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Article

Synthesis, Characterization and *in vitro* Antioxidant Activity of New Chiral *N*-boc Organotellurium Compounds, $(CH_3)_3OC(O)NHCH(R)C(O)NHCH_2$-$CH_2Te$-$C_6H_4$-4-$OCH_3$, Containing Carbamate and Peptide Groups

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Synthesis, characterization and antioxidant activity of a new series of chiral *N*-boc oraganotellurium compounds, $(CH_3)_3OC(O)NHCH(R)C(O)NHCH_2CH_2Te$-$C_6H_4$-4-$OCH_3$, containing carbamate and peptide groups have been reported in this paper. These chiral peptides were synthesized in good to excellent yields, via acid-amine coupling reaction of *N*-boc *L*-amino acids with 2-(4-methoxyphenyltelluro) ethylamine in presence of dicyclohexyl carbodimide (DCC) at room temperature. The elemental analyses, Fourier transform infrared (FTIR), ^1H and $^{13}C\{^1H\}$ nuclear magnetic resonance (NMR) spectra and mass spectra were characteristic. Specific optical rotation (SOR) was also determined. *In vitro* antioxidant activity of these multi-functional compounds in methanol has been evaluated against 2,2-diphenyl-1-picrylhydrazyl (DPPH) radicals with 2,6-di-*tert*-butyl-4-methylphenol (BHT) as a standard reference compound. The IC_{50} (inhibitory concentration 50) values of these chiral peptides revealed significant inhibition against DPPH radicals and found to be effective antioxidants.

Keywords: organochalcogen, aminoacid derivative, antioxidant

Introduction

An antioxidant is "any substance that delays or prevents oxidation of an oxidisable species".[1,2] Oxidative stress, induced by reactive oxygen species (ROS) produced in the body, is one of the main factors of current slow killer diseases, that population suffering from, like cancer, diabetes, cardiovascular, neurological (Alzheimer's and Parkinson's), inflammatory viral diseases and digestive disorders.[3-6]

Since the discovery of "Ebselen", a natural antioxidant, a number of organochalcogen (S, Se, Te) compounds have been designed, synthesized and investigated as free radical scavengers or antioxidants to mimic the natural ones.[7-30] The divalent organochalcogen compounds have the potential to act as catalytic antioxidants because they readily react with many types of oxidants such as peroxides, peroxynitrites, singlet oxygen and ozone resulting tetravalent organochalcogens (that is chalcogenides to chalcogenoxides and chalcogenols to dichalcogenides) which in turn reduced by many mild reducing agents. The antioxidant activity of organochalcogen compounds is also related to their redox potentials and rates of oxidation in solutions.[31-35] Even though a large number of antioxidants are available, they have many disadvantages such as they are costly and many of them cause various side effects due to the toxic byproducts.[36-40,22]

Organotellurium compounds have shown many advantages as free radical scavengers or antioxidants. They act as both peroxide decomposers and chain-breaking, donating antioxidants even under biologically relevant conditions. They have also demonstrated higher radical scavenging efficiency than the corresponding S and Se compounds.[41,42]

Organotellurium compounds have been much less explored in biology unlike the compounds of its lower congeners (S and Se), even though tellurium exhibit various similar properties of sulfur and selenium[43-46] which may be due to the fact that tellurium was considered non-essential biological trace element, commercial non-availability of a wide variety of organotellurium compounds as starting materials and some misconception that they are air sensitive, foul smelling and even toxic. A few reasons among enhanced interest currently in the biological chemistry of organotellurium compounds are the availability of modern analytical techniques (^{125}Te Fourier transform nuclear magnetic resonance, FT-NMR; atomic absorption spectroscopy, AAS; and inductively coupled plasma-atomic

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emission spectrometry, ICP-AES) to study and understand the solution behavior of Te containing systems, such an option does not exist for sulfur compounds, the secondary interactions (Te···X where X = O, Cl, Br, I or M) arises from the hypervalent nature of Te, thus increases the stability of organotellurium compounds and higher redox activity of the tellurium.

Numerous organochalcogen compounds containing amine, peptide/amide and carbamate groups enhances the rates of their redox reactions[16,22,23,47] and the effect of these groups on the activity of organotellurium compounds was expected to be more pronounced than that of corresponding organoselenium compounds.[47,23] The biological activity of chiral organochalcogen compounds may be specific. Recently reported that the organoselenium and tellurium compounds which contain the secondary interactions between chalcogen atom and other heteroatoms [TeX, X = N, O, S, Cl, Br, I] through internal chelation play an important role in the catalytic antioxidant activity.[48-50]

There are numerous synthetic and natural chiral organoselenium compounds[20-26,43-46] but there has not been studied antioxidant properties of chiral organotellurium compounds containing peptide and carbamate functionalities.

In view of the above advantages and to expand the applications of chiral organotellurium compounds in biological activities[51] particularly as antioxidants, we have reported in this paper the synthesis, spectral and analytical characterization data of chiral *N*-boc organotellurium compounds containing amide and carbamate groups. These chiral multi-functionalized compounds (**4a**-**4g**) synthesized from *N*-boc *L*-amino acids and 2-(4-methoxyphenyltelluro) ethylamine via condensation in presence of dicyclohexyl carbodimide (DCC). The *in vitro* antioxidant activity of these compounds against 2,2-diphenyl-1-picrylhydrazyl (DPPH) radicals has been studied. All the compounds showed significant antioxidant activity when compared to 2,6-di-*tert*-butyl-4-methylphenol (BHT).

