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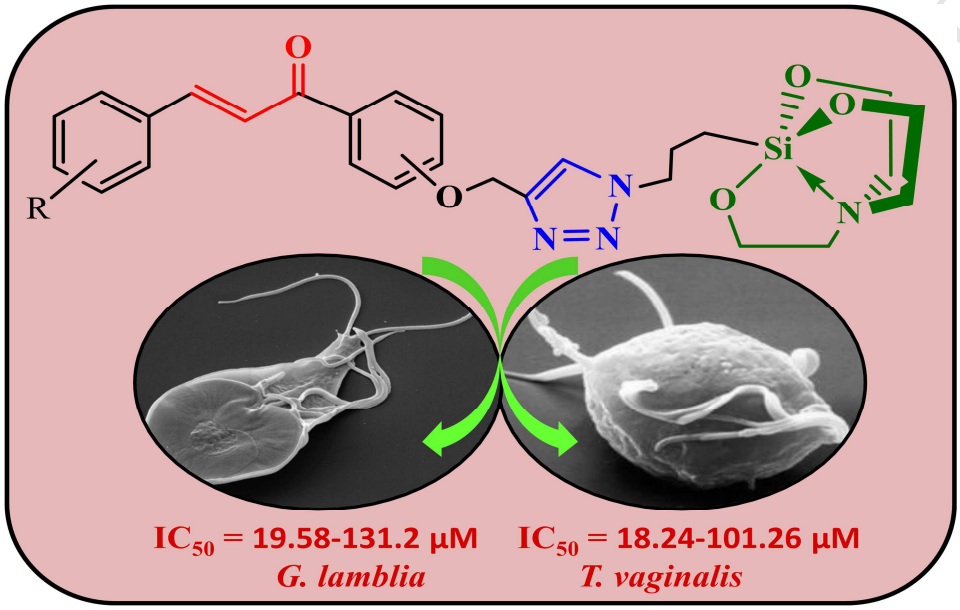
A series of 1,2,3-triazole and chalcone allied organosilatranes (**7a-7g**,**8a-8g**,**9a-9g**) are synthesized and well characterized by various spectroscopic techniques. The synthesized compounds are passed through the computer based screeing for their physicochemical properties and then tested for their antigiardial and antitrichomonal activities. The compounds showing good activites are then tested for their cytotoxicity against Hek-293 and HeLa cells.



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Abstract

A series of chalconyl blended triazole allied silatranes (**7a-7g/8a-8g/9a-9g**) were synthesized in good yields using a simple, economical and biocompatible synthetic route. The blend of three different pharmacologically active moieties into a single scaffold resulted into synergistic effect in their bio-activity. Various substitutions were tried to study the structure activity relationship (SAR) of the synthesized compounds on the basis of biological results. All the newly synthesized compounds were well characterized by IR, ^{1}H and ^{13}C NMR, low resolution mass spectroscopy and elemental analysis. The structures of **7a** and **7c** were authenticated by single crystal X-ray crystallography. These compounds were screened by using Molinspiration software for their physicochemical properties and all the compounds showed good oral bioavailability. The antiparasitic activity of the newly synthesized compounds was evaluated against unicellular parasites (*Giardia lamblia* and *Trichomonas vaginalis*) in comparison to standard drug (metronidazole) by 3-(4,5-Dimethylthiazol-yl)-diphenyl tetrazoliumbromide (MTT) assay. All the compounds displayed significant activity against *G. lamblia* and *T. vaginalis* with IC_{50} values ranging from 19.58-131.2 µM and 18.24-101.26 µM respectively. The entire library of compounds was found to be more active than metronidazole except **9a**, **9f** and **9g**. Notably, **9e** and **7e** were found to be most significant against *G. lamblia* and *T. vaginalis* respectively.

Key Words: Chalcone - 1,2,3-Triazole - Silatrane - Giardicidal activity - Trichomonacidal activity - Metronidazole - 3-(4,5-Dimethylthiazol-yl)-diphenyl tetrazoliumbromide (MTT)

1. Introduction

Parasitic diseases are an important public health problem in developing countries [1]. Among the diarrhoea causing agents, giardiasis is an important parasitic cause, commonly

treated with metronidazole [2]. Apart from causing diarrhoea, it can lead to wide range of clinical manifestations such as abdominal pain, nausea, dehydration, vomiting, and malabsorption syndrome producing adverse effect on growth and development [3-6]. Around 280 million people, especially children, are infected around the world [7-9].

Trichomoniasis is another parasitic disease caused by a single-celled protozoan parasite *T. vaginalis*. It is a sexually transmitted disease leading to clinical manifestations such as malodorous vaginal discharge, dysuria, lower abdominal pain and damage of vaginal epithelium, increasing the risk to HIV infection and cervical neoplasia [10-13]. Most commonly used drugs for the treatment of giardiasis and trichomoniasis are metronidazole **1** (Fig.1), tinidazole, furazolidone, paramomycin or nitazoxanide **2** (Fig. 1) [14,15].

Metronidazole affects electron transport and it is metabolized to produce a reactive reduced form which is cytotoxic for parasites [16]. A recently reported broad spectrum antiparasitic agent, nitroheterocycle nitazoxanide (NTZ) has got few unpleasant effects such as nausea and vomiting [17]. Mendez *et al.* have latterly reported a new analog of NTZ **3** (Fig. 1) and tested their antigiardial activities [18]. These chemotherapeutic antiparasitic agents are usually associated with several side effects such as treatment failures, activity against normal intestinal flora, parasite resistance and possible carcinogenicity [5,19-22]. These issues lead to an imperative quest for more effective, selective and less toxic drugs to treat both these diseases.

In the development of new drugs, it is convenient to have a range of diverse chemical structures with the desired pharmacological activity [12]. “Molecular hybridization” is one of the many strategies, which has been successfully applied for the design, and development of new and efficient hybrids [23-25]. It involves the combination of two or more chemical entities to form new hybrid moieties exhibiting additive pharmacological activities [26]. Considering this, the design of our synthesis is based on the individual activities of the

selected moieties with the anticipation of their higher activity in the hybrid molecules. Chalcones, 1,2,3-triazoles and silatranes have been investigated as important fragments possessing wide range of biological activities.

Chalcones (1,3-diarylprop-2-en-1-one) are well known for their diverse activites such as antileishmanial [27], antibacterial [28], antifungal [29], antitumour [30], antimalarial [31,32], antiviral [33], antitubercular [34], antiinvasive [35], anticancer [36], antioxidant [37], antihyperglycemic [38], antiinflammatory [39], analgesic [40], antiplatelet [41], antiulcerative [42] and a large list yet to be mentioned. Moreover, they can be readily synthesized by simple and inexpensive Claisen-Schmidt reaction [43] and various modifications can be made by introducing different substituents on the aromatic rings of chalcones to give a large number of analogues showing immense activities [44-46].

1,2,3-triazoles are an important class of heterocyclic compounds that received significant attention for the past few decades because of the broad spectrum of their applications in biochemical, pharmaceutical, and material sciences [47-60]. These are attractive connecting units, since they are stable to metabolic degradation, oxidative/reductive conditions and actively participate in dipole-dipole interactions and hydrogen bonding [61]. So, these moieties can be shaped into powerful pharmacophores that can play an important role in bio-conjugation. The copper (I) catalysed synthesis of 1,2,3-triazoles [62] from azides and terminal alkynes is an increasingly common method for rapid synthesis of organic and bioorganic compounds in high yields and purity [63]. Therefore, the well recognized click route [64] is followed to generate 1,2,3-triazole derivatives.

Silatranes are intracomplex silicon triethanolamine esters of general formula XSi $(OCH_2CH_2)_3N$. The unique structure, specific physicochemical properties, biological activity and prospects of applications as drugs [65-70] have necessitated the search for novel effective methods for synthesizing the new compounds of this type. The unusual trigonal bipyramidal

structure of silatranes leads to their high dipole moment and high electronegativity which favours the chemisorption of these molecules on the surface of proteins and lipid layer of cellular membranes either by forming hydrogen bonds with equatorial oxygens or by dipole-dipole interactions. Silatranes also form sorptive layer over cellular membranes to avoid penetration of peroxy radicals and toxins. Their ability to donate silicon that acts as an essential microelement for all living organisms and form triethanolamine as the hydrolysis product which is also biologically active makes them even more fascinating [71].

