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Note

Synthesis of 1-aryl-(1,2-dideoxy-α-D-glucofurano)-[2,1-*d*]imidazolidine-2-selones and the crystal structure of the 1-*p*-bromophenyl derivative *

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Although the reaction of 2-amino-2-deoxy sugars with isocyanates and isothiocyanates to give glycofuranoimidazolidin-2-ones and -2-thiones is well known[1,2], no reactions with isoselenocyanates have been reported.

We now report the synthesis, in yields of 77–88%, of the crystalline 1-aryl-(1,2-dideoxy-α-D-glucofurano)[2,1-*d*]imidazolidine-2-selones (**1–3**) by the reaction of 2-amino-2-deoxy-D-glucose with aryl isoselenocyanates[3] in aqueous ethanol containing 10% of acetic acid. The intermediates **4**, which were detected by TLC (see Experimental), are analogous to those isolated in the corresponding reactions with aryl isothiocyanates[2]. The rates of formation of bicyclic selones were **2** > **1** > **3**, which reflects the inductive effects of the 4-methoxy and 4-bromine substituents, respectively.

Compounds **1–3** are similar to chiral oxazolidine-2-selones that have been used[4] for quantitative detection of remote chiral centres using ^{77}Se NMR spectroscopy.

The structures **1–3** were assigned on the basis of analytical, UV, IR, ^{1}H and ^{13}C NMR, and MS data (see Experimental). The ^{1}H and ^{13}C NMR data (Tables I and II) are similar to those of the 2-one and 2-thione analogues[2], except that the resonances of N-H and C-2 are shifted downfield, reflecting the participation of the resonance structure with partial positive charge on N-1 and N-3 and negative

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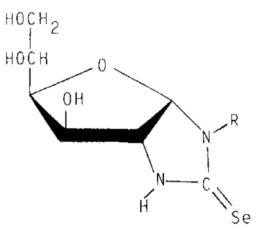
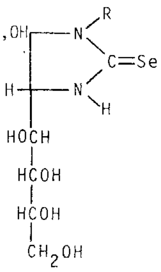


1 R = Ph

2 R = p-MeOC$_6$H$_4$

3 R = p-BrC$_6$H$_4$



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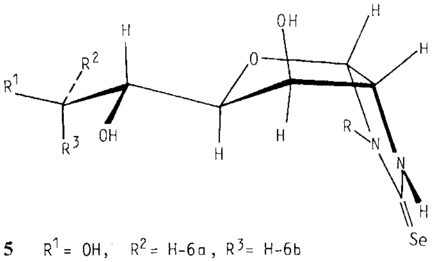
charge on Se. This view is corroborated by the C–Se bond length obtained from the X-ray diffraction data of **3** (see below). The ^{13}C resonance of C=Se appeared at ~ 178 ppm, whereas those of C=O and C=S appeared at 157 and 181 ppm, respectively. The $^{3}J_{H,H}$ values indicated[5,6] an equilibrium between the conformers **5** and **6**, with the furan ring in the E_4 form[7] and the C-2/6 chain in a planar zigzag form with the usual chain-end flexibility.



5 R^1 = OH, R^2 = H-6a, R^3 = H-6b

6 R^1 = H-6a, R^2 = H-6b, R^3 = OH

The mass spectra of **1**–**3** contained peaks for M^+, and Scheme 1 summarises the pathways of fragmentation, and the base peaks are $(B + H)^+$ for **1** and $(B + H - Se)^+$ for **2** and **3**. Similar fragments were found[2] for the thione analogues. Selenium-containing fragments showed a typical pattern of six lines, but the line for ^{80}Se (natural occurrence, 49.8%) is the only one considered. The UV spectra of **1**–**3** contained bands with λ_{max} at ~ 270 nm (cf. ~ 240 nm for the thione analogues[8,9] and ~ 230 nm for the 2-one analogues[2]).

