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New Mercurated and Tellurated Sulpha Compounds: Synthesis, *Invitro* Anticancer Study and DFT Calculation.

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Abstract

The current study includes mercuration and telluration of some sulpha compounds; these compounds were prepared by reaction of 4-aminobenzenesulfonic acid and 4,4'-sulfonyldianiline with mercuric(II) acetate reagent to produce Arylmercuric(II)chloride, which was subjected to transmetallation reactions by using $TeBr_4$ to form the Aryltellurium(IV) tribromide. Additionally, the reactions between (2-amino-5-sulfophenyl)mercury(II) chloride and 3,4-dihydroxybenzaldehyde on one hand, and 4,4'-sulfonylbis[2-chloromercuric aniline] with benzaldehyde, on the other, produce mercurated sulpha compounds containing azomethine- group**.** These obtained compounds react with $TeBr_4$ to form new tellurated sulpha compounds containing azomethine-group. These newly created compounds were subjected to various analyses, including C.H.N.S analysis, proton-NMR, FT-IR, and Carbon-13 NMR. The synthesised compounds were tested for cytotoxicity using in-vitro analyses on two human cancer cell lines, PC3 (prostate cancer cell) and T24 (bladder cancer cell). The prepared organotellurium compounds are effective, especially **4** and **6** compounds. DFT calculations of HOMO and LUMO energy levels and certain quantum parameters indicate that the organomercury compounds are relatively stable and exhibit lesser reactivity when compared to their organotellurium counterparts. Additionally, theoretical results validate the results obtained by the measurement of cancer effectiveness.

Keywords: Organomercury; Organotellurium; Anti-cancer; DFT; Metrical studio/DMol3

1. Introduction

Organomercury compounds represented by the formulae R_2Hg and RHgX (R is an alkyl or aryl group; X is a halide group) have been studied keenly over the past few decades in the pursuit of reagents that are highly versatile during controlled transmetallation processes [1]. Organomercury(II) derived compounds have been used to prepare organometallic compounds of the transition group metals and the main groups too. The classic reduction process by Grignard reagent or lithiation is unsuccessful in producing these compounds [2]. Compounds containing mercury are harmful, and that remains a consideration that should be factored in during preparation. However, using mercury has its advantages, one of which is the ability to make functionalised organomercury-derived compounds. Additionally, the transmetallation reaction is highly selective, which is another advantage [3].

Synthesising several organotellurium compounds using transmetallation of organomercury substances has been widely studied and reported in several publications [4-7]. Aromatic compounds, when reacting with tellurium tetrahalides, undergo a direct substitution reaction, and the obtained yield is low. Sometimes, the reactions are not feasible. However, tellurium tetrahalides undergo a substitution reaction with arylmercuric chloride with a high yield of aryltellurium trihalide [8, 9].

The previous few decades have seen a steady increase in the production and application of organotellurium compounds. These compounds have shown promising results to use as alternatives in synthetic processes, such as the reactions involving carbon-carbon bond formation, as well as several other interconversions between functional groups [10-12]. Moreover, these organotellurium compounds and several transition metal complexes have been proven to possess anticarcinogenic, antibacterial,

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anti-inflammatory, antifungal, and antioxidative properties, which make these compounds potential pharmacological agents [13-20]. AS101 and SAS are two examples of tellurium complex compounds that are known to inhibit tumour survival proteins like survivin. They also inactivate cysteine proteases like cathepsin B and obstruct IL-10 tumour production. These anticarcinogenic effects are attributed to the redox-modulation caused by Te(IV) [21, 22].

Aromatic organotellurium compounds having an electron-donating nitrogen atom in the ortho position are highly stable because of the intramolecular forces between nitrogen and tellurium atoms. The synthesis of these compounds has been of great interest in the scientific community [23-25]. Theoretical analyses of organotellurium compounds by using density functional theory (DFT) have been successfully used in many theoretical studies of organotellurium compounds [6, 26, 27].

The objective of this study is to explore ways to synthesise new tellurated and mercurated sulpha compounds and analyse their activity against tumours. Additionally, specific electronic characteristics were explored with the help of computational chemistry. Finally, the link between the practical observations and theory would be devised.

2. Experimental

2.1 Chemical

All chemicals used in the experiments were procured from reputed commercial chemical suppliers and were used in their pristine form without any further purification. Tellurium tetrabromide, mercuric acetate, sodium chloride, 1,4-dioxane, 4-aminobenzenesulfonic acid, and 4,4'-sulfonyldianiline supplied from Sigma-Aldrich company. 3,4-dihydroxybenzaldehyde and benzaldehyde from Merck company. While ethanol 99.8%, methanol, benzene, and dichloromethane were supplied from Fischer Chemical company.

