Synthesis, Characterisation and *In-silico* Studies of Novel Heterocyclic Organotellurium Dithiocarbamates

Shamsi M. Maaz.[1], Bajpai S.[1*], Singh A.[2], Srivastava N.[1] and Pandey G.[3]
1. Department of Chemistry, Amity School of Applied Sciences, Amity University, Lucknow Campus, INDIA
2. Department of Chemistry, Lucknow University, Lucknow, INDIA
3. Department of Chemistry, SRMIST Delhi NCR Campus, Modinagar, Ghaziabad, INDIA
*sbajpai1@amity.edu

Abstract

A series of novel di-alkyl dithiocarbamate derivatives viz. $C_4H_8Te(S_2CNR)_2$ and $C_4H_8TeI(S_2CNR)$ where R=C_8H_{18}(dibutyl), C_7H_8(benzyl), C_6H_{14}(hexyl), C_4H_{10}(butyl) and C_8H_{10}(2-phenylethyl) have been synthesized by the reaction of corresponding silver salt of dithiocarbamates with $C_4H_8TeI_2$ (1,1,2,3,4,5-Hexahydro-1,1-diiodo tellurophene). Protection of metal displacement and facile synthesis was done using silver salts. They have been characterized by elemental analysis, IR, ^{1}H NMR, ^{13}C NMR, UV and molar conductance. Molar conductance values showed that all complexes were non- electrolytic in nature.

The studies favour monodentate coordination of the dithiocarbamate moiety with tellurium. Molecular docking studies were being performed to bind the respective synthesized complex (ligand) into the crystal structure of cyclooxygenase-2 (prostaglandin synthase-2) and alpha-hemolysin from staphylococcus aureus at the specific active sites to examine the feasible binding sites and principal binding interaction. In silico, docking studies were done to evaluate the binding free energy of the present inhibitor inside the macromolecule using the Autodock 4.2. The important parameters i.e. binding energy, RMSD and hydrogen bond interaction are examined. The result indicate that the selected ligand (organotellurium compound) shows the binding energy in the range of -6.43 kcal /mol to -8.25 kcal /mol for Cyclooxygenase-2 and -4.49 kcal/mol to -6.80 Kcal/mol for alpha-hemolysin and their protein-ligand interaction are shown by using the two programs that are protein-ligand interaction profiler and pymol.

Keywords: Novel, Organotellurium, Dithiocarbamates, *In silico*, Molecular Docking, Protein.

Introduction

The persistent enthusiasm for tellurium mixes including sulphur-giver ligands is to a great extent because of the range of structures attainable with these kinds of ligands. Specifically, the basic assorted variety accomplished by tellurium mixes containing 1, 1-dithiolate ligands (dithiocarbamate) results from a few variables. The capacity of these ligands to show numerous coordination designs (due to the presence of variety of binding modes in its anionic N-CS_2 species) and the limit of tellurium to build its coordination number by intra-sub-atomic connections and the nearness of stereo chemically active lone pairs on the tellurium molecule give rise to mono-, bi- and bridged dentate complexes.

Various reports on synthesis, spectroscopic characterisation and structure determination of select organotellurium dithiocarbamates are available.[1-3,5,8,9,10-12,17,21,22] Tellurium (IV) dithiocarbamates have been utilized as quickening agents in rubber vulcanization[25] and as stabilizers for polypropylene.

Studies on Te-S assisted supramolecular networks are also available[6,7]. Progressing reports from Srivastava et al[26,27] portrays the supramolecular relationship in various non-cyclic and cyclic organotellurium(IV) backups R_2TeX_2, R_2TeIX and R_2TeClX [R_2 = $(C_2H_5)_2$, (n-$C_3H_7)_2$, C_4H_8, $C_4H_7(CH_3)$, C_5H_{10}, C_8H_8; X = $OCOC_6H_5$, $OCOC_6H_3(NO_2)$2-3,5, $OCOCH{=}C_6H_5$, $OCOC_6H_4(NO_2)$-4, $S_2CN(C_2H_5)_2$, $S_2CNC_4H_8O$ and $S_2CNC_5H_{10}$] formed through intramolecular Te-S assistant bonds between sub-nuclear Te - (X = I, S, O) helper bonds and C-H - O hydrogen bonds.

As an augmentation of our examinations with respect to the stereochemistry and holding of hypervalent tellurium mixes, we currently report on the synthesis and the structural characterization of novel mono- and di-substituted organotellurium dithiocarbamate derivatives of the type [$C_4H_8Te(S_2CNR)_2$] and [$C_4H_8TeI(S_2CNR)$] where R= C_8H_{18}(dibutyl),C_7H_8(benzyl),C_6H_{14}(hexyl),C_4H_{10}(butyl),C_8H_{10}(2-phenylethyl).

These new compounds have been characterized through elemental analysis and IR, ^{1}H-NMR and ^{13}C-NMR spectral studies. *In silico* molecular docking of $C_4H_8Te(S_2CNR)_2$ and $C_4H_8TeI(S_2CNR)$ complexes have been performed.

Material and Methods

Physical Measurements: Elemental analysis was carried out on an Elemental Analyser Elementar Vario EL III (Accuracy: + 5%). Tellurium was estimated volumetrically[28]. IR spectra were recorded using a Shimadzu 8210 PC FTIR spectrometer in the frequency range 4000-350cm^{-1}with the samples in KBr discs. The (^{1}H, ^{13}C) NMR spectra were recorded on a Varian VXR 3005 spectrometer in $CDCl_3$ for all the complexes except those of 1,1,2,3,4,5-Hexahydro-1,1-diiodotellurophene ($C_4H_8TeI_2$) (1).

Synthesis: 1,1,2,3,4,5-Hexahydro-1,1-diiodotellurophene ($C_4H_8TeI_2$) (1) was prepared by literature methods [23] and was recrystallized from benzene to obtain bright red prism (m.p. 149-150°C). Reported method [19] was employed for the synthesis of sodium salts of Dibutyl-, Benzyl -, Hexyl-, Butyl- and 2-PhenylEthyl dithiocarbamates. Silver salt of di-alkyl dithiocarbamates (AgS_2CNR) were prepared by mixing aqueous solutions of $AgNO_3$ and corresponding sodium salt of dithiocarbamates, NaS_2CNR (R=C_8H_{18}, C_7H_8, C_6H_{14}, C_4H_{10} and C_8H_{10}) in equimolar ratio. White solid obtained was filtered and dried.