Results and Discussion

Synthesis and characterization of chiral *N*-boc organotellurated peptides (**4a-4g**)

A new series of chiral *N*-boc organotellurated compounds (**4a-4g**, Figure 1) were synthesized by condensation of *N*-boc *L*-amino acids and 2-(4-methoxyphenyltelluro) ethylamine in presence of DCC as a dehydrating agent according to the reactions given in the Scheme 1. The reactions were carried out in dry dichloromethane. The products were purified by flash column chromatography. The compounds, **4a**-**4g**, were obtained with good to excellent yields of about 80-95%.

FTIR spectra of chiral *N*-boc organotellurated peptides (**4a**-**4g**)

Fourier transform infrared (FTIR) spectra were recorded in the range of 400-4000 cm^{-1}. In the IR spectra of compounds, **4a**-**4g**, characteristic bands were obtained for NH, C–H, C=C, C=O, C–O, C–S and C–Te functional groups. The –NH– stretching bands were observed at around at 3300-3450 cm^{-1} and the C=O stretching vibrational bands were obtained at 1630-1660 cm^{-1}. The C–S stretching band in **4d** and **4e** were appeared at 733 cm^{-1}. The C–Te aryl stretching vibrational band was appeared in the region of 510 ± 5 cm^{-1}.[52-55]

^{1}H NMR spectra of chiral *N*-boc organotellurated peptides (**4a**-**4g**)

The ^{1}H NMR spectra of the compounds **4a**-**4g** were found characteristic. The CH_2Te and CH_2N signals were observed at δ, 2.734-2.814 and 3.290-3.375 ppm and appeared as triplets and multiplets respectively. These signals were found deshielded about 0.4 to 0.5 ppm when compared to 2-(4-methoxyphenyltelluro) ethylamine.[55] There are two types of NH groups such as the carbamate (Boc-NH–) and amide (>CO–NH–). The carbamate NH proton gave a doublet in the range of δ, 6.5 to 6.9 ppm while the amide NH gave a triplet between 7.95 to 8.25 ppm due to coupling with CH and CH2 protons respectively. In all the compounds a singlet was observed at around 1.35 ppm for all the 9 protons of t-Bu group. In **4a** the methyl group showed a doublet at 1.118-1.136 ppm. In **4b** the benzylic CH2 protons were split into two doublets of a doublet at 2.672-2.705 and 2.891-2.924 ppm due to their diastereotopic nature. In **4c** the CH, CH2 and CH3 protons all gave multiplets between 0.77 to 1.25 ppm. The protons of $–CH_2–CH_2–S–CH_3$ group in **4d** were appeared as a multiplet, triplet and a singlet at 1.698-1.771, 2.384-2.423 and 2.013 ppm respectively. In **4e**, the $-CH_2SCH_2Ph$, protons were observed as two multiplets. In 4f the phenolic OH was obtained as a singlet at 9.12 ppm. The aromatic protons present at meta and ortho to Te were observed at 6.804-6.9 and 7.606-7.663 ppm respectively in all the compounds which were in agreement with that reported for 2-(4-methoxyphenyltelluro) ethylamine.[55] The peaks for other aromatic protons were characteristic.

^{13}C NMR spectra of chiral *N*-boc organotellurated peptides (**4a**-**4g**)