2.2 Instrument

The FT-IR Shimadzu spectrophotometer was used to measure the IR spectra. Specifically, IR Affinity-1 was the equipment model, and measurement was done in the 4000-400cm^{-1} range using KBr discs. The experiments were conducted at the Chemistry department of the Education for Pure Sciences Faculty at Basrah University in Iraq. Bruker 500 MHz spectrometer at the Tehran University laboratory was used to record hydrogen and carbon-13 nuclear magnetic resonance spectra. DMSO-d6 was used as the solvent, and tetramethylsilane (TMS) acted as an internal reference. C.H.N.S analysis was performed at Tarbiat Modares analytical lab of the Tehran University, Iran. Specifically, CHNS-O Perkin Elmer model 2400-11 was the equipment used for the analysis. Anti-tumour studies were conducted at the Changchun Institute of Applied Chemistry (CIAC), Chinese Academy of Sciences (CAS) Changchun, Jilin Province, China.

2.3 Synthesis

***2-amino-5-sulfophenyl)mercury(II) chloride* 1**

A mixture of (3.82 g, 12 mmol) of mercuric acetate and (1.73 g, 10 mmol) 4-aminobenzenesulfonic acid was boiled and stirred for 14 h. in a solution of (50 mL) EtOH. Subsequently, NaCl (0.7 g, 12 mmol) in a solution of boiling MeOH was added to the mixture. It was then cooled with continuous stirring for one hour. A white powder was obtained after the precipitate was filtered, washed with water and EtOH, followed by drying over $CaCl_2$. Yield: 3.36 g, 82%. m.p.: 236- 238°C (dec.). ^{1}H NMR (500 MHz, DMSO- d_6): δ = 10.10 (s, 1H, O- H, H^a), 7.69 (s, 1H, Ar- H, H^b), 6.85 (d, 1H, Ar- H, H^c), 6.51 (d, 1H, Ar- H, H^d), 5.62 (s, 2H, -NH_2, H^e) ppm. FT- IR (KBr): ῡ = 3550 (OH), 3213 (N-H), 3074 (arom.CH), 1620 (C=C), 1315 (S=O) cm^{-1}. Anal.Calcd. for $C_6H_6ClHgNO_3S$: C, 17.65; H, 1.48; N, 3.43; S, 7.85. Found: C, 17.71; H, 1.49; N, 3.37; S, 7.81%.

***4-amino-3-(tribromo- λ^4-tellanyl)benzenesulfonic acid* 2**

(1.79 g, 4 mmol) of tellurium tetrabromide was mixed with an equivalent molar amount of (2-amino-5-sulfophenyl) mercury(II)chloride **1** weighing 1.63 g., 4 mmol in 40 mL of 1,4-dioxane and refluxed for 6 hours under argon atmosphere. Upon cooling, a 1:2 addition compound of mercury(II) halide and dioxane was isolated as white sheets and filtered. Subsequently, a rotary evaporator was used to dry the filtrate. The obtained residue was recrystallized two times using a 1:2 solution of DCM and MeOH. Finally, a solid brown crystal was obtained. Yield: 1.48 g, 69%. m.p.: 213- 215°C(dec.). ^{1}H NMR (500 MHz, DMSO- d_6): δ = 10.23 (s, 1H, O- H, H^a), 7.69 (s, 1H, Ar- H, H^b), 6.98 (d, 1H, Ar- H, H^c), 6.52 (d, 1H, Ar- H, H^d), 6.08 (s, 2H, -NH_2, H^e) ppm. ^{13}C NMR (125 MHz, DMSO- d_6): δ = 149.44 (C-NH_2), 141.65 (C-SO_3H), 127.81 (C-Te), 119.30 (C- H), 116.68(C- H) ppm. FT- IR (KBr): ῡ = 3600-3350 (OH) and (N-H), 1624 (C=C), 1345 (S=O) cm^{-1}.Anal.Calcd. for $C_6H_6Br_3NO_3STe$: C, 13.36; H, 1.12; N, 2.60; S, 5.94. Found: C, 13.42; H, 1.14; N, 2.53; S, 5.82%.

