# 1,3,4-Selenadiazole

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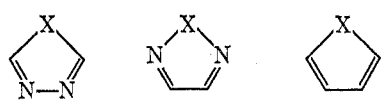
*Received July 28, 1969*

The synthesis and physical properties of 1,3,4-selenadiazole, the parent and only known member of a new heterocyclic ring system, are described. The compound has recently been shown to have the smallest angle, 81.8°, yet found in a planar five-membered ring.[2]

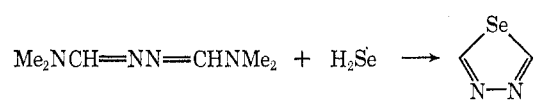
The acquisition of incontrovertible evidence for the presence of a rate-enhancing d-orbital participation in the deprotonation of thiamine and other heteroaromatic sulfur compounds has proved to be an elusive goal in both this[3] and other laboratories.[4] Recently, during the course of our own studies in this area, we required several selenium heterocycles, including a sample of 1,3,4-selenadiazole (IA), but on searching the literature we discovered that, not only was this parent heterocycle itself unknown, but no example of the substituted ring system had been synthesized. In contrast, the sulfur (IB)[5a-c] and oxygen (IC)[5d] analogs, along with all members of the other symmetrical X-adiazole systems (II, X = Se, S, O)[6] and the simplest compounds of this class, selenophene (IIIA), thiophene (IIIB), and furan (IIIC), have been prepared. In fact these structures (IB, IC, II, III) are so well characterized that bond angles and bond lengths are even known to high precision using microwave spectroscopy.[7] From these



IA, X = Se; B, X = S; C, X = O — IIA, X = Se; B, X = S; C, X = O — IIIA, X = Se; B, X = S; C, X = O

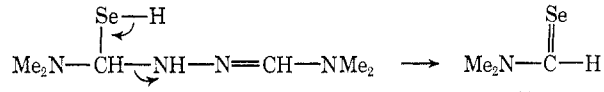
microwave results it was readily apparent that a similar structural analysis of 1,3,4-selenadiazole would provide the key reference data necessary to the understanding of the bonding in these other compounds and, even more important, aid in a more rigorous interpretation and definition of the concept of heteroaromaticity in ring systems containing higher row elements.

Thus with both our own needs and the further incentive of synthesizing a theoretically valuable compound as the inducements, we set out to make 1,3,4-selenadiazole. On paper the most encouraging approach involved the direct adaptation of the Föhlisch[5c] synthesis of 1,3,4-thiadiazole (IB) from the readily available N,N-dimethylformamide azine (IV)[5c] and hydrogen sulfide. However, when we ran the reaction of IV with hydrogen selenide using the Föhlisch procedure we did not obtain IA, but instead a protonated cation of IV. This problem could be circumvented by the addition of 0.08 equiv of pyridine (product yields decrease rapidly as the amount of pyridine is changed in either direction from this optimum value) to the reaction, medium, and, after several changes in addition methods, reaction times and temperatures, and in isolation procedures, we were able to obtain IA in 25% yield along



IV IA

with an equal amount of N,N-dimethylselenoformamide (VI).[8] This latter compound is undoubtedly derived by elimination of the alternative amidrazone leaving group from the expected intermediate (V).



V VI

1,3,4-Selenadiazole is a colorless liquid, bp 58° (0.5 mm), which slowly decomposes in air but which is stable in storage at 0° in the dark under vacuum. The mass spectrum (Figure 1) is complicated by the fact that five isotopes of selenium are found in significant natural abundance ($^{76}$Se 9.02%, $^{77}$Se 7.58%, $^{78}$Se 23.52%, $^{80}$Se 49.82%, $^{82}$Se 9.19%), but evidence for the following major fragments has been obtained: $SeCHN^+$, $CHSe^+$, $Se^+$, and $HCN^+$. As would be expected IA exhibits a single peak, though at exceedingly low field, in its nmr spectrum, a peak which moves from $\tau$ −0.89 in the neat liquid to +0.04 at infinite dilution in carbon tetrachloride; the $^{13}$C–H coupling constant is 214.3 cps. The presence of a nuclear spin of $^1/_2$ in the $^{77}$Se isotope suggested the possibility of finding the coupling inter-