The structure of **3** was confirmed by X-ray analysis and a view[10] of the molecule with the atomic numbering is shown in Fig. 1. Bond lengths and angles are shown in Table III. The mean value C–C in the phenyl group is 1.36(5) Å. The bond lengths and angles in the glucofurano-imidazolidine-2-selone group are normal, except for the C-1–C-2 and C-4–C-5 bonds which are longer than the normal C(sp^3)–C(sp^3) single bond. The Se–C bond length of 1.79(2) Å is intermediate of those for Se–C single (1.98 Å) and double bonds (1.67 Å). This partial double-bond

TABLE I

^{1}H NMR data (δ in ppm, J in Hz) for solutions of **1**–**3** in $(CD_3)_2SO$

Compound	H-1	H-2	H-3	H-4	H-5	H-6a	H-6b	NH	HO-3	HO-5	HO-6
1	5.95d	4.16d	4.14dd	3.63dd	3.74m	3.58m	3.40m	9.65s	5.43d	4.80d	4.56t
2	5.87d	4.13d	4.10dd	3.63dd	3.73m	3.58m	3.40m	9.55s	5.40d	4.78d	4.53t
3	5.97d	4.14d	4.12dd	3.62dd	3.73m	3.56m	3.40m	9.76s	5.45d	4.80	4.56t
Compound	$J_{1,2}$	$J_{2,3}$	$J_{3,4}$	$J_{4,5}$	$J_{5,6a}$	$J_{5,6b}$	$J_{6a,6b}$	$J_{3,OH}$	$J_{5,OH}$	$J_{6,OH}$	
1	6.4	~ 0	2.2	8.6	2.5	5.0	11.1	5.0	6.0	5.5	
2	6.4	~ 0	2.2	8.8	2.4	5.2	11.2	5.1	6.0	5.5	
3	6.3	~ 0	2.1	8.8	2.5	5.0	11.2	5.0	6.0	5.6	

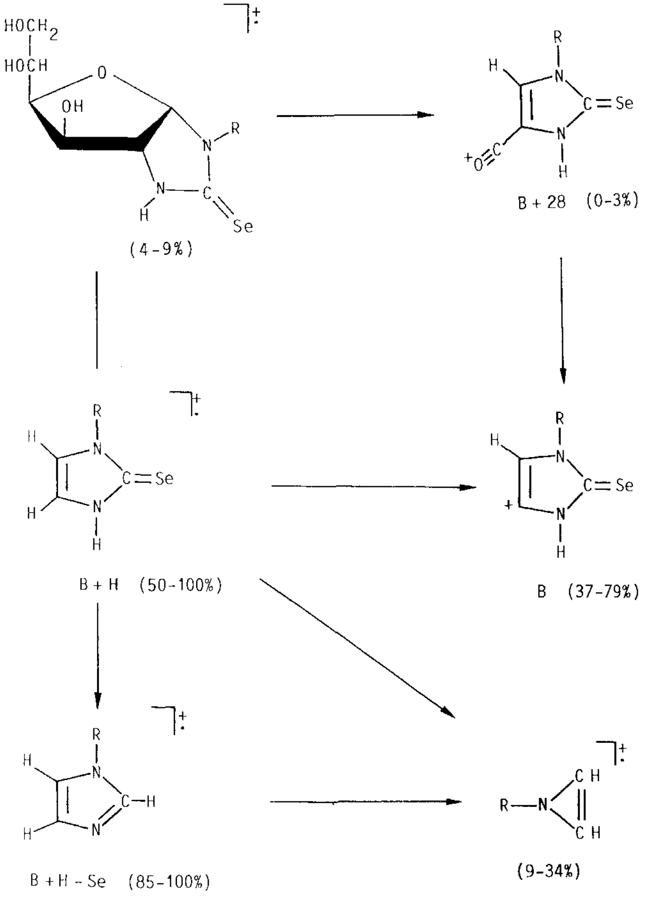
TABLE II

^{13}C NMR data (δ in ppm) for solutions of **1**–**3** in $(CD_3)_2SO$

Compound	C-1	C-2	C-3	C-4	C-5	C-6	C=Se	Aromatic			
								C-1	C-2,6	C-3,5	C-4
1	94.8	66.7	73.3	79.2	67.9	63.6	178.0	139.1	127.6	128.3	126.9
2	95.0	66.6	73.5	79.1	67.9	63.6	178.5	131.8	129.5	113.7	158.3
3	94.6	66.8	73.2	79.3	67.8	63.5	177.9	138.4	129.0	144.4	159.3

character reflects the resonance of the selenourea system. The phenyl and the imidazolidine groups are planar, and the maximum deviations from the best planes are 0.04 and 0.06 Å, respectively. The Br and Se substituents are at 0.04 and 0.08 Å from the respective planes.