***{2-[(3,4-dihydroxybenzylidene)amino]-5-sulfophenyl}mercury(II) chloride* 3**

A mixture of (0.55 g, 4 mmol) of 3,4-dihydroxybenzaldehyde and (1.63g, 4 mmol) of (2-amino-5-sulfophenyl)mercury(II) chloride **1** was refluxed in a solution containing (30 mL) EtOH and 2-3 drops of sulphuric acid and stirred for two hours. Once the solution cooled, the precipitate was filtered and washed with EtOH several times. The solid residue was recrystallized two times from a 2:3 mixture and benzene and alcohol. Finally, a yellowish solid was obtained. Yield: 1.70 g, 81%. m.p.: 176- 178°C(dec.). ^{1}H NMR (500 MHz, DMSO- d_6): δ = 10.92 and 10.76 (s, 1H, Phenolic O-H, H^a), 10.24 (s, 1H, O- H, H^b), 10.16 (s, 1H, -N=CH, H^c), 7.69- 7.17 (m, 6H, Ar- H, H^d) ppm. Anal. FT- IR (KBr): ῡ = 3480 (OH), 1624 (C=C), 1582 (C=N), 1300 (S=O) cm^{-1}. Calcd. for $C_{13}H_{10}ClHgNO_5S$: C, 29.55; H, 1.1.91; N, 2.65; S, 6.07. Found: C, 30.01; H, 1.89; N, 2.55; S, 6.13%.

***4-[(3,4-dihydroxybenzylidene)amino]-3-(tribromo-λ^4-tellanyl)benzenesulfonic acid* 4**

The same procedure of compound **2** was used to synthesise the compound **4** but used (2.11 g, 4 mmol) of (2-((3,4-dihydroxybenzylidene) amino)-5-sulfophenyl)mercury(II) chloride **3** and (1.79 g, 4 mmol) of tellurium tetrabromide. The formation product was a brown solid crystal. Yield: 1.58g, 60%. m.p.: 213- 215°C (dec.). ^{1}H NMR (500 MHz, DMSO- d_6): δ = 11.27 and 11.12 (s, 1H, Phenolic O-H, H^a), 10.35 (s, 1H, O- H, H^b), 10.16 (s, 1H, -N=CH, H^c), 7.95- 7.31 (m, 6H, Ar- H, H^d) ppm. ^{13}C NMR (125 MHz, DMSO- d_6): δ = 165.25(C-N=), 161.13 (CH=N), 152.13(C-OH), 150.89 (C-OH), 147.06 (C-SO_3H), 130.5 3(C-Te), 127.77 (C- H), 124.09 (C- H), 121.62 (C- H), 119.30 (C-H), 118.77 (C- H), 117.38(C- H) ppm. FT- IR (KBr): ῡ = 3436 (OH), 2910 (aliph. CH) , 1622 (C=C), 1595 (C=N), 1355 (S=O) cm^{-1}. Anal.Calcd. for $C_{13}H_{10}Br_3NO_5STe$: C, 23.67; H, 1.53; N, 2.12; S, 4.86. Found: C, 23.77; H, 1.60; N, 2.31; S, 4.72%.

***4,4'-sulfonylbis[2-chloromercuric aniline* 5**

The same procedure of compound **1** was used to synthesise the compound **5**, but used (2.48 g, 10 mmole) of 4,4'-sulfonyldianiline and (7.63 g, 24 mmole) of mercuric acetate and (1.40 g, 24 mmole) of NaCl . The formation product was a white powder. Yield: 5.52 g, 77%. m.p.: 213- 215°C (dec.). ^{1}H NMR (500 MHz, DMSO- d_6): δ = 7.67 (d, 1H, Ar- H, H^a), 7.55 (d, 1H, Ar- H, H^b), 6.57 (s, 1H, Ar- H, H^c), 5.91(s, 2H, -NH_2, H^d) ppm. ^{13}C NMR (125 MHz, DMSO- d_6): δ = 150.55 (C-NH_2), 136.54 (C-SO_2), 127.84 (C-HgCl), 123.82 (C- H), 121.64 (C-H), 115.98 (C- H) ppm. FT- IR (KBr): ῡ = 3448 and 3350 (N-H), 3220 (arom.CH), 1620 (C=C), 1288 (S=O) cm^{-1}. Anal.Calcd. for $C_{12}H_{10}Cl_2Hg_2N_2O_2S$: C, 20.06; H, 1.40; N, 3.90; S, 4.46. Found: C, 21.11; H, 1.43; N, 3.92; S, 4.49%.

***4,4'-sulfonylbis[(2-(tribromo- λ^4-tellanyl)aniline]* 6**

The compound **6** synthesized in the same way as compound **2** but used (1.43 g, 2 mmol) of bis(4-amino-3-chloromercuricphenyl) sulfone **5** and (1.79 g, 4 mmol) of tellurium tetrabromide. The formation product was a brown solid crystal. Yield: 1.31 g, 67%. m.p.: 213- 215°C(dec.). ^{1}H NMR (500 MHz, DMSO- d_6): 7.69 (d, 1H, Ar- H, H^a), 7.49 (d, 1H, Ar- H, H^b), 6.64 (s, 1H, Ar- H, H^c), 6.19 (s, 2H, -NH_2, H^d) ppm. FT- IR (KBr): ῡ = 3455 and 3360 (N-H), 3228 (arom.CH), 1622 (C=C), 1279(S=O) cm^{-1}. Anal.Calcd. for $C_{12}H_{10}Br_6N_2O_2STe_2$: C, 14.69; H, 1.03; N, 2.86; S, 3.27. Found: C, 15.42; H, 1.09; N, 2.92; S, 3.33%.