Compounds (2-6) and (7-11) were prepared opting similar procedure in 1:2 and 1:1 molar ratio of $C_4H_8TeI_2$: AgS_2CNR respectively. In each case, to the clear solution of 1,1,2,3,4,5-hexahydro-1,1-diiodo tellurophene ($C_4H_8TeI_2$) in 30 ml dry dichloromethane, was added corresponding silver salt of N-alkyl dithiocarbamates and N-aryl dithiocarbamates. The reaction mixture was stirred for 3 h at room temperature. The reaction mixture was filtered to eliminate the unidentified material. The filtrate was concentrated to 15 ml and a layer of petroleum-ether (40–60°C) was laid on it. It was kept overnight. The resulting crystalline /amorphous solid obtained was filtered, dried and weighed. The colour of the obtained solid, isolated yields, melting points, analytical data, molar conductance and their spectroscopic characterization for the compounds (2-11) are given in their synthesis.

Synthesis of 1,1,2,3,4,5-hexahydro-1,1-bis dibutyl dithiocarbamate tellurophene [$C_4H_8Te(S_2CNC_8H_{18})_2$](2): Compound (2) was synthesised by the reaction of $C_4H_8TeI_2$ (2.20 g, 1 mmol) and silver salt of N-dibutyl dithiocarbamate (3.14g, 2mmol) in 30 ml of dichloromethane. The resulting product gave pale yellow crystals, m.p. 98°C, yield: 1.12 g (83%). Elemental Anal. Calc. for $C_{22}H_{44}N_2S_4Te$: Found (Calculated) (%): C, 44.60 (44.63); H, 7.40 (7.44); N, 4.70 (4.73); S, 21.61(21.63); Te, 21.0 (21.57). IR (cm^{-1}):1425 s, 1386 m (ν CN); 937 s, 1083 m (ν CS); 534 s (ν$TeCH_2$); ^{1}HNMR ($CDCl_3$, δ ppm): 2.60 (m, 1H, Te-CH_2), 1.99 (m, 1H, Te-CCH_2), 0.89 (m, 3H, C-CH_3), 1.64 (m, 2H, C-CH_2), 1.27 (m, 6H, C-$CH_2CH_2CH_2CH_2$), 8.50 (t, 1H, N-H), 3.50 (tdd, 2H, N-CH_2); ^{13}CNMR (100.60 MHz, $CDCl_3$, δ ppm): 39.27 (s, Te-CH_2), 21.37(s, Te-CCH_2), 201.11 (s, S_2CN), 44.78 (s, N-CH_2), 28.45 (s, N-CCH_2), 23.87 (s, N-C_2CH_2), 29.45 (d, N-C_3CH_2), 29.45 (d, N-C_4CH_2), 31.88 (s, N-C_5CH_2), 22.70 (s, N-C_6CH_2), 14.08 (s, N-C_7CH_3); UV-Vis (λ_{max}, nm): 371 nm (ε = 22178 M^{-1} cm^{-1}), 321 nm (ε = 25387 M^{-1} cm^{-1}), 294 nm (ε = 27392 M^{-1} cm^{-1}) and 260 nm (ε = 47654 M^{-1} cm^{-1}).

Synthesis of 1,1,2,3,4,5-hexahydro-1,1-bis benzyl dithiocarbamate tellurophene [$C_4H_8Te(S_2CNC_7H_8)_2$](3): Compound (3) was synthesised by the reaction of $C_4H_8TeI_2$(1.28 g, 1 mmol) and silver salt of benzyl dithiocarbamate (1.70 g,2 mmol) in 30 ml of dichloromethane. The resulting product gave yellow amorphous solid, m.p. 110° C yield: 1.18 g (80%). Elemental Anal. Calc. for $C_{20}H_{24}N_2S_4Te$: Found (Calculated) (%): C, 43.80 (43.83); H, 4.35 (4.38); N, 4.99, (5.11); S, 23.35 (23.38); Te, 23.00 (23.30). IR (cm^{-1}): 1431 s, 1390 m (νCN); 947 s, 1083 m (ν CS); 563 m (ν$TeCH_2$); ^{1}HNMR ($CDCl_3$, δ ppm): 2.60 (m, 1H, Te-CH_2), 1.99 (m, 1H, Te-CCH_2), 7.26 (m, 1H, C-H(Benzyl)) 7.32 (m, 9H, C_6H_5), 8.80 (t, 1H, N-H), 4.78 (m, 2H, N-CH_2); ^{13}CNMR (100.60 MHz, $CDCl_3$, δ ppm): 39.27 (s, Te-CH_2), 21.37 (s, Te-CCH_2), 200.34 (s, S_2CN), 127.60 ,128.80 ,127.94 (s, C-H(Benzyl)), 48.42 (s, N-CH_2). 140.21 (s, N-CH_2-C); UV-Vis (λ_{max}, nm): 365 nm (ε = 22965 M^{-1} cm^{-1}), 327 nm (ε = 26530 M^{-1} cm^{-1}), 292 nm (ε = 28707 M^{-1} cm^{-1}) and 252 nm (ε = 49124 M^{-1} cm^{-1}).

Synthesis of 1,1,2,3,4,5-hexahydro-1,1-bis hexyl dithiocarbamate tellurophene [$C_4H_8Te(S_2CNC_6H_{14})_2$] (4): Compound (4) was synthesised by the reaction of $C_4H_8TeI_2$(0.743 g, 1 mmol) and silver salt of n-hexyl dithiocarbamate (0.96 g,2 mmol) in 30 ml of dichloromethane. The resulting product gave orange amorphous solid, m.p. 160°C, yield: 0.752 g (80%). Elemental Anal. Calc. for $C_{18}H_{36}N_2S_4Te$: Found (Calculated) (%): C, 40.30 (40.32); H, 6.70 (6.72); N, 5.20 (5.23); S, 23.89 (23.90); Te, 23.20 (23.83). IR (cm^{-1}):1405 s, 1350 m (ν CN); 970 s, 1080 m (ν CS); 565 m (ν$TeCH_2$); ^{1}HNMR ($CDCl_3$, δ ppm): 2.60 (m, 1H, Te-CH_2), 1.99 (m, 1H, Te-CCH_2), 0.89 (m, 6H, C-CH_3), 1.65 (m, 2H, C-CH_2), 1.30 (m, 4H, C-$CH_2CH_2CH_2$), 8.50 (t, 1H, N-H), 3.49 (td, 4H, N-CH_2); ^{13}CNMR (100.60 MHz, $CDCl_3$, δ ppm): 39.27 (s, Te-CH_2), 22.11 (s, Te-CCH_2), 201.11 (s, S_2CN), 44.78 (s, N-CH_2), 28.49 (s, N-CCH_2), 26.40 (s, N-C_2CH_2), 31.11 (d, N-C_3CH_2), 22.11 (d, N-C_4CH_2), 14.08 (s, N-C_5CH_3); UV-Vis (λ_{max}, nm): 366 nm (ε = 22543 M^{-1} cm^{-1}), 322 nm (ε = 25897 M^{-1} cm^{-1}), 288 nm (ε = 27986 M^{-1} cm^{-1}) and 251 nm (ε = 50312 M^{-1} cm^{-1}).

