Synthesis of 4,4′-substituted 2,2′-[ethane-1,2-diylbis(selanediyl)]bis(1*H*-imidazol-5(4*H*)-ones)

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Synthesis of new bis(seleno-imidazolone) derivatives bearing the alkyl and aryl moieties at the N(1) atom of the five-membered ring was developed. Cytotoxicity of the synthesized compounds against A549, VA-13, MCF-7, and HEK293T cell lines was evaluated.

Key words: imidazolone, 2-selenohydantoine, bis(seleno) derivatives, organoselenium compounds, alkylation, cytotoxicity, MTT test, *in vitro*.

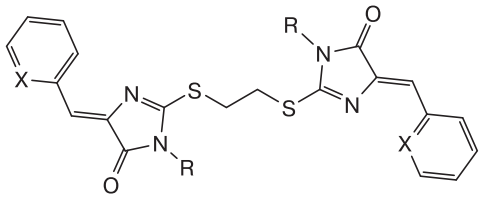
To date, a wide variety of the organoselenium derivatives have been described that show antioxidant,[1—6] antitumor,[7] antiviral,[8] antimicrobial,[9] antithyroid[10] effects and other biological activities.[11] Interest in organoselenium chemistry increased significantly after finding that selenium is present in glutathione peroxidase, the mammalian enzyme that regulates the concentration of the reactive oxygen species in cells.[12] Lysova and coworkers[13] have reported the synthesis of metal-organic frameworks based on N-donor Se-containing ligand; luminescence of the synthesized structures was found to be due to intraligand transitions.

Bis-thioimidazolone derivatives[14,15] were used as the ligands to obtain complexes of different metals (Cu^{+1}, Cu^{+2}, Co^{+2})[16—22] and some of them were developed as compounds with potential antifungal activity.[23]

Bis-selenoimidazolone derivatives and their biological properties are less studied. Synthesis of complex compounds of selenoimidazolones with Co^{+2}, Ni^{+2}, Cu^{+2}, and Cu^{+1} and their electrochemical properties (oxidation and reduction potentials) were first reported in 2012.[24] Biological activities of 3-aryl-5-arylidene-2-selenohydantoins were studied.[25] It was found that in the pairs of 2-thiohydantoin and 2-selenohydantoin derivatives with the same substituents, the Se-containing compounds are more active.

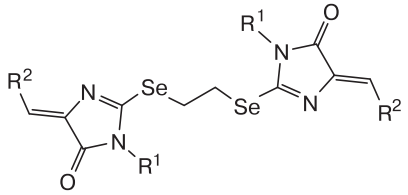
The aim of the present work is to synthesize 4-alkylidene- and 4-arylidene-substituted derivatives of 2-selenohydantoin dimers and study their antitumor activity *in vitro*. It should be noted that dispiro derivatives of 2-selenohydantoin with promising antioxidant and cytotoxic activities were recently synthesized.[26]

Bis-thioimidazolone derivatives



R = Alk, Ar, HetAr
X = CH, N

Bis-selenoimidazolone derivatives



R^1, R^2 = Alk, Ar

Results and Discussion

Compound **1** used as the starting material in the synthesis of 4-alkylidene- and 4-arylidene-substituted derivatives was synthesized as earlier described.[25] Selenoureas **2a—c** and 2-selenohydantoins **3a—f** were prepared as shown in Scheme 1 following the known procedures.[27,28]

Previously,[24] compound **3d** was synthesized in 25% yield; while the method reported in the present work provides the target compounds in the yields above 55%.

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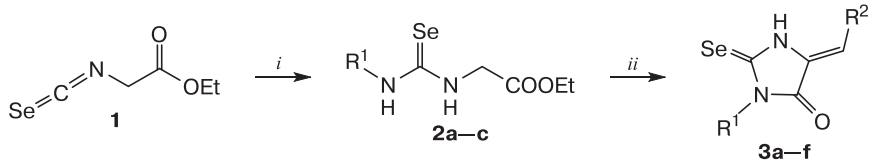
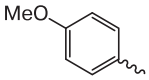
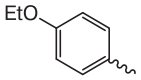
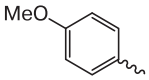
Scheme 1



Reagents and conditions: *i.* R^1NH_2, DMAP (1 mol.%) or base-free, Et_2O; *ii.* 1) R^2CHO, KOH (2%), EtOH; 2) NH_4Cl/H_2O.

