](1,2,5)selenadiazole-4-amine (**4**) by initial treatment with dimethylformamide dimethyl acetal (DMFDMA) (2) followed by selective reduction using ammonium bromide in methanol. Compound **4** afforded the selenadiazolo[3,4-*i*][1]benzazepine derivatives (**7**, **10**, **13**, **15**) upon treatment with malononitrile (**5**), ethyl cyanoacetate (**8**) and cyanoacetamide (**11**) respectively.

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INTRODUCTION

In continuation of our interest in synthesizing new seven membered rings, with anticipated biological importance using nitriles [1] as a simple and cheap staring materials, this work describes the syntheses of selenadiazolobenzazepine derivatives starting from simple nitriles.

Azepine derivatives are weak modulators of ligand response in Gα-protein coupled α_{2A} adrenoceptors [2], also, in adrenoceptor identification [3], potent integrin receptor antagonist [4], allosteric modulators of musacrinic receptors [5], a new GABA uptake inhibitors [6].

This paper communicates the first preparation of selenadiazolobenzazepine derivatives with an illustration of their synthetic use en route to nitrogen heterocycles.

RESULTS AND DISCUSSION

Scheme I outlines the synthetic sequence employed in our laboratory for preparation of the key intermediate (*E*)-5-(2-dimethylamino)vinylbenzo[*c*][1,2,5]selenadiazole-4-amine (**4**).

The strategy for the synthesis of **4** was based on the condensation of 5-methyl-4-nitro-2,1,3-benzoselena-diazole **(1)** [7] with *N*,*N*-dimethylformamide dimethyl acetal (DMFDMA) (**2**) in DMF to give the *trans* isomer (*J* = 13.1 Hz) of enamine **3** [8] in 84% yield. The reduction of the nitro enamine **3** using ammonium bromide in methanol [9] under neutral conditions leads to the selective reduction of the nitro group leaving the double bond of the enamine intact. The reduction completion was monitored by TLC which gave a single spot after 10 hours. This approach leads to (*E*)-5-(2-methylamino)-vinylbenzo[*c*](1,2,5)selenadiazole-4-amine **(4)** in a good yield.

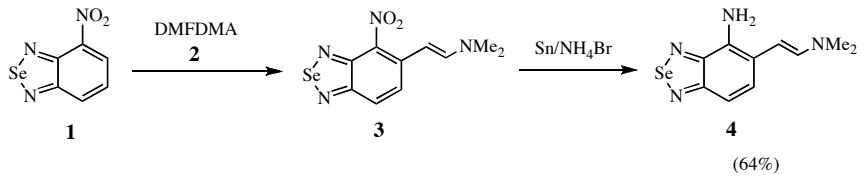
Treatment of **4** with active methylene compounds **5**, **8** and **11** in refluxing ethanol containing a catalytic amount of piperidine resulted in the formation of the unknown 1,2,5-selenadiazolo[3,4-*i*][1]benzazepine derivatives **7**, **10**, **13**, and **15** respectively (Scheme II). The formation of the selenadiazolo[3,4-*i*][1]benzazepine structure **7** was elucidated based on correct elemental analysis and spectral data. Thus ^{1}H-nmr spectrum of **7** shows the presence of two doublets at 6.33 and 7.7 ppm for H-6 and H-7 splitting each other, which is characteristic of the azepine structure.

Structure **10** was assigned for the product obtained by reaction of **4** with ethyl cyanoacetate (**8**) based on correct spectral data. ^{1}H-nmr revealed the presence of doublet-doublet signal for H-6 and doublet-triplet signal for H-7. Also, ^{13}C-nmr exhibits a signal at δ =168 ppm corresponding to amidic carbonyl function.

