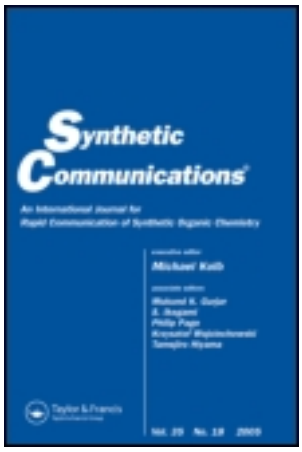

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1,4-PENTADIEN-3-ONES. A SOURCE FOR SELENANO 1,2,3- SELENA AND THIADIAZOLES

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1,4-PENTADIEN-3-ONES. A SOURCE FOR SELENANO 1,2,3-SELENA AND THIADIAZOLES

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ABSTRACT

The 4-Selenanols (**2,3**) and 4-selenanones (**4**) were obtained by the reaction of 1,4-pentadien-3-ones (**1**) with sodium hydrogen selenide under different conditions. The fused 1,2,3-selenadiazoles (**6**) and 1,2,3-thiadiazoles (**7**) were prepared from **4** on oxidative cyclization with SeO_2 and Hurd–Mori reaction with $SOCl_2$.

In continuation of our interest on the incorporation of heteroatoms as part of six-membered cyclic ketones which were the source for fused heterocycles,[1–3] we extended our studies to 4-selenanones. The present communication deals with the results obtained in such processes.

By refluxing an equimolar mixture of 1,5-diphenyl-1,4-pentadien-3-one (**1a**) with sodium hydrogen selenide, generated *in situ* from selenium and sodium borohydride in 1 : 2 ratio under nitrogen atmosphere and

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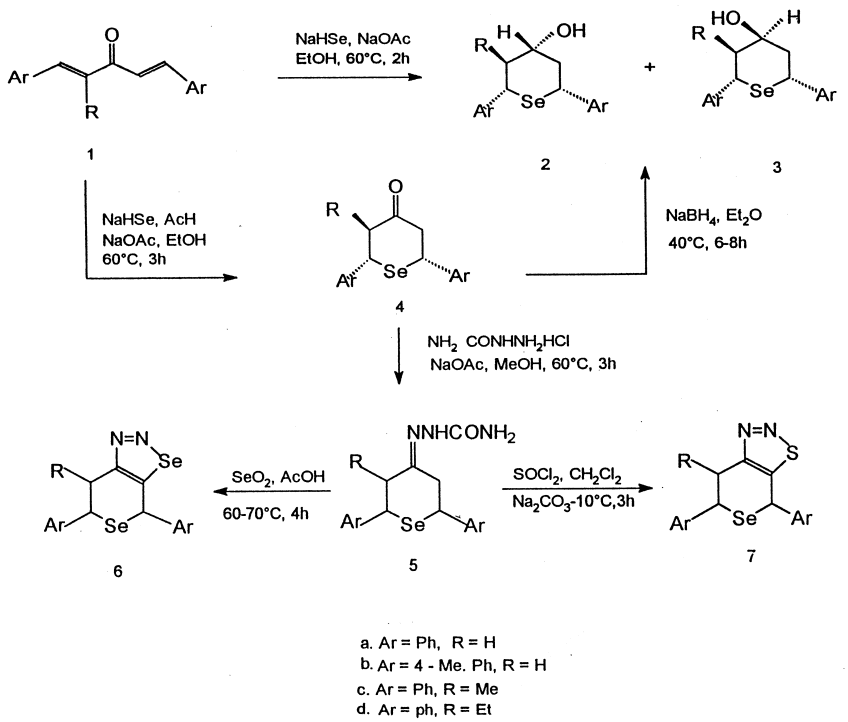
sodium acetate gave 4-selenanols (**2a**) and (**3a**) over 80% yield (Scheme). The **2** with equatorial -OH was found to be a major product (~70%) while **3** with axial -OH was separated as a minor one (~15%). Repetetion of this work with 1,5-diaryl-1,4-pentadien-3-ones **1b–d** resulted only **2** as major and **3** as minor products.