Compound	R^1	R^2	Yield (%)
2a		—	97
2b	Ph	—	41
2c		—	82
3a			69
3b		Ph	91
3c			98
3d	Ph	Ph	58
3e	Ph		76
3f			55

The intermediate selenohydantoins of type **3** are capable of undergoing selenol-selenone tautomerism and, therefore, show high SeH acidity (*cf.* pK_a (Me—SeH)[29] = 5.2; pK_a (Ph—SeH)[30] = 5.9). These compounds are readily deprotonated on treatment with inorganic bases in polar aprotic solvents (DMSO, DMF).

When compounds **3a—f** were treated with excess K_2CO_3 in DMF, the color of the reaction mixture changed to red due to the selenolate formation. To the obtained solution of selenolate, 1,2-dibromoethane was added portionwise at −10 °C. 1,2-Dibromoethane reacted with selenolate to form an ethylene bridge between two selenohydantoin moieties. The full conversion was achieved within 8—9 h (Scheme 2). The reaction conditions for the synthesis of compounds **4a—f** were optimized with respect of the base (Cs_2CO_3, K_2CO_3) and solvent (DMSO, DMF). It was found that both Cs_2CO_3 and K_2CO_3 provide nearly the same yields of the target products, therefore, less expensive K_2CO_3 was preferred. In DMSO, the content of monoalkylation products was higher and prolongation of the reaction time led to resinification of the reaction mixture.

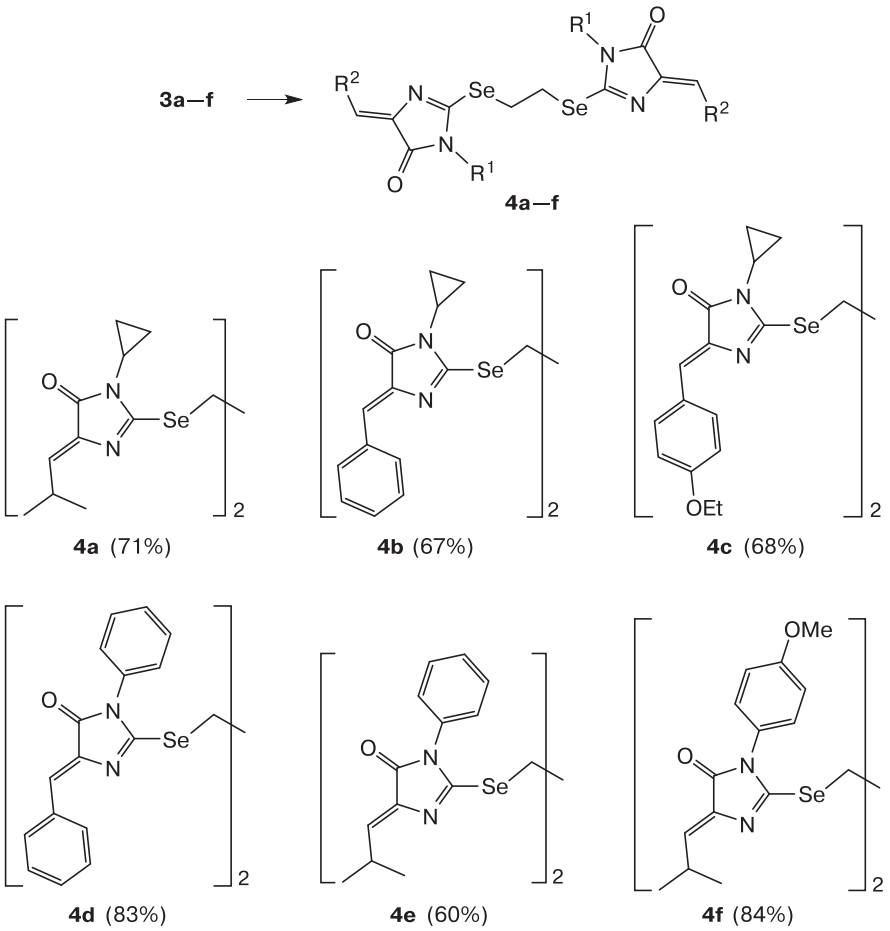
Thus, we synthesized a series of 2-selenohydantoin dimers **4a—f** bearing aliphatic and aromatic substituents at N(1).