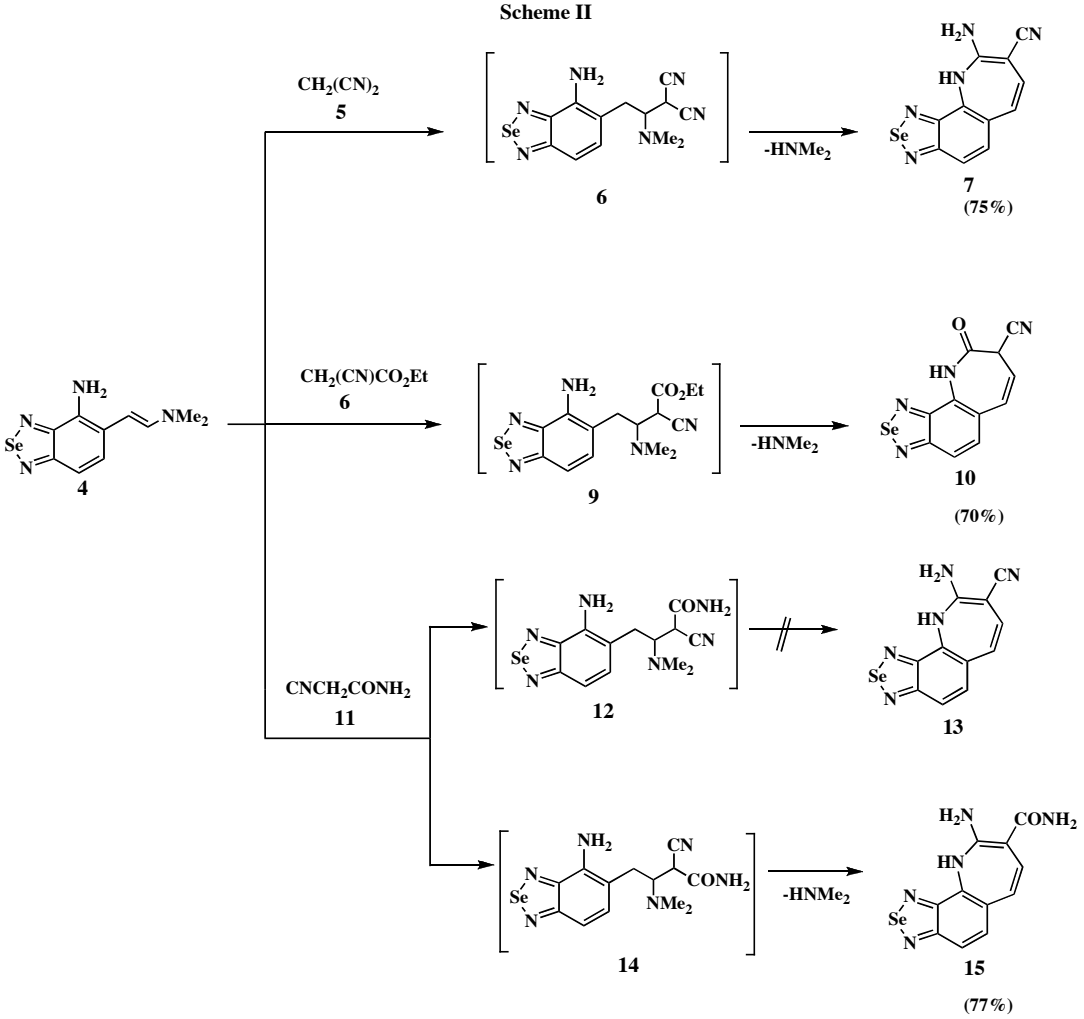
Two possible structures have been proposed for the reaction of **4** with cyanoacetamide. Structure **13** was eliminated based on correct elemental analysis and spectral data. IR spectrum shows the presence of absorption band at 1690 cm^{-1} which indicates the presence of amidic carbonyl function. Also, ^{13}C-nmr reveals the presence of a carbonyl signal at δ = 179 which is characteristic to structure **15**.