In the ^{13}C nuclear magnetic resonance (NMR) spectra of

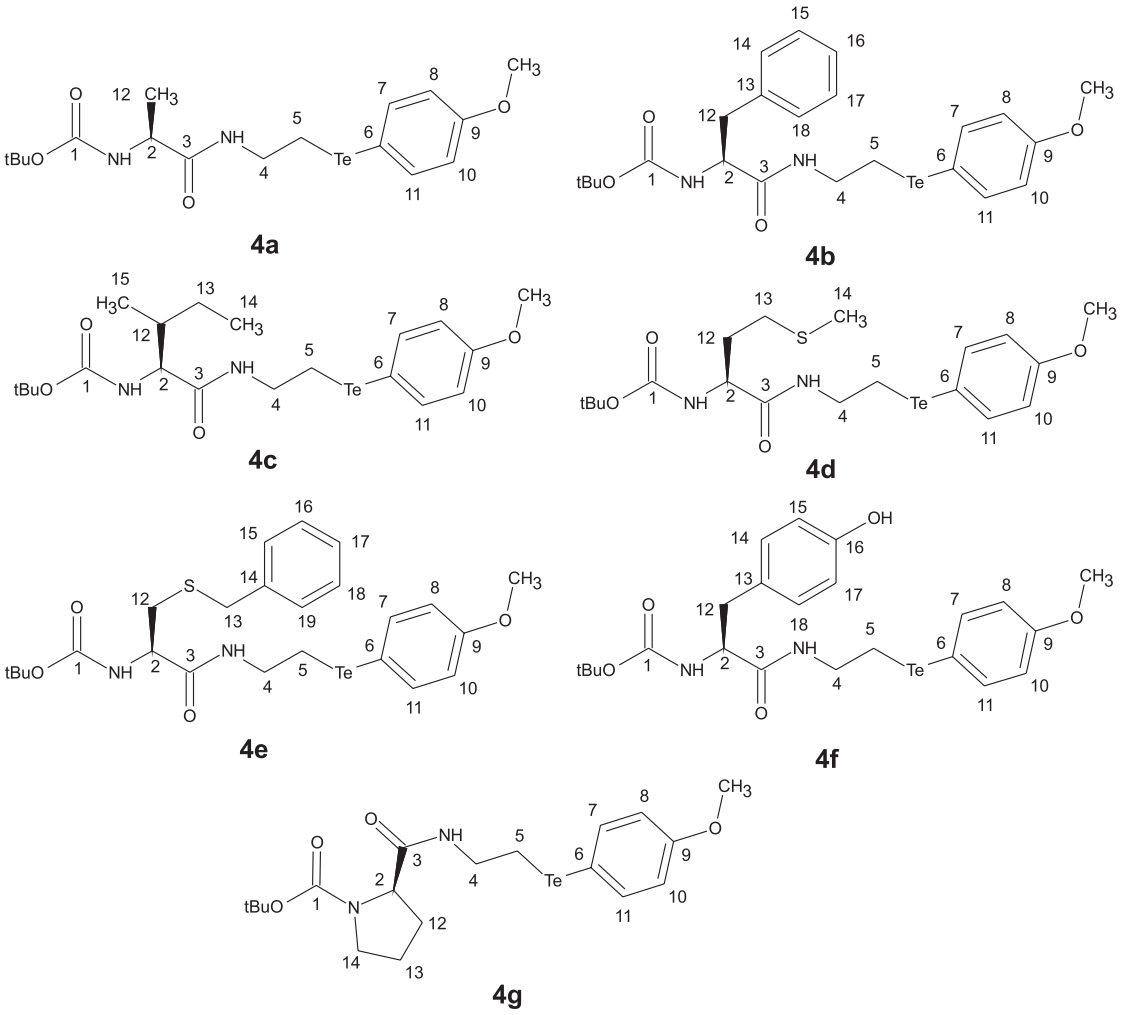
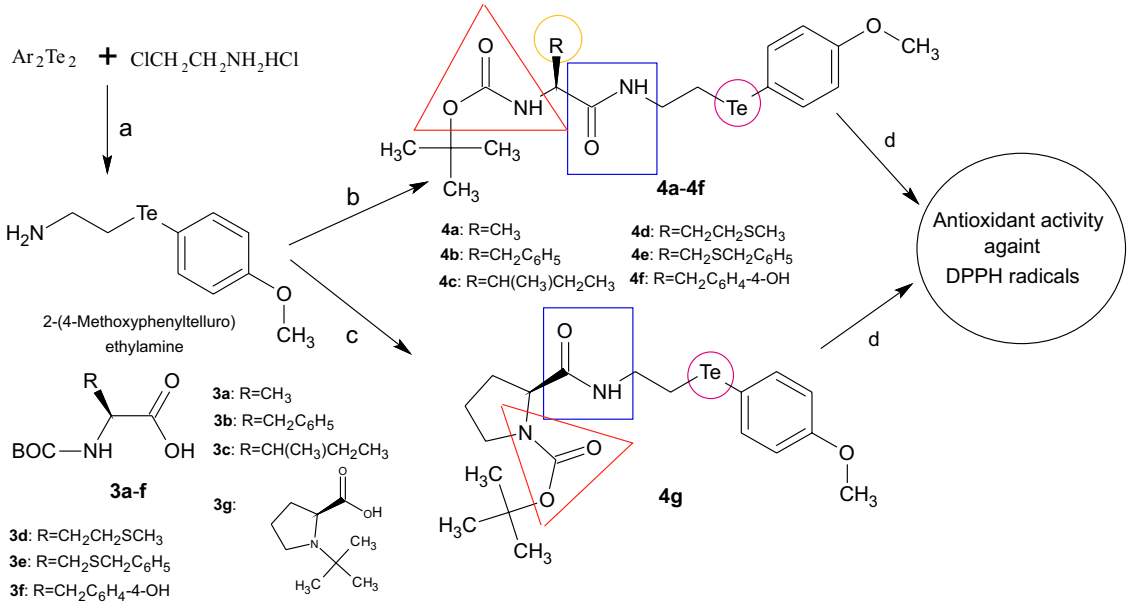


Figure 1. Structure of chiral *N*-boc organotellurated peptides (**4a**-**4g**).



Scheme 1. Synthesis of chiral *N*-boc organotellurated peptides (**4a**-**4g**): (a) EtOH, $NaBH_4$/aq. NaOH, CH_2Cl_2; (b) **3a-3f**, DCC, THF; (c) **3g**, DCC, THF; (d) antioxidant activity against DPPH radicals.