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(7) IB: B. Bak, L. Nygaard, E. J. Pedersen, and J. Rastrup-Andersen, *J. Mol. Spectrosc.*, **19**, 283 (1966); IC: B. Bak, J. T. Nielsen, O. F. Nielsen, L. Nygaard, J. Rastrup-Andersen, and P. A. Steiner, *ibid.*, **19**, 458 (1966); IIA: G. L. Blackman, R. D. Brown, F. R. Burden, and J. E. Kent, *Chem. Phys. Lett.*, **1**, 379 (1967); IIB: S. V. Dobyns and L. Pierce, *J. Amer. Chem. Soc.*, **85**, 3553 (1963); IIC: E. Saegebarth and A. P. Cox, *J. Chem. Phys.*, **43**, 166 (1965); IIIA: R. D. Brown, F. R. Burden, and P. G. Godfrey, *J. Mol. Spectrosc.*, **25**, 415 (1968); IIIB: B. Bak, D. Christensen, L. Hansen-Nygaard, and J. Rastrup-Andersen, *ibid.*, **7**, 58 (1961); IIIC: B. Bak, D. Christensen, W. Dixon, L. Hansen-Nygaard, J. Rastrup-Andersen, and M. Schottländer, *ibid.*, **9**, 124 (1962).

(8) C. Collard-Charon and M. Renson, *Bull. Soc. Chim. Belges*, **72**, 304 (1963). We have found that small amounts of N,N-dimethylthioformamide are also formed in the Föhlisch synthesis of IB though this is not reported in the original article.[5c]

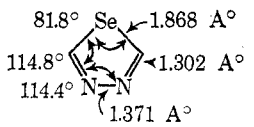
TABLE I

| | IA[a] | IB[b] | IC[c] | IIA[d] |
|---|---|---|---|---|
| Bp, °C (mm) | 58 (0.5) | 82–83.5 (13) | 150 (760) | 138 (760) |
| Mp, °C | 22.5–23.5 | 42–43 | | 20.5–21 |
| *d*, g/ml (temp, °C) | 2.05 (25) | | 1.25 (25)[a] | 2.10 (24) |
| $n_D$ (temp, °C) | 1.5933 (25) | | 1.4300 (25) | 1.6158 (24) |
| $\lambda_{max}$, mμ (ε), solvent | 232 (2350), 204 (1850), 95% EtOH | 211 (2600), 95% EtOH | End absorption, 95% EtOH | 285 (6300), MeOH |
| Nmr, τ | | | | |
| Neat | −0.89 | | +0.72[a] | |
| $CCl_4$ (infinite diln) | +0.04 | +0.89[a] | +1.67[a] | +0.72 |
| $J_{^{13}C-H}$, cps | 214.3 | 212.9[a] | 236.0[a] | 188 |
| Dipole moment, D | 3.40[e] | 3.28[f] | 3.04[g] | 1.11[h] |

[a] This work. [b] Reference 5a, except where noted. [c] Reference 5d, except where noted. [d] Reference 6, IIA, except where noted. [e] Reference 2. [f] B. Bak, D. Christensen, L. Hansen-Nygaard, L. Lipschitz, and J. Rastrup-Andersen, *J. Mol. Spectrosc.*, **9**, 225 (1962). [g] Reference 7, IC. [h] Reference 7, IIA.

action between this atom and hydrogen. This coupling, in fact, is quite large $J_{^{77}Se-C-H}$ = 55.3 cps, even though a carbon atom intervenes between the two coupled atoms [in agreement with our assignment is the fact that the ratio of intensities (7:1) of the $^{77}Se$–C–H side band to the $^{13}C$–H side band is in accord with the natural abundances of the two atoms: $^{77}Se$ = 7.58%, $^{13}C$ = 1.11%]. The $J_{^{77}Se-C_2-H}$ coupling constant in selenophene is also large (48 cps[9]). A comparison of the physical properties of 1,3,4-selenadiazole (IA) with those of the related sulfur (IB) and oxygen (IC) compounds, and the isomeric 1,2,5-selenadiazole (IIA) is summarized in Table I.[10]