In conclusion, reaction of active methylene compounds with the (*E*)-5-(2-dimethylamino)vinylbenzo[*c*][1,2,5]-selenadiazole-4-amine (**4**) have been successfully applied. Since the azepine unit has important biological activity, we believe that access to selenadiazolobenzazepine

Scheme I



Scheme II



derivatives will find many applications for biological screening purposes.

EXPERIMENTAL

All melting points are uncorrected. IR spectra were recorded in KBr disks using a Shimadzu IR-740 spectrophotometer. ^{1}H- and ^{13}C-NMR spectra were recorded on a Bruker AC-300 spectrometer with [$^2H_6$]DMSO as solvent and TMS as internal standard; chemical shifts are reported in δ units (ppm). Mass spectra were measured on GCLMS INCOS XL Finnigan MAT. Microanalysis was performed on LECOCHNS-932.

5-Methyl-4-nitro-2,1,3-benzoselenadiazole (**1**). Prepared as in lit. [7] m.p.: 196-8 °C. ir (KBr): 3084, 1617, 1527, 1504, 1493, 1381 cm^{-1}. ^{1}H nmr (DMSO-d_6): δ 7.98 (d, 1H, *J* = 9.2, 7-H), 7.60 (d, 1H, *J* = 9.2, 6-H), 2.44 (s, 3H, Me). ^{13}C nmr (DMSO-d_6): δ 158.25, 150.63, 141.69, 131.92, 131.61, 125.46 (vinyle carbons), 16.99 (CH_3).

(*E*)-5-[2-(Dimethylamino)ethenyl-4-nitro-2,1,3-benzoselenadiazole (3). Prepared as in lit. [8] m.p. 186-7 °C, ir (KBr): 2919, 2802, 1620, 1599, 1484 cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 7.99 (d, 1H, *J* = 9.8, 7H), 7.92 (d, 1H, *J* = 13.1, 2'H), 7.68 (dd, *J* = 9.85, 0.5, 6-H), 5.41 (d, 1H, *J* = 13.1, 1'-H), 3.01 (s, 6H, *N*-Me).

(*E*)-5-[2-Dimethylamino)vinylbenzo[*c*][1,2,5]selenadiazolo-4-amine (4). A mixture of **3** (0.29g, 1mmol), and 30 mmol of tin metal (cut into small pieces) and ammonium bromide (20 mmol) in methanol (10 ml) were placed in a two necked 50 ml rbm and was stirred at atmospheric pressure and room temperature for 10 hours (TLC: petrol/EtOAc 1:1). After completion, the reaction was

quenched by adding little water and organic compound was extracted into diethyl ether (2 x 25 ml). The combined ether extract was washed with dil. HCl and neutralized with $NaHCO_3$ and was taken into ether. The ether part was dried and the solvent evaporated to get the pure product. The resulting solid was crystallized from isopropanol to give compound **4** as brown crystals, yield 64 %; m.p. 230 °C; ir (KBr): 3250 (NH_2), 1620, 1599 (C=N) cm^{-1}. ^1H nmr (DMSO-d_6): δ 7.98 (1H, d, *J* = 9.2, 7-H), 7.92 (1H, d, *J* = 13.1), 7.6 (1H, d, *J* = 9.2, 6 H), 5.41 (1H, d, *J* = 13.1), 4.8 (s, 2H, NH_2), 3.01 (6 H, s, N-Me). MS: m/z 264 (M^+) 100%. *Anal*. Calcd. For $C_{10}H_{12}N_4Se$: C, 44.95; H, 4.53; N, 20.97. Found: C, 44.81; H, 4.50; N, 21.10.

General procedure for the preparation of compounds 7, 10, 15, 18. To a solution of compound **4** (10 mmol) in ethanol (30 mL) containing piperidine (0.5 mL), was added (10 mmol) methylene compounds **5**, **8**, **11** or benzylidinemalononitrile **(16)** respectively. The reaction mixture was then heated under reflux for 6 hours. The reaction mixture was left to cool at room temperature and the deposited solid was collected by filtration to give compounds 7, **10**, **15** and **18** respectively.