4a-**4g**, the CH_2Te and CH_2N carbon signals were appeared between δ, 22-25 ppm and 40-41 ppm, respectively.[56] The methyl carbons of ^{t}Bu group in **4d** and **4f** are slightly deshielded and appeared at 28.63 and 29.87 ppm, respectively, whereas in others these carbon were appeared at 28.07-28.16 ppm. The quaternary carbon peaks of ^{t}Bu group were produced at δ ca. 78 ppm. The carbons atoms present at position *meta* and *ortho* to Te were appeared at around 115.5 and 140.0 ppm, respectively. The carbamate [$(CH_3)_3CO(CO)NH-$] and amide [$-NH(CO)CH<$] carbons are highly deshielded and appeared in the range of 155.0-155.5 and 170-171 ppm, respectively, in all **4a**-**4g**. The methyl carbon was observed at 18.29 ppm in **4a**. In **4b** and **4f** the benzylic methylene carbon signal was appeared at ca. 37 ppm. In **4d** the carbons of $CH_3SCH_2CH_2-$ chain were obtained at 15.09, 32.21 and 30.24 ppm, respectively. The signals for CH_2SCH_2- carbons were observed at 35.10 and 47.44 ppm, respectively, in **4e**. The carbon atoms *meta* and *ortho* to Te were observed between 115.2-115.7 and 139.0-140.5 ppm, respectively in **4a**-**4g**.[56] The other aromatic signals are characteristic for their respective carbons.

Mass spectra of **4a**, **4b** and **4g**

Mass spectra of compounds **4a**, **4b** and **4g** were recorded using atmospheric-pressure chemical ionization (APCI) in the positive mode. The [M + 1] ion peak were obtained at *m/z* 450.9, 527 and 476.9 with 20, 30 and 10% abundance. In all, the peaks were also obtained with [M + 1 + H_2O] at 467.9, 545 and 494.9 with 100% abundance.

Radical scavenging activity of chiral *N*-boc organotellurated peptides (**4a**-**4g**)

In order to understand the influence of tellurium atom along with carbamate and amide groups by varying the substituent at chiral carbon in the biological activity, such as the antioxidant activity of compounds **4a**-**4g** in comparison with BHT, a common antioxidant that finds application in the food industry,[57,58] was determined by DPPH assay *in vitro* as given in Table 1.

DPPH is characterized as a stable free radical by virtue of the delocalization of the single electron over the molecule as a whole, so that the molecules do not dimerise, as would be the case with most other free radicals. The delocalization also gives rise to the deep violet color, characterized by an absorption band in ethanol solution centered at about 520 nm.

When a solution of DPPH is mixed with that of a substance that can donate an electron or hydrogen atom, then this gives rise to the reduced form with the loss of this violet color.[52-55] This latter will then undergo further reactions which control the overall stoichiometry, that is, the number of molecules of DPPH reduced (decolorized) by one molecule of the reductant. The reaction is therefore intended to provide the link with the reactions taking place in an oxidizing system, such as the autoxidation of a lipid or other unsaturated substance; the DPPH molecule is thus intended to represent the free radicals formed in the system whose activity to be suppressed by the substance.

Table 1. Antioxidant capacities of chiral *N*-boc organotellurated peptides (**4a**-**4g**)

Concentration / μM	Inhibition / %						
	4a	**4b**	**4c**	**4d**	**4e**	**4f**	BHT
0	0	0	0	0	0	0	0
4	20	30	33	33	30	31	38
8	42	48	53	51	51	49	60
12	59	57	66	58	62	63	67
16	64	61	68	64	64	65	70

Antioxidant potential of chiral *N*-boc organotellurated amides were assessed through DPPH radicals with varying concentration as given in the Table 1 and also shown in Figure 2 which demonstrated that these multi-functionalized compounds (**4a**-**4g**) are effective antioxidants than BHT towards DPPH radicals due to the presence of Te and which is also influenced by carbamate and amide groups.

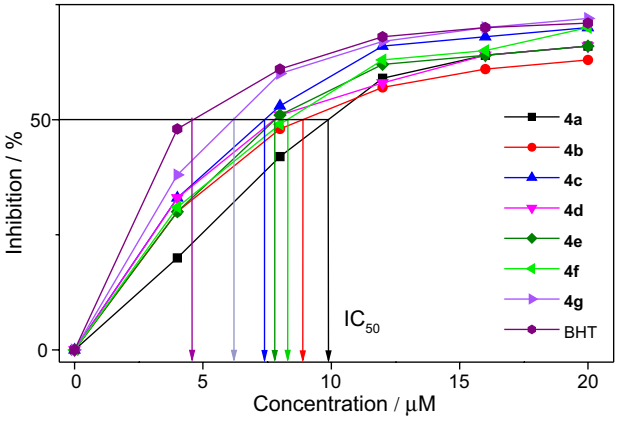


Figure 2. Graphical representation of antioxidant activity of **4a**-**4g** against DPPH radicals.

The IC_{50} (inhibitory concentration 50) values (sample concentration required to inhibit 50% of the radicals) of **4a**-**4g** are in the range of 6.00 to 10.00 μM mL^{-1} as given in the Table 2 and also represented graphically in Figure 3. These values suggested that the chiral *N*-boc organotellurated compounds containing carbamate and amide functionalities showed good antioxidant activities.