Earlier, 4-selenanones were prepared by doping selenium into 1,5-diaryl-1,4-pentadien-3-ones using hydrogen selenide, which was generated *in situ* from aluminium selenide.[4] This reagent was not found to be conve-



Scheme.

nient due to the poisonous character, unpleasant odour and instability.[5] Furthermore, the generation of hydrogen selenide from aluminium selenide was slow inspite of refluxing the reaction mixture for longer times.

In order to overcome these problems, sodium hydrogen selenide generated from selenium and sodium borohydride has been used. The reaction of **1** with sodium hydrogen selenide in the presence of sodium acetate under

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nitrogen atmosphere gave a mixture of products. The latter were separated and were identified as epimeric 4-selenanols (**2** and **3**) instead of the expected 4-selenanones (**4**) by spectral parameters. Then, the reaction was monitored at frequent intervals to ascertain whether doping of selenium or the reduction of keto group under priority. Had it been the reduction, the resultant 1,5-diaryl-1,4-pentadien-3-ol has no conjugation and hence cyclization would not be effective. On the other hand, if cyclization took place first, the resultant 4-selenanone may undergo reduction with excess sodium borohydride present in the reaction mixture, thus leading to only 4-selenanols. Indeed, 4-selenanone on reduction with lithium aluminium hydride gave 4-selenanols almost in similar ratio.[6,7]

The configuration and conformations of 4-selenanols was assigned on the basis of ^{1}H NMR (Figure 1). In **2a** the methine protons at C-2 and C-6 showed a doublet of doublet at 4.32 ppm. Further, two double doublets observed at 2.58 and 2.19 were due to axial and equatorial methylene protons at C-3 and C-5 whereas the proton at C-4 showed a multiplet in the region 3.66–3.88 ppm. These observations are contrary to the earlier values.[6,7] The hydroxylic proton at C-4 exhibited a broad singlet at 1.49 ppm. On the other hand the ^{1}H NMR spectrum of **3a** displayed two multiplets for methine (C-2 and C-6) and methylene (C-3 and C-5) protons at 4.65–4.78 and at 2.18–2.36 ppm. A broad singlet at 4.20 was observed for the proton at C-4 and the hydroxyl proton showed a multiplet in the region 1.62–1.84 ppm. Thus, the ^{1}H NMR spectra of the epimeric 4-selenanols indicate that an axial hydroxyl group was found to deshield the diaxial protons at C-2 and C-6 by $\sim$0.25–0.35 ppm.

In order to confirm the reaction process, the excess sodium borohydride present in the ethanolic solution of sodium hydrogen selenide was decomposed by adding acetaldehyde dropwise. When the resultant sodium hydrogen selenide in ethanol was used the product obtained was only 4-selenanone (**4**). The latter when subjected to reduction with sodium borohydride gave **2** and **3** in almost same ratio as obtained from **1**.

In fact the α-keto methylene functionality in **4** was primarily responsible for the formation of annelated bicyclic systems. This has been accomplished by the oxidative cyclization of the semicarbazones of **4** (**5**) with

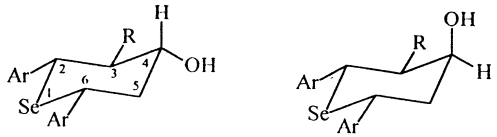

Figure 1.

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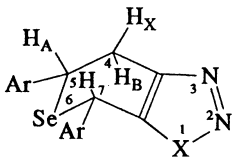

Figure 2.

selenium dioxide and thionyl chloride to obtain 5,7-diaryl(-4-alkyl)selenano[3,4-*d*][1,2,3]selenadiazole/thiadiazole (**6**/**7**). The IR spectra of **6** and **7** showed absorption bands in the regions 1460–1478, 683–707 cm^{-1} for N=N and C-Se/S groups, respectively. In the ^1H NMR of **6a** and **7a** the ring protons of selenacyclohexene moiety showed ABX splitting pattern. The H_A at C-5, H_B and H_x at C-4 appeared as doublet of doublets due to their geminal and vicinal couplings. Apart from this, a sharp singlet was observed for the proton at C-7. This splitting pattern confirms the puckering nature of the selenan ring when it is fused with selenadiazole or thiadiazole moieties (Figure 2).