In light of above findings, we are presenting an efficient way for the molecular stitching of different pharmacophoric elements of silatranes, triazole and chalcones in a single chemical framework resulting into a library of chalcones and further investigation of *in vitro* antiparasitic activity of these compounds on intestinal unicellular parasite (*G. lamblia*) and a urogenital tract parasite (*T. vaginalis*).

2. **Results and discussion**

2.1. Drug Design

We have designed the compounds **7a-7g**/**8a-8g**/**9a-9g** on the basis of individual activities of three different biologically potent moieties. In order to coalesce the activity of these groups, molecular nailing was done in an efficient and productive way so that the active group of the three moieties appear together in the final product showing some kind of synergistic effect. Our approach is to substitute ring A of the chalcone moiety with the triazole substituted silatrane. The drug design was also based on the computer aided prediction of the physicochemical properties of the molecules like polar surface area, number of rotational bonds, hydrogen bond donating or accepting ability and lipophilicity values that play an important role in predicting the drug bioavailability [72,73]. The aim of computational analysis is to filter the compounds considered unsuitable for screening purposes. Polar surface area illustrates drug absorption thus predicting that the molecules

with PSA > 140 have low oral bioavailability. The number of rotational bonds in a molecule is the measure of molecule's flexibility and is found to be a very good descriptor of drug's permeability. The hydrogen bonding capacity is based on the presence of oxygen and nitrogen atoms in the molecule and somehow affects drug's permeation rate. The lipophilic character can be predicted from clogP values and the values ≤ 5 are considered ideal for orally active drugs. These parameters were calculated using Molinspiration software [74] and the results demonstrate that almost all the compounds meet the above mentioned criteria making their important place in drug development.

The jointure of combinatorial chemistry and high throughput screening instigated us to develop such molecules that can be further exploited for their pharmacological activities. Further, different substitutions are trialled to study the structure activity relationship (SAR) of the chalconyl blended triazole encapped silatranes.

2.2. Chemistry

Variously substituted acetylinic chalcones have been synthesized by the most widely used base catalyzed Claisen–Schmidt reaction. Commercially available o/m/p-hydroxyacetophenones are subjected to O-alkylation with 1.2 equiv of propargyl bromide in the presence of an excess amount of K_2CO_3 (1.5 equiv) in DMF. Acetylinic acetophenones **1/2/3** are obtained in excellent yields which then undergo aldol condensation with variedly substituted aldehydes in the presence of methanolic NaOH resulting into acetylinic chalcones **4a-4g**/**5a-5g**/**6a-6g** in quite high yields. The solid chalcones are purified by recrystallization (**4a-4g**/**5e-5g**/**6a-6g**) while the liquid products (**5a-5d**) are purified by column chromatography.

3-azidopropyltriethoxysilane (3-AzPTES) is remodelled into its more stable and biologically potential analogue 3-azidopropylsilatrane (3-AzPSa) by transesterification

reaction with triethanolamine in toluene as solvent and presence of catalytic amount of KOH. The alkyne terminated chalcones are then clicked onto 3-AzPSa in THF/Et_3N solvent system at 60 °C with the catalyst loading of Cu catalyst [$CuBr(PPh_3)_3$] to incure 1,2,3-triazole bound organosilatranes **7a-7g**/**8a-8g**/**9a-9g** (Scheme 1) in excellent yields (87-93%). The melting points and yields of the products are listed in Table 2. All the newly synthesized compounds were characterized by IR, ^1H and ^{13}C NMR, low resolution mass spectroscopy and elemental analysis. Compounds **7a** and **7c** have also been characterized by single crystal X-ray crystallography. All the organosilatranes were synthesized under dry nitrogen atmosphere using a vacuum glass line.

Multinuclear (^1H and ^{13}C) NMR spectra are very well consistent with the structure of the synthesized compounds. Doublets around 7.23-7.52 ppm and 7.49-8.12 ppm appear in the NMR spectra of all compounds corresponding to vinyl hydrogen atoms, α and β respectively with a high *J* value of around 15 Hz confirming the (E)-configuration of the chalcones. In the NMR spectra of acetylinic chalcones (**4a-4g**/**5a-5g**/**6a-6g**), alkynyl proton appears around δ ≈ 2.4 ppm that upon cyclisation with 3-AzPSa shows a shift to δ = 7.3-7.6 ppm (for **7a-7g**/**8a-8g**/**9a-9g**) confirming the cyclisation of alkynyl moiety into triazole unit. Additionally, shifting of -OCH_2 protons of acetylene group from δ = 4.7 ppm to δ ≈ 5.2 ppm certifies the formation of cyclised product. Also, a major shift in the protons of the carbon attached with the azide group in 3-AzPSa from 3.2 ppm to 4.2 ppm affirms the formation of the desired product. Further, two equivalent triplets appear around δ = 2.7-2.8 ppm and δ = 3.6-3.7 ppm corresponding to -NCH_2 and -OCH_2 protons respectively of $Si(OCH_2CH_2)_3N$ skeleton. Parallel shifting is scrutinized in the carbon spectrum of the respective compounds.

In ^{13}C NMR spectra of all compounds, the carbonyl carbon appears as the least shielded carbon in the region δ = 188.0-193.4 ppm. The vinyl carbons of the chalcone moiety appear at δ = 120.7-124.4 ppm and δ = 142.1-144.9 ppm for α and β carbons respectively. Two

carbons of alkynyl moiety (for **4a-4g**/**5a-5g**/**6a-6g**) appear in the range of δ = 76.0-78.8 ppm that shift around δ = 120.0-122.9 ppm and δ = 137.8-143.0 ppm in cyclised compounds (**7a-7g**/**8a-8g**/**9a-9g**), that confirms the cyclisation of alkyne functionality to triazole unit. In the final compounds, the peaks at δ = 49.7-51.5 ppm and δ = 56.1-58.0 ppm are assigned to -NCH_2 and -OCH_2 carbons of silatranyl moiety. Carbon attached to silicon appears as the most shielded carbon at δ = 12.1-13.2 ppm clearly indicating the hypervalency in the final compounds.

2.3. Crystallography

Single crystals of compound **7a** and **7c** were grown by slow evaporation of their corresponding solutions in chloroform at room temperature. The ORTEP plots of both the compounds (thermal ellipsoids drawn at 50% probability) are shown in Fig. 3. Details of data collection and structure refinement, and selected bond lengths and bond angles of both the compounds are listed in Table 2 & 3 respectively.

Single crystal X-ray diffraction study of the compounds **7a** & **7c** confirms that both the molecules crystallize in monoclinic crystal system with space group P121/c1 and C12/c1 respectively. Both the compounds possess typical silatrane structure containing Si atom where coordination of tripodal trianionic $N(CH_2CH_2O–)_3$ entities act as tetradentate coordinating unit to Si and forms a penta-membered ring via a trans Si–N bond. The lattice array for **7a** favours to form a hydrophobic-hydrophilic layer arrangement along ac-plane. A simplifier model for lattice arrangement is shown for **7a** (Fig. 4) and **7c** (Fig. 5). Overall skeletal looks like a “tadpole-like” structure where the Si-bound centre resembles head region and the chalcone-functionalized alkyl moiety resembles tail region. The tail region (~ 18 Å) is around 8 times longer than head (~ 2.3 Å) component. The five membered chalcone moiety is almost normal (~86 º) to functionalized alkyl part (Fig. S1). Similarly in case of compound

