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Synthesis and Spectral Analysis of Some 4-Substituted-5,7-diarylpyridino[3,4-d]-1,2,3-selenadiazoles

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Several novel 5,7-diarylpyridino[3,4-d]-1,2,3-selenadiazoles (**1-6**) are prepared from their respective semicarbazones of 2,6-diarylpiperidin-4-ones. The products are analyzed by IR, ^{1}H, ^{13}C NMR studies and C, H, N analysis by comparing the parent selenadiazole (**1**) which is prepared from the semicarbazone of 2,6-diphenylpiperidin-4-one. Similarly a set of 5,7-diaryl-4-methylpyridino[3,4-d]-1,2,3-selenadiazoles (**7-13**), 5,7-diaryl-4-ethylpyridino[3,4-d]-1,2,3-selenadiazoles (**14-19**) and 5,7-diaryl-4-isopropylpyridino[3,4-d]-1,2,3-selenadiazole (**20-25**) are synthesized and characterized.

Key Words: Selenadiazoles, Semicarbazones, Piperidones, Spectral studies.

INTRODUCTION

Most of the organoselenium compounds[1] are known to be toxic in nature. However, the essential role of selenium in the animal body has been reported[2]. The 1,2,3-selenadiazoles and 1,2,5-selenadiazoles have potent antibacterial and antiviral activity[3,4]. Synthesis and spectral studies of 1,2,5-selenadiazolo-[3,4-d]pyridines from 2,3-diaminopyridines are well documented[5]. But the synthesis of 1,2,3-selenadiazolo[3,4-d]pyridines from diaminopyridines are not possible. The only available method for this synthesis is conversion of semicarbazone of respective piperidin-4-one into selenadiazolo[3,4-d]-pyridines by selenium dioxide in acetic acid medium[5]. Hence, it prompted us to synthesis some substituted 1,2,3-selenadiazoles from the semicarbazones of 3-substituted-2,6-diphenylpiperidin-4-ones.

EXPERIMENTAL

The elemental analysis was done on a Heraeus-C, H, N rapid analyzer. IR spectra were recorded in Jasco-700 infrared spectrometer using KBr pellets. ^{13}C NMR spectra were recorded on a DRX 500 and AMX 400 spectra

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operating at 125.7 and 100 MHz, respectively using 10 mm sample tubes. Solution for the measurement of spectra were prepared by dissolving 0.5 of the sample in 2.5 mL of chloroform-d containing 1 % TMS and acetone-d. All the chemical shift values are with reference to TMS.

Proton NMR spectra were recorded on a DRX 500 NMR and AMX 400 NMR spectrometer operating at 500 and 400 MHz, respectively. Samples were prepared by dissolving about 10mg of sample in 0.5 mL of acetone and chloroform-d containing 1 % TMS. All the chemical shifts are with reference to TMS.

The column was packed with silica gel (100-200 mesh) in hexane (1:50: compound:silica gel). The eluting solvents were benzene, benzene-chloroform (4:1). The separated compounds were checked with co-TLC. The compounds were found to be separated in benzene-chloroform (4:1).

Preparation of 3-substituted-2,6-diarylpiperidin-4-ones: The 2,6-diarylpiperidones were prepared following the procedure adopted by Noller and Baliah[6]. Ammonium acetate (100 mmol), benzaldehyde (200 mmol) and appropriate ketone (200 mmol) were dissolved in 95 % alcohol (80 mL) and the solution was heated on a hot plate with gentle swirling until the colour of the mixture changed to orange. The mixture was cooled and poured into ether (100 mL) and concentrated hydrochloric acid (14 mL) was added. The precipitated 2,6-diarylpiperidin-4-one hydrochloride was collected by filtration and re-crystallization from ethanol-ether. The hydrochloride was dispersed in acetone and concentrated ammonia was added drop-wise until a clear solution was obtained. The clear solution was poured into cold water and the solid precipitated was collected and crystallized from ethanol. The observed melting points are in excellent agreement with those of the reported ones.