Cytotoxicity of the synthesized compounds **4a—f** was evaluated *in vitro* (Table 1) against MCF-7 (metastatic breast cancer), A549 (lung adenocarcinoma), VA-13 (slow-growing human lang fibroblasts), and HEK293T (easily transducable human embryonic kidney 293 cells expressing a mutant variant of SV40 large T antigen) cell lines using standard MTT assay.[31] Enzalutamide (antiandrogen)[32,33] and Nutlin-3a (inhibitor of the p53/MDM2 interaction)[34,35] were used as the reference drugs.

Table 1. Cytotoxicity (CC_{50}) of the synthesized compounds **4a—f**

Compound	CC_{50}/μmol L^{-1}			
	VA-13	A549	MCF-7	HEK293T
4a	3.3±0.5	2.7±0.4	17.5±2.3	9.9±0.7
4b	7.5±1.4	25.0±5.8	52.7±16	54.1±12.5
4c	13.9±3.1	8.0±0.7	32.7±5.5	4.7±0.7
4d	16.9±3.2	4.6±1	131.8±46.4	3.1±0.9
4e	1.9±0.3	1.7±0.1	4.8±0.5	4.5±0.3
4f	14.4±1.1	11.6±0.9	33.5±5.1	12.5±0.8
Nutlin-3a	—	15.1	8.3	—
Enzalutamide	63.4	21.2	>100	5.1±0.3

Scheme 2



Reagents and conditions: 1,2-dibromoethane (0.5 equiv.), K_2CO_3 (1.5 equiv.), DMF, −10 °C.

All studied compounds exhibited high nonspecific cytotoxicity against the test cell lines. Compounds **4c** and **4d** showed selective cytotoxic effect against HEK293T and A549 cells as compared to the non-cancerous cell line VA-13. Compound **4e** occurred most cytotoxic; its CC_{50} value is almost an order of magnitude higher than that of the reference compounds and compounds **4a** and **4f** bearing the isopropylidene substituents at the position 5 of the imidazolone ring. For more detailed evaluation of the cytotoxicity effect of the synthesized compounds, a broader array of the cell lines is required as well as additional studies of the mechanism of cytotoxicity, for instance, the studies of binding of the compounds with bovine serum albumin, their ability to intercalate into the DNA duplex, proteasome inhibitory activity, *etc*.

Experimental

All starting reagents are commercially available and were used as purchased. The reaction course was monitored by TLC using precoated plates Merck Silicagel 60 F_{254}. ^{1}H NMR and ^{13}H NMR spectra were recorded on Bruker Avance 400 instrument in $CDCl_3$ and DMSO-d_6. IR spectra were recorded with a UR-20 IR spectrometer in Nujol and a Termo Nicolet IR200 FT-IR spectrometer at a resolution of 4 cm^{-1}. The reactions were monitored by LC/MS using Thermo Dionex Ultimate 3000 and ABSciex 3200 Qtrap instruments equipped with a quadruple detector and a Thermo Scientific Acclaim RSLC 120 C18 3 μm column (150×4.6 mm). High-resolution electrospray ionization mass spectrometry was performed with a Bruker microTOF II instrument. Melting points of the synthesized compounds were measured with an OptiMelt MPA100 automated melting point system with the heating rate from 0.1 to 20 °deg min^{-1} (maximum temperature of 400 °C, accuracy of 0.1 °C).

Synthesis of ethyl 2-[3-alkyl(aryl)selenoureido]acetates (2a—c) was described in detail in our previous publication.[27] To a solution of amine (1 equiv.) in anhydrous diethyl ether, ethyl 2-isoselenocyanoacetate **1** (1.1 equiv.) was added dropwise. The reaction mixture was stirred for 30 min and DMAP (1 mol.%) was added. Stirring was continued for 2—12 h. The precipitated selenoureas **2a—c** were collected by filtration using filtration funnels with glass sintered disc, washed with small amount of chilled diethyl ether, and dried under vacuum of the water jet pump.