7c, there is an additional -OMe group at the tail region as compared to **7a**. The minuscule difference later forces compound **7c** to a differently layered structure along ab-plane but less dense type arrangement along ac-palce. Again the five-membered chalcone moiety is tilted towards (~ 31º) one side with respect to functionalized alkyl part (Fig. S2). In both the molecules, the central Si atom achieves a coordination number five where the O atoms of the tripodal trianionic unit occupy equatorial positions and the N donor is present at apical site. Among various variable structural parameters around the Si centre, the Si–N bond lengths are 2.180(1) and 2.163(5) Å and N–Si–Cax bond angles are found to be 179.18(8), 179.51(2)° for **7a** and **7c** respectively. All the Si–N bonds and angles around Si are within range of reported values [75]. Both complexes of **7a** and **7c** are discrete monomer type with geometry very close to trigonal bipyramidal (TBP) geometry around the Si atom as confirmed from the value of τ 1.014–1.015. The distortion parameter τ = (β–α)/60 was calculated from the structural data where the value of τ should be 0 for perfect square-pyramidal geometry and 1 for a perfect TBP structure and is applicable to five co-ordinate structures as an index of the degree of trigonality [76]. In terms of the percentage, trigonal bipyramidal character was also calculated by taking in account the three apical-to-equatorial bond angles and three equatorial-to-equatorial bond angles via following equations [77]:

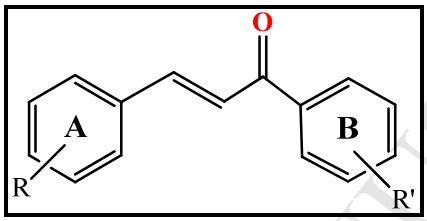
$$\%TBPax = 100*[\{109.51/3(\sum\theta n)\}/(109.5–90.0)$$

$$\%TBPeq = 100*[\{1/3(\sum\phi n)– 109.5\}/120.0–109.5)$$

where θn is average of angles Oeq—Si—Cax and ϕn is average of angles Oeq—Si—Oeq. Based on the above equations, % TBPax and % TBPeq for compounds **7a** and **7c** are found to be 64.82, 61.48 % and 86.57, 84.0 % respectively. Apart from the structural differences, there are few short interactions of –CH···O/N type, present in both the compounds.

2.4. In vitro antiparasitic effect

In this study, twenty one new silatrane derivatives have been synthesized and evaluated for their antiparasitic activities against *G. lamblia* and *T. vaginalis*. The biological assay results against the parasites are summarized in Table 4. The antiparasitic activities of the newly synthesized compounds were compared with the standard drug metronidazole (Met). Various substitutions have been incorporated on the two aromatic rings of chalcones to give a number of analogues with potential biological activities.



Firstly, we compared the activities of chalcones **7a-7g** possessing p-substitution on ring A and variedly substituted ring B against *T. vaginalis* and it was found that the compound **7a** with no ring substitution was less active than the substituted ones with IC_{50} = 27.24 µM. Comparisons were made to determine if increasing the number of electron donating groups on ring B made any difference in their activity. However, no specific trend could be delineated on this basis. Compound **7e** endowed with three $–OCH_3$ groups and **7g** with electron withdrawing –Cl functionality were comparatively more potent than the two $–OCH_3$ (**7d**) or $–CH_3$ (**7f**) substituted compounds. The compounds **8a-8g** with o-substitution on ring A showed less trichomonacidal activities as compared to the p-substituents with IC_{50} ranging from 21.265-50.025 µM but the ring B substitution follows the same trend. On the other hand, m-substituted chalcones **9a-9g** displayed two-fold less activity than their o/p-isomers with the IC_{50} range of 30.275-101.265 µM. Among all the tested compounds, **7e** with IC_{50} = 18.245 µM demonstrated excellent efficacy against *T. vaginalis* (Fig. 6). This compound was

also found to have excellent physicochemical properties, acceptable polar surface area of 115.67 and admirable clogP value of 3.1.

Biological assay results against *G. lamblia* showed that most of the compounds exhibited comparatively low bioactivity with IC_{50} ranging from 19.58-131.2 µM. The compounds substituted at o/p- position of ring A were found to be more potent than the m-substituted compounds. Compounds with tri-methoxy substitution on ring B portrayed better activity compared to other substitutions and compound **9e** with m-position of ring A and three methoxy groups on ring B came out as the most promising antigiardial agent with IC_{50} = 19.58 µM. Thus, 90% of the compounds assayed against *T. vaginalis* and 71% of the compounds tested against *G. lamblia* were found to be more effective than the control drug metronidazole that presented IC_{50} = 55.85 µM and 62.48 µM for both the parasites respectively.

An interesting trend can be outlined from the structure activity relationship of the tested compounds. The compounds whether with ortho, meta or para substitution at ring-A and tri-methoxy substituent at ring-B exhibited the best giardicidal and trichomonacidal activities among the screened compounds while the organosilatranes bearing methyl group at ring-B were found to be less effective against both the parasites. The moieties having chlorine as the ring-B substituent displayed intermediate activities. This may be due to the presence of bulky methoxy groups that are responsible for the better activities of these compounds in comparison to the unsubstituted or methyl substituted analogues. Moreover, the physicochemical results also show better PSA values for tri-methoxy substituents supporting its good oral bioavailability.

2.5. In vitro cytotoxic effect

To study the effect of compounds on mammalian cells, their toxicity was evaluated. For this, six compounds (**7e, 7f, 8a, 8d, 9b** and **9e**) presenting exquisite parasitic activities were treated with Hek-293 and HeLa cells. It was evident from Table 5 that at respective 20X of IC_{50} values none of the compounds showed any toxicity. The selectivity index (SI) of the compounds defined as the ratio of cytotoxicity to biological activity (SI = CC_{50} Hek-293 or HeLa/ IC_{50} of the parasites) was calculated. Notably all six compounds with significant *in vitro* antiparasitic activity (giardicidal and trichomonacidal) possess good selectivity index.

3. Experimental

3.1. Chemistry

3.1.1. Starting Material

Propargyl bromide (80% in toluene) (Sigma-Aldrich), o/m/p-hydroxyacetophenones (AVRA), potassium carbonate (Thomas), substituted aldehydes (Sigma-Aldrich), sodium hydroxide (AVRA), sodium sulphate (Finar), Bromotris(triphenylphosphine)copper(I) (Sigma-Aldrich) were used as received. The organic solvents were dried according to standard procedures. 3-azidopropylsilatrane (3-AzPSa) and acetylinic chalcones (**4a-4g**/**5a-5g**/**6a-6g)** were synthesized by known procedure from literature [32,78,79].

3.1.2. Measurements

Infrared spectrum was obtained as Neat on a Thermo Scientific Fischer spectrometer. CHN analysis was obtained on Perkin Elmer Model 2400 CHNS elemental analyser. The NMR spectra (^{1}H and ^{13}C) were recorded on a JEOL (AL 300 MHz) and BRUKER (400 MHz) spectrometer using $CDCl_3$ as internal reference and chemical shifts were reported relative to tetramethylsilane. J values are given in Hz. The abbreviations used to explain NMR are as: s, singlet; d, doublet; q, quartet; dd, doublet of doublet; t, triplet; m, multiplet.

Mass spectral measurements (TOF MS ESþ 1.38 eV) were carried out on Waters QQ–TOF micro Mass Spectrometer. Melting points were measured in a Mel Temp II device using sealed capillaries and were uncorrected. Column chromatography was performed with silica gel plates (Kieselgel 60, 230-400 mesh). Analytical thin layer chromatography was performed employing 0.2 mm coated commercial silica gel plates (E. Merck, DC-Aluminum sheets, Kieselgel 60 F254). Physicochemical properties of the compounds were predicted using the Molinspiration software.