Preparation of semicarbazone (B-1 to B-25): A mixture of respective 2,6-diarylpiperidin-4-one (1 g, 0.0027 mol), semicarbazide hydrochloride (0.316, 0.0027 mol) and sodium acetate (0.750 g) in ethanol (40 mL) was refluxed for 2 h on a steam bath and cooled. The separated solid was filtered, washed with water and re-crystallized from ethanol.

Preparation of 4-substituted-5,7-diarylpyridino[3,4-d]-1,2,3-selenadiazoles (1-25): The method of Reddy *et al.*[7] was adopted to prepare these compounds. Appropriate semicarbazone (0.500 g, 0.0012 mol) was treated with selenium dioxide (0.135 g, 0.0012 mol) in glacial acetic acid (20 mL) and the mixture was gently heated (50-60 ºC) with stirring until the evolution of gas ceased. The reaction mixture was cooled, filtered and then poured into crushed ice. The product obtained was subjected to column chromatography. The analytical data of the synthesized compounds **1-25** is given in Table-1.

TABLE-1
ANALYTICAL DATA OF 1,2,3-SELENADIAZOLES DERIVATIVES (**1-25**)

Compd.	m.f. / (m.w.)	m.p. (ºC) / Yield (%)	R	X	Elemental analysis (%): Found (Calcd.)		
					C	H	N
1	$C_{17}H_{11}N_3Se$ / (336.25)	123 / (20)	H	H	60.40 (60.67)	3.17 (3.27)	12.20 (12.49)
2	$C_{17}H_9N_3Cl_2Se$ / (405.14)	127-128 / (17)	H	*p*-Cl	50.09 (50.35)	2.11 (2.22)	10.03 (10.36)
3	$C_{17}H_9N_3Cl_2Se$ / (405.14)	111-112 / (22)	H	*o*-Cl	50.13 (50.35)	2.15 (2.22)	10.10 (10.36)
4	$C_{19}H_{15}N_3Se$ / (364.30)	130-131 / (23)	H	*p*-Me	62.41 (62.56)	4.02 (4.12)	11.30 (11.52)
5	$C_{17}H_9N_5O_4Se$ / (426.24)	140-143 / (21)	H	*m*-NO_2	47.53 (47.86)	2.01 (2.11)	16.20 (16.42)
6	$C_{17}H_9N_5O_4Se$ / (426.24)	147-149 / (18)	H	*p*-NO_2	47.60 (47.86)	2.09 (2.11)	16.25 (16.42)
7	$C_{18}H_{13}N_3Se$ / (350.28)	110 / (40)	CH_3	H	61.53 (61.66)	3.60 (3.71)	11.47 (11.99)
8	$C_{18}H_{11}N_3Cl_2Se$ / (419.17)	117 / (36)	CH_3	*p*-Cl	51.33 (51.53)	2.52 (2.62)	9.89 (10.02)
9	$C_{18}H_{11}N_3Cl_2Se$ / (419.17)	123 / (39)	CH_3	*o*-Cl	51.39 (51.53)	2.58 (2.62)	9.96 (10.02)
10	$C_{20}H_{17}N_3Se$ / (378.33)	129 / (33)	CH_3	*p*-Me	63.30 (63.43)	4.38 (4.49)	11.01 (11.10)
11	$C_{20}H_{17}N_3O_2Se$ / (410.33)	125 / (35)	CH_3	*p*-OMe	58.52 (58.49)	4.16 (4.14)	10.27 (10.23)
12	$C_{18}H_{11}N_5O_4Se$ / (440.27)	133 / (30)	CH_3	*m*-NO_2	49.10 (49.06)	2.52 (2.50)	16.03 (15.99)
13	$C_{18}H_{11}N_5O_4Se$ / (440.27)	139 / (27)	CH_3	*p*-NO_2	49.03 (49.06)	2.41 (2.50)	15.91 (15.99)
14	$C_{19}H_{15}N_3Se$ / (364.30)	94 / (40)	C_2H_5	H	62.40 (62.58)	4.02 (4.11)	11.38 (11.53)
15	$C_{19}H_{13}N_3Cl_2Se$ / (433.19)	100 / (28)	C_2H_5	*p*-Cl	52.60 (52.63)	2.90 (3.0)	9.60 (9.69)
16	$C_{19}H_{13}N_3Cl_2Se$ / (433.19)	108 / (32)	C_2H_5	*o*-Cl	52.61 (52.63)	2.93 (3.0)	9.36 (9.69)
17	$C_{21}H_{19}N_3Se$ / (392.36)	106 / (37)	C_2H_5	*p*-Me	64.28 (64.22)	4.88 (4.84)	10.73 (10.70)
18	$C_{21}H_{19}N_3O_2Se$ / (424.35)	117 / (29)	C_2H_5	*p*-OMe	59.25 (59.38)	4.40 (4.47)	9.82 (9.89)
19	$C_{19}H_{13}N_5O_4Se$ / (454.30)	125 / (36)	C_2H_5	*m*-NO_2	50.09 (50.18)	2.80 (2.86)	15.35 (15.40)
20	$C_{20}H_{17}N_3Se$ / (378.33)	102 / (30)	$(CH_3)_2CH$	H	63.20 (63.43)	4.22 (4.44)	11.02 (11.01)
21	$C_{20}H_{15}N_3Cl_2Se$ / (447.22)	109 / (20)	$(CH_3)_2CH$	*p*-Cl	53.41 (53.66)	3.27 (3.35)	9.30 (9.39)
22	$C_{20}H_{15}N_3Cl_2Se$ / (447.22)	112 / (22)	$(CH_3)_2CH$	*o*-Cl	53.42 (53.66)	3.29 (3.35)	9.32 (3.39)
23	$C_{22}H_{21}N_3Se$ / (406.38)	119 / (36)	$(CH_3)_2CH$	*p*-Me	64.78 (64.96)	5.08 (5.17)	10.20 (10.34)
24	$C_{22}H_{21}N_3O_2Se$ / (438.38)	124 / (33)	$(CH_3)_2CH$	*p*-OMe	60.20 (60.22)	4.75 (4.79)	9.55 (9.58)
25	$C_{20}H_{15}N_5O_4Se$ / (468.32)	133 / (27)	$(CH_3)_2CH$	*m*-NO_2	51.12 (51.24)	3.18 (3.20)	14.90 (14.94)