Synthesis of 1,1,2,3,4,5-hexahydro-1,1-bis butyl dithiocarbamate tellurophene [$C_4H_8Te(S_2CNC_4H_{10})_2$] (5): Compound (5) was synthesised by the reaction of $C_4H_8TeI_2$(1.02 g, 1 mmol) and silver salt of n-butyl dithiocarbamate (1.2 g, 2 mmol) in 30 ml of dichloromethane. The resulting product gave yellow amorphous solid, m.p. 102°C, yield: 1.24 g (75%). Elemental Anal. Calc. for $C_{14}H_{28}N_2S_4Te$: Found (Calculated) (%): C, 34.97(35.03); H, 5.80 (5.84); N, 5.79 (5.84); S, 26.65 (26.69); Te, 26.10 (26.60). IR (cm^{-1}):1420 s, 1340 m (ν CN); 967 s, 1085 m (ν CS); 525 s (ν$TeCH_2$); ^{1}HNMR ($CDCl_3$, δ ppm): 2.97 (m, 1H, Te-CH_2), 1.99 (m, 1H, Te-CCH_2), 0.92 (t, 6H, C-CH_3), 1.65 (m, 2H, C-CH_2), 1.29 (m, 2H, C-CH_2CH_2), 8.55 (t, 1H, N-H), 3.47 (td, 4H, N-CH_2); ^{13}CNMR (100.60 MHz, $CDCl_3$, δ ppm): 39.27 (s, Te-CH_2), 21.37 (s, Te-CCH_2), 201.11 (s, S_2CN), 44.60 (s, N-CH_2), 31.05 (s, N-CCH_2), 20.45 (s, N-C_2CH_2) 13.76 (s, N-C_3CH_3);UV-Vis (λ_{max}, nm): 369 nm (ε = 22365 M^{-1} cm^{-1}), 324 nm (ε = 25098 M^{-1} cm^{-1}), 299 nm (ε = 28021 M^{-1} cm^{-1}) and 255 nm (ε = 51615 M^{-1} cm^{-1}).

Synthesis of 1,1,2,3,4,5-hexahydro-1,1-bis 2-phenylethyl dithiocarbamate tellurophene [$C_4H_8Te(S_2CNC_8H_{10})_2$](6): Compound (6) was synthesised by the reaction of $C_4H_8TeI_2$ (1.07 g, 1 mmol) and silver salt of 2-phenylethyl dithiocarbamate (1.5 g,2 mmol) in 30 ml of dichloromethane. The resulting product gave orange amorphous solid, m.p. 130°C, yield: 1.57 g (60%). Elemental Anal. Calc. for $C_{22}H_{28}N_2S_4Te$: Found (Calculated) (%): C, 45.85 (45.87); H, 4.83(4.86); N, 4.80 (4.86); S, 22.20(22.24); Te, 21.69 (22.17). IR (cm^{-1}):1415 s, 1375 m (ν CN); 930 s, 1075 m (ν CS); 537 m (νTeCH2). ^{1}HNMR ($CDCl_3$, δ ppm): 2.60 (m, 1H, Te-CH_2), 1.99 (m, 1H, Te-CCH_2), 2.94 (ttd, 7H, C-CH_2) 7.26,7.20 (m, 10H, C-H(Phenyl)), 8.96 (t, 1H, N-H), 3.69 (tdd, 4H, N-CH_2); ^{13}CNMR (100.60 MHz, $CDCl_3$, δ ppm): 39.27 (s, Te-CH_2), 21.37 (s, Te-CCH_2), 201.07 (s, S_2CN), 127.12 ,129.05 (d) (s, C-H (Benzyl)), 46.32(s, N-CH_2), 34.58(s, N-CCH_2), 139.99 (s, N-CH_2-C); UV-Vis (λ_{max}, nm): 368nm (ε = 22830 M^{-1} cm^{-1}), 321 nm (ε = 26210 M^{-1} cm^{-1}), 283 nm (ε = 28621 M^{-1} cm^{-1}) and 257 nm (ε = 49543 M^{-1} cm^{-1}).

Synthesis of 1,1,2,3,4,5-hexahydro-1-Iodo,1-dibutyl dithiocarbamate tellurophene [$C_4H_8TeI(S_2CNC_8H_{18})$] (7): Compound (7) was synthesised by the reaction of [$C_4H_8TeI_2$] (2.20 g, 1 mmol) and silver salt of N- Dibutyl dithiocarbamate (3.14g, 1mmol) in 30 ml of dichloromethane. The resultant product gave orange amorphous solid, m.p. 99°C, yield: 2.1 g (78%).Elemental Anal. Calc. for $C_{13}H_{26}INS_2Te$:Found (Calculated) (%): C, 30.30(30.32); H, 5.02(5.05); I, 24.63(24.67); N, 2.69(2.72); S, 12.39(12.44); Te: 24.24(24.80). IR (cm^{-1}):1422 s, 1355 m (νCN); 965 s, 1081 m (ν CS); 525 s (νTeCH$_2$). ^{1}HNMR ($CDCl_3$, δ ppm): 3.13 (m, 1H, Te-CH_2), 2.00 (m, 1H, Te-CCH_2), 0.89 (m, 3H, C-CH_3), 1.64 (m, 2H, C-CH_2), 1.28 (m, 6H, C-$CH_2CH_2CH_2CH_2$), 8.26 (t, 1H, N-H), 3.50 (tdd, 2H, N-CH_2); ^{13}CNMR (100.60 MHz, $CDCl_3$, δ ppm): 48.27 (s, Te-CH_2), 21.79 (s, Te-CCH_2), 200.11 (s, S_2CN), 44.74 (s, N-CH_2), 28.45 (s, N-CCH_2), 23.87 (s, N-C_2CH_2), 29.45 (d, N-C_3CH_2), 29.45 (d, N-C_4CH_2), 31.88 (s, N-C_5CH_2), 22.70 (s, N-C_6CH_2), 14.08 (s, N-C_7CH_3); UV-Vis (λ_{max}, nm): 360 nm (ε = 22856 M^{-1} cm^{-1}), 329 nm (ε = 25942 M^{-1} cm^{-1}), 281 nm (ε = 28990 M^{-1} cm^{-1}) and 259 nm (ε = 53765 M^{-1} cm^{-1}).