An analysis of the microwave spectrum of 1,3,4-selenadiazole has recently been accomplished by Levine, Krugh, and Gold, and their interpretation of the data including a comparison of experimental bond angles and bond lengths with those of the related heterocycles in series I–III has been published.[2] A short summary of the Gold values for IA is also diagrammed below. *Note that the C–Se–C angle of 81.8° is the smallest known angle in a planar five-membered ring.*




## Experimental Section

Infrared spectra were taken on a Perkin-Elmer Model 137 recording spectrophotometer (calibrated against the 6.24 μ band of polystyrene), and a Coleman Hitachi 124 double-beam spectrophotometer was used to measure the ultraviolet spectra. Nmr spectra were run on a Varian HA-100 nmr spectrometer; the chemical shifts are expressed in τ units using an internal tetramethylsilane standard (side bands generated by an audio-oscillator monitored by a frequency counter were used as an aid in obtaining accurate measurements of chemical shift, $J_{^{13}C-H}$, and $J_{^{77}Se-H}$). An AEI-MS-902 mass spectrometer was used to record the mass spectra. The refractive indices were measured on a Valentine refractometer. Vapor phase chromatography was carried out on a Varian Aerograph Model 700 gas chromatograph with a thermoconductivity detector. The comparison samples of 1,3,4-thiadiazole (IB) and 1,3,4-oxadiazole (IC) were obtained by known procedures.[5c,d]

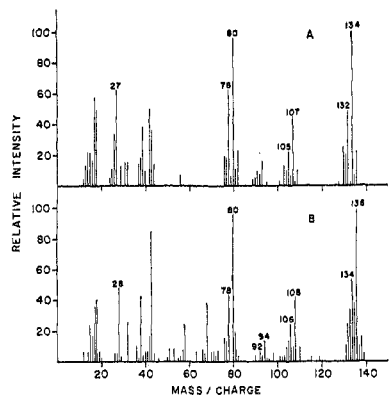



Figure 1.—Spectra at 70 eV. A is 1,3,4-selenadiazole; B is 1,3,4-selenadiazole-$d_2$ (~75%), -$d_1$ (~25%).

**1,3,4-Selenadiazole.**—N,N-Dimethylformamide azine dihydrochloride (prepared by the reaction of N,N′-diformylhydrazine and dimethylformamidoyl chloride)[5c] was converted into N,N-dimethylformamide azine, mp 74–75° (lit.[5c] 75–76°), by reaction with 2 equiv of sodium ethoxide.

The N,N-dimethylformamide azine (5.5 g, 0.039 *M*) and pyridine (0.25 ml, 0.003 *M*) were then mixed in methanol (60 ml) and placed in a 200-ml flask equipped with a condenser and a gas inlet from a hydrogen selenide generator. While the reaction solution was stirred with a magnetic stirrer and cooled in an ice bath, hydrogen selenide was bubbled in. [The hydrogen selenide was generated by slowly adding distilled water to 35.0 g of freshly ground aluminum selenide (City Chemical Corp.) and the gas was dried by passing it through calcium chloride.] After the first half hour the ice bath was removed, though hydrogen selenide was bubbled in for an additional half hour. The reaction mixture was left to stand overnight. The methanol was then removed by evaporation at aspirator pressure, leaving a thick black oily tar, which was triturated 7–8 times with 50-ml portions of anhydrous ethyl ether. The ether extract was filtered, dried over sodium sulfate, and finally vacuum evaporated leaving an oil, which on distillation, bp 50–62° (0.2 mm), afforded a mixture of two products which were successfully separated by vpc, using a 10 ft × 0.25 in. column, with 20% Se-52 on 60–80 Gas-Chrom Q, at 142° (He flow, 82 ml/min; retention time using 50-μl samples, for compound 1, 6.0–12.0 min, and, for compound 2, 14.0–26.0 min), and were identified as the desired 1,3,4-selenadiazole [IA, compound 1: ir (μ, neat) 3.31 (medium), 3.62 (short), 7.17 (long), 8.20 (s), 8.46 (m), 10.72 (m), 11.43 (m), 12.20 (l, broad); micro bp 58° (0.5 mm)] and N,N-dimethylselenoformamide [VI, compound 2: nmr τ −0.58 (s), 6.68 (s); ratio 1:6, $CDCl_3$; lit.[3] bp 79° (0.4 mm)]. Based on nmr analysis, the two compounds are formed in about a 1:1 ratio; IA was generated in *ca.* 25% yield.