N,N'-{sulfonylbis[(2-chloromercuric)-4,1-phenylene]}bis[1-phenylmethanimine] 7

The same procedure of compound **3** was used to synthesise the compound **7** but used (2.15 g, 3 mmol) of bis(4-amino-3-chloromercuricphenyl) sulfone **5** and (0.63 g, 6 mmol) of benzaldehyde .The formation product gave a yellowish solid. Yield: 2.24 g, 84%. m.p.: 213- 215°C (dec.). ^{1}H NMR (500 MHz, DMSO- d_6): δ = 9.88 (s, 1H, -N=CH, H^a), 7.79- 6.97 (m, 8H, Ar- H, H^b) ppm. FT- IR (KBr): ῡ = 3195(arom.CH) , 2910 (aliph. CH), 1625(C=C), 1597(C=N), 1299(S=O) cm^{-1}. Anal.Calcd. for $C_{26}H_{18}Cl_2Hg_2N_2O_2S$: C, 34.91; H, 2.03; N, 3.13; S, 3.58. Found: C, 35.29; H, 2.09; N, 3.39; S, 3.62%.

N,N'-{sulfonylbis[2-(tribromo-λ^4-tellanyl)-4,1-phenylene]}bis[1-phenylmethanimine] 8

The compound **8** synthesized in the same way as compound **2** but used (1.79 g, 2 mmol) of bis (4-benzylideneamino-3-chloromercuricphenyl) sulfone **7** and (1.79 g, 4.00 mmol) of tellurium tetrabromide. The formation product was a brown solid crystal. Yield: 1.64 g, 71%. m.p.: 213- 215°C(dec.). ^{1}H NMR (500 MHz, DMSO- d_6): δ = 9.99 (s, 1H, -N=CH, H^a), 7.63- 6.90 (m, 8H, Ar- H, H^b) ppm. ^{13}C-NMR (125 MHz, DMSO- d_6): δ = 165.21(C-N=), 155.68 (CH=N), 137.90 (C-SO_2), 133.15 (C-Te), 130.68 (C-H), 129.08 (C-H), 128.31 (C-H), 127.16 (C-H), 123.81 (C-H), 122.47 (C-H), 120.52 (C-H), 120.41 (C-H) ppm. FT- IR (KBr): ῡ = 3080(arom.CH), 1612 (C=C), 1597 (C=N), 1296 (S=O) cm^{-1}.Anal.Calcd. for $C_{26}H_{18}Br_6N_2O_2STe_2$: C, 26.99; H, 1.57; N, 2.42; S, 2.77. Found: C, 27.91; H, 1.64; N, 2.50; S, 2.81%.

2.4 Anti-tumor activity.

The compounds were analysed for cytotoxicity on the cells using an MTT assay as previously mentioned [28]. T24 and PC3 cells were seeded in 96-well plates, with a cell density of 10,000 cells per well. After the overnight growth of cells, they were incubated in 100 µL in complete culture media that had a different concentration of each compound. Specifically, the incubation was done in triplicate using 0, 3, 6, 12, 25, 50, and 100 µM concentration of each compound. The cells were allowed to incubate for 24 hours. Subsequently, the wells were analysed for the growth of the cells, which was found by the addition of 10 µL MTT (5 mg/ml in phosphate-buffered saline solution) to each well followed by incubation for 4 hours. 150 µL of DMSO was added to each well after removing the medium, followed by gentle shaking. The ELX 800 plate reader from BIO-TEK Instruments Inc. was used to record the absorbance at 490 *nm* wavelength.

2.5 Theoretical details

Calculations for all eight molecules were done using the Density Function Theory (DFT) method using the Perdew, Burke, and Enzerhof (PBE) theory level [29]. The basis set used was a double numerical plus polarisation (DNP) [26]. Material Studio-DMol3 ver. 5.5 software was used to extract the output file. Molecular orbital energy values E_{LUMO} and E_{HOMO} were extracted from the file, and several quantum chemical parameters were calculated using the equations mentioned below [30].