Synthesis of 1,1,2,3,4,5-hexahydro-1-Iodo,1-benzyl dithiocarbamate tellurophene [$C_4H_8TeI(S_2CNC_7H_8)$] (8): Compound **(**8) was synthesised by the reaction of [$C_4H_8TeI_2$] (2.00 g, 1 mmol) and silver salt of benzyl dithiocarbamate (1.32 g, 1mmol) in 30 ml of dichloromethane. The resultant product gave orange amorphous solid, m.p. 99°C, yield: 2.6 g (65%). Elemental Anal. Calc. for $C_{12}H_{16}INS_2Te$: Found (Calculated) (%): C, 29.20(29.24); H, 3.21(3.25); I, 25.69(25.77); N, 2.79(2.84); S, 12.95(12.99), Te: 25.52(25.91);IR (cm^{-1}): 1410 s, 1365 m (νCN); 955 s, 1079 m (ν CS); 535 m (νTeCH$_2$); ^{1}HNMR ($CDCl_3$, δ ppm): 3.13 (m, 1H, Te-CH_2), 1.98 (m, 1H, Te-CCH_2), 7.26 (m, 1H, C-H(Benzyl)) 7.32 (m, 9H, C_6H_5), 8.27 (t, 1H, N-H), 4.78 (m, 2H, N-CH_2); ^{13}CNMR (100.60 MHz, $CDCl_3$, δ ppm): 48.35 (s, Te-CH_2), 21.79 (s, Te-CCH_2), 198.90 (s, S_2CN), 127.60 ,127.80 ,127.94 (s, C-H(Benzyl)), 48.35 (s, N-CH_2). 140.21 (s, N-CH_2-C); UV-Vis (λ_{max}, nm): 364 nm (ε = 22076 M^{-1} cm^{-1}), 328 nm (ε = 25934 M^{-1} cm^{-1}), 280 nm (ε = 28928 M^{-1} cm^{-1}) and 254 nm (ε = 52983 M^{-1} cm^{-1}).

Synthesis of 1,1,2,3,4,5-hexahydro-1-Iodo,1- hexyl dithiocarbamate tellurophene [$C_4H_8TeI(S_2CNC_6H_{14})$] (9): Compound **(**9) was synthesised by the reaction of [$C_4H_8TeI_2$] (2.5 g, 1 mmol) and silver salt of hexyl dithiocarbamate (1.62 g,1mmol) in 30 ml of dichloromethane. The resultant product gave dark brown amorphous solid, m.p.100°C, yield: 2.4 g (71%).Elemental Anal. Calc. for $C_{11}H_{22}INS_2Te$: Found (Calculated) (%): C, 27.09(27.13); H, 4.49(4.52); I, 26.01(26.08); N, 2.79(2.88); S, 13.09(13.16), Te: 26.16(26.23). IR (cm^{-1}):1435 s, 1360 m (νCN); 930 s, 1075 m (νCS); 570 s (νTeCH$_2$); ^{1}HNMR ($CDCl_3$, δ ppm): 3.12 (m, 1H, Te-CH_2), 2.00 (m, 1H, Te-CCH_2), 0.89 (m, 6H, C-CH_3), 1.65 (m, 2H, C-CH_2), 1.30 (m, 4H, C-$CH_2CH_2CH_2$), 8.26 (t, 1H, N-H), 3.50 (td, 4H, N-CH_2); ^{13}CNMR (100.60 MHz, $CDCl_3$, δ ppm): 48.27 (s, Te-CH_2), 21.79 (s, Te-CCH_2), 200.11 (s, S_2CN), 44.74 (s, N-CH_2), 28.49 (s, N-CCH_2), 26.40 (s, N-C_2CH_2), 31.11 (d, N-C_3CH_2), 22.11 (d, N-C_4CH_2), 14.08 (s, N-C_5CH_3); UV-Vis (λ_{max}, nm): 354 nm (ε = 22245 M^{-1} cm^{-1}), 325 nm (ε = 26943 M^{-1} cm^{-1}), 297 nm (ε = 28557 M^{-1} cm^{-1}) and 256 nm (ε = 49941 M^{-1} cm^{-1}).

Synthesis of 1,1,2,3,4,5-hexahydro-1-Iodo,1-butyl dithiocarbamate tellurophene [$C_4H_8TeI(S_2CNC_4H_{10})$] (10): Compound (10) was synthesised by the reaction of [$C_4H_8TeI_2$] (2.5 g, 1 mmol) and silver salt of butyl dithiocarbamate (1.53 g,1 mmol) in 30 ml of dichloromethane. The resultant product gave orange amorphous solid, m.p. 97°C, yield: 2.3 g (78%). Elemental Anal. Calc. for $C_9H_{18}INS_2Te$: Found (Calculated) (%): C, 23.52(23.55); H, 3.90(3.93); I, 27.65(27.68); N, 3.01(3.05); S, 13.91(13.96), Te: 27.44(27.83). IR (cm^{-1}):1417 s, 1367 m (νCN); 938 s, 1084 m (νCS); 535 m (νTeCH2); ^{1}HNMR ($CDCl_3$, δ ppm): 3.13 (m, 1H, Te-CH_2), 2.00 (m, 1H, Te-CCH_2), 0.92 (t, 6H, C-CH_3), 1.65 (m, 2H, C-CH_2), 1.29 (m, 2H, C-CH_2CH_2), 8.06 (t, 1H, N-H), 3.53 (td, 4H, N-CH_2); ^{13}CNMR (100.60 MHz, $CDCl_3$, δ ppm): 48.27 (s, Te-CH_2), 21.79 (s, Te-CCH_2), 200.00 (s, S_2CN), 44.58 (s, N-CH_2), 31.05 (s, N-CCH_2), 20.45 (s, N-C_2CH_2) 13.76 (s, N-C_3CH_3); UV-Vis (λ_{max}, nm): 369 nm (ε = 27235 M^{-1} cm^{-1}), 332 nm (ε = 25638 M^{-1} cm^{-1}), 287 nm (ε = 28772 M^{-1} cm^{-1}) and 258 nm (ε = 54700 M^{-1} cm^{-1}).