(9) M. L. Hefferman and A. A. Humffray, *Mol. Phys.*, **7**, 527 (1961). In this compound $J_{^{77}Se-C_2-C_3-H}$ is 9.5 cps, while the similar coupling, $J_{^{77}Se-N-C-H}$, in 1,2,5-selenadiazole, is 27.9: P. Bucci, V. Bertini, G. Ceccarelli, and A. de Munno, *Chem. Phys. Lett.*, **1**, 473 (1967).

(10) Attempts to determine the basicity of IA and IB by the potentiometric titration procedure described in detail by P. Haake and L. P. Bausher [*J. Phys. Chem.*, **72**, 2213 (1968)] were unsuccessful. There were no detectable inflections in the titration curves indicating that the $pK_a$ values for these compounds are <1. No significant change in the ultraviolet spectrum of IA was observed on addition of concentrated HCl to aqueous solutions of this substrate.

*Anal.* Calcd for $C_2H_2N_2Se$: C, 18.06; H, 1.52; N, 21.06. Found: C, 17.88; H, 1.77; N, 21.24.

**Dideuterio-1,3,4-selenadiazole.**—The crude distillate above (1.0 g), containing both 1,3,4-selenadiazole and N,N-dimethylselenoformamide, was dissolved in 20 ml of 0.2 *N* sodium carbonate in $D_2O$ (Diaprep 99.8%) and left to stand for 12 hr at room temperature. The deuterated selenadiazole was extracted from the heavy water with ethyl ether (six 50-ml portions) and the ether solution dried over magnesium sulfate. The ether was evaporated and the product purified by vpc (same conditions as above). From the mass spectrum the product contained about 75% dideuterio species and 25% monodeuterio compound. The infrared spectrum contained a strong C–D stretching band at 4.35 $\mu$ (neat).

**Registry No.**—IA, 289-13-4; IB, 289-06-5; IC, 288-99-3.

**Acknowledgments.**—We wish to thank Professor L. P. Gold for several valuable discussions. This research was supported by a grant from the U. S. Public Health Service (GM-13980).

# 1,2,4-Triazoles. XXIII. Chlorination of *s*-Triazolo[4,3-*a*]pyridine-3-thiol and the Formation of 3,5,6,7,7,8-Hexachloro-5,6,7,8-tetrahydro-*s*-triazolo[4,3-*a*]pyridine[1]

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*Received May 19, 1969*

Chlorination of *s*-triazolo[4,3-*a*]pyridine-3-thiol gave, as the major product, the above hexachloro compound together with small amounts of 3,8-dichloro- and 3,6,7,8-tetrachloro-*s*-triazolo[4,3-*a*]pyridine. Similar products were obtained from methyl-substituted derivatives of the ring system. Treatment of the thiols with aqueous sodium hypochlorite solution ("Clorox") gave the corresponding monochloro product in good yield.

Chlorination of various heterocyclic thiols under oxidizing conditions is a convenient route to sulfonyl chlorides and, in certain cases, to the corresponding chloro compounds.[2] Our interest in chloro-substituted heterocycles as precursors for the synthesis of polynuclear heterocyclic systems with bridgehead nitrogen atoms[3] led us to study the oxidative chlorination of *s*-triazolo[4,3-*a*]pyridine-3-thiol (1, R = R′ = H) as a possible route to the 3-chloro compound. This study has resulted in some interesting polychlorinated products of this bicyclic ring system.