Synthesis of 2-selenohydantoins 3a—f (general procedure).[27,28] Selenoureas **2** (1 equiv.) were added to 2% solution of KOH in EtOH (10 mL) under vigorous stirring. After 5 min, the mixture acquired a deep violet color. Then the appropriate aldehyde (1.2 equiv.) was added. The reaction mixture was stirred at 20 °C for 2 h, neutralized to pH 4.5 with a saturated aqueous ammonium hydrochloride solution, and extracted with dichloromethane (3×50 mL). The combined organic layers were dried with Na_2SO_4 and the solvent was removed *in vacuo*. The residue was subjected to flash column chromatography (elution with dichloromethane). The eluates containing the target product were concentrated *in vacuo* to dryness. The obtained solid was recrystallized from glacial AcOH to give pure *Z* isomers of compounds **3a—f**.

Physicochemical and spectral data of compounds **3a,c,d,f** coincide with those published earlier.[27,28]

(*Z*)-5-Benzylidene-3-cyclopropyl-2-selenoxoimidazolidin-4-one (3b) was prepared from ethyl 2-(3-cyclopropylselenoureido) acetate (**2a**) (0.25 g) and benzaldehyde (0.115 mL). Yield 0.28 g (91%). Orange crystals. M.p. 155—156 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ: 0.95—1.01 (m, 4 H, CH_{2Cyclo}); 2.86 (ddd, 1 H, CH_{Cyclo}, *J* = 11.1 Hz, *J* = 7.3 Hz, *J* = 4.1 Hz); 6.65 (s, 1 H, CH); 7.41—7.45 (m, 3 H, H_{Ar}); 7.78—7.80 (m, 2 H, H_{Ar}); 12.80 (s, 1 H, NH). ^{13}C NMR (101 MHz, DMSO-d_6), δ: 6.7 (2 C), 25.4, 113.2, 126.7, 128.8 (2 C), 129.5, 130.3 (2 C), 132.4, 164.0, 180.6. IR (KBr), ν/cm^{-1}: 451, 554, 579, 690, 724, 760, 821, 874, 958, 925, 1027, 1054, 1088, 1169, 1206, 1236, 1313, 1266, 1326, 1435, 1497, 1461, 1651, 1728, 1740, 3011, 3058, 3200. HRMS (FTMS + *c*ESI): found *m/z* 293.0188 $[M + H]^+$; calculated for $C_{13}H_{12}N_2OSe$ 293.0188.

(*Z*)-5-(2-Methylpropylidene)-3-phenyl-2-selenoxoimidazolidin-4-one (3e) was prepared from ethyl 2-(3-phenylselenoureido)acetate (**2b**) (035 g) and isobutyraldehyde (125 mL). Yield 0.274 g (76%). Yellow crystals. M.p. 202—203 °C. ^{1}H NMR (400 MHz, DMSO-d_6), δ: 1.07 (d, 6 H, 2 Me, *J* = 6.5 Hz); 3.01 (qd, 1 H, CH, *J* = 13.0 Hz, *J* = 6.6 Hz); 5.84 (d, 1 H, CH, *J* = 10.5 Hz); 7.34 (d, 2 H, H_{Ar}, *J* = 7.1 Hz); 7.47 (m, 3 H, H_{Ar}); 12.95 (s, 1 H, NH). ^{13}C NMR (75 MHz, DMSO-d_6), δ: 21.6 (2 C), 26.5, 125.7, 128.2, 128.7 (2 C), 128.8, 128.9 (2 C), 134.0, 162.2, 177.8. IR (KBr), ν/cm^{-1}: 409, 440, 501, 522, 607, 627, 668, 687, 734, 754, 860, 880, 903, 943, 968, 989, 1015, 1056, 1084, 1123, 1145, 1156, 1171, 1211, 1242, 1272, 1308, 1369, 1382, 1433, 1452, 1471, 1483, 1576, 1645, 1700, 2937, 3222. HRMS (FTMS + cESI): found *m/z* 293.0196 $[M - H]^-$; calculated for $C_{13}H_{14}N_2OSe$ 293.0198.