Synthesis of 1,1,2,3,4,5-hexahydro-1-Iodo,1-2-phenylethyl dithiocarbamate tellurophene [$C_4H_8TeI(S_2CNC_8H_{10})$] (11): Compound (11) was synthesised by the reaction of [$C_4H_8TeI_2$] (2.5g, 1 mmol) and silver salt of 2-phenylethyl dithiocarbamate (1.7 g,1mmol) in 30 ml of dichloromethane. The resultant product gave orange amorphous solid, m.p. 80°C, yield: 2.2 g (76%). Elemental Anal. Calc. for $C_{13}H_{18}INS_2Te$: Found (Calculated) (%): C, 30.77(30.80); H, 3.49(3.55); I, 25.01(25.05); N, 2.71(2.77);

S, 12.60(12.64); Te, 24.88 (25.19);IR (cm^{-1}):1428 s, 1370 m (νCN); 944 s, 1080 m(νCS); 530 s (νTeCH2); ^{1}HNMR ($CDCl_3$, δ ppm): 3.12 (m, 1H, Te-CH_2), 2.00 (m, 1H, Te-CCH_2), 2.94 (td, 7H, C-CH_2) 7.26,7.19 (m, 10H, C-H(Phenyl)), 8.51 (t, 1H, N-H), 3.69 (tdd, 4H, N-CH_2); ^{13}CNMR (100.60 MHz, $CDCl_3$, δ ppm): 48.27 (s, Te-CH_2), 21.79 (s, Te-CCH_2), 200.01 (s, S_2CN), 127.12 ,129.05 (d) (s, C-H (Benzyl)), 46.32(s, N-CH_2), 34.58(s, N-CCH_2), 139.99 (s, N-CH_2-C); UV-Vis (λ_{max}, nm): 369 nm (ε = 22590 M^{-1} cm^{-1}), 337 nm (ε = 25786 M^{-1} cm^{-1}), 280 nm (ε = 28781 M^{-1} cm^{-1}) and 253 nm (ε = 50879 M^{-1} cm^{-1}).

Computational studies

Molecular docking: Molecular docking studies were performed to insert molecule i.e. our ligand into the crystal structures cyclooxygenase-2 (prostaglandin synthase-2) and of alpha-hemolysin from staphylococcus aureus at active sites to determine the possible binding mode and predominant binding interactions. Molecular docking studies were done to assess the binding free energy of the inhibitor inside the target molecule using Autodock. Protein preparation was done by Autodock 4.2. The ligands $R_2Te(dtc)_2$ and $R_2TeI(dtc)$ were being modelled by the use of chemdraw software and also CS chem. 3D for energy minimization. Three important parameters like binding energy, RMSD and non-covalent interaction (hydrogen bond and hydrophobic interaction) were determined.

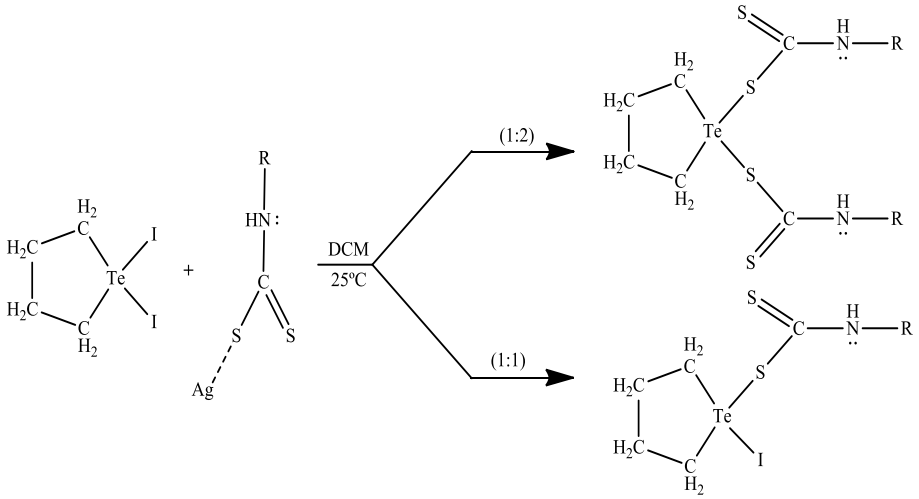
Preparation of target compounds for docking: Autodock 4.2 have been used for *in-silico* interaction analysis of Cyclooxygenase-2 (prostaglandin synthase-2) complexed with a selective inhibitor, SC-558 in i-222 space group (PDB id: 6COX) as target and representative compound ($C_4H_8TeI(S_2CNC_7H_8)$ as ligand[24]. Docking study has been done with initiation of protein preparation by Autodock 4.2 with Kollaman charge as -30.00, non-polar H as 11, number of rotatable bond as 2 and aromatic carbons with 16. After the protein preparation, ligand was prepared by no. of torsions as 12. Size of grid box was taken as 60, 60, 60 as the center of the grid box for x, y and z axis were analysed on scale of co-ordinate dimension as 24.076*24.077*36.961. Docking preparation include 27000 generation.

Autodock 4.2 again was used for the *in-silico* interaction analysis of alpha-hemolysin from *staphylococcus aureus* (PDB id: 7AHL) as target and representative compound (C_4H_8TeI ($S_2CNC_7H_8$) as ligand [(24)]. Docking study have been done with initiation of protein preparation by Autodock 4.2 with Kollaman charge as -29.15, non-polar H as 13, number of rotatable bond as 2 and aromatic carbons with 16. After the protein preparation, ligand was prepared by no. of torsions as 5. Size of grid box was taken as 90, 70, 70 as the centre of the grid box for x, y and z axis were analysed on scale of co-ordinate dimension as (50.702*27.375*44.027). Docking preparation include 27000 generation.

Identification and confirmation of binding sites: In docking, the binding pockets present in the complex i.e. protein taken are really important for giving a site to the ligand to bind. These binding pockets were equated via literatures After docking, the protein-ligand interactions were studied by using two programs pymol and protein ligand interaction profiler.

Results and Discussion

Characterisation analysis: The reaction between 1,1,2,3,4,5-hexahydro-1,1-diiodo tellurophene with silver salt of di-alkyl dithiocarbamate in dichloromethane produced the corresponding di-substituted and mono-substituted compounds: [C_4H_8Te ($S_2CNC_8H_{18})_2$] (2), [C_4H_8Te ($S_2CNC_7H_8)_2$] (3), [C_4H_8Te ($S_2CNC_6H_{14})_2$] (4), [C_4H_8Te ($S_2CNC_4H_{10})_2$] (5), [C_4H_8Te ($S_2CNC_8H_{10})_2$] (6), [C_4H_8TeI ($S_2CNC_8H_{18}$)] (7), [C_4H_8TeI ($S_2CNC_7H_8$)] (8), [C_4H_8TeI ($S_2CNC_6H_{14}$)] (9), [C_4H_8TeI ($S_2CNC_4H_{10}$)] (10) and [C_4H_8TeI ($S_2CNC_8H_{10}$)] (11) (Scheme 1). The molar conductance values for the synthesized complexes in DMSO at room temperature lie between 1.09-1.47 ohm^{-1} cm^2 mol^{-1} which indicates that these are non-electrolytes.