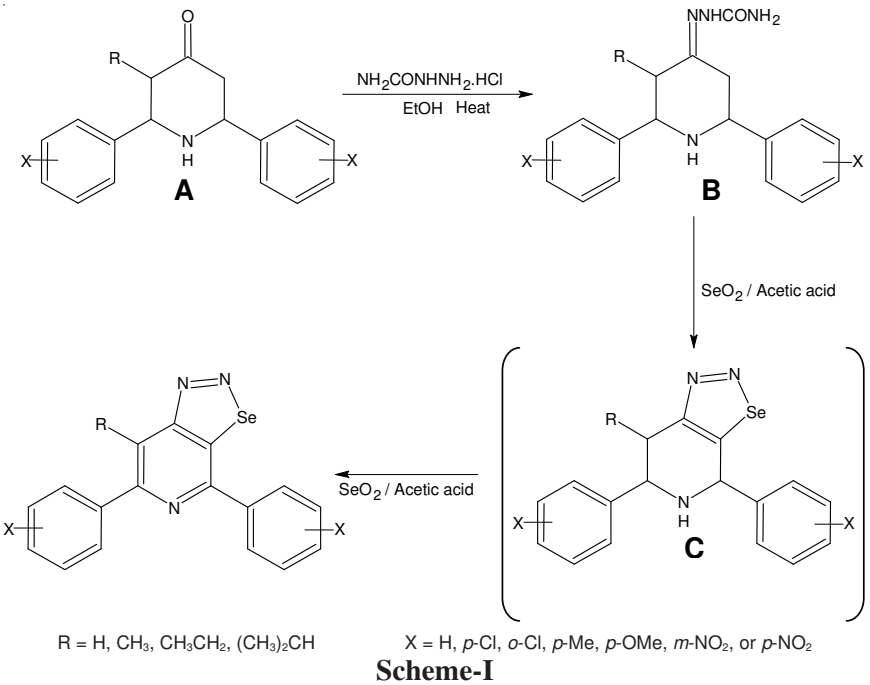
The compounds show characteristic absorption for aromatic C-H stretching, aliphatic C-H stretching C=C ring stretching and C=C ring stretching. The IR spectral values of selenadiazoles are given in Table-2.