In the mass spectra of **6a** and **7a** moderate intense M^+ peaks were observed at 404 and 357 corresponding to their chemical composition, $C_{17}H_{14}N_2Se_2$ and $C_{17}H_{14}N_2SSe$, respectively. In both the compounds an ion at *m*/*z* 297 was observed which might be due to expulsion of N_2 and Se/S. The phenylacetylene radical cation (*m*/*z* 101) appeared as base peak in both the systems.

In conclusion we have developed a one-pot reaction for the synthesis of 4-selenanols and a new reagent for doping selenium into 1,5-diaryl-1,4-pentadien-3-ones. The selena and thiadiazole rings were developed on 4-selenanones by exploiting α-keto methylene group in the latter compounds.

EXPERIMENTAL

Melting points were determined on a Mel–Temp apparatus and are uncorrected. IR spectra (KBr disc) were recorded on a Beckmann IR-18 Spectrophotometer. NMR Spectra were recorded in $CDCl_3$/DMSO-d_6 using 200 MHz on a varian EM-360 Spectrophotometer, all chemical shifts were reported in ppm from TMS as an internal standard. The mass spectra were recorded on Jeol JMS-D 300 instrument at 70 eV. Elemental analyses were obtained from RSIC, Punjab University, Chandigarh, India.

The starting materials, 1,5-diaryl-1,4-pentadien-3-ones (**1a**, **b**) and 1,5-diaryl-2-alkyl-1,4-pentadien-3-ones (**1c**, **d**) were prepared as per the literature procedure.[2]

2,6-Diaryl(-3-alkyl)-4-selenanols (2 and 3)

General procedure: To a well stirred suspension of selenium powder (1.39 g, 12.5 mmol) in 15 mL ethanol at room temperature, sodium borohydride (0.93 g, 25 mmol) in ethanol (20 mL) was added dropwise. Soon a vigorous reaction sets in with the evolution of hydrogen gas. After few minutes a colourless solution of sodium hydrogen selenide was formed to which 1,5-diaryl-1,4-pentadien-3-one (15 mmol) and sodium acetate (1.0 g) dissolved in absolute ethanol (25 mL) was added and refluxed for 2 h on a water bath. After completion of the reaction, the solution was cooled and kept in an ice box overnight. The solid separated was filtered and recrystallized from a mixture of benzene and *n*-hexane (1 : 1). This is a major product **2**. The filtrate on concentration gave a syrupy substance which was filtered through a column of silica gel to furnish **3**.