Scheme 1: [R=C_8H_{18}, C_7H_8,C_6H_{14},C_4H_{10} and C_8H_{10}; DCM=Dichloromethane]

The choice of using silver salts of dithiocarbamates was (i) to protect metal displacement phenomenon due to which the yields observed in these novel compounds was increased as compared with the reactions with its sodium salts and (ii) Facile synthesis due to the formation of corresponding silver iodides with ease.

The IR (KBr) spectra of the reported compounds (2-11) were assigned by comparison with the literature data of similar compounds.[4,6,13,15,21] In all the newly synthesized organotellurium dithiocarbamates, the spectra shows the sharp absorptions in the range 1390 - 1435 cm^{-1} which is affiliated to N-CS_2 stretching mode thereby indicating the shifting of υC-N of NCS_2 group towards the higher energies due to strong delocalization of electrons in the dithiocarbamate moiety The presence of υC-S absorption band is characteristic of the coordination mode of the dithiocarbamate ligands[20].

Two signals with medium intensity owing to the stretching mode of the C-S bonds were observed in the regions 950 ± 20 cm^{-1} and 1079 ±4 cm^{-1} in the reported compounds (2-11) respectively. The difference in wave numbers of these two bands is greater than 20cm^{-1}, thus owing towards monodentate coordination of the dithiocarbamate ligands to the tellurium [(4)]. The υ($TeCH_2$) of C_4H_8Te bunch show their standard positions.

In the ^{1}H NMR spectra of the synthesised novel organotellurium compounds, the corresponding signals of the tellurocycle moiety and the dithiocarbamate ligand are observed and their integration corresponds to expected for mono-substituted and di-substituted compounds. In the ^{1}H NMR spectra of compounds (2-11), the chemical shift for δ(Te-CH_2), δ(Te-C-CH_2) were spotted as multiplet and the range for δ(Te-CH_2) is from2.60 to 3.12 ppm and for δ(Te-C-CH_2) lies between 1.98 to 2.03 ppm respectively. Further the signals corresponding to δ (N-CH_2) lies in the region from 3.47 to 4.78 ppm as triplet of doublet of doublets except the compounds (3,8) multiplet and (4,5,9,10) triplet of doublets spotted.

The signals corresponding to δ(N-H) appear as triplet in all the compounds detected in the range from 8.06 to 8.96 ppm. These four chemical shifts were common in all the ten compounds (2-11). Some unique signals were also spotted in the synthesized compound, but these signals were detected in the specific compounds and the details are as follows:

In compounds (2,4,5,7,9,10), the signals corresponding to δ(C-CH_3) ranging from 0.89 to 0.92 ppm were noticed as multiplet but triplet in compounds (5,10). For the compound (2,4,5,6,7,9,10,11) the signals corresponding to δ(C-CH_2) appear as multiplet but in compound (6,11) the signal was spotted as triplet of doublet in the region from 1.31 to 2.94 ppm . Furthermore, in the compound (5,10), the signals corresponding to δ(C-CH_2-CH_2) appear as1.29 multiplet. In compound (4, 9), δ(C-CH_2-CH_2-CH_2) signal was noticed as 1.30 ppm multiplet. In compound (2,7), δ(C-CH_2-CH_2-CH_2-CH_2) again were noticed as multiplet from 1.27 to 1.28 ppm.

The signals corresponding to δ((C-H) benzyl) in compound (3,8) appear as multiplet with the single value to be 7.26 ppm and the signals corresponding to δ((C-H) phenyl) in compounds (6,11) appear as 7.26 multiplet and 7.20 doublets of doublets of triplets in both the compounds. For δ(C_6H_5) the signal appears as 7.32 ppm multiplet in compounds (3,8).

Furthermore, the ^{13}C-NMR spectra of compounds (2-11) exhibit a signal of the nitrogen atom attached to the methylene carbons. δ(N-CH_2) appear as singlet in the range 44.58 to 48.42 ppm. In addition, the signals δ(Te-CH_2) appears as singlet and the range for δ(Te-CH_2) from 39.27 to 48.35 ppm respectively. The signals corresponding to δ(Te-CCH_2) lies in the region 21.37 to 22.11 ppm as singlet. In comparison to the remaining signals, the signals corresponding to δ(S_2CN) carbon atoms are of relatively small intensity and appear in the range from 198.90 to 201.11 ppm as singlet.

So, like in ^{1}HNMR, here also we obtained four signals which are common in all compounds i.e. (2-11). Likewise, some unique signals were detected in the specific synthesized compounds and the details are as follows. In the compounds (2,4,5,6,7,9,10,11), the signals corresponding to δ(N-CCH_2) ranges from 28.45 to 34.58 ppm were spotted as singlet. For the compounds (2,4,5,7,9,10), the signals corresponding to δ(N-C_2CH_2) appear as singlet in the region from 20.45 to 26.40 ppm.

Moreover in the compounds (2,4,7,9), the signals corresponding to δ(N-C_3CH_2) appears as singlet in compounds (4,9) and doublet in (2,7) ranging from 29.45 to 31.11 ppm and signals corresponding to δ(N-C_4CH_2) in the same compound appears as singlet in compounds (4,9) and doublet in (2,7) ranging from 22.11 to 29.45 ppm. In the compounds (2,7), the signals corresponding to δ(N-C_5CH_2) were noticed as 31.88 ppm singlet and signals corresponding to δ(N-C_6CH_2) in the same compounds appears as 22.70 ppm singlet.

In the compounds (5,10), δ(N-C_3CH_3) were noted as 13.76 ppm singlet. Signals corresponding δ(N-C_5CH_3) in compounds (4,9) appear as 14.08 ppm singlet and in compounds (2,7), the signals corresponding to δ(N-C_7CH_3) appear as 14.08 ppm singlet. The signals corresponding to δ(CH benzyl) in compounds (3,6,8,11) appears in the region 127.12 to 129.05 ppm as singlet but in compounds (6,11), doublets were also detected along with singlet and the signals corresponding to δ(N-CH_2-C), (N-CH_2-CH_2-C) appears as 139.99 ppm singlet and 140.21 ppm singlet.

The comparison of the electronic spectra of the newly synthesized organotellurium dithiocarbamate with the corresponding sodium salts of dithiocarbamic acid reveals

that the absorption around 250 nm in the spectra of the compounds is due to the transition located in the CS_2 group of the ligand.[14,16,18]

The presence of single intense absorption at 250±5 nm in the spectra of all newly synthesized dithiocarbamate derivatives (2-11) suggests a monodentate nature of dithiocarbamate groups.