Synthesis of 4,4′-substituted 2,2′-[ethane-1,2-diylbis(selanyldiyl)]bis[1*H*-imidazol-5(4*H*)-ones] (4a—f) (general procedure). To a solution of (*Z*)-3-substituted 5-[(alkyl/aryl)idene]-2-selenoxoimidazolidin-4-one **3** (1 equiv.) in DMF, K_2CO_3 (1.5 equiv.) was added. The obtained mixture was stirred for 10 min, cooled to −10 °C, and treated portionwise with 1,2-dibromoethane (0.5 equiv.). After 3—4 h, the reaction mixture was warmed to ~20 °C, this resulted in the change in the color of the reaction mixture from red to yellow. After the reaction completion (TLC monitoring), the mixture was diluted with water, the precipitate obtained was collected by filtration using filtration funnels with glass sintered disc, and successively washed with EtOH and diethyl ether. The obtained dry powder was subjected to column chromatography. The eluates containing the target products were concentrated *in vacuo* and recrystallized from dichloromethane—petroleum ether to give pure products **4**.

(4*Z*,4′*Z*)-2,2′-[Ethane-1,2-diylbis(selanediyl)]bis[1-cyclopropyl-4-(2-methylpropylidene)-1*H*-imidazol-5(4*H*)-one] (4a) was prepared from (*Z*)-3-cyclopropyl-5-(2-methylpropylidene)-2-selenoxoimidazolidin-4-one (**3a**) (90 mg) and 1,2-dibromoethane (33 mg). Yield 67 mg (71%). White crystals. M.p. 172—173 °C. ^{1}H NMR (400 MHz, $CDCl_3$), δ: 0.96 (ddd, 8 H, 4 CH_{2Cycl}; *J* = 6.5 Hz, *J* = 3.8 Hz, *J* = 2.5 Hz); 1.11 (d, 12 H, 4 Me, *J* = 6.7 Hz); 2.57 (dq, 2 H, 2 CH_{Cycl}, *J* = 6.5 Hz, *J* = 4.2 Hz); 3.18 (qd, 2 H, 2 CH_{iobut}, *J* = 13.3 Hz, *J* = 6.6 Hz); 3.72 (s, 4 H, 2 CH_2); 6.14 (d, 2 H, 2 CH, *J* = 9.6 Hz). ^{13}C NMR (101 MHz, $CDCl_3$), δ: 6.5 (4 C), 22.4 (4 C), 22.5 (2 C), 26.6 (2 C), 27.5 (2 C), 138.0 (2 C), 139.8 (2 C), 160.9 (2 C), 169.0 (2 C). IR (diamond), ν/cm^{-1}: 577, 662, 712, 755, 826, 934, 971, 1032, 1100, 1114, 1131, 1180, 1229, 1286, 1370, 1397, 1455, 1509, 1663, 1719, 1728, 2866, 2963, 3015. HRMS (FTMS + *c*ESI): found 543.0766 $[M + H]^+$; calculated for $C_{22}H_{30}N_4O_2Se_2$ 543.0772.

(4*Z*,4′*Z*)-2,2′-[Ethane-1,2-diylbis(selanediyl)]bis[4-benzylidene-1-cyclopropyl-1*H*-imidazol-5(4*H*)-one] (4b) was prepared from (*Z*)-5-benzylidene-3-cyclopropyl-2-selenoxoimidazolidin-4-one (**3b**) (80 mg) and 1,2-dibromoethane (22 mg). Yield 56 mg (67%). Yellow crystals. M.p. 236—237 °C. ^{1}H NMR (400 MHz, $CDCl_3$), δ: 1.02—1.07 (m, 8 H, 4 CH_{2Cycl}); 2.64—2.70 (m, 2 H, 2 CH_{Cycl}); 3.91 (s, 4 H, 2 CH_2); 6.87 (s, 2 H, 2 CH); 7.37—7.41 (m, 6 H, H_{Ar}); 8.10—8.12 (m, 4 H, H_{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$), δ: 6.5 (4 C), 22.6 (2 C), 26.7 (2 C), 124.5 (2 C), 128.7 (4 C), 130.1 (2 C), 132.0 (4 C), 134.5 (2 C), 139.0 (2 C), 163.4 (2 C), 169.9 (2 C). IR (diamond), ν/cm^{-1}: 539, 552, 581, 617, 656, 693, 727, 783, 765, 829, 873, 938, 954, 1007, 1029, 1107, 1153, 1179, 1196, 1212, 1288, 1315, 1329, 1237, 1374, 1351, 1399, 1427, 1449, 1570, 1491, 1636, 1717, 3047. HRMS (FTMS + *c*ESI): found *m/z* 611.0450 $[M + H]^+$; calculated for $C_{28}H_{26}N_4O_2Se_2$ 611.0459.