Treatment of *s*-triazolo[4,3-*a*]pyridine-3-thiol (1, R = R′ = H) with an excess of chlorine at 0–10° in aqueous chloroform gave three products. Representation of the major product (29% yield) as 3,5,6,7,7,8-hexachloro-5,6,7,8-tetrahydro-*s*-triazolo[4,3-*a*]pyridine (2) is consistent with the following evidence. The molecular formula, $C_6H_3Cl_6N_3$, was established by, analytical and molecular weight data, the latter being determined from its mass spectrum which showed the appropriate isotopic chlorine clusters (Table I). Its nmr spectrum consisted of an AX pattern at $\tau$ 3.50 and 4.97 (rel intensity 1:1) with $J$ = 5.6 Hz and a singlet (1 H) at $\tau$ 4.84. These data suggest the presence of vicinal hydrogens at positions 5 and 6 in a diaxial relationship and a proton at position 8 of the nucleus, the 7 position being occupied by a *gem* dichloro group. The absence of a low field signal (below $\tau$ 2.00) attributable to a 3-hydrogen atom in *s*-triazolo[4,3-*a*]-pyridine[4] places the sixth chlorine atom in the 3 position. The ultraviolet absorption spectrum ($\lambda_{max}$ 275, 220 m$\mu$; log $\epsilon$ 3.89, 3.98) indicated that the conjugated system present in 3-chloro-*s*-triazolo[4,3-*a*]pyridine (8, R′ = H) ($\lambda_{max}$ 297, 265, 258, 208 m$\mu$; log $\epsilon$ 3.79, 3.79, 3.83, 4.69) was no longer present in the hexachloro product and the infrared spectrum was devoid of any characteristic absorption in the carbon–carbon double-bond region.

TABLE I

MASS SPECTRAL DATA[a] FOR SEVERAL DERIVATIVES OF THE *s*-TRIAZOLO[4,3-*a*]PYRIDINE SYSTEM

| Compound | *m/e* (rel intensity) |
|---|---|
| 2 | 327(5.5), 294(100), 292(80), 223(49), 221(52), 187(52), 127(26), 99(20) |
| 3, R = R′ = H | 187(100), 127(95), 100(29) |
| 4 | 257(100), 255(70), 194(44), 167(12.5), 133(22), 98(12.5) |
| 3, R = H; R′ = $CH_3$ | 201(100), 166(22), 140(11), 105(10), 85(9), 79(9), 65(9) |
| 6 | 273(13), 238(33), 203(66), 201(100), 166(16), 140(12), 105(13), 78(20), 75(10), 64(8), 63(10), 62(10), 61(8), 60(5) |
| 3, R = R′ = $CH_3$ | 215(100), 214(7), 180(7), 153(7), 127(5), 119(25), 92(8), 78(7), 77(5), 67(6), 66(7), 65(5) |

[a] Determined at 70 eV.

The following chemical transformations show that no skeletal rearrangement had occurred and offer support for the above assignments.[5] Reaction of the hexachloro compound 2 with dilute ammonia or barium hydroxide gave a product 4 which was also found as a minor constituent of the original chlorination reaction. The

(1) (a) Partial financial support of this work by U. S. Public Health Service Research Grant No. CA 08495, National Cancer Institute, and USAMRDC Contract No. DA-49-193-MD-3012, is gratefully acknowledged; (b) Communication No. 728 in the U. S. Army Research Program on Malaria.

(2) For papers detailing earlier work in this area, see R. O. Roblin, Jr., and J. W. Clapp, *J. Amer. Chem. Soc.*, **72**, 4890 (1950); C. W. Noell and R. K. Robins, *ibid.*, **81**, 5997 (1959); R. K. Robins, *J. Org. Chem.*, **26**, 447 (1961); N. K. Basu and F. L. Rose, *J. Chem. Soc.*, 5660 (1963); W. Broadbent, C. W. Miller, and F. L. Rose, *ibid.*, 3369 (1965); G. S. Sidhu, S. Naqui, and D. S. Iyengar, *J. Heterocycl. Chem.*, **3**, 158 (1966); H. L. Yale and J. J. Piala, *J. Med. Chem.*, **9**, 42 (1966).

(3) For example, see K. T. Potts, U. P. Singh, and J. Bhattacharyya, *J. Org. Chem.*, **33**, 3766 (1968).

(4) K. T. Potts, H. R. Burton, T. H. Crawford, and S. W. Thomas, *ibid.*, **31**, 3522 (1966).

(5) It is recognized that our data do not rigorously exclude the possibility that this hexachloro product could be an isomeric one. However, its relationship to the tetrachloro and dichloro products, together with mechanistic considerations, lead us to put more emphasis on the proposed structure. Tlc analysis always indicated that we were dealing with only one hexachloro product.