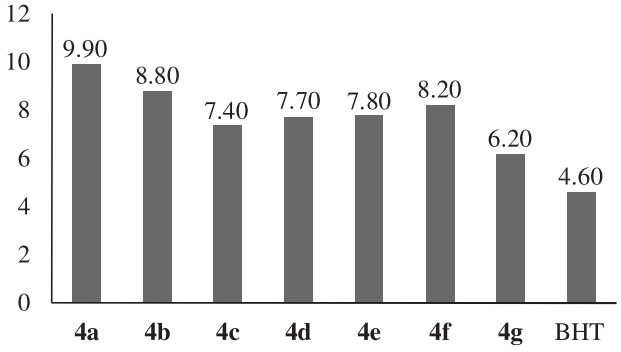


Figure 3. IC_{50} values of chiral *N*-boc organotellurated peptides (**4a-4g**).

Table 2. IC_{50} values of **4a**-**4g**

Compound	IC_{50} / μM
4a	9.9
4b	8.8
4c	7.4
4d	7.7
4e	7.8
4f	8.2
4g	6.2

IC_{50}: inhibitory concentration 50.

Conclusions

In summary, we presented the synthesis of new chiral *N*-boc oraganotellurium compounds (**4a**-**4g**) containing carbamate and peptide groups from *N*-boc *L*-amino acids and 2-(4-methoxyphenyltelluro) ethylamine in presence of DCC. All these compounds were characterized by elemental analysis, FTIR, ^{1}H, and ^{13}C {^{1}H} NMR spectroscopy and mass spectrometry. Specific optical rotations were determined for **4a**-**4g**. *In vitro* antioxidant activity of **4a**-**4g** in methanol has been investigated against DPPH radicals with BHT as a standard reference compound. The IC_{50} values of the chiral *N*-boc organotellurrated peptides (**4a-4g**) were found in the range of 6 to 10 μM concentration. These results revealed that the new chiral *N*-boc organotellurated peptides (**4a**-**4g**) proved to possess significantly high antioxidant activity against DPPH radicals and among which compound **4g**, *L*-proline based peptide showed highest antioxidant activity.

Experimental

Analytical techniques

^{1}H and ^{13}C {^{1}H} NMR spectra were recorded on a Bruker DPX-400 Hz or AVANCE II Bruker 400 Hz spectrometer at 399.65 and 100.64 Hz, respectively. Spectra were recorded in dimethyl sulfoxide, DMSO-d_6, solutions. Chemical shifts were reported in parts *per* million (ppm) with tetramethylsilane (TMS) as a reference standard. Specific optical rotations (SOR) were measured using Rudolph Autopol-I automatic Polarimeter in a cell of 100 mm path length. Melting points were recorded in open capillary tubes and are reported uncorrected. FTIR spectra were recorded on a JASCO FTIR-4100 instrument in the range of 400 to 7000 cm^{-1}. Column chromatography was performed using Merck silica gel (230-400 mesh). Thin layer chromatography (TLC) was performed using Merck 60 F254 silica gel on pre-coated aluminum sheets. Compounds were visualized on TLC with UV-light, potassium permanganate stain, iodine vapor or with ninhydrin.

Materials

Solvents such as tetrahydrofuran (THF) and benzene were dried using sodium metal and benzophenone. *N*-boc *L*-aminoacids, sodium borohydride, elemental tellurium, anisole, 2-chloroethylamine hydrochloride, DCC, DPPH and BHT were purchased from Sigma Aldrich Ind. Ltd., and they were used as received. The following precursor compounds were prepared according to literature procedures: 1,2-bis(4-methoxyphenyl) ditellane,[59] 2-(4-methoxyphenyltelluro) ethylamine.[52-55]

General procedure for the synthesis of chiral *N*-boc *L*-organotellurated amides (**4a-4f**)

The stirred solution of *N*-boc *L*-amino acids, (10 mmol) in dry CH_2Cl_2 (50 mL) was cooled to 0 °C and then was added DCC (2.063 g, 10 mmol). The reaction mixture was slowly brought to room temperature and continued the stirring for about 2-3 h. A solution of 2-((4-methoxyphenyl) tellanyl) ethylamine dissolved in 15-20 mL of CH_2Cl_2 was added dropwise. The whole reaction mass was further stirred at room temperature. The progress of the reaction was checked by TLC. After completion of the reaction, the resulting mixture was diluted with CH_2Cl_2 and the organic layer was washed thrice with brine (3 × 50 mL). The combined organic layers were dried over anhydrous Na_2SO_4 and then filtered. The solvent was removed under reduced pressure. The crude product obtained above was subjected to column chromatography hence gave compounds **4a**-**4f**.