TABLE-2
IR SPECTRAL DATA OF 1,2,3-SELENADIAZOLES (**1-25**)

Compd.	Aromatic (C-H *str*. (cm^{-1})	Aliphatic (C-H *str*. (cm^{-1})	C=C *str*. (cm^{-1})	C=N *str*. (cm^{-1})
1	3050	2910	1628	1452
2	3048	2923	1648	1456
3	3040	2923	1645	1457
4	3039	2922	1617	1457
5	3052	2911	1620	1450
6	3045	2927	1633	1451
7	3010	2950	1703	1440
8	3008	2924	1702	1457
9	3012	2923	1734	1458
10	3015	2923	1682	1417
11	3011	2926	1698	1459
12	3008	2925	1652	1460
13	3014	2925	1654	1462
14	3014	2900	1650	1442
15	3006	2928	1654	1416
16	3068	2933	1659	1439
17	3032	2927	1659	1416
18	3005	2928	1717	1438
19	3050	2926	1718	1435
20	3022	2912	1702	1445
21	3047	2930	1715	1442
22	3067	2961	1717	1459
23	3029	2963	1717	1463
24	3042	2959	1703	1406
25	3078	2961	1710	1460

RESULTS AND DISCUSSION

4-Substituted-5,7-diarylpyridino[3,4-d]-1,2,3-selenadiazoles are synthesized from the semicarbazones of various 3-substituted-2,6-diarylpiperidin-4-ones by the action of selenium dioxide in acetic acid *via* the formation of the intermediate C as shown in **Scheme-I**. The products are analyzed by IR, ^{1}H, ^{13}C NMR studies and C, H, N studies. It is expected that the compound C is formed from its respective semicarbazone (**B**) and undergoes dehydrogenation by SeO_2 to give selenadiazoles. The stoichiometry (1:2::semicarbazone:SeO_2) of the reaction is also supported by the formation of the selenadiazoles. The attempts to isolate C for all substituents are unsuccessful. A mechanism proposed by Lalezari *et al.*[8] has been adopted for the formation of selenadiazoles.



Scheme-I

5,7-Diarylpyridino[3,4-d]-1,2,3-selenadiazoles (1-6)

^{13}C NMR data: In compounds **2-6**, the chemical shifts are assigned for respective carbons by comparing[9] with that of compound **1**. The signal for C-4 carbon can be easily distinguished from other carbons based on their intensities. Thus, the upfield signal in the region of 112.48-114.93 ppm is assigned to C-4 carbon. In aromatic systems, introduction of nitrogen containing substituents is expected to shield the *ortho* carbon. Among the remaining signals, the upfield signal in the region of 134.81-137.63 ppm is assigned to C-8 carbon. The downfield signal in the region of 165.68-168.47 ppm is due to the C-9 carbon, because it is directly attached to the more electronegative atom nitrogen. Based on the substituent effects, the down field signals in the region of 153.36-156.99 ppm and 154.91-158.23 ppm are assigned to C-5 and C-7, respectively. The chemical shift values in the region of 140.46-143.74 ppm and 138.1-140.64 ppm are due to the *ipso* carbons of the phenyl rings attached at C-5 and C-7 positions are having good agreement with the *ipso* carbon chemical shift values of 2,6-diphenyl-piperidin-4-one[10]. The C-7 carbon is at downfield when compared to C-5 carbon because it is nearer to a five membered ring system. So the signal in the region of 140.46-143.74 ppm is assigned to the ipso carbon attached to C-7 carbon and the other signal between 138.1-140.64 ppm is assigned to C-5. The other chemical shift values in the region of 125.70-132.81 ppm

are assigned to the aromatic carbons in the phenyl rings. For compound **4**, the methyl carbon in the *para* position of the phenyl ring appears at 21.49 ppm.