The furanose ring is not planar and, in terms of ring-puckering co-ordinates[11], the amplitude and phase magnitudes are Q = 0.33(3) Å and ϕ = 67(5)° for C-1–O–



Scheme 1.

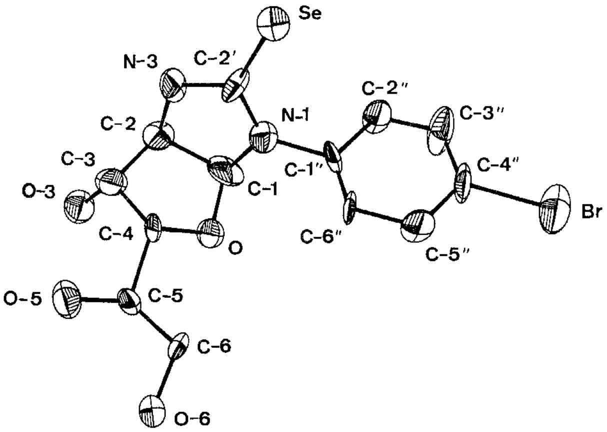


Fig. 1. ORTEP view of **3** along the *c* axis, showing the atomic numbering. The ellipsoids enclose 50% probability.

TABLE III

Bond lengths (Å) and angles (°) for **3**

Se–C-2′	1.79(2)	C-4–C-3	1.42(4)
Br–C-4″	1.90(2)	C-5–C-4	1.63(3)
N-1–C-2′	1.34(3)	C-5–O-5	1.40(3)
N-1–C-1″	1.50(3)	C-5–C-6	1.50(4)
O-3–C-3	1.39(4)	C-2′–N-3	1.35(3)
O-6–C-6	1.39(3)	C-1″–C-2″	1.38(3)
C-1–O	1.45(3)	C-2″–C-3″	1.33(3)
C-1–N-1	1.46(5)	C-4″–C-5″	1.39(5)
C-2–C-1	1.61(4)	C-4″–C-3″	1.34(5)
C-2–N-3	1.45(4)	C-6″–C-1″	1.30(4)
C-2–C-3	1.52(4)	C-6″–C-5″	1.40(4)
C-4–O	1.44(3)		
Se–C-2′–N-1	128(2)	C-2–C-1–O	102(2)
Se–C-2′–N-3	126(2)	C-2–N-3–C-2′	116(2)
Br–C-4″–C-3″	123(1)	C-2–C-3–O-3	107(1)
Br–C-4″–C-5′	115(2)	C-2–C-3–C-4	100(2)
N-1–C-2′–N-3	104(2)	C-4–C-5–C-6	113(1)
N-1–C-1″–C-6″	120(2)	C-4–C-5–O-5	105(1)
N-1–C-1″–C-2″	114(2)	C-4–C-3–O-3	109(2)
N-3–C-2–C-3	110(2)	C-5–C-4–C-3	120(2)
O–C-1–N-1	111(3)	C-5–C-4–O	103(1)
O–C-4–C-3	112(2)	C-5–C-6–O-6	108(2)
O-5–C-5–C-6	113(2)	C-2′–N-1–C-1″	124(2)
C-1–C-2–C-3	106(2)	C-1″–C-6″–C-5″	118(3)
C-1–C-2–N-3	101(2)	C-1″–C-2″–C-3″	116(3)
C-1–O–C-4	104(2)	C-4″–C-5″–C-6″	118(3)
C-1–N-1–C-1″	117(2)	C-4″–C-3″–C-2″	121(3)
C-1–N-1–C-2′	117(2)	C-5″–C-4″–C-3″	120(2)
C-2–C-1–N-1	99(2)	C-6″–C-1″–C-2″	124(2)