2a: Yield 76%; m. p. 176–177°C; IR ν_{max} (cm^{-1}) 3380, 1030; ^{1}H NMR δ: 1.49 (d, 1H, OH), 2.19 (dd, 2H, H_{ax}-3 and 5, $J = 12.9$ and 13.8), 2.58 (dd, 2H, H_{eq}-3 and 5, $J = 3.4$ and 13.8), 3.66–3.88 (m, 1H, H-4), 4.32 (dd, 2H, H-2 and 6, $J = 3.4$ and 12.9), 7.20–7.80 (m, 10H, H_{arom}); MS *m*/*z* 318, 316, 300, 237. **2b**: Yield 64%; m. p. 205–206°C; IR ν_{max} (cm^{-1}) 3362, 1026; ^{1}H NMR δ: 1.64 (d, 1H, OH), 2.14 (dd, 2H, H_{ax}-3 and 5, $J = 11.5$ and 17.6), 2.58 (dd, 2H, H_{eq}-3 and 5, $J = 3.8$ and 17.6), 2.32 (s, 6H, CH_3), 3.71–3.86 (m, 1H, H-4), 4.90 (dd, 2H, H–2 and 6, $J = 3.8$ and 11.5), 6.95–7.55 (m, 8H, H_{arom}). **2c**: Yield 65%; m.p. 158–159°C; IR ν_{max} (cm^{-1}) 3410, 1040; ^{1}H NMR δ: 0.84 (d, 3H, CH_3), 1.68 (d, 1H, OH), 2.20 (dd, 1H, H_{ax}-5 , $J = 12.5$ and 16.4), 2.65 (dd, 1H, H_{eq}-5 $J = 3.6$ and 16.4), 2.89 (d, 1H, H_{ax}-3,$J = 11.5$), 3.75–3.82 (m, 1H, H-4), 4.19 (d, 1H, H_{ax}-2, $J = 11.5$), 4.85 (dd, 1H, H_{ax}-6, $J = 3.6$ and 12.5), 6.84–7.55 (m, 10H, H_{arom}). **2d**: Yield 69%; m.p. 102–103°C; IR ν_{max} (cm^{-1}) 3310, 1038. **3a**: Yield 11%; m.p. 130–131°C; IR ν_{max} (cm^{-1}) 3340, 1020; ^{1}H NMR δ: 1.92 (d, 1H, OH), 2.09 (dd, 2H, H_{ax}-3 and 5, $J = 12.0$ and 17.2), 2.58 (dd, 2H, H_{eq}-3 and 5, $J = 3.6$ and 17.2), 4.41 (bs, 1H, H-4), 4.76 (dd, 2H, H-2 and 6, $J = 3.6$ and 12.0), 7.16–7.58 (m, 10H, H_{arom}). **3b**: Yield 16%; m.p. 132–133°C; IR ν_{max} (cm^{-1}) 3280, 1009; ^{1}H NMR δ: 1.96 (d, 1H, OH), 2.15 (s, 6H, CH_3), 2.23 (dd, 2H, H_{ax}-3 and 5, $J = 11.6$ and 16.8), 2.60 (dd, 2H, H_{eq} -3 and 5, $J = 3.0$ and 11.6), 4.39 (bs, 1H, H-4), 4.75 (dd, 2H, H-2 and 6, $J = 3.0$ and 11.6), 7.02–7.58 (m, 8H, H_{arom}). **3c**: Yield 17%; m.p. 150–151°C; IR ν_{max} (cm^{-1}) 3340, 1006; **3d**: Yield 14%; m.p. 106–107°C; IR ν_{max} (cm^{-1}) 3340,

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1001; ^{1}H NMR δ: 0.66 (t, 3H, CH_2-$\underline{CH_3}$), 0.75–0.91 (m, 2H, $\underline{CH_2}$-CH_3), 2.20 (dd, 1H, H_{ax}-5, $J = 12.0$ and 16.8), 2.36 (d, 1H, OH), 2.55 (dd, 1H, H_{eq}-5, $J = 3.6$ and 16.8), 2.81 (d, 1H, H_{ax}-2, $J = 11.9$), 4.31 (bs, 1H, H-4), 4.54 (d, 1H, H_{ax}-2, $J = 11.9$), 4.86 (dd, 1H, H_{ax}-6, $J = 3.6$ and 12.0), 7.00–7.60 (m, 10H, H_{arom}).

2,6-Diaryl(-3-alkyl)-4-selenanone (4)

General procedure: To a colourless solution of sodium hydrogen selenide obtained as described in the above procedure, acetaldehyde was added dropwise while stirring in order to decompose the excess $NaBH_4$. A vigorous reaction sets in immediately with a slight foaming, which was cooled to room temperature. To this, 1,5-diaryl-1,4-pentadien-3-one (15 mmol) and sodium acetate (1.0 g) dissolved in absolute ethanol (25 mL) was added and refluxed for 3 h on a water bath. After completion of the reaction the solvent was removed with flash evaporator. The residue was extracted with hot benzene, and concentrated under vacuo. The residual portion was diluted with pet.ether (60–80°C) (15 mL) and refrigerated overnight. The solid separated was filtered off, dried and recrystallized from pet.ether (60–80°C) to yield **4**.