3.1.3. General Procedure for the synthesis of 3-azidopropylsilatrane

To the stirred solution of sodium azide (5.4 g, 83.1 mmol) in dry DMF (150 ml), 5.0 g (20.7 mmol) of 3-chloropropyltriethoxysilane was added dropwise within 10 min. The reaction mixture was stirred at 90 °C for 4 h. The removal of DMF was carried out under reduced pressure. The crude mixture was then diluted with diethylether and filtered under inert atmosphere. The diethyl ether was removed in vacuo and the crude oil obtained was distilled at 130 °C under reduced pressure of 5 mm of Hg resulting into 3-AzPTES (3-azidopropyltriethoxysilane) as colourless oil. 3-AzPTES (1 ml, 4.0 mmol) was taken in a two-necked round bottom flask. 20 ml toluene was added to the silane followed by the addition of triethanolamine (0.6 g, 4.0 mmol). Catalytic amount of KOH was then added to the reaction mixture and the reaction was allowed to reflux for 4h in order to azeotropically remove the ethanol formed during the reaction with the help of Dean-Stark assembly. Afterwards, solvent was removed under vacuum and 15 ml hexane was added. The contents were then left for overnight stirring followed by filtration under nitrogen and drying under vacuum. Yield: 91 %; NMR (300 MHz, $CDCl_3$, 25 °C) δ_H = 0.38 (t, *J* = 8.1 Hz, 2H, -Si*CH*$_2$-), 1.63 (m, 2 H, -C*CH*$_2$C-), 2.76 (t, *J* = 5.7 Hz, 6H, -N*CH*$_2$), 3.18 (t, *J* = 6.9 Hz, 2H, N_3*CH*$_2$$CH_2$), 3.70 (t, *J* = 5.7 Hz, 6H, -O*CH*$_2$).

3.1.4. General Procedure for the synthesis of acetylinic acetophenones (1,2,3)

o/m/p-hydroxyacetophenone (1.0 g, 7.4 mmol) was dissolved in small amount of DMF (5-10 ml) followed by the addition of anhydrous K_2CO_3 (1.52 g, 11.0 mmol). The resulting suspension was stirred for 30 min at room temperature which was then cooled to 0 °C. To this, propargyl bromide (1.09 ml, 11.9 mmol) was subsequently added dropwise over a period of 10 min under stirring and the resulting mixture was allowed to stir at 25 °C for 16 h. The reaction was monitored by TLC and on consumption of starting materials, quenched by ice cold water resulting into the formation of precipitate. The precipitate so obtained was filtered, washed with water and recrystallized from MeOH to afford the crystalline product (**1/2/3**) in excellent yield. The spectroscopic data of the resulting compounds correlate well with the literature reports.

3.1.5. General Procedure for the synthesis of acetylinic chalcones (4a-4g/5a-5g/6a-6g)

Methanolic NaOH (5 ml) (3% w/v) was added to a solution of the acetylenic acetophenone **1/2/3** (1.0 g, 5.7 mmol) in MeOH (20 ml). The resulting mixture was stirred at 25 °C for 30 min followed by the addition of a methanolic solution of the commercially available substituted aldehyde (1.0 equiv). The mixture was then stirred for 16 h at room temperature. The reaction was monitored by TLC and on consumption of starting materials, quenched by ice cold water resulting into the formation of precipitate (for **4a-g**,**5e-5g**,**6a-6g**). The precipitate so obtained was filtered, washed with water and recrystallized from MeOH to afford the crystalline product. For the reactions in which no precipitation occurred (for **5a-5d**), the product mixture was diluted with water, neutralized with 10% HCl and extracted with ethyl acetate (20 ml) and the combined organic layers were washed twice with ice cold water (2×20 ml). The organic layer was dried over anhydrous Na_2SO_4 and the solvent was evaporated under reduced pressure to afford yellow brown viscous oil. The crude was then

subjected to column chromatography with EtOAc/Hexane 3:7, as eluent. The spectroscopic data of the chalcones correlate well with the literature reports.

3.1.6. General Procedure for the synthesis of chalconyl silatranes (***7a-7g/8a-8g/9a-9g***)

To the stirred solution of acetylinic chalcones (**4a-4g/5a-5g/6a-6g)** in THF/Et_3N solvent system, taken in a two necked round bottomed flask, was added catalytic amount of Bromotris(triphenylphosphine)copper(I) (0.01 mmol/alkyne function) followed by the addition of 3-AzPSa. The reaction mixture was then refluxed at 60 °C for 4 h. Thereafter, the solvent was evaporated under vacuum and on slow addition of hexane (10 ml), solid precipitated out. The solid so obtained was left for overnight stirring and then filtered under nitrogen and dried under vacuum resulting into desired organosilatranes **7a-7g/8a-8g/9a-9g** in excellent yields.

3.1.6.1. (E)-1-(4-((1-(3-(silatranyl)propyl)-1H-1,2,3-triazol-4-ylmethoxyphenyl-3-phenylprop-2-en-1-one (**7a**)

The quantities used were as **4a** (1.0 g, 3.8 mmol), 3-AzPSa (0.98 g, 3.8 mmol). Yellow solid, Yield: 1.82 g, 3.5 mmol, 92 %. IR (neat, cm^{-1}): 563 (N→Si), 758, 1087 (Si-O), 1648 (C=O), 2941 (C=C-H). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ 0.35 (m, 2H, -$SiCH_2$-), 1.95 (m, 2H, -CCH_2C-), 2.75 (t, *J* = 5.8 Hz, 6H, -CH_2N-), 3.70 (t, *J* = 5.8 Hz, 6H, -O*CH*$_2$$CH_2$-), 4.30 (t, *J* = 7.4 Hz, 2H, -N_3CH_2-), 5.26 (s, 2H, -OCH_2-), 7.04 (d, *J* = 8.9 Hz, 2H, H2, H6), 7.30-7.37 (m, 4H, Tz-H, H9-H11), 7.49 (d, *J* = 15.6 Hz, 1H, Hα), 7.60 (d, *J* = 8.3 Hz, 2H, H8, H12), 7.74 (d, *J* = 15.6 Hz, 1H, Hβ), 7.99 (d, *J* = 8.9 Hz, 2H, H3, H5). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ 13.0 ($SiCH_2$), 26.3 (C**C**H_2C), 51.3 (CH_2**C**H_2N), 53.4 (N_3CH_2), 57.7 (O**C**$H_2$$CH_2$), 62.5 ($OCH_2$), 115.0 (C2, C6), 122.1, 143.0 (Tz-C), 122.7 (Cα), 128.6 (C8, C12), 129.1 (C10), 130.4 (C9, C11), 131.0 (C4), 131.7 (C3, C5), 135.5 (C7), 144.0 (Cβ), 162.4 (C1), 188.1 (C=O). MS: m/z (relative abundance (%)): 543 (53), 521 (76), 246 (32), 214 (31), 167 (36),

158 (89), 149 (100). Anal. Calcd. for $C_{27}H_{32}N_4O_5Si$: C, 62.29; H, 6.19; N, 10.76. Found: C, 62.15; H, 6.18; N, 10.63.

3.1.6.2. (E)-1-(4-((1-(3-(silatranyl)propyl)-1H-1,2,3-triazol-4-ylmethoxyphenyl-3-(4-methoxyphenyl)prop-2-en-1-one (**7b**)

The quantities used were as **4b** (1.0 g, 3.4 mmol), 3-AzPSa (0.88 g, 3.4 mmol). Yellow solid, Yield: 1.68 g, 3.1 mmol, 90 %. IR (neat, cm^{-1}): 580 (N→Si), 771, 1028 (Si-O), 1658 (C=N), 2945 (C=C-H). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ 0.29 (m, 2H, -$SiCH_2$-), 1.89 (m, 2H, -CCH_2C-), 2.70 (t, *J* = 5.8 Hz, 6H, -CH_2N-), 3.64 (t, *J* = 5.8 Hz, 6H, -O*CH*$_2$$CH_2$-), 3.79 (s, 3H, -$OCH_3$), 4.26 (t, *J* = 7.4 Hz, 2H, -N_3CH_2-), 5.22 (s, 2H, -OCH_2-), 6.83 (d, *J* = 8.6 Hz, 2H, H9, H11), 6.98 (d, *J* = 8.7 Hz, 2H, H2, H6), 7.32 (d, *J* = 15.5 Hz, 1H, Hα), 7.50 (d, *J* = 8.6 Hz, 2H, H8, H12), 7.56 (s, 1H, Tz-H), 7.66 (d, *J* = 15.5 Hz, 1H, Hβ), 7.93 (d, *J* = 8.7 Hz, 2H, H3, H5). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ 13.2 ($SiCH_2$), 26.5 (C**C**H_2C), 51.5 (CH_2**C**H_2N), 53.7 (N_3CH_2), 55.8 (OCH_3), 58.0 (O**C**H_2CH_2), 62.7 (OCH_2), 111.6 (C9, C11), 115.1 (C2, C6), 121.2, 140.0 (Tz-C), 123.2 (Cα), 129.7 (C8, C12), 131.2 (C7), 131.8 (C4), 132.3 (C3, C5), 142.3 (Cβ), 159.2 (C10), 162.4 (C1), 189.4 (C=O). MS: m/z (relative abundance (%)): 573 (38), 551 (100). Anal. Calcd. for $C_{28}H_{34}N_4O_6Si$: C, 61.07; H, 6.22; N, 10.17. Found: C, 60.98; H, 6.21; N, 10.12.