(4*Z*,4′*Z*)-2,2′-[Ethane-1,2-diylbis(selanediyl)bis[1-cyclopropyl-4-(4-ethoxybenzylidene)-1*H*-imidazol-5(4*H*)-one] (4c) was prepared from (*Z*)-3-cyclopropyl-5-(4-ethoxybenzylidene)-2-selenoxoimidazolidin-4-one (**3c**) (73 mg) and 1,2-dibromoethane (18 mg). Yield 51 mg (68%). Yellow crystals. M.p. 231—232 °C. ^{1}H NMR (400 MHz, $CDCl_3$), δ: 1.01 (s, 8 H, 4 CH_{2Cycl}); 1.42—1.45 (t, 6 H, 2 $OCH_2C\underline{H}_3$, *J* = 6.2 Hz); 2.63—2.69 (s, 2 H, 2 CH_{Cycl}); 3.90 (s, 4 H, 2 CH_2); 4.07 (q, 4 H, 2 $OC\underline{H}_2CH_3$, *J* = 11.8 Hz, *J* = 6.0 Hz); 6.85 (s, 2 H, 2 CH), 6.89 (d, 4 H, H_{Ar}, *J* = 7.4 Hz); 8.07 (d, 4 H, H_{Ar}, *J* = 7.2 Hz). ^{13}C NMR (101 MHz, $CDCl_3$), δ: 6.52 (4 C), 14.9 (2 C), 22.6 (2 C), 26.7 (2 C), 63.7 (2 C), 114.8 (4 C), 124.8 (2 C), 127.2 (2 C), 133.9 (4 C), 137.2 (2 C), 160.6 (2 C), 161.4 (2 C), 170.0 (2 C). IR (diamond), ν/cm^{-1}: 488, 540, 560, 581, 660, 724, 757, 811, 834, 873, 893, 923, 954, 1003, 1031, 1042, 1085, 1109, 1148, 1175, 1211, 1240, 1306, 1348, 1253, 1369, 1396, 1423, 1443, 1495, 1565, 1508, 1630, 1599, 1710, 2925, 2982, 3083. HRMS: (FTMS + *c*ESI): found *m/z* 699.0974 $[M + H]^+$; calculated for $C_{32}H_{34}N_4O_4Se_2$ 699.0984.

(4*Z*,4′*Z*)-2,2′-[Ethane-1,2-diylbis(selanediyl)]bis[4-benzylidene-1-phenyl-1*H*-imidazol-5(4*H*)-one] (4d) was prepared from (*Z*)-5-benzylidene-3-phenyl-2-selenoxoimidazolidin-4-one (**3d**) (100 mg) and 1,2-dibromoethane (28 mg). Yield 86 mg (83%). Yellow crystals. M.p. 245—246 °C. ^{1}H NMR (400 MHz, $CDCl_3$), δ: 3.94 (s, 4 H, 2 CH_2); 7.00 (s, 2 H, CH); 7.33—7.38 (m, 10 H, H_{Ar}); 7.47—7.55 (m, 6 H, H_{Ar}); 8.14 (d, 4 H, H_{Ar}, *J* = 4.1 Hz). ^{13}C NMR (101 MHz, $CDCl_3$), δ: 26.9 (2 C), 125.5 (2 C), 127.2 (4 C), 128.8 (4 C), 129.5 (2 C), 129.8 (4 C), 130.3 (2 C),

132.2 (4 C), 133.0 (2 C), 134.4 (2 C), 138.3 (2 C), 160.9 (2 C), 168.7 (2 C). IR (diamond), ν/cm^{-1}: 559, 639, 658, 689, 717, 760, 727, 774, 891, 925, 946, 1026, 1063, 1107, 1152, 1206, 1228, 1284, 1304, 1320, 1349, 1361, 1398, 1448, 1488, 1571, 1595, 1634, 1728, 3021, 3423. HRMS (FTMS + *c*ESI): found *m*/*z* 683.0470 [M + H]$^+$; calculated for $C_{34}H_{26}N_4O_2Se_2$ 683.0459.