^{1}H NMR data: For compounds **2-6**, the signals are assigned for respective carbons by comparing[9] with that of compound **1**. A singlet observed around 8.9 ppm is due to the H-4 proton. A multiplet appear between 6.75-8.4 ppm is due to the aromatic protons in the phenyl rings. For compound **4**, the methyl protons give a sharp peak around 2.3 ppm.

5,7-Diaryl-4-methylpyridino[3,4-d]-1,2,3-selenadiazoles (7-13)

^{13}C NMR data: For compounds **8-13**, the signals are assigned for respective carbons by comparing with that of compound **7**. The signal in the range of 17.29-17.95 ppm is assigned to methyl carbon at C-4. Introduction of an alkyl group at C-4 is expected to affect the chemical shifts of C-4 and nearby carbons. Based on the a effect, the methyl group at C-4 appears between 125.60-127.91 ppm. For the carbons C-8 and C-9, the signal between 165.44-168.21 ppm is assigned to C-9 carbon, since it is directly attached to more electronegative atom nitrogen. Hence the other value in the region of 135.00-136.94 ppm is assigned to C-8 carbon. The signals in the region of 151.05-153.08 ppm and 154.35-159.69 ppm are assigned for the C-5 and C-7 carbons, respectively. The signals in the range of 140.07-143.86 ppm and 138.88-140.03 ppm correspond to the *ipso* carbons of the two phenyl rings at C-7 and C-5 carbons. The methyl carbons in the phenyl ring appear at 21.05 and 20.92 ppm due to the different orientation of the phenyl ring. The CH_3 group in the C-4 position limits the rotation of the phenyl ring. For compound **11**, the methoxy group in the phenyl rings merged due to the fast rotation of the phenyl rings on NMR scale. So a single line is observed at 55.40 ppm. The other signals in the region of 127.41-133.40 ppm are due to the aromatic carbons in the phenyl rings.

^{1}H NMR data: In compounds **8-13**, the chemical shifts are assigned for respective carbons by comparing with that of compound **7**. A sharp peak in the region of 2.9-3.1 ppm is due to the methyl proton at C-4 carbon. A multiplet in the region of 7.0-8.2 ppm is due to the aromatic protons in the phenyl rings. For compound **10**, a singlet observed at 2.3 ppm is due to the methyl protons in the *para* position of the phenyl ring. For compound **11** a singlet observed at 3.8 ppm is assigned for the methoxy protons in the *para* position of the phenyl ring.

5,7-Diaryl-4-ethylpyridino[3,4-d]-1,2,3-selenadiazoles (14-19)

^{13}C NMR data: The signals for compounds **15-19** are assigned by comparing the chemical shift values with that of compound **14**. The signal in the range of 23.60-24.79 ppm is assigned to methylene carbon and the signal in the region of 16.38-18.36 ppm is assigned to methyl carbon of

ethyl group. The signals at 152.28-153.32 ppm and 156.25-158.78 ppm are due to C-5 and C-7 carbons. As expected, there is no appreciable difference in chemical shifts between compounds **7-13** and **14-19**. The upfield signal in the region of 135.86-138.14 ppm is assigned to C-8 carbon and the signal between 164.45-167.93 ppm is obviously due to C-9 carbon. The absorption in the range of 132.31-134.92 ppm is due to C-4 carbon. The chemical shifts in the region of 141.25-143.46 ppm and 139.34-142.57 ppm are due to ipso carbons of the phenyl ring carbons. The chemical shift values between 125.87-133.07 ppm are due to the aromatic carbons of the phenyl rings. For compound **17**, two signals are obtained at 21.54 and 21.59 ppm for the methyl group in the phenyl ring. This is due to the different orientation adopted by the phenyl rings. The bulky ethyl group controls the free rotation of phenyl rings. For compound **18**, two signals is obtained at 55.10 and 55.12 ppm, which correspond to the methoxy protons in the phenyl rings. This is also due to the difference in the orientation of the phenyl rings. The bulky ethyl group limits the free rotation of phenyl rings.