C-4–C-3–C-2. The endocyclic torsion angles of the furanose ring are: C-4–O–C-1–C-2 = −23(3)°, O–C-1–C-2–C-3 = 3(3)°, C-1–C-2–C-3–C-4 = 18(3)°, C-2–C-3–C-4–O = −35(3)°, and C-3–C-4–O–C-1 = 39(3)°. The asymmetry parameters[12] are ΔCs (C-H) = 0.023(17), ΔC_2 (C-2) = 0.046(14), and ΔC_2 (C-1) = 0.079(14), so that the conformation is E with a pseudomirror plane through C-4, O-3 axial, and C-5 quasi-equatorial. This conformation accords with the E_4 form deduced by ^{1}H NMR spectroscopy. The angles between planes are as follows: furan–imidazolidine, 71°; phenyl–imidazolidine, 75°; and phenyl–furan, 23°.

The molecules are linked into chains along the a axis by the following hydrogen bonds:

C-3 $\cdots$ O-5($x-1/2,\ -y+3/2,\ -z+1$) = 3.08(4) Å, C-3–H $\cdots$ O-5 = 99(1)°
C-2 $\cdots$ O-5($x-1/2,\ -y+3/2,\ -z+1$) = 2.91(3) Å, C-2–H $\cdots$ O-5 = 100(1)°
O-3 $\cdots$ O-6($x-1/2,\ -y+3/2,\ -z+1$) = 2.67(2) Å, O-3–H $\cdots$ O-6 = 92(1)°
N-3 $\cdots$ O-5($x-1/2,\ -y+3/2,\ -z+1$) = 2.94(3) Å, N-3–H $\cdots$ O-5 = 111(1)°
O-5 $\cdots$ O-3($x,\ y,\ z+1$) = 2.80(3) Å, O-5–H $\cdots$ O-3 = 117(1)°
O-3 $\cdots$ O-5($x,\ y,\ z-1$) = 2.80(3) Å, O-3–H $\cdots$ O-5 = 97(1)°
O-6 $\cdots$ O-3($x+1/2,\ -y+3/2,\ -z+1$) = 2.67(2) Å, O-6–H $\cdots$ O-3 = 145(2)°

EXPERIMENTAL

General methods.—Melting points are uncorrected. Optical rotations were measured with a Perkin–Elmer 241 polarimeter. FTIR spectra (KBr discs) were recorded with a Bomem MB-120 spectrometer and UV spectra with a Philips PU 8710 UV/VIS spectrometer on solutions in MeOH. The ^{1}H (200 MHz) and ^{13}C NMR (50.3 MHz) spectra were recorded with a Varian XL-200 instrument. EI (70 eV)-mass spectra were obtained using a Kratos MS-80 RFA instrument, with an ionising current of 100 μA, an accelerating voltage of 4 kV, and a resolution of 1000 (10% valley definition). The elemental composition of the ions was determined with a resolution of 10,000 (10% valley definition).

*1-Phenyl-(1,2-dideoxy-α-*D*-glucofurano)[2,1-*d*]imidazolidine-2-selone* (**1**).—A mixture of 2-amino-2-deoxy-D-glucose hydrochloride (323 mg, 1.5 mmol), NaHCO$_3$ (126 mg, 1.5 mmol), and phenyl isoselenocyanate (328 mg, 1.8 mmol) in EtOH–water (2:1, 15 mL) was boiled for 30 min under reflux. TLC (CH$_2$Cl$_2$–MeOH, 5:1) revealed only one compound, R_F 0.43. Acetic acid (1.5 mL) was added, and the solution was boiled under reflux for a further 1 h until the intermediate disappeared, then concentrated. Column chromatography (CH$_2$Cl$_2$–MeOH, 7:1) of the residue and crystallisation of the product (445 mg, 88%) from EtOH–water (1:1) gave **1**, mp 208–209° (dec.); $[\alpha]_D^{22}$ +53°, $[\alpha]_{578}^{22}$ +54°, $[\alpha]_{546}^{22}$ +58°, $[\alpha]_{435}^{22}$ +82° (c 1, pyridine); R_F 0.53; λ_{max}^{MeOH} 273 nm (ϵ_{mM} 9.1); ν_{max} 3418, 3383, 3264 (NH, OH), 1477 (NH), 1595, 1585, 1495, 1440, and 698 cm^{-1} (Ph). Mass spectrum: m/z 344.0177 (M$^+$, 8%), 264.1120 (M$^+$ − Se, 3), 250.9924 (B$^+$ + 28, 3), 223.9832 (B$^+$ + H, 100), 222.9773 (B$^+$, 79), 144.0528 (B$^+$ + H − Se, 85), 117.0580 (PhNC$_2$H$_2$$^+$, 34), 77 (Ph$^+$, 19). The ^{1}H and ^{13}C NMR data are given in Tables I and II.