(4*Z*,4′*Z*)-2,2′-[Ethane-1,2-diylbis(selanediyl)]bis[4-(2-methylpropylidene)-1-phenyl-1*H*-imidazol-5(4*H*)-one] (4e) was prepared from (*Z*)-5-(2-methylpropylidene)-3-phenyl-2-selenoxoimidazolidin-4-one (**3e**) (80 mg) and 1,2-dibromoethane (26 mg). Yield 42 mg (60%). White crystals. M.p. 166—167 °C. ^{1}H NMR (400 MHz, $CDCl_3$), δ: 1.14 (d, 12 H, 4 Me_{isobut}, J = 6.7 Hz); 3.24 (qd, 2 H, 2 CH_{isobut}, J = 13.5 Hz, J = 6.7 Hz); 3.74 (s, 4 H, 2 CH_2); 6.30 (d, 2 H, 2 CH, J = 9.7 Hz); 7.26—7.30 (m, 4 H, H_{Ar}); 7.43—7.50 (m, 6 H, H_{Ar}). ^{13}C NMR (101 MHz, $CDCl_3$), δ: 22.3 (4 C), 26.9 (2 C), 27.7 (2 C), 127.2 (4 C), 127.3 (2 C), 129.4 (2 C), 129.7 (4 C), 129.82 (2 C), 129.84 (2 C), 133.0 (2 C), 139.2 (2 C). IR (diamond), ν/cm^{-1}: 422, 506, 585, 613, 631, 660, 707, 750, 721, 842, 767, 881, 921, 943, 971, 1026, 1055, 1073, 1112, 1129, 1173, 1211, 1285, 1356, 1383, 1397, 1452, 1596, 1513, 1662, 1733, 2869, 2928, 2965, 3052. HRMS (FTMS + *c*ESI): found *m*/*z* 615.0764 [M + H]$^+$; calculated for $C_{28}H_{30}N_4O_2Se_2$ 615.0772.

(4*Z*,4′*Z*)-2,2′-[Ethane-1,2-diylbis(selanediyl)]bis[1-(4-methoxyphenyl)-4-(2-methylpropylidene)-1*H*-imidazol-5(4*H*)-one] (4f) was prepared from (*Z*)-3-(4-methoxyphenyl)-5-(2-methylpropylidene)-2-selenoxoimidazolidin-4-one (**3f**) (70 mg) and 1,2-dibromoethane (21 mg). Yield 61 mg (84%). White crystals. M.p. 119—120 °C. ^{1}H NMR (400 MHz, $CDCl_3$), δ: 1.13 (d, 12 H, 4 Me_{isobut}, J = 6.7 Hz); 3.18—3.27 (m, 2 H, 2 CH_{isobut}); 3.72 (s, 4 H, 2 CH_2); 3.83 (s, 6 H, 2 OMe); 6.28 (d, 2 H, 2 CH, J = 9.7 Hz); 6.97 (d, 4 H, H_{Ar}, J = 8.8 Hz); 7.19 (d, 4 H, H_{Ar}, J = 8.7 Hz). ^{13}C NMR (101 MHz, $CDCl_3$), δ: 22.3 (4 C), 26.7 (2 C), 27.7 (2 C), 55.7 (2 C), 114.9 (4 C), 125.4 (2 C), 128.7 (4 C), 128.8 (2 C), 138.9 (2 C), 139.3 (2 C), 160.3 (2 C), 168.0 (2 C). IR (diamond), ν/cm^{-1}: 534, 593, 734, 745, 754, 834, 936, 947, 1024, 1108, 1131, 1172, 1185, 1211, 1299, 1283, 1259, 1360, 1446, 1454, 1506, 1514, 1606, 1655, 1729, 2864, 2961. HRMS (FTMS + *c*ESI): found *m*/*z* 675.0976 [M + H]$^+$; calculated for $C_{30}H_{34}N_4O_4Se_2$ 675.0983.

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This paper does not contain descriptions of studies on animals or humans.

The authors declare no competing interests.

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