^{1}H NMR data: In compounds **15-19**, the chemical shifts are assigned for respective carbons by comparing with that of compound **14**. Due to the splitting by neighboring methyl group, a quartet is observed for methylene protons in the region of 3.01-3.76 ppm. However, for methyl protons, due to diastereomeric nature of methylene protons a multiplet is observed in the region of 1.27-1.76 ppm. A multiplet between 6.71-9.07 ppm is due to the aromatic protons of the phenyl rings. For compound **17**, two signals appear clearly at 2.45 and 2.49 ppm for the methyl protons in the phenyl rings. Similarly for compound **18**, two signals appear in the region of 4.17 and 4.24 ppm due to the methoxy protons in the *para* positions of the phenyl rings. This is due to the different orientation of the phenyl rings.

5,7-Diaryl-4-isopropylpyridino[3,4-d]-1,2,3-selenadiazoles (20-25)

^{13}C NMR data: The assignment of signals is also carried out by comparing the chemical shifts with that of compound **20**. Introduction of a bulky isopropyl group at C-4 position alters the chemical shifts of C-4 as expected. Because of the isopropyl group at C-4, in compounds **20-25**, the C-4 is more deshielded when compared to the C-4 carbon of compound **1**. So the signal in the range of 138.11-139.66 ppm is assigned to C-4. The signals between 151.85-152.20 ppm and 156.55-158.63 ppm are due to the C-5 and C-7 carbons, respectively. For other carbons there is no appreciable difference in the chemical shifts, when compared with that of compound **1**. The signals between 135.56-137.86 ppm and 162.02-168.93 ppm are obviously due to C-8 and C-9 carbons, respectively. The signal in the region of 29.68-31.8 ppm corresponds to methine carbon and the signal in the region of 23.10-23.8 ppm corresponds to -$(CH_3)_2$ carbons. The chemical

shift values in the region of 141.19-143.33 ppm and 140.11-142.55 ppm are assigned to ipso carbons. The chemical shift values in the region of 124.85-131.57 ppm are due to the aromatic carbons of the phenyl ring. For compound **23**, two signals appear at 21.87 and 21.72 ppm for the methyl group in the *para* position of the phenyl rings. Similarly, two peaks appear at 55.50 and 55.72 ppm for the methoxy protons in the *para* position of the phenyl ring. This is due to the different orientation of the phenyl rings.

^{1}H NMR data: In compounds **21-25**, the signals are assigned for respective carbons by comparing with that of compound **20**. A doublet is observed for -$(CH_3)_2$ group between 0.9-1.0 ppm where as a multiplet is observed in the region of 3.5-3.7 ppm for methine protons. A multiplet is observed in the region of 6.62-7.97 ppm and this corresponds to the aromatic protons of the phenyl ring. For compound **23**, two signals appear at 2.32 and 2.35 ppm. This is due to the different orientation adopted by the phenyl rings. For compound **24**, the signals are found to merged and appear at 3.83 ppm.

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REFERENCES

1. K.W. Frank, *J. Nutr.*, **8**, 597 (1934).
2. K. Schwarz and C.M. Foltz, *J. Am. Chem. Soc.*, **79**, 3292 (1957).
3. H. Mirshamsi, I. Lalezari, M. Kamali, G. Niloufari and N. Rezvani, *Arch. Virusforch.*, **29**, 267 (1970).
4. I. Lalezari and A. Vahdat, *J. Med. Chem.*, **14**, 59 (1971).
5. F. Kurzer, in ed.: J.C. Barret, Thiadiazoles and Selenadiazoles, in Aliphatic Organo-Sulphur Compounds, Compounds with Exocyclic Sulphur Functional Groups, and Their Selenium and Tellurium Analogues, Academic Press, New York (1978).
6. C.R. Noller and V. Baliah, *J. Am. Chem. Soc.*, **70**, 3853 (1948).
7. D.B. Reddy, M.V.R. Reddy and V. Padmavathy, *Indian J. Chem.*, **36B**, 923 (1997).
8. I. Lalezari, A. Shafiee and S. Yalpani, *Tetrahedron. Lett.*, **58**, 5105 (1969).
9. N.M.D. Brown and P. Bladon, *Tetrahedron*, **24**, 6577 (1968).
10. V. Suganya, Ph.D. Thesis, Annamalai University, Annamalai Nagar, India (1999).

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