3.1.6.3. (E)-1-(4-((1-(3-(silatranyl)propyl)-1H-1,2,3-triazol-4-ylmethoxyphenyl-3-(2-methoxyphenyl)prop-2-en-1-one (**7c**)

The quantities used were as **4c** (1.0 g, 3.4 mmol), 3-AzPSa (0.88 g, 3.4 mmol). Yellow solid, Yield: 1.67 g, 3.1 mmol, 89 %. IR (neat, cm^{-1}): 586 (N→Si), 752, 1053 (Si-O), 1646 (C=N), 2946 (C=C-H). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ 0.30 (m, 2H, -$SiCH_2$-), 1.90 (m, 2H, -CCH_2C-), 2.71 (t, *J* = 5.8 Hz, 6H, -CH_2N-), 3.65 (t, *J* = 5.8 Hz, 6H, -O*CH*$_2$$CH_2$-), 3.86 (s, 3H, -$OCH_3$), 4.26 (t, *J* = 7.3 Hz, 2H, -N_3CH_2-), 5.21 (s, 2H, -OCH_2-), 6.83-6.92 (m, 2H, H9,

H11), 6.99 (d, *J* = 8.8 Hz, 2H, H2, H6), 7.27 (t, *J* = 7.0 Hz, 1H, H10), 7.50-7.57 (m, 3H, Hα, H8, Tz-H), 7.92-8.00 (m, 3H, Hβ, H3, H5). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ 12.9 ($SiCH_2$), 26.2 (C**C**H_2C), 51.2 (CH_2**C**H_2N), 53.4 (N_3CH_2), 55.5 (OCH_3), 57.6 (O**C**H_2CH_2), 62.4 (OCH_2), 111.2 (C11), 114.8 (C2, C6), 120.9 (C7), 122.9, 139.6 (Tz-C), 124.4 (Cα), 125.7 (C9), 129.4 (C8), 130.9 (C10), 131.5 (C4), 132.0 (C3, C5), 144.1 (Cβ), 158.9 (C12), 162.1 (C1), 189.1 (C=O). MS: m/z (relative abundance (%)): 573 (100), 551 (40), 150 (15). Anal. Calcd. for $C_{28}H_{34}N_4O_6Si$: C, 61.07; H, 6.22; N, 10.17. Found: C, 60.93; H, 6.19; N, 10.09.

3.1.6.4. (E)-1-(4-((1-(3-(silatranyl)propyl)-1H-1,2,3-triazol-4-ylmethoxyphenyl-3-(2,4-dimethoxyphenyl)prop-2-en-1-one (**7d**)

The quantities used were as **4d** (1.0 g, 3.1 mmol), 3-AzPSa (0.80 g, 3.1 mmol). Yellow solid, Yield: 1.63 g, 2.8 mmol, 91 %. IR (neat, cm^{-1}): 579 (N→Si), 764, 1095 (Si-O), 1651 (C=N), 2929 (C=C-H). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ 0.30 (m, 2H, -$SiCH_2$-), 1.90 (m, 2H, -CCH_2C-), 2.71 (t, *J* = 5.3 Hz, 6H, -CH_2N-), 3.65 (t, *J* = 5.3 Hz, 6H, -O*CH*$_2CH_2$-), 3.85 (s, 3H, -OCH_3), 3.78 (s, 3H, -OCH_3), 4.26 (t, *J* = 7.5 Hz, 2H, -N_3CH_2-), 5.21 (s, 2H, -OCH_2-), 6.37 (s, 1H, H11), 6.43 (d, *J* = 7.5 Hz, 1H, H9), 6.98 (d, *J* = 7.2 Hz, 2H, H2, H6), 7.14 (d, *J* = 7.5 Hz, 1H, H8), 7.43 (d, *J* = 15.5 Hz, 1H, Hα), 7.57 (s, 1H, Tz-H), 7.88-7.93 (m, 3H, Hβ, H3, H5). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ 12.8 ($SiCH_2$), 26.0 (C**C**H_2C), 50.8 (CH_2**C**H_2N), 53.1 (N_3CH_2), 55.1 (OCH_3), 55.2 (OCH_3), 57.3 (O**C**H_2CH_2), 62.0 (OCH_2), 98.3 (C11), 105.2 (C9), 114.4 (C7), 117.2 (C2, C6), 120.0, 139.4 (Tz-C), 122.6 (Cα), 128.2 (C8), 130.5 (C4), 131.9 (C3, C5), 142.7 (Cβ), 160.2 (C12), 161.7 (C10), 162.8 (C1), 188.7 (C=O). MS: m/z (relative abundance (%)): 603 (32), 581 (100). Anal. Calcd. for $C_{29}H_{36}N_4O_7Si$: C, 59.98; H, 6.25; N, 9.65. Found: C, 59.83; H, 6.15; N, 9.58.

3.1.6.5. (E)-1-(4-((1-(3-(silatranyl)propyl)-1H-1,2,3-triazol-4-ylmethoxyphenyl-3-(2,3,4-trimethoxyphenyl)prop-2-en-1-one (**7e**)

The quantities used were as **4e** (1.0 g, 2.8 mmol), 3-AzPSa (0.72 g, 2.8 mmol). Yellow solid, Yield: 1.53 g, 2.5 mmol, 90 %. IR (neat, cm^{-1}): 580 (N→Si), 761, 1091 (Si-O), 1652 (C=N), 2933 (C=C-H). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ 0.29 (m, 2H, -$SiCH_2$-), 1.89 (m, 2H, -CCH_2C-), 2.70 (t, *J* = 5.8 Hz, 6H, -CH_2N-), 3.64 (t, *J* = 5.8 Hz, 6H, -O*CH*$_2CH_2$-), 3.80 (s, 3H, -OCH_3), 3.84 (s, 3H, -OCH_3), 3.88 (s, 3H, -OCH_3), 4.25 (t, *J* = 7.4 Hz, 2H, -N_3CH_2-), 5.21 (s, 2H, -OCH_2-), 6.60 (d, *J* = 8.8 Hz, 1H, H9), 6.98 (d, *J* = 8.8 Hz, 2H, H2, H6), 7.26 (d, *J* = 8.8 Hz, 1H, H8), 7.45 (d, *J* = 15.7 Hz, 1H, Hα), 7.56 (s, 1H, Tz-H), 7.83 (d, *J* = 15.7 Hz, 1H, Hβ), 7.92 (d, *J* = 8.8 Hz, 2H, H3, H5). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ 12.9 ($SiCH_2$), 26.2 (C**C**H_2C), 51.1 (CH_2**C**H_2N), 53.3 (N_3CH_2), 56.0 (OCH_3), 57.5 (O**C**H_2CH_2), 60.7 (OCH_3), 61.3 (OCH_3), 62.3 (OCH_2), 107.8 (C7, C9), 114.7 (C2, C6), 121.2 (C8), 122.8, 139.2 (Tz-C), 123.8 (Cα), 128.4 (C4), 130.8 (C3, C5), 139.2 (C11), 142.8 (Cβ), 154.0 (C12), 155.8 (C10), 162.1 (C1), 188.5 (C=O). MS: m/z (relative abundance (%)): 633 (100), 611 (38). Anal. Calcd. for $C_{30}H_{38}N_4O_8Si$: C, 59.00; H, 6.27; N, 9.17. Found: C, 58.89; H, 6.18; N, 9.11.