Electronegativity	$\chi = -1/2\ (E_{HOMO}+E_{LUMO})$
Chemical potential	$\mu = -\chi = 1/2\ (E_{HOMO}+E_{LUMO})$
Chemical hardness	$\eta = -1/2\ (E_{HOMO}-E_{LUMO})$
Global softness	$S = -1/2\ \eta$
Global electrophilicity	$\omega = \mu^2/2\eta$
Absolute softness	$\sigma = 1/\eta$

3. Results and Discussion

3.1 Synthesis

This work describes the synthesis of new tellurated and mercurated compounds. Compounds **1** and **5** are sulpha organomercury in nature, and the yield has been satisfactory because the synthesis process allowed 4,4'-sulfonyldianiline and 4-aminobenzenesulfonic acid to react first with mercuric acetate followed by sodium chloride using ethyl alcohol as a solvent. Compounds **2** and **6** are the brown-precipitated tellurated forms of **1** and **5** and were formed by reacting the compounds **1** and **5** with tellurium tetrabromide. On the other hand, sulpha organomercury compounds containing azomethine **3** and **7** precipitated as a yellowish powder by reacting compound **1** with 3,4-dihydroxy benzaldehyde, and compound **5** with benzaldehyde. Sulpha organotellurium compounds-containing azomethine **4** and **8** were synthesised by reaction of compounds **3** and **7** with tellurium tetrabromide and were obtained in a brown coloured crystallised form, scheme 1.

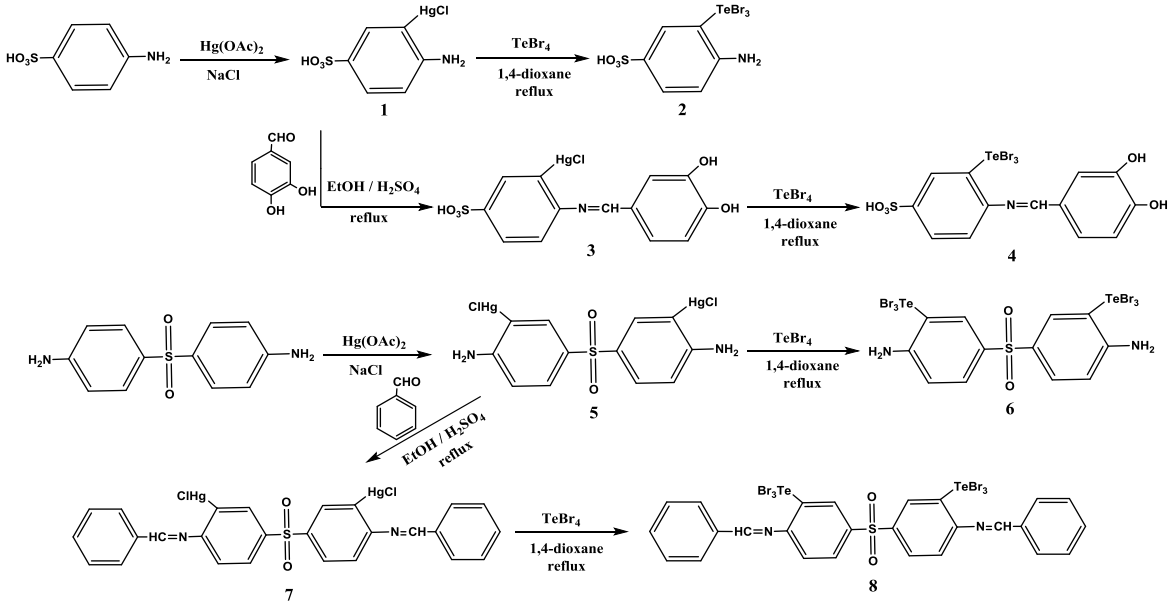
The processes used to prepare the new compounds are mentioned in Scheme 1. Yield, colour, melting point, and C.H.N.S analyses for these compounds were in agreement with the obtained values, which are mentioned in the experimental section.

Compounds **1**, **2**, **5**, and **6** are found to have two weak bands in their infrared spectra at 3600-3213 and 3360-3350 cm^{-1}. The symmetrical properties of the amino group could be the reason for this observation. Additionally, there is a presence of overlap with *ν*(O-H) in compounds **1** and **2**. The IR spectra of compounds **3**, **4**, **7**, and **8** have a vibration frequency at 1597-1582 cm^{-1}, and the presence of azomethine group (-C=N-) is confirmed. Compounds **1** to **4** had a presence of strong, broad bands in the 3600-3350 cm^{-1} range owing to *ν*(O-H). All compounds were found to have medium and strong bands in the range 1355-1279 cm^{-1} attributed to the stretching vibration of the sulfinyl (S=0) group.