Molecular Docking

(a) Docking result of[$C_4H_8TeI(S_2CNC_7H_8)$]: The docking results of cyclooxygenase-2 (prostaglandin synthase-2) (PDB id: 6COX) with [C_4H_8TeI ($S_2CNC_7H_8$)] analyzed by Autodock 4.2 are given in table 1. Out of best 10 run, run 9 indicate the best with lowest binding energy -8.25 kcal /mol and RMSD 57.43. Hydrogen and hydrophobic bond interaction of cyclooxygenase-2 (prostaglandin synthase-2) (PDB id: 6COX) with ligands are given in figure 1.

Table 1
Binding energy values obtained during docking analysis of [$C_4H_8TeI(S_2CNC_7H_8)$] as ligand andcyclooxygenase-2 (prostaglandin synthase-2) (PDB ID: 6COX) as target protein

S.N.	Run	Binding energy score	RMSD
1	1	-7.22	54.73
2	2	-6.78	45.84
3	3	-7.38	55.41
4	4	-6.70	48.84
5	5	-7.37	54.58
6	6	-7.19	54.68
7	7	-7.53	54.49
8	8	-6.43	48.62
9	**9**	**-8.25**	**57.43**
10	10	-7.46	57.41

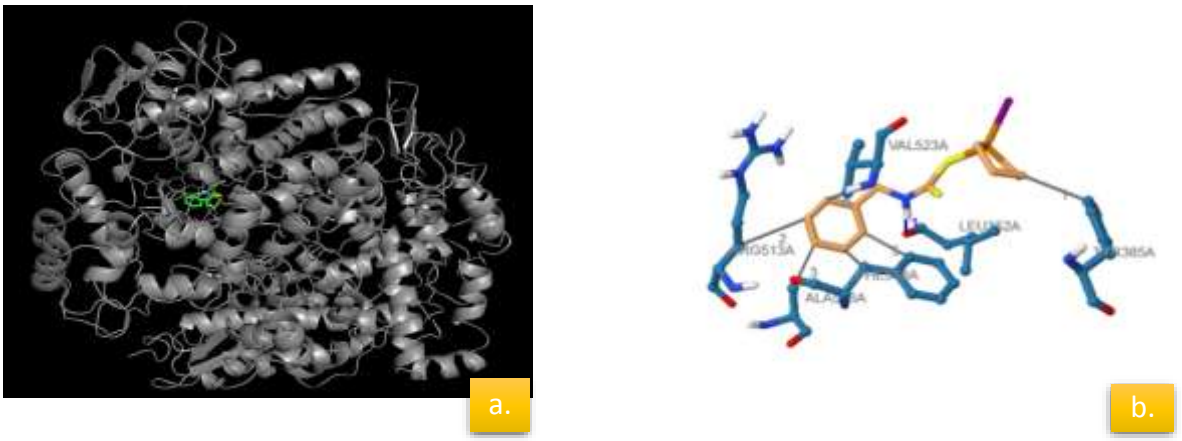


Figure 1: (a) Binding pose of [C_4H_8TeI ($S_2CNC_7H_8$)] with cyclooxygenase-2 (Pdb id: 6 COX) (b) 2-D Interaction diagram of cyclooxygenase-2 (prostaglandin synthase-2) (Pdb id: 6 COX with [C_4H_8TeI ($S_2CNC_7H_8$)]

Table 2
Binding energy values obtained during docking analysis of [$C_4H_8TeI(S_2CNC_7H_8)$] as ligand and Alpha-Hemolysin from staphylococcus aureus (PDB ID: 7AHL) as target protein

S.N.	Run	Binding energy score	RMSD
1	1	-4.53	86.37
2	2	-5.91	61.16
3	3	-4.79	76.22
4	4	-4.55	78.77
5	5	-6.19	61.82
6	6	-4.49	77.07
7	**7**	-6.80	66.52
8	8	-6.50	59.80
9	9	-6.05	60.05
10	10	-6.27	69.55

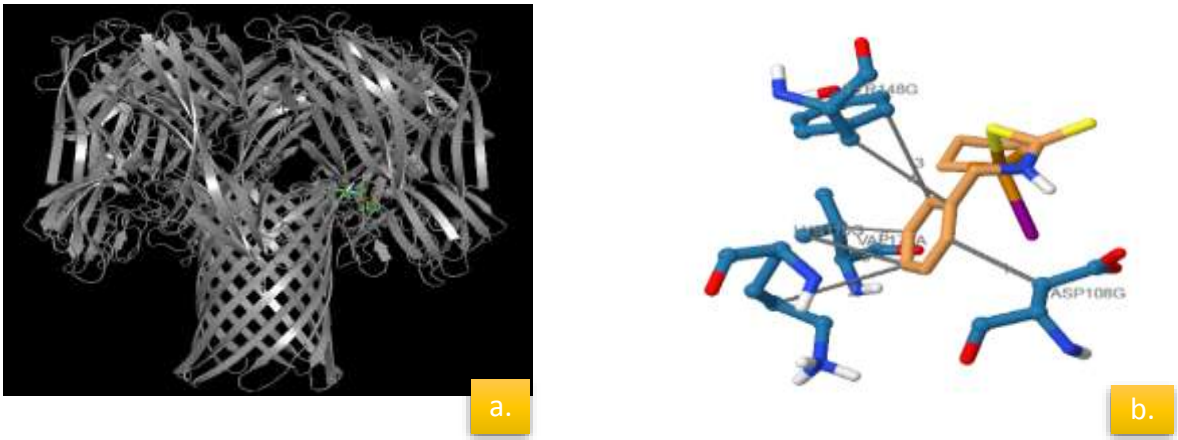


Figure 2: (a) Binding pose of [C_4H_8TeI ($S_2CNC_7H_8$)] with alpha-haemolysin from staphylococcus aureus (Pdb id: 7AHL) (b) 2-D Interaction diagram of alpha-haemolysin from staphylococcus aureus (Pdb id: 7AHL) with [C_4H_8TeI ($S_2CNC_7H_8$)]

The results show the interaction of ligand clear indicated the H-bond with oxygen atom of leucine and N of ligand with 1.80 distances. Also there exist hydrophobic interaction between tyrosine, argnine, alanine, phenylalanine and valine amino acid and ligand. These interactions indicate the significant binding of ligand with target.