Anal. Calcd for $C_{16}H_{16}N_2O_4Se$: C, 45.49; H, 4.70; N, 8.16. Found: C, 45.82; H, 4.69; N, 7.96.

*1-*p*-Methoxyphenyl-(1,2-dideoxy-α-*D*-glucofurano)[2,1-*d*]imidazolidine-2-selone* (**2**).—A mixture of 2-amino-2-deoxy-D-glucose hydrochloride (1.5 mmol), $NaHCO_3$ (1.5 mmol), and *p*-methoxyphenyl isoselenocyanate (382 mg, 1.8 mmol) in EtOH–water (2:1, 1.5 mL) was boiled for 30 min under reflux. Acetic acid (1.5 mL) was added and, after boiling under reflux for 15 min, TLC (CH_2Cl_2–MeOH, 5:1) revealed the disappearance of the intermediate. The solution was cooled, and the resulting crystals (437 mg, 78%) were collected, washed with EtOH–water (1:1), and recrystallised from EtOH–water (1:1) to give **2**, mp 224–226° (dec.); $[\alpha]_D^{22}$ +57°, $[\alpha]_{578}^{22}$ +60°, $[\alpha]_{546}^{22}$ +67°, $[\alpha]_{435}^{22}$ +112° (*c* 1, pyridine); λ_{max}^{MeOH} 270 nm (ϵ_{mM} 11.9); ν_{max} 3433, 3364, 3188, 3105 (NH, OH), 1475 (NH), 1607, 1583, 1516, 1437, and 837 cm^{-1} (aryl, *p*-substituted). Mass spectrum: *m/z* 374.0342 (M^+, 4%), 294.1160 ($M^+ -$ Se, 2), 281.9858 ($B^+ +$ 28, 2), 253.9915 ($B^+ +$ H, 65), 252.9870 (B^+, 37), 174.0788 ($B^+ +$ H − Se, 100), 147 ($MeOC_6H_4NC_2H_2^+$, 9), 77 (Ph^+, 5). The ^1H and ^{13}C NMR data are given in Tables I and II.

Anal. Calcd for $C_{14}H_{18}N_2O_5Se$: C, 45.05; H, 4.86; N, 7.51. Found: C, 45.25; H, 4.93; N, 7.70.

*1-*p*-Bromophenyl-(1,2-dideoxy-α-*D*-glucofurano)[2,1-*d*]imidazolidine-2-selone* (**3**).—2-Amino-2-deoxy-D-glucose hydrochloride (78 mg, 0.36 mmol), $NaHCO_3$ (31 mg, 0.36 mmol), and *p*-bromophenyl isoselenocyanate (112 mg, 0.43 mmol) in EtOH–water (2:1, 4 mL) were reacted, as described for **2**, to give **3** (116 mg, 77%), mp 238–240° (dec.); $[\alpha]_D^{22}$ +57°, $[\alpha]_{578}^{22}$ +61°, $[\alpha]_{546}^{22}$ +104° (*c* 0.8, pyridine); λ_{max}^{MeOH} 269 nm (ϵ_{mM} 10.7); ν_{max} 3427, 3360, 3190, 3152 (NH, OH), 1475 (NH), 1641, 1494, 1438, and 826 cm^{-1} (aryl, *p*-substituted). Mass spectrum: *m/z* 423.9387 and 421.9355 (M^+, 4 and 9%), 303.8863 and 301.8872 ($B^+ +$ H, 50 and 60), 302.8916 and 300.8902 (B^+, 48 and 51), 223.9783 and 221.9805 ($B^+ +$ H − Se, 94 and 100), 196.9676 and 194.9667 ($BrC_6H_4NC_2H_2^+$, 19 and 19), 156.9484 and 154.9608 ($C_6H_4Br^+$, 19 and 30). The ^1H and ^{13}C NMR data are given in Tables I and II.