(*S*)-*tert*-Butyl(1-((2-((4-methoxyphenyl)tellanyl)ethyl) amino)-1-oxopropan-2-yl) carbamate (**4a**)

Light brown viscous liquid; yield 85%; $[\alpha]_D^{28.5}$ –20.0 (*c* 1.0, $CHCl_3$); IR (KBr) ν / cm^{-1} 3338, 3306, 2976, 2926,

2849, 1686, 1644, 1524, 1488, 1449, 1365, 1320, 1280, 1240, 1162, 1065, 1024, 810, 638, 585, 511, 463, 446, 419; ^{1}H NMR (399.65 Hz, DMSO-d_6) δ 1.118-1.136 (d, 3H, *J* 7.2 Hz, H12), 1.357 (s, 9H, ^{t}Bu), 2.779-2.814 (t, 2H, *J* 7.59 Hz, H5), 3.290-3.375 (m, 2H, H4), 3.73 (s, 3H, OCH_3), 3.843-3.879 (m, 1H, H2), 6.804-6.833 (m, 3H, H8, H10, NH), 7.612-7.663 (d, 2H, *J* 8.4 Hz, H7, H11), 7.964-7.993 (t, H, *J* 5.99 Hz, NH); ^{13}C NMR (100.64 Hz, DMSO-d_6) δ 18.29 (CH_3), 24.43 (C5), 28.17 (^{t}Bu), 40.72 (C2), 40.72 (C4), 55.23 (OCH_3), 77.93 (^{t}BuCO), 100.18 (C6), 115.57 (C8, C10), 139.90 (C7, C11), 154.94 (C1), 159.27 (C9), 172.34 (C3); MS (+ pESI) *m/z*, calcd. for $C_{17}H_{26}N_2O_4Te$ [M$^+$]: 450; found (% abundance): 150 (90), 288 (30), 330 (70), 450.9 (20), 467.9 (100).

(*S*)-*tert*-Butyl(1-((2-((4-methoxyphenyl)tellanyl)ethyl) amino)-1-oxo-3-phenylpropan-2-yl) carbamate (**4b**)

Colourless solid; yield 90%; $[\alpha]_D^{29.0}$ –9.5 (*c* 1.0, $CHCl_3$); mp 108-110 °C; elemental anal. calcd. for $C_{23}H_{30}N_2O_4Te$ (found): C 52.51 (52.98), H 5.75 (5.75), N 5.32 (5.41); IR (KBr) ν / cm^{-1} 3392, 3061, 2968, 2935, 1688, 1656, 1585, 1525, 1487, 1455, 1389, 1365, 1302, 1285, 1243, 1175, 1159, 1066, 1029, 1005, 948, 846, 817, 788, 754, 701, 659, 635, 589, 511; ^{1}H NMR (399.65 Hz, DMSO-d_6) δ 1.279 (s, 9H, ^{t}Bu), 2.672-2.705 (dd, 1H, *J* 13.18 Hz, H12), 2.739-2.777 (t, 2H, *J* 7.59 Hz, H5), 2.891-2.924 (dd, 1H, *J* 13.18 Hz, H12), 3.288-3.396 (m, 2H, H4), 3.726 (s, 3H, OCH_3), 4.058-4.068 (m, 1H, H2), 6.809-6.831 (d, 2H, *J* 8.4 Hz, H8, H10), 6.849-6.870 (d, 1H, *J* 8.39 Hz, NH), 7.162-7.240 (m, 5H, H14 to H18), 7.614-7.636 (d, 2H, *J* 8.7 Hz, H7, H11), 8.117 (bt, H, NH); ^{13}C NMR (100 Hz, $CDCl_3$) δ 25.05 (C5), 28.07 (^{t}Bu), 37.61 (C12), 40.79 (C4), 55.69 (C2), 54.95 (OCH_3), 77.87 (^{t}BuCO), 100.21 (C6), 115.29 (C8, C10), 126.06 (C16), 127.91 (C14, C18), 129.10 (C15,17), 138.08 (C13), 139.80 (C7, C11), 155.07 (C1), 159.23 (C9), 171.17 (C3); MS (+ pESI) *m/z*, calcd. for $C_{23}H_{30}N_2O_4Te$ [M$^+$]: 526.1; found (% abundance): 365 (40), 404 (70), 527 (30), 545 (100).

(*S*)-*tert*-Butyl((2*S*,3*S*)-1-((2-((4-methoxyphenyl)tellanyl) ethyl)amino)-3-methyl-1-oxopentan-2-yl) carbamate (**4c**)

Colourless solid; yield 95%; $[\alpha]_D^{27.5}$ –13.5 (*c* 1.0, $CHCl_3$); mp. 61-62 °C; elemental anal. for $C_{20}H_{32}N_2O_4Te$: calcd. (found): C 48.82 (48.90), H 6.55 (6.55), N 5.69 (5.75); IR (KBr) ν / cm^{-1} 3314, 3061, 3085, 2962, 2930, 2876, 2853, 1679, 1644, 1518, 1486, 1281, 1243, 1164, 1019, 640, 586, 512, 447, 420; ^{1}H NMR (400.23 Hz, DMSO-d_6) δ 0.769-0.807 (m, 6H, H14, H15), 1.011-1.065 (m, 2H, H13), 1.197-1.247 (m, 1H, H12), 1.357 (s, 9H, ^{t}Bu), 2.779-2.817 (t, 2H, *J* 7.99 Hz, H5), 3.328-3.413 (m, 2H, H4), 3.692-3.794 (m, 1H, H2), 3.731 (s, 3H, OCH_3), 6.591-6.613 (d, 1H, *J* 8.79 Hz, NH), 6.799-6.835 (d, 2H, *J* 8.4 Hz, H8, H10), 7.606-7.642 (d, 2H, *J* 8.7 Hz, H7, H11), 8.068 (bt, 1H, NH); ^{13}C NMR (100.64 Hz, DMSO-d_6) δ 10.97 (C10), 15.47 (C18), 24.38 (C13), 25.30 (C5), 28.16 (^{t}Bu), 40.15 (C2), 40.77 (C4), 54.99 (OCH_3), 77.90 (^{t}BuCO), 100.23 (C6), 115.33 (C8, C10), 139.91 (C7, C11), 155.26 (C1), 159.28 (C9), 171.09 (C3).