^{1}H NMR spectra of compounds **1**, **2**, **5**, and **6** had a singlet broad signal in the 6.10-5.62 ppm range, and this is due to the protons in the aromatic amino group. Hydroxyl group (phenolic and carboxylic) protons in compounds **1** to **4** were observed to have a singlet signal in the 11.27-10.10 ppm range. Compounds **3**, **4**, **7**, and **8** demonstrated additional evidence to support the formation of azomethine group (-CH=N-) in the form of a singlet signal in the 10.16-9.88 ppm range that is in agreement with the previous reports [6]. Compounds **1**, **2**, **5**, and **6** had three aromatic protons that appeared as two duplet signals in the 7.69-6.85 ppm range while there was one singlet in the 7.69-6.51 ppm range. In contrast, aromatic protons in compounds **3**, **4**, **7**, and **8** exhibited multiplet signals in the 7.95-6.90 ppm range.

The chemical structure of the compounds as proposed in the study was confirmed by the ^{13}C - NMR signals. These signals for compounds **2**, **5**, **4**, and **8,** respectively, were at 149.44, 150.55, 165.25, and 165.21 ppm. The signals correspond to carbon atoms in the aromatic ring attached with nitrogen. Compound **4** has two signals at 150.89 and 152.13 ppm that can be attributed to attachment carbon and

oxygen atoms. Attachments of carbon and sulphur observed at levels 141.65, 147.06, 136.54, and 137.90 ppm, respectively. Signals at 127.81, 130.53, and 133.15 ppm for compounds **2, 4,** and **8** respectively are characteristic of carbon and tellurium atom attachment [31]. Compounds **4** and **8** have an atoms in the case of compounds **2**, **4**, **5,** and **8** were azomethine group whose aliphatic carbon signal was in a low field at 161.13 and 155.68 ppm. Other Ar-C signals appeared in the 130.68-115.98 ppm range.



Scheme 1. Preparation pathway of organomercury and organotellurium compounds.

3.2 Invitro anti-tumor activity

In this study, the compounds were tested for anticarcinogenic activity towards T24 bladder cells and PC-3 human prostate cells, *invitro*. Compounds **2**, **4**, **6**, and **8** demonstrated anticarcinogenic activity. Compounds **4** and **6** showed significant activity toward these two types of cancer cells more than compounds **2** and **8**, as highlighted in Table 1.

This activity may be attributed to active atoms like sulphur, oxygen, nitrogen, and tellurium [32-36]. Tellurium has demonstrated the ability to inhibit enzymes that facilitate tumour growth [37]. Moving forward, PC-3 and T24 cells were tested in a dose ranging 3 to 100 µM of compounds **4** and **6**. The cell growth inhibition ratio of PC3 and T24 is shown in Figure 1. At 100 µM concentration, inhibition activity stood at 72.88% and 96.02% for compounds **4** and **6**, respectively. IC_{50} is the half-maximal inhibitory concentration and measures the efficacy of a compound as a biological inhibitor. IC_{50} value for compound **6** is greater than that for compound **4** against tumour cells. The results, as specified in Table 1, show the higher activity of compound **4** compared to compound **6**. This could be attributed to the presence of phenolic, azomethine groups, and intermolecular chalcogen bonding via Tellerium atoms that can interact with cancer cell proteins and act as an inhibitor

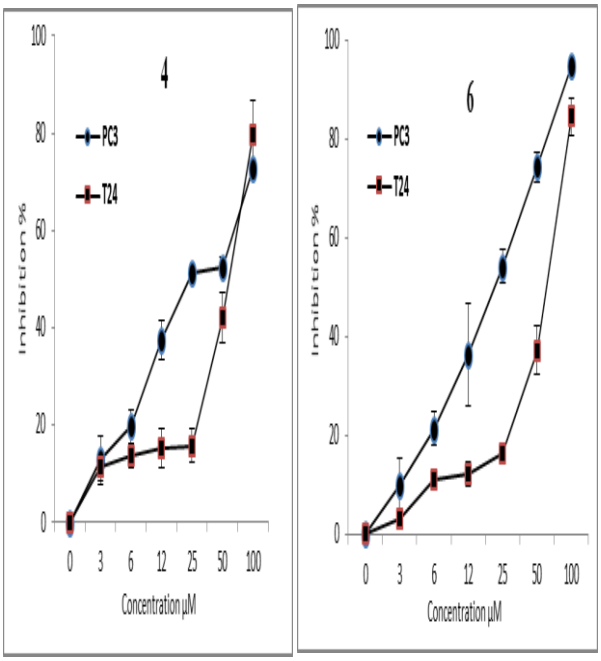


Figure 1. T24 and PC3 tumor cell growth inhibition of compounds **4** and **6**

Table 1. Anticarcinogenic activity and IC50 values of the compounds against PC-3 cells and T24 cells