4a: Yield 60%; m.p. 107–108°C; IR ν_{max} (cm^{-1}) 1696; ^{1}H NMR δ: 2.56 (dd, 2H, H_{ax}-3 and 5), 2.94 (dd, 2H, H_{eq}-3 and 5), 4.16 (dd, 2H, H_{ax}-2 and 6). **4b**: Yield 61%; m.p. 134–135°C; IR ν_{max} (cm^{-1}) 1690. **4c**: Yield 64%; m.p. 121–122°C; IR ν_{max} (cm^{-1}) 1701; ^{1}H NMR δ: 0.95 (d, 3H,CH_3), 2.95 (m, 1H, H_{ax}-3), 3.16 (dd, 1H, H_{ax}-5 $J = 10.4$ and 16.5), 3.54 (dd, 1H, H_{eq} -5, $J = 4.6$ and 16.5), 4.17 (d, 1H, H-2, $J = 11.0$), 4.56 (dd, 1H, H-6, $J = 4.6$ and 10.4). **4d**: Yield 65%; m.p. 101–102°C; IR ν_{max} (cm^{-1}) 1705.

Reduction of (4)

General procedure: To a well stirred slurry of sodium borohydride (0.44 g, 12 mmol) in dry ether (25 mL) was added dropwise, a solution of 4-selenanone (**4**) (10 mmol) in dry ether (25 mL). The contents were stirred at 40°C for 6–8 h. After completion of the reaction the excess hydride was carefully decomposed by the drop-wise addition of acetaldehyde. The solvent was removed under reduced pressure. The product obtained was separated by column chromatography to result **2** and **3**.

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4-Semicarbazono-2,6-diaryl(-3-Alkyl)selenan (5)

General procedure: A mixture of semicarbazide hydrochloride (1.67 g, 15 mmol), sodium acetate (2.72 g, 20 mmol) and **4** (10 mmol) in methanol (30 mL) was refluxed for 3 h. The solution was concentrated, cooled and poured onto crushed ice. The semicarbazone thus formed was filtered, washed with water and dried. It was recrystallized from ethanol.

5a: Yield 78%; m.p. 141–142°C. IR ν_{max} (cm^{-1}) 3368, 3280, 1700. **5b**: Yield 74%; m.p. 156–158°C; IR ν_{max} (cm^{-1}) 3460, 3340, 1708. **5c**: Yield 71%; m.p. 148–150°C; IR ν_{max} (cm^{-1}) 3379, 3295, 1695. **5d**: Yield 74%; m.p. 171–172°C; IR ν_{max} (cm^{-1}) 3350, 3262, 1715.

5,7-Diaryl(-4-alkyl)selenano[3,4-*d*] [1,2,3] Selenadiazole (6)

General procedure: The semicarbazone **5** (5 mmol) was taken in glacial acetic acid (15 mL) and the solution was stirred at 60–70°C. After all the solid has been dissolved, the powdered selenium dioxide (0.61 g, 5.5 mmol) was added in portions. The stirring was continued at the same temperature until the evolution of gas ceased. After completion of the reaction the mixture was cooled and filtered to remove precipitated selenium. The filtrate was poured onto crushed ice and the crude product obtained was filtered through a column of silica gel to get a pure compound.