3.1.6.6. (E)-1-(4-((1-(3-(silatranyl)propyl)-1H-1,2,3-triazol-4-ylmethoxyphenyl-3-p-tolyl-prop-2-en-1-one (**7f**)

The quantities used were as **4f** (1.0 g, 3.6 mmol), 3-AzPSa (0.93 g, 3.6 mmol). Yellow solid, Yield: 1.73 g, 3.2 mmol, 90 %. IR (neat, cm^{-1}): 576 (N→Si), 756, 1094 (Si-O), 1659 (C=N), 29437 (C=C-H). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ 0.30 (m, 2H, -$SiCH_2$-), 1.90 (m, 2H, -CCH_2C-), 2.33 (s, 3H, -CH_3), 2.71 (t, *J* = 5.8 Hz, 6H, -CH_2N-), 3.65 (t, *J* = 5.8 Hz, 6H, -O*CH*$_2CH_2$-), 4.26 (t, *J* = 7.4 Hz, 2H, -N_3CH_2-), 5.21 (s, 2H, -OCH_2-), 6.99 (d, *J* = 8.8 Hz, 2H, H2, H6), 7.13 (d, *J* = 8.0 Hz, 2H, H9, H11), 7.23 (d, *J* = 15.6 Hz, 1H, Hα), 7.45 (d, *J* = 8.0 Hz, 2H, H8, H12), 7.57 (s, 1H, Tz-H), 7.67 (d, *J* = 15.6 Hz, 1H, Hβ), 7.94 (d, *J* = 8.8 Hz, 2H,

H3, H5). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ 12.9 ($SiCH_2$), 21.5 (CH_3), 26.2 ($C\mathbf{C}H_2C$), 51.1 ($CH_2\mathbf{C}H_2N$), 53.3 (N_3CH_2), 57.6 ($O\mathbf{C}H_2CH_2$), 62.4 (OCH_2), 114.8 (C2, C6), 121.0, 142.8 (Tz-C), 122.8 (Cα), 128.4 (C8, C12), 128.5 (C4), 129.8 (C9, C11), 130.9 (C7), 131.7 (C3, C5), 140.6 (C10), 144.1 (Cβ), 162.2 (C1), 188.4 (C=O). MS: m/z (relative abundance (%)): 557 (34), 535 (100). Anal. Calcd. for $C_{28}H_{34}N_4O_5Si$: C, 62.90; H, 6.41; N, 10.48. Found: C, 62.87; H, 6.35; N, 10.43.

3.1.6.7. (E)-1-(4-((1-(3-(silatranyl)propyl)-1H-1,2,3-triazol-4-ylmethoxyphenyl-3-(4-chlorophenyl)prop-2-en-1-one (**7g**)

The quantities used were as **4g** (1.0 g, 3.4 mmol), 3-AzPSa (0.87 g, 3.4 mmol). Yellow solid, Yield: 1.64 g, 3.0 mmol, 88 %. IR (neat, cm^{-1}): 571 (N→Si), 761, 1085 (Si-O), 1655 (C=N), 2925 (C=C-H). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ 0.29 (m, 2H, -$SiCH_2$-), 1.90 (m, 2H, -CCH_2C-), 2.71 (t, *J* = 5.8 Hz, 6H, -CH_2N-), 3.64 (t, *J* = 5.8 Hz, 6H, -O*CH*$_2CH_2$-), 4.25 (t, *J* = 7.4 Hz, 2H, -N_3CH_2-), 5.21 (s, 2H, -OCH_2-), 7.00 (d, *J* = 8.8 Hz, 2H, H2, H6), 7.30 (d, *J* = 8.5 Hz, 2H, H9, H11), 7.42 (d, *J* = 15.6 Hz, 1H, Hα), 7.50 (d, *J* = 8.5 Hz, 2H, H8, H12), 7.57 (s, 1H, Tz-H), 7.63 (d, *J* = 15.6 Hz, 1H, Hβ), 7.93 (d, *J* = 8.8 Hz, 2H, H3, H5). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ 12.9 ($SiCH_2$), 26.2 ($C\mathbf{C}H_2C$), 51.2 ($CH_2\mathbf{C}H_2N$), 53.4 (N_3CH_2), 57.6 ($O\mathbf{C}H_2CH_2$), 62.4 (OCH_2), 114.9 (C2, C6), 122.5, 142.5 (Tz-C), 122.7 (Cα), 129.4 (C8, C12), 129.6 (C9, C11), 131.0 (C4), 131.4 (C3, C5), 133.4 (C7), 133.7 (C10), 142.9 (Cβ), 162.6 (C1), 188.0 (C=O). MS: m/z (relative abundance (%)): 577 (23), 555 (100). Anal. Calcd. for $C_{27}H_{31}ClN_4O_5Si$: C, 58.42; H, 5.63; N, 10.09. Found: C, 58.38; H, 5.56; N, 9.89.

3.1.6.8. (E)-1-(2-((1-(3-(silatranyl)propyl)-1H-1,2,3-triazol-4-ylmethoxyphenyl-3-phenylprop-2-en-1-one (**8a**)

The quantities used were as **5a** (1.0 g, 3.8 mmol), 3-AzPSa (0.98 g, 3.8 mmol). Yellow solid, Yield: 1.70 g, 3.3 mmol, 88 %. IR (neat, cm^{-1}): 558 (N→Si), 755, 1094 (Si-O), 1660 (C=N),

2931 (C=C-H). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ 0.19 (m, 2H, -$SiCH_2$-), 1.73 (m, 2H, -CCH_2C-), 2.68 (t, *J* = 5.7 Hz, 6H, -CH_2N-), 3.61 (t, *J* = 5.7 Hz, 6H, -O*CH*$_2$$CH_2$-), 3.99 (t, *J* = 7.2 Hz, 2H, -N_3CH_2-), 5.21 (s, 2H, -OCH_2-), 6.97 (t, *J* = 7.5 Hz, 1H, H2), 7.06 (d, *J* = 7.6 Hz, 1H, H4), 7.19-7.31 (m, 5H, H8-H12), 7.36-7.40 (m, 2H, H3, Hα), 7.41 (s, 1H, Tz-H), 7.49 (d, *J* = 15.9 Hz, 1H, Hβ), 7.59 (d, *J* = 7.6 Hz, 1H, H5). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ 12.8 ($SiCH_2$), 26.1 (C**C**H_2C), 51.1 (CH_2**C**H_2N), 53.1 (N_3CH_2), 57.6 (O**C**H_2CH_2), 63.1 (OCH_2), 113.1 (C2), 121.4, 142.4 (Tz-C), 122.7 (C4, C6), 123.9 (Cα), 127.6 (C8, C12), 128.5 (C10), 129.0 (C9, C11), 131.0 (C5), 133.2 (C7), 135.3 (C3), 142.9 (Cβ), 157.3 (C1), 192.0 (C=O). Anal. Calcd. for $C_{27}H_{32}N_4O_5Si$: C, 62.29; H, 6.19; N, 10.76. Found: C, 62.25; H, 6.16; N, 10.62.

3.1.6.9. (E)-1-(2-((1-(3-(silatranyl)propyl)-1H-1,2,3-triazol-4-ylmethoxyphenyl-3-(4-methoxyphenyl)prop-2-en-1-one (**8b**)

The quantities used were as **4a** (1.0 g, 3.4 mmol), 3-AzPSa (0.88 g, 3.4 mmol). Yellow solid, Yield: 1.65 g, 3.0 mmol, 86 %. IR (neat, cm^{-1}): 558 (N→Si), 755, 1094 (Si-O), 1660 (C=N), 2930 (C=C-H). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ 0.20 (m, 2H, -$SiCH_2$-), 1.75 (m, 2H, -CCH_2C-), 2.67 (t, *J* = 5.7 Hz, 6H, -CH_2N-), 3.60 (t, *J* = 5.7 Hz, 6H, -O*CH*$_2$$CH_2$-), 3.76 (s, 3H, -$OCH_3$), 4.04 (t, *J* = 7.2 Hz, 2H, -N_3CH_2-), 5.20 (s, 2H, -OCH_2-), 6.79 (d, *J* = 8.5 Hz, 2H, H9, H11), 6.93-7.06 (m, 2H, H2, H4), 7.22 (d, *J* = 8.5 Hz, 2H, H8, H12), 7.33-7.44 (m, 2H, H3, Hα), 7.47 (s, 1H, Tz-H), 7.57 (d, *J* = 14.8 Hz, 1H, Hβ), 7.73 (d, *J* = 8.3 Hz, 1H, H5). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ 12.8 ($SiCH_2$), 26.1 (C**C**H_2C), 51.2 (CH_2**C**H_2N), 53.2 (N_3CH_2), 55.2 (OCH_3), 57.7 (O**C**H_2CH_2), 63.1 (OCH_2), 113.1 (C9, C11), 113.6 (C2), 114.6 (C6), 120.3, 142.5 (Tz-C), 121.5 (Cα), 124.9 (C4), 125.5 (C8, C12), 128.1 (C7), 130.3 (C5), 133.0 (C3), 143.2 (Cβ), 157.3 (C10), 161.6 (C1), 191.9 (C=O). Anal. Calcd. for $C_{28}H_{34}N_4O_6Si$: C, 61.07; H, 6.22; N, 10.17. Found: C, 60.97; H, 6.12; N, 10.13.

3.1.6.10. (E)-1-(2-((1-(3-(silatranyl)propyl)-1H-1,2,3-triazol-4-ylmethoxyphenyl-3-(2-methoxyphenyl)prop-2-en-1-one (**8c**)

The quantities used were as **5c** (1.0 g, 3.4 mmol), 3-AzPSa (0.88 g, 3.4 mmol). Yellow solid, Yield: 1.65 g, 3.0 mmol, 88 %. IR (neat, cm^{-1}): 586 (N→Si), 749, 1095 (Si-O), 1654 (C=N), 2929 (C=C-H). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ 0.21 (m, 2H, -$SiCH_2$-), 1.74 (m, 2H, -CCH_2C-), 2.70 (t, *J* = 5.7 Hz, 6H, -CH_2N-), 3.64 (t, *J* = 5.7 Hz, 6H, -O*CH*$_2$$CH_2$-), 3.79 (s, 3H, -$OCH_3$), 3.99 (t, *J* = 7.2 Hz, 2H, -N_3CH_2-), 5.24 (s, 2H, -OCH_2-), 6.80-6.89 (m, 2H, H9, H11), 6.98-7.09 (m, 2H, H2, H4), 7.19-7.29 (m, 2H, H8, H10), 7.37-7.44 (m, 2H, H3, Hα), 7.58 (s, 1H, Tz-H), 7.80-7.89 (m, 2H, Hβ, H5). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ 12.8 ($SiCH_2$), 26.1 (C**C**H_2C), 51.1 (CH_2**C**H_2N), 53.0 (N_3CH_2), 55.3 (OCH_3), 57.5 (O**C**H_2CH_2), 63.3 (OCH_2), 111.1 (C11), 113.1 (C2, C7), 121.0 (C9), 121.4 (C4, C6), 122.6, 137.8 (Tz-C), 124.3 (Cα), 128.1 (C8), 128.9 (C10), 130.9 (C5), 132.9 (C3), 143.1 (Cβ), 157.2 (C12), 158.7 (C1), 192.3 (C=O). Anal. Calcd. for $C_{28}H_{34}N_4O_6Si$: C, 61.07; H, 6.22; N, 10.17. Found: C, 60.96; H, 6.12; N, 10.13.

3.1.6.11. (E)-1-(2-((1-(3-(silatranyl)propyl)-1H-1,2,3-triazol-4-ylmethoxyphenyl-3-(2,4-dimethoxyphenyl)prop-2-en-1-one (**8d**)

The quantities used were as **5d** (1.0 g, 3.1 mmol), 3-AzPSa (0.80 g, 3.1 mmol). Yellow solid, Yield: 1.64 g, 2.8 mmol, 91 %. IR (neat, cm^{-1}): 579 (N→Si), 755, 1096 (Si-O), 1638 (C=N), 2925 (C=C-H). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 0.33 (m, 2H, -$SiCH_2$-), 1.87 (m, 2H, -CCH_2C-), 2.78 (t, *J* = 5.8 Hz, 6H, -CH_2N-), 3.71 (t, *J* = 5.8 Hz, 6H, -O*CH*$_2$$CH_2$-), 3.80 (s, 3H, -$OCH_3$), 3.83 (s, 3H, -$OCH_3$), 4.13 (t, *J* = 7.2 Hz, 2H, -N_3CH_2-), 5.28 (s, 2H, -OCH_2-), 6.44 (s, 1H, H11), 6.50 (d, *J* = 8.6 Hz, 1H, H9), 7.05 (t, *J* = 7.5 Hz, 1H, H4), 7.13 (d, *J* = 8.0 Hz, 1H, H2), 7.34-7.47 (m, 3H, H8, Hα, H3), 7.54 (s, 1H, Tz-H), 7.62 (d, *J* = 7.6 Hz, 1H, H5), 7.87 (d, *J* = 16.0 Hz, 1H, Hβ). ^{13}C NMR (101 MHz, $CDCl_3$, 25 °C): δ 13.1 ($SiCH_2$), 26.3 (C**C**H_2C), 51.0 (CH_2**C**H_2N), 53.3 (N_3CH_2), 55.5 (2×OCH_3), 57.5 (O**C**H_2CH_2), 63.3 (OCH_2),

98.4 (C11), 105.4 (C9), 113.1 (C7), 117.1 (C2), 121.3, 138.6 (Tz-C), 122.7 (Cα), 125.5 (C6), 128.3 (C6), 130.2 (C8), 130.4 (C5), 132.5 (C3), 143.4 (Cβ), 156.8 (C12), 160.1 (C10), 162.9 (C1), 193.4 (C=O). Anal. Calcd. for $C_{29}H_{36}N_4O_7Si$: C, 59.98; H, 6.25; N, 9.65. Found: C, 59.86; H, 6.13; N, 9.56.

3.1.6.12. (E)-1-(2-((1-(3-(triethoxysilatranyl)propyl)-1H-1,2,3-triazol-4-ylmethoxyphenyl-3-(2,3,4-trimethoxyphenyl)prop-2-en-1-one (**8e**)

The quantities used were as **5e** (1.0 g, 2.8 mmol), 3-AzPSa (0.72 g, 2.8 mmol). Yellow solid, Yield: 1.51 g, 2.5 mmol, 89 %. IR: 574 (N→Si), 758, 1096 (Si-O), 1641 (C=N), 2927 (C=C-H). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 0.33 (m, 2H, -$SiCH_2$-), 1.88 (m, 2H, -CCH_2C-), 2.77 (t, *J* = 5.8 Hz, 6H, -CH_2N-), 3.71 (t, *J* = 5.8 Hz, 6H, -O*CH*$_2$$CH_2$-), 3.86 (m, 9H, 3×-$OCH_3$), 4.18 (t, *J* = 7.2 Hz, 2H, -N_3CH_2-), 5.28 (s, 2H, -OCH_2-), 6.68 (d, *J* = 8.5 Hz, 1H, H9), 7.04 (t, *J* = 7.5 Hz, 1H, H4), 7.12 (d, *J* = 8.5 Hz, 1H, H8), 7.20 (d, *J* = 8.8 Hz, 1H, H2), 7.36 (d, *J* = 16.0 Hz, 1H, Hα), 7.43-7.46 (m, 1H, H3), 7.56 (s, 1H, Tz-H), 7.63 (d, *J* = 7.5 Hz, 1H, H5), 7.82 (d, *J* = 16.0 Hz, 1H, Hβ). ^{13}C NMR (101 MHz, $CDCl_3$, 25 °C): δ 12.1 ($SiCH_2$), 25.2 (C**C**H_2C), 49.9 (CH_2**C**H_2N), 52.3 (N_3CH_2), 55.1 (OCH_3), 56.5 (O**C**H_2CH_2), 59.9 (OCH_3), 60.5 (OCH_3), 62.0 (OCH_2), 106.7 (C9), 108.4 (C7), 112.1 (C2), 120.3 (C6), 121.0, 141.3 (Tz-C), 121.8 (Cα), 122.1 (C4), 125.2 (C8), 129.5 (C5), 131.7 (C3), 137.0 (C11), 142.1 (Cβ), 152.6 (C12), 154.6 (C10), 155.8 (C1), 191.9 (C=O). Anal. Calcd. for $C_{30}H_{38}N_4O_8Si$: C, 59.00; H, 6.27; N, 9.17. Found: C, 58.94; H, 6.23; N, 9.18.

3.1.6.13. (E)-1-(2-((1-(3-(silatranyl)propyl)-1H-1,2,3-triazol-4-ylmethoxyphenyl-3-p-tolyl-prop-2-en-1-one (**8f**)

The quantities used were as **5f** (1.0 g, 3.6 mmol), 3-AzPSa (0.93 g, 3.6 mmol). Yellow solid, Yield: 1.67 g, 3.1 mmol, 87 %. IR (neat, cm^{-1}): 576 (N→Si), 756, 1094 (Si-O), 1660 (C=N), 2933 (C=C-H). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ 0.22 (m, 2H, -$SiCH_2$-), 1.75 (m, 2H, -

CCH_2C-), 2.33 (s, 3H, -CH_3), 2.71 (t, *J* = 5.8 Hz, 6H, -CH_2N-), 3.64 (t, *J* = 5.8 Hz, 6H, -O*CH_2*CH_2-), 4.01 (t, *J* = 7.2 Hz, 2H, -N_3CH_2-), 5.23 (s, 2H, -OCH_2-), 6.99 (t, *J* = 7.5 Hz, H4), 7.06-7.12 (m, 3H, H2, H9, H11), 7.31 (d, *J* = 6.6 Hz, 2H, H8, H12), 7.37-7.40 (m, 2H, H3, Hα), 7.42 (s, 1H, Tz-H), 7.49 (d, *J* = 15.9 Hz, 1H, Hβ), 7.59 (d, *J* = 7.5 Hz, 1H, H5). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ 12.9 ($SiCH_2$), 21.4 (OCH_3), 26.1 (C**C**H_2C), 50.9 (CH_2**C**H_2N), 53.2 (N_3CH_2), 57.5 (O**C**H_2CH_2), 63.0 (OCH_2), 113.1 (C2), 121.3, 140.8 (Tz-C), 121.4 (C4), 122.8 (Cα), 126.5 (C8, C12), 128.5 (C9, C11), 129.7 (C5), 130.6 (C3), 132.3 (C7), 133.1 (C10), 142.9 (Cβ), 157.1 (C1), 192.8 (C=O). Anal. Calcd. for $C_{28}H_{34}N_4O_5Si$: C, 62.90; H, 6.41; N, 10.48. Found: C, 62.83; H, 6.38; N, 10.34.

3.1.6.14. (E)-1-(2-((1-(3-(silatranyl)propyl)-1H-1,2,3-triazol-4-ylmethoxyphenyl-3-(4-chlorophenyl)prop-2-en-1-one (**8g**)

The quantities used were as **5g** (1.0 g, 3.4 mmol), 3-AzPSa (0.87 g, 3.4 mmol). Yellow solid, Yield: 1.62 g, 2.9 mmol, 87 %. IR (neat, cm^{-1}): 583 (N→Si), 757, 1097 (Si-O), 1667 (C=N), 2923 (C=C-H). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ 0.29 (m, 2H, -$SiCH_2$-), 1.90 (m, 2H, -CCH_2C-), 2.71 (t, *J* = 5.8 Hz, 6H, -CH_2N-), 3.65 (t, *J* = 5.8 Hz, 6H, -O*CH_2*CH_2-), 4.25 (t, *J* = 7.2 Hz, 2H, -N_3CH_2-), 5.21 (s, 2H, -OCH_2-), 7.08 (t, *J* = 7.4 Hz, 1H, H4), 7.14 (d, *J* = 8.3 Hz, 1H, H2), 7.35 (d, *J* = 8.3 Hz, 2H, H9, H11), 7.40 (s, 1H, Tz-H), 7.43 (d, *J* = 8.0 Hz, 2H, H8, H12), 7.48-7.50 (m, 2H, Hα, H3), 7.54 (d, *J* = 15.9 Hz, 1H, Hβ), 7.60 (d, *J* = 7.3 Hz, 1H, H5). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ 13.6 ($SiCH_2$), 26.5 (C**C**H_2C), 50.1 (CH_2**C**H_2N), 52.7 (N_3CH_2), 56.7 (O**C**H_2CH_2), 61.4 (OCH_2), 114.2 (C2), 121.0, 138.9 (Tz-C), 122.6 (Cα), 123.9 (C4), 128.0 (C8, C12), 128.7 (C9, C11), 129.6 (C5), 130.1 (C7), 133.4 (C10), 135.2 (C3), 142.4 (Cβ), 158.3 (C1), 188.6 (C=O). Anal. Calcd. for $C_{27}H_{31}ClN_4O_5Si$: C, 58.42; H, 5.63; N, 10.09. Found: C, 58.37; H, 5.63; N, 10.02.

3.1.6.15. (E)-1-(3-((1-(3-(silatranyl)propyl)-1H-1,2,3-triazol-4-ylmethoxyphenyl-3-phenylprop-2-en-1-one (**9a**)

The quantities used were as **6a** (1.0 g, 3.8 mmol), 3-AzPSa (0.98 g, 3.8 mmol). Yellow solid, Yield: 1.84 g, 3.5 mmol, 93 %. Yellow solid: 0.95 g, Yield: 93 %. IR (neat, cm^{-1}): 580 (N→Si), 771, 1028 (Si-O), 1658 (C=N), 2945 (C=C-H). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 0.42 (m, 2H, -$SiCH_2$-), 2.00 (m, 2H, -CCH_2C-), 2.80 (t, *J* = 5.8 Hz, 6H, -CH_2N-), 3.75 (t, *J* = 5.8 Hz, 6H, -O*CH*$_2CH_2$-), 4.34 (t, *J* = 7.5 Hz, 2H, -N_3CH_2-), 5.26 (s, 2H, -OCH_2-), 7.22 (d, *J* = 8.2 Hz, 1H, H2), 7.35 (s, 1H, Tz-H), 7.40-7.44 (m, 3H, H9-H11), 7.52 (d, *J* = 15.7 Hz, 1H, Hα), 7.62 (d, *J* = 7.7 Hz, 1H, H4), 7.63-7.67 (m, 3H, H7, H8, H12), 7.68 (s, 1H, H6), 7.81 (d, *J* = 15.7 Hz, 1H, Hβ). ^{13}C NMR (101 MHz, $CDCl_3$, 25 °C): δ 13.2 ($SiCH_2$), 26.3 (C**C**H_2C), 51.0 (CH_2**C**H_2N), 53.4 (N_3CH_2), 57.5 (O**C**H_2CH_2), 62.3 (OCH_2), 114.5 (C6), 119.6 (C2), 121.3, 143.0 (Tz-C), 122.2 (Cα), 122.9 (C4), 128.5 (C8, C12), 129.0 (C10), 129.7 (C9, C11), 130.5 (C3), 134.9 (C7), 139.6 (C5), 144.9 (Cβ), 158.7 (C1), 190.2 (C=O). Anal. Calcd. for $C_{27}H_{32}N_4O_5Si$: C, 62.29; H, 6.19; N, 10.76. Found: C, 62.23; H, 6.13; N, 10.68.

3.1.6.16. (E)-1-(3-((1-(3-(silatranyl)propyl)-1H-1,2,3-triazol-4-ylmethoxyphenyl-3-(4-methoxyphenyl)prop-2-en-1-one (**9b**)

The quantities used were as **6b** (1.0 g, 3.4 mmol), 3-AzPSa (0.88 g, 3.4 mmol). Yellow solid, Yield: 1.71 g, 3.1 mmol, 91 %. IR (neat, cm^{-1}): 573 (N→Si), 753, 1086 (Si-O), 1660 (C=N), 2933 (C=C-H). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 0.32 (m, 2H, -$SiCH_2$-), 1.96 (m, 2H, -CCH_2C-), 2.83 (t, *J* = 5.8 Hz, 6H, -CH_2N-), 3.73 (t, *J* = 5.8 Hz, 6H, -O*CH*$_2CH_2$-), 3.86 (s, 3H, -OCH_3), 4.32 (t, *J* = 7.3 