Compounds	PC-3 cells	T24 cells	IC_{50} value µM	
			PC-3	T24
1	-	-		
2	+	-		
3	-	-		
4	++	++	22.26±3.21	24.12±4.44
5	-	-		
6	++	++	27.53±4.72	48.82±4.84
7	-	-		
8	+	+		

3.3 Theoretical study

Material Studio 5.5/DMol3 was used to perform geometry optimisation for the new compounds as shown in Figure 2. Molecular orbital energies of HOMO (π donor) and LUMO (π acceptor) are crucial parameters for quantum chemical calculations. The HOMO orbital act as the primary electron donor while the LUMO orbital acts as the electron acceptor. Both molecular orbital energy values are negative and confirm that the synthesised compounds are stable [42]. The energy gap (E_{LUMO}–E_{HOMO}) measures the stability of the molecule and helps define the kinetic stability and chemical reactivity of the molecule [43]. Higher energy gap, the molecule is more stable and less reactive. Moreover, a small energy gap may be polarised easily and typically associated with low kinetic stability and exhibits high chemical reactivity. Molecules with low orbital energy gap are known as soft molecules [44].

Referring to the data specified in Table 2, it is determined that the prepared molecules are stable, assigning negative values of E_{HOMO} and E_{LUMO} orbitals. The energy gap ($\Delta E_{(LUMO-HOMO)}$), chemical softness(S), chemical hardness (η), and absolute softness(ϭ) are associated with the chemical properties of the molecules. Molecules **1** and **5** exhibit high ΔE and hardness; however, they have lower values of absolute softness and softness. Therefore, these two compounds are relatively stable and hard molecules compared to other compounds. In the case of compounds **4**, **6**, and **8**, chemical hardness and ΔE values are low, whereas the values for absolute softness are high, which confirms that these compounds are more reactive than the others. Thus, there is flexibility in their use for biological cases [45, 46].

Chemical potential (μ) is the average of the energy values of the HOMO and LUMO orbitals. Electronegativity (χ) is the negative of chemical potential. These are two opposite values that are used to determine the dipolar degree at the molecular level [47]. Electronegativity is the potential to attract electrons from other chemical species and is an important parameter that helps determine inhibitive performance at the molecular level [48]. Molecules **2**, **4**, **6**, and **8** had the highest electronegativity compared with other compounds, molecule **4** having the highest value among them. The results validate the agreement with the anti-cancer study results.

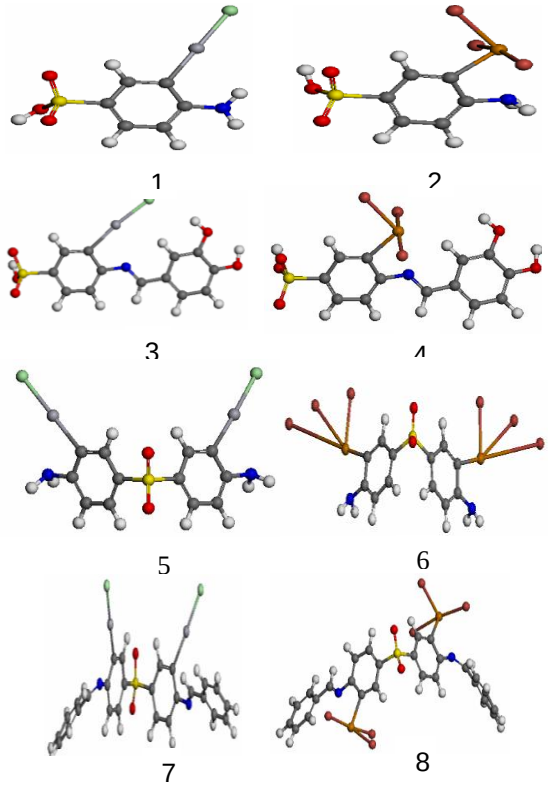


Figure 2. Geometry optimization of the molecules structure

Global electrophilicity (ω) serves as an important marker of reactivity and may be used to compare molecules on their electron-donating ability [49]. High global electrophilicity implies that the molecule behaves as an electrophile. In the study, molecules **4**, **6**, and **8** are electrophilic, this behaviour is attributed to the presence of Br, O, N, Te, and S atoms that contain free electron lone pairs.