(*S*)-*tert*-Butyl(1-((2-((4-methoxyphenyl)tellanyl)ethyl) amino)-4-(methylthio)-1 oxobutan-2-yl)carbamate (**4d**)

Light brown viscous liquid; yield 80%; $[\alpha]_D^{28.0}$ –2.0 (*c* 1.0, $CHCl_3$); IR (KBr) ν / cm^{-1} 3320, 3061, 2974, 2929, 1696, 1586, 1520, 1489, 1439, 1391, 1366, 1283, 1245, 1174, 1046, 1025, 963, 861, 822, 788, 758, 695, 635, 587, 515, 485; ^{1}H NMR (399.65 Hz, DMSO-d_6) δ 1.361 (s, 9H, ^{t}Bu), 1.698-1.771 (m, 2H, H12), 2.013 (s, 3H, H14), 2.384-2.423 (t, 2H, *J* 7.19 Hz, H13), 2.791-2.825 (t, 2H, *J* 6.39 Hz, H5), 3.295-3.409 (m, 2H, H4), 3.730 (s, 3H, OCH_3), 3.887-3.939 (m, 1H, H2), 6.896-6.916 (d, 1H, *J* 7.99 Hz, NH), 6.804-6.826 (d, 2H, *J* 8.4 Hz, H8, H10), 7.611-7.633 (d, 2H, *J* 8.7 Hz, H7, H11), 8.022-8.049 (t, H, *J* 5.59 Hz, NH); ^{13}C NMR (100.64 Hz, DMSO-d_6) δ 15.09 (C12), 28.63 (^{t}Bu), 30.24 (C14), 32.21 (C13), 33.79 (C5), 41.17 (C4), 47.96 (C2), 55.46 (OCH_3), 78.50 (^{t}BuCO), 100.66 (C6), 115.79 (C8, C10), 140.36 (C7, C11), 155.76 (C1), 159.74 (C9), 171.81 (C3).

(*S*)-*tert*-Butyl(3-(benzylthio)-1-((2-((4-methoxyphenyl) tellanyl)ethyl)amino)-1-oxopropan-2-yl) carbamate (**4e**)

Bright yellow solid; yield 95%; $[\alpha]_D^{27.0}$ –6.5 (*c* 1.0, $CHCl_3$); mp 89-90 °C; elemental anal. for $C_{24}H_{32}N_2O_4STe$ calcd. (found): C 50.38 (50.38), H 5.64 (5.65), N 4.90 (4.95); IR (KBr) ν / cm^{-1} 3357, 3323, 3058, 3023, 2925, 2850, 1685, 1654, 1514, 1487, 1456, 1365, 1282, 1244, 1227, 1156, 1018, 697, 608, 563, 507, 464, 436; ^{1}H NMR (399.65 Hz, DMSO-d_6) δ 1.394 (s, 9H, ^{t}Bu), 2.672-2.720 (dd, 1H, *J* 5.59 Hz, C12), 2.803-2.839 (t, 2H, *J* 6.79 Hz, H5), 3.354-3.442 (m, 1H, C13), 3.701-3.735 (m, 2H, H4), 3.740 (s, 3H, OCH_3), 4.075-4.131 (m, 1H, H2), 6.815-6.837 (d, *J* 8.4 Hz, 2H, H8, H10), 6.899-6.920 (d, 1H, *J* 8.39 Hz, NH), 7.221-7.308 (m, 5H, H15 to H19), 7.624-7.646 (d, *J* 8.7 Hz, 2H, H7, H11), 8.210-8.237 (t, H, *J* 5.19 Hz, NH); ^{13}C NMR (100.64 Hz, DMSO-d_6) δ 24.39 (C5), 28.12 (^{t}Bu), 35.10 (C12), 40.86 (C4), 47.44 (C13), 53.70 (C2), 54.95 (OCH_3), 78.16 (^{t}BuCO), 100.20 (C6), 115.28 (C8, C10), 126.73 (C17), 128.25 (C15, C19), 128.83 (C16, C18), 138.32 (C14), 139.86 (C7, C11), 155.14 (C1), 159.24 (C9), 170.14 (C3).