6a: Yield 62%; m.p. 112–114°C; IR ν_{max} (cm^{-1}) 702, 1680; ^{1}H NMR δ: 2.58 (dd, 1H, H_A, $J = 4.6$ and 10.4), 2.74 (dd, 1H, H_B, $J = 10.4$ and 16.2), 4.18 (dd, 1H, H_x, $J = 4.6$ and 16.2), 4.58 (s, 1H, H-7), 6.80–7.66 (m, 10H, H_{arom}); MS *m/z* 404, 376, 324, 297. Anal. Calcd. for $C_{17}H_{14}N_2Se_2$: C, 50.50, H, 3.49, N, 6.94; Found: C, 50.65, H, 3.54, N, 6.80. **6b**: Yield 60%; m.p. 105–107°C IR ν_{max} (cm^{-1}) 695, 1468; ^{1}H NMR δ: 2.14 (s, 6H, CH_3), 2.52 (dd, 1H, H, $J = 4.4$ and 10.5), 2.71 (dd, 1H, H_B, $J = 10.5$ and 16.3), 4.17 (dd, 1H, H_x, $J = 4.4$ and 16.3), 4.52 (s, 1H, H-7), 7.00–7.80 (m, 8H, H_{arom}); Anal. Calcd. for $C_{19}H_{18}N_2Se_2$: C, 52.78, H, 4.19, N, 6.49; Found: C, 52.66, H, 4.25, N, 6.60. **6c**: Yield 65%; m.p. 122–124°C; IR ν_{max} (cm^{-1}) 707, 1474; ^{1}H NMR δ: 2.20 (d, 3H, CH_3), 2.68–2.77 (m, 1H, H-4), 4.12 (d, 1H, H-5, $J = 11.1$), 4.57 (s, 1H, H-7), 6.85–7.55 (m, 10H, H_{arom}); Anal. Calcd. for $C_{18}H_{16}N_2Se_2$: C, 51.68, H, 3.85, N, 6.71; Found: C, 51.79, H, 3.81, N, 6.85. **6d**: Yield 64%; m.p. 109–111°C; IR ν_{max} (cm^{-1}) 683, 1478.

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5,7-Diaryl(-4-alkyl)selenano[3,4-*d*][1,2,3] Thiadiazole (7)

General procedure: The appropriate semicarbazone **5** (5 mmol) was added portionwise to an excess of thionyl chloride (5 mL) at 0°C. After complete addition, the reaction mixture was allowed to attain the room temperature and kept aside for another 2 h. Then dichloromethane (25 mL) was added to the contents and the excess thionyl chloride was decomposed with saturated sodium carbonate solution. The dichloromethane extract was washed with water and dried (an. Na_2SO_4). The solvent was removed under vacuo. The gummy product so obtained was filtered through a column of silica gel using ethyl acetate and hexane as eluents to get **7**.

7a: Yield 66%; m.p. 135–136°C; IR ν_{max} (cm^{-1}) 707, 1475; ^{1}H NMR δ: 2.65 (dd, 1H, H_A, $J = 4.5$ and 10.4), 2.88 (dd, 1H, H_B, $J = 10.4$ and 16.3), 4.40 (dd, 1H, H_x, $J = 4.5$ and 16.3), 4.60 (s, 1H, H-7), 6.90–7.50 (m, 10H, H_{arom}); MS *m*/*z* 357, 324, 297, 277; Anal. Calcd. for $C_{17}H_{14}N_2SSe$: C, 57.13, H, 3.95, N, 7.85; Found: C, 57.25, H, 3.89, N, 7.76. **7b**: Yield 70%; m.p. 129–130°C; IR ν_{max} (cm^{-1}) 685, 1450; ^{1}H NMR δ: 2.20 (s, 6H, CH_3), 2.59 (dd, 1H, H_A, $J = 4.3$ and 10.0), 2.85 (dd, 1H, H_B , $J = 10.0$ and 16.2), 4.42 (dd, 1H, H_x $J = 4.3$ and 16.2), 4.62 (s, 1H, H-7), 7.05–7.70 (m, 8H, H_{arom}); Anal. Calcd. for $C_{19}H_{18}N_2SSe$: C, 59.20, H, 4.70, N, 7.28; Found: C, 59.12, H, 4.64; N, 7.16. **7c**: Yield 69%; m.p. 118–119°C; IR ν_{max} (cm^{-1}) 702, 1466; ^{1}H NMR δ: 2.25 (d, 3H, CH_3), 2.66–2.79 (m, 1H, H-4), 4.28 (d, 1H, H-5, $J = 11.4$), 4.59 (s, 1H, H-7), 6.98–7.40 (m, 10H, H_{arom}); Anal. Calcd. for $C_{18}H_{16}N_2SSe$: C, 58.20, H, 4.34, N, 7.56; Found: C, 58.13, H, 4.40, N, 7.49. **7d**: Yield 68%; m.p. 126–127°C; IR ν_{max} (cm^{-1}) 705, 1474.

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