9-Amino-10H-1,2,5-selenadiazolo[3,4-*i*][1]Benzazepine-8-carbonitrile (7). Compound **7** was obtained as yellow crystals from ethanol; yield 75%; m.p. 245°C; ir (KBr): 3350, 3250 (NH, NH_2), 2190 (CN), 1620, 1599 (C=N) cm^{-1}. ^1H nmr (DMSO-d_6): δ 9.6 (br s, 1H, NH), 8.35 (d, *J* = 8.8 Hz, 1H), 8.1 (d, *J* = 8.8, 1H), 7.7 (d, *J* = 7.9 Hz, 1H), 6.33 (d, 1H, *J* = 7.9, 1H), 4.85 (br s, 2H, NH_2). ^{13}C nmr (DMSO-d_6): δ 164.2, 160.5 (imin-carbons), 161.9, 135.8, 133.0, 129.8, 121.2, 120.3, 120, 61.7 (vinyl- carbons), 115.7 (CN). MS: m/z 288 (M^+) 100%. *Anal*. Calcd. For $C_{11}H_7N_5Se$: C, 45.85; H, 2.45; N, 24.30. Found: C, 45.66; H, 2.50; N, 24.23.

9-Oxo-9,10-dihydro-8*H*-1,2,5-selenadiazolo[3,4-*i*][1]benzazepine-8*H*-carbonitrile (10). Compound **10** was obtained as yellow crystals from ethanol; yield 70%; m.p. 233°C; ir (KBr): 3350 (NH), 2190 (CN), 1690 (C=O), 1620, 1599 (C=N) cm^{-1}. ^1H nmr (DMSO-d_6): δ 10.5 (br s, 1H, NH), 8.55 (d, *J* = 8.8 Hz, 1H), 8.1 (d, *J* = 8.8, 1H) 7.70 (d, *J* = 8.8 Hz, 1H), 6.33 (d, 1H, *J* = 5.1, 1H), 5.77 (1H, dd, *J* = 2.6 and 9.9, 7-H), 4.46 (1H, dt, *J* = 1.8 and 9.9, 6H).^{13}C nmr (DMSO-d_6): δ 168.0 (CO-amide), 164.0, 160.8 (imine-carbons), 133.6, 123.0, 125.0, 120.0, 119.0, 118.0 (vinyl-carbons), 115.0 (CN), 34.0 (CH-aliphatic). MS: m/z 289 (M^+) 100%. *Anal*. Calcd. For $C_{11}H_6N_4OSe$: C, 45.69; H, 2.09; N, 19.38. Found: C, 45.66; H, 2.00; N, 19.43.

9-Amino-1,2,5-selenadiazolo[3,4-*i*][1]Benzazepine-8-carboxamide (15). Compound **15** was obtained as yellow crystals form Ethanol/DMF; yield 77%; m.p. 254°C; ir (KBr): 3380, 3300 (NH, NH_2), 1690 (CO-amide), 1590 (C=N) cm^{-1}. ^1H nmr (DMSO-d_6): δ 9.8 (br s, 1H, NH), 8.35 (d, *J* = 8.8 Hz, 1H), 8.1 (d, *J* = 8.8, 1H), 7.51 (d, *J* = 7.9 Hz, 1H), 6.33 (d, 1H, *J* = 7.9, 1H), 4.88 (br s, 2H, NH_2). ^{13}C nmr (DMSO-d_6): δ 172.0 (CO-amide), 164.8, 160.00 (imine-carbons), 153.00, 136.00, 136.00, 122.0, 121.50, 121.00 120.00, 87.00 (vinyle- carbons). MS: m/z 307 (M^+) 100%. *Anal*. Calcd. For $C_{11}H_9N_5OSe$: C, 43.15; H, 2.96; N, 22.87. Found: C, 43.46; H, 2.91; N, 22.63.

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