(*S*)-*tert*-Butyl(3-(4-hydroxyphenyl)-1-((2-((4-methoxyphenyl) tellanyl)ethyl)amino)-1-oxopropan-2-yl) carbamate (**4f**)

Light brown solid; yield 80%; $[\alpha]_D^{26.0}$ –5.7 (*c* 1.0, $CHCl_3$); mp 96-97 °C; elemental anal. for $C_{23}H_{30}N_2O_5Te$ calcd. (found): C 50.96 (50.75), H 5.58 (5.60), N 5.17 (5.25); IR (KBr)

ν / cm^{-1} 3319, 2927, 2850, 1646, 1513, 1487, 1438, 1364, 1242, 1158, 1023, 820, 641, 587, 515, 463, 413; ^{1}H NMR (400.33 Hz, DMSO-d_6) δ 1.30 (s, 9H, ^{t}Bu), 2.570-2.627 (m, 1H, H12), 2.764-2.807 (t, 2H, *J* 7.60 Hz, H5), 2.844-2.924 (dd, 1H, *J* 14.80 Hz, H12), 3.334-3.405 (m, 1H, H4), 3.486 (bs, 1H, H4), 3.731 (s, 3H, OCH_3), 3.913-3.973 (m, 1H, H2), 6.809-6.829 (d, *J* 8.4 Hz, 2H, H7, H10), 6.696-6.717 (d, 1H, *J* 8.40 Hz, NH), 6.614-6.633 (d, 2H, *J* 8.7 Hz, H14, H18), 6.976-6.995 (d, 2H, *J* 8.4 Hz, H15, H17), 7.612-7.633 (d, 2H, *J* 8.7 Hz, H7, H11), 8.034 (bt, H, NH), 9.123 (bs, 1H, OH); ^{13}C NMR (100.64 Hz, DMSO-d_6) δ 25.88 (C5), 29.87 (^{t}Bu), 37.40 (C12), 41.28 (C4), 47.96 (C2), 55.46 (OCH_3), 78.35 (^{t}BuCO), 100.72 (C6), 115.24 (C7, C10), 115.80 (C15, C17), 128.54 (C13), 130.49 (C14, C18), 140.30 (C7, C11), 155.56 (C16), 156.53 (C1), 159.73 (C9), 171.83 (C3).

(*S*)-*tert*-Butyl2-((2-((4-methoxyphenyl)tellanyl)ethyl) carbamoyl)pyrolidine-1-carboxylate (**4g**)

Colourless solid; yield 90%; $[\alpha]_D^{28.5}$ −36.7 (*c* 1.0, $CHCl_3$); mp 105-106 °C; elemental anal. for $C_{19}H_{28}N_2O_4Te$, calcd. (found): C 47.94 (47.54), H 5.93 (5.65), N 5.88 (6.01); IR (KBr) ν / cm^{-1} 3077, 3305, 2998, 2974, 2934, 2870, 2835, 1677, 1658, 1584, 1544, 1486, 1455, 1415, 1368, 1343, 1280, 1244, 1160, 1122, 1060, 1027, 918, 890, 832, 812, 777, 753, 673, 586, 539, 513; ^{1}H NMR (400.23 Hz, DMSO-d_6) δ 1.306 (s, 9H, ^{t}Bu), 1.609-1.652 (dd, 1H, *J* 4.00 Hz, H13), 1.730-1.748 (m, 4H, H12-H14), 2.048-2.069 (dd, 1H, *J* 5.79 Hz, H2), 2.790-2.830 (t, 2H, H5), 3.215-3.275 (m, 2H, H4), 3.729 (s, 3H, OCH_3), 3.907-3.949 (dd, 1H, *J* 6.79 Hz, H2), 6.809-6.829 (d, 2H, *J* 8.4 Hz, H8, H10), 7.609-7.631 (d, 2H, *J* 8.7 Hz, H7, H11), 8.047-8.061 (t, H, *J* 5.59 Hz, NH); ^{13}C NMR (100.64 Hz, DMSO-d_6) δ 23.13 (C13), 25.30 (C5), 28.13 (^{t}Bu), 30.97 (C12), 40.82 (C2), 46.62 (C4), 47.48 (C14), 55.25 (OCH_3), 78.37 (^{t}BuCO), 100. 27 (C6), 115.32 (C8, C10), 139.81 (C7, C11), 153.61 (C1), 159.28 (C9), 172.18 (C3); MS (+ pESI) *m/z*, calcd. for $C_{19}H_{28}N_2O_4Te$ [M^+]: 476.04, found (% abundance): 315 (50), 354 (70), 377 (25), 476.9 (15), 494.9 (100).

Antioxidant activity DPPH radical scavenging evaluation of compounds (**4a**-**4g**)

Antioxidant activity was evaluated for the series of newly synthesized chiral *N*-boc organotellurated peptides, **4a**-**4g**, *in vitro* using DPPH assay following the modified method of Brand-Williams.[60] DPPH is a stable free radical with purple color which is generally used for determination of electron donating capacity of an antioxidant compound *in vitro*.[61] In the presence of an antioxidant, the DPPH radical decays and the change in absorbance at 520 nm was measured by spectrophotometry. Hence the scavenging activity of compounds was determined. The solutions of concentrations of 4, 8, 16 and 20 μM of compounds, **4a**-**4g**, in 50% methanol were prepared. To this 140 μL of 1 mM DPPH were added and then incubated at 37 °C for 30 min. The absorbance's for these solutions were measured at 520 nm against 50% methanol as blank by UV-Vis, spectrophotometer. A control reaction was also carried out without addition of the test sample. The actual absorbance was taken as the difference in the absorbance of the control and the test samples and hence IC_{50} (inhibitory concentration 50) values were determined.

Supplementary Information

Supplementary data (NMR, MS and FTIR spectra) are available free of charge at http://jbcs.sbq.org.br as PDF file.

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