Table 2. Conformational parameters (eV.) for all optimized structures

Compounds	EHOMO (eV)	ELUMO (eV)	ΔELUMO-HOMO (eV)	χ (eV)	μ (eV)	η (eV)	S (eV)	ω (eV)	ϭ (eV)
1	-5.893	-2.183	3.710	4.030	-4.038	1.855	-0.928	4.395	0.539
2	-6.340	-3.734	2.606	5.037	-5.037	1.303	-0.652	9.736	0.767
3	-5.767	-3.376	2.391	4.571	-4.572	1.195	-0.598	8.741	0.836
4	-6.156	-4.002	2.154	5.079	-5.079	1.077	-0.539	11.980	0.928
5	-6.573	-2.638	3.935	4.605	-4.606	1.967	-0.984	5.390	0.508
6	-5.402	-3.991	1.411	4.696	-4.697	0.705	-0.353	15.630	1.417
7	-5.824	-3.308	2.516	4.566	-4.566	1.258	-0.629	8.286	0.794
8	-6.035	-4.071	1.964	5.053	-5.053	0.982	-0.491	13.000	1.018

The electrostatic potential maps of the active molecules **4**, **6**, and **8** and the shapes of the HOMO and LUMO orbitals are described in Figure 3. It is observed that there is HOMO orbital localisation primarily on bromine, tellurium, oxygen, and nitrogen atoms moieties. LUMO orbitals with π behaviour are primarily concentrated around the phenyl ring. Molecular electrostatic potential maps are immensely useful in understanding the points where an electrophilic attack may happen. The maps are indicators of electron density and help to understand nucleophilic reactions and also hydrogen bonding [47]. The shape maps indicate that sites with high electron density are active sites, the electron density concentrated around bromine, sulphur, tellurium, and oxygen atoms.

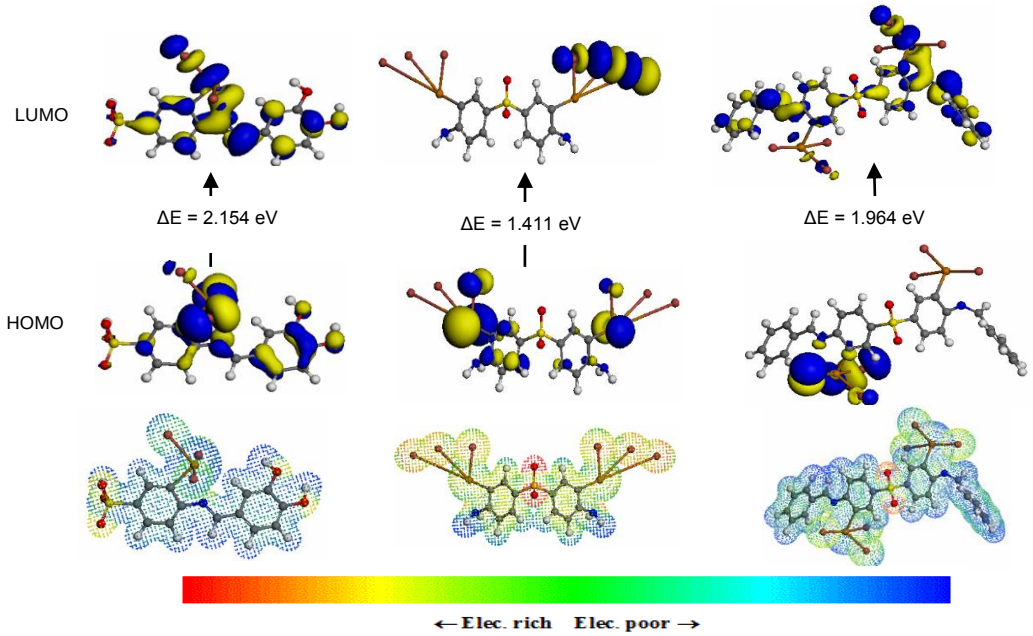


Figure 3. HOMO, LUMO orbital's and molecular electrostatic potential maps of the active molecules **4**, **6** and **8**

4. Conclusions

Analysis of structural information derived from the synthesised compounds matched the data presented in the paper. The reaction between tellurium and mercury is considered successful because the transmetallation reaction has the final products with an acceptable yield. The organotellurium compounds, especially **4** and **6**, were observed to have anti-tumour properties

against two types of tested cells – PC3 and T24. However, organomercury compounds exhibited no such anti-tumour activity.

Based on orbital energy calculations (HOMO and LUMO) and analysis of specific quantum parameters proved that organomercury substances are relatively stable but less effective than their organotellurium counterparts. Additionally, molecules **4**, **6**, and **8** proved to be more effective, which could be attributed to the presence of bromine, sulphur, tellurium, and oxygen atoms. It is thus concluded that the results obtained by the theoretical study are in agreement with the results of the anti-cancer study.

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