(b) Docking result of [C_4H_8TeI ($S_2CNC_7H_8$)]: The docking results of alpha-haemolysin from staphylococcus aureus (Pdb id: 7AHL) with [C_4H_8TeI ($S_2CNC_7H_8$)] analysed by Autodock 4.2 are given in table 2. Out of best 10 run, run 7 indicate the best with lowest binding energy -6.80 kcal /mol and RMSD 66.52. Hydrogen and hydrophobic bond interaction of alpha-haemolysin from staphylococcus aureus (Pdb id: 7AHL) with ligands are given in figure 2. Also there exist hydrophobic interaction between lysine, aspartic acid, tyrosine and valine amino acid and ligand. These interactions indicate the significant binding of ligand with target.

Conclusion

Ten novel organotellurium dithiocarbamates were synthesised in increased yields via facile synthetic approach using silver salts of dithiocarbamates. Elemental analysis and spectral studies proved the formation of expected mono- and di substituted novel organotellurium dithiocarbamates. In all these novel complexes of tellurium, the dithiocarbamate moiety depicts monodentate chelating ligand behaviour. *In silico* molecular docking studies of the synthesized organotellurium dithiocarbamate $C_4H_8Te(S_2CNR)_2$ and $C_4H_8TeI(S_2CNR)$ with cyclooxygenase-2 (prostaglandin synthase-2) and alpha-hemolysin from staphylococcus aureus show various interactions.

By examining the binding energy and RMSD value of all the ten ligands i.e. $C_4H_8Te(S_2CNR)_2$ and $C_4H_8TeI(S_2CNR)$, we conclude the best ligand as ($C_4H_8TeI(S_2CNC_7H_8)$ in cyclooxygenase-2 (prostaglandin synthase-2) and ($C_4H_8TeI(S_2CNC_7H_8)$ in alpha-hemolysin from staphylococcus aureus.

Acknowledgement

The authors are thankful to Amity School of Applied Sciences, Amity University, Lucknow and Lucknow University, Lucknow, India for providing the research facilities and infrastructural support.

References

1. Bailey J.H.E. and Drake J.E., *Can. J. Chem.*, **71(1),** 42-50 **(1993)**

2. Bailey J.H.E., Drake J.E. and Wong M.L.Y., *Can. J. Chem.*, **69(12),** 1948 **(1991)**

3. Bogason J.O., Dakternieks D., Husebye S., Maartmann-Moe K. and Zhu H., *Phosphorus Sulfur Silicon Rel. Elem*., **71(1-4),** 13-24 **(1992)**

4. Bonati F. and Ugo R., *J. Organomet. Chem.*,**10(2)**, 257-268 **(1967)**

5. Canseco-Melchor G., Montalvo V.G., Toscano R.A. and Cea-Olivares R., *J. Organomet. Chem*., **631(1-2),** 99 **(2001)**

6. Cotero-Villegas A.M., García P.G., Hopfl H., del Carman Perez-Redondo M., Martinez-Salas P., Lopez-Cardoso M. and Olivares R.C., *J. Organomet. Chem.*, **695(8),** 1246-1252 **(2010)**

7. Cotero-Villegas A.M., García P.G., Hopfl H., del Carman Perez-Redondo M., Martinez-Salas P., Lopez-Cardoso M. and Olivares R.C., *J. Organomet. Chem.*, **696(10),** 2071-2078 **(2011)**

8. Dakternieks D., Di Giacomo R., Gable R.W. and Hoskins B.F., *J. Am. Chem. Soc.*, **110(20),** 6753-6761 **(1988)**

9. Dakternieks D., Di Giacomo R., Gable R.W. and Hoskins B.F., *J. Organomet. Chem*., **353(1),** 35- 43 **(1988)**

10. Drake J.E., Drake R.J., Khasrou L.N. and Ratnani R., *Inorg. Chem.*, **35(10),** 2831-2840 **(1996)**

11. Drake J.E., Khasrou L.N., Mislankar A.G. and Ratnani R., *Inorg. Chem.*, **38(18),** 3994-4004 **(1999)**

12. Drake J.E. and Yang J., *Inorg. Chem.*, **36(9),** 1890-1903 **(1997)**

13. Durgaprasad G., Sathyanarayana D.N. and Patel C.C, *Can. J. Chem.*, **47(4)**, 631-635 **(1969)**

14. Ewald A.H., Martin R.L., Ross I.G. and White A.H., *Proc. R. Soc. London*, **280(1381),** 235-257 **(1964)**

15. Herlimger A.W., Wenhold S.N. and Long T.V., *J. Am. Chem. Soc.*, **92**, 6474 **(1970)**

16. Holloway C.E. and Gitlitz M.H., *Can. J. Chem.*, **45**, 2659 **(1967)**

17. Husebye S., Maartmann-Moe K., Steffensen W., Beattie D.T., Krogsgaard Larsen P., Maartmann-Moe K. and Wold S., *Acta Chem. Scand.*, **44,** 139-143 **(1990)**

18. Janssen M.J., *Recl. Trav. Chim. Pays. Bas Belg.*, **79(5),** 464-473 **(1960)**

19. Khoudary K., Mona S., Matar M. and Haffar S., *Asian Journal of Chemistry*, **25(2)**, 962-964 **(2013)**

20. Mohammad A., Varshney C. and Nami S.A.A., *Spectrochim Acta*, Part A, **73 (1)**, 20-24 **(2009)**

21. Montalvo V.G., Marcelo-Polo A., Montoya R., Toscano R.A., Ortega S.H. and Cea-Olivares R., *J. Organomet. Chem*., **623(1-2),** 74-80 **(2001)**

22. Montalvo V.G., Toscano R., Delgado A.B. and Olivares R.C., *Polyhedron.*, **20(203)**, 1831-1853 **(2001)**

23. Morgan G.T. and Burstall F.H., *J. Chem. Soc*., 180-184 **(1931)**

24. Morris G.M., Huey R., Lindstrom W., Sanner M.F., Belew R.K., Goodsell D.S. and Olson A.J., *J. Comput. Chem.*, **30(16)**, 2785-2791 **(2009)**

25. Singh A.K. and Basumatary, *J. Organomet. Chem.*, **364(1-2),** 73-77 **(1989)**

26. Srivastava P.C., Dwivedi S., Singh V., Pujan T., Bhuj A.K., Butcher R.J., Krishna M.B.M. and Rao D.N., *Inorg. Chim. Acta*, **388(40),** 175-183 **(2012)**

27. Srivastava P.C., Singh V., Dwivedi S., Pujan T., Bhuj A.K., Butcher R.J., Krishna M.B.M. and Rao D.N., *Polyhedron.*, **42(1),** 36-42 **(2012)**

28. Vogel A.I., Longman, London, Quantitative Inorganic Analysis, 267 **(1975)**.

(Received 20th January 2021, accepted 28th February 2021)