Anal. Calcd for $C_{13}H_{15}BrN_2O_4Se$: C, 36.99; H, 3.58; N, 6.64. Found: C, 37.04; H, 3.60; N, 6.55.

Crystal analysis *.—Compound **3** crystallised as prisms from EtOH, with approximate dimensions 0.11 × 0.05 × 0.22 mm; preliminary Weissenberg photographs indicated that crystals belonged to the orthorhombic system with systematic absences consistent with $P2_12_12_1$. Accurate cell dimensions and crystal orientation matrix, determined on a CAD-4 diffractometer by a least-squares treatment of the setting angles of 25 reflections in the range $4 < \theta < 20°$, were $a = 10.076(3)$, $b = 31.800(7)$, $c = 4.697(5)$ Å, $Z = 4$. The unit cell volume (V) was 1505.0(1) Å^3,

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* Lists of the observed and calculated structure factors, the anisotropic thermal parameters, and the non-hydrogen and hydrogen atomic co-ordinates are deposited with, and can be obtained from, Elsevier Science Publishers B.V., BBA Data Deposition, P.O. Box 1527, Amsterdam, Netherlands. Reference should be made to No. BBA/DD/507/*Carbohydr. Res.*, 237 (1992) 303–311.

and the absorption coefficient (μ) was 5.11 mm^{-1}. D_c was 1.86 Mg.m^{-3} and D_m measured by flotation, was 1.86 Mg.m^{-3}; $F(000) = 832$, at room temperature.

An Enraf–Nonius CAD-4 diffractometer was used with graphite monochromator and MoK_α radiation (0.7107 Å), the $\omega/2\theta$ mode, and $2\theta_{max} = 40°$ ($0 \leqslant h \leqslant 10$, $0 \leqslant k \leqslant 31$, $0 \leqslant l \leqslant 4$). Two reference reflections ($\bar{4}$ 3 0 and 4 $\bar{3}$ 0) were measured each hour in order to monitor crystal stability, and were re-centered after every 100 measured reflections in order to monitor crystal orientation. No significant changes in the intensities were noted. From 984 unique reflections measured, 602 were observed with $I > 2\sigma(I)$. Data were corrected for Lorentz polarisation, and an empirical absorption correction following the DIFABS procedure[13] was applied to the isotropically refined data. The structure was solved by Patterson techniques (Br and Se) and remaining non-H atoms from a single cycle of DIRDIF[14]. After anisotropic refinement by full-matrix least-squares of all the 21 non-hydrogen atoms in the asymmetric units, the hydrogen atoms (except OH from differences synthesis) were placed in calculated positions (C–H = 1.0 Å), and were assigned the same isotropic thermal parameters as the atoms to which they were bonded, and were included, but not refined, in the final stage of refinement.

Refinement was based on F (structure amplitudes) to minimise the function $\Sigma\omega(|F_o| - |F_c|)^2$ with $\omega = 1/\sigma^2(F_o)$; 190 parameters were refined (9 parameters per atom plus 1 for the scale); the over-determination ratio was 6.08 reflections/parameter. The refinement led to a final convergence with $R = 0.07$. The high R factor and esd's, as well as the discrepancies between F_o and F_c, were due to the poor quality of the crystals. The maximum shift/error was 0.16 and goodness-of-fit parameters $S = 0.86$. Atomic scattering factors were taken from the International Tables for X-Ray Crystallography[15] and all calculations were performed with the X-Ray System of crystallographic programs[16].

The bond lengths (Å) and angles (°) in Table III were calculated by the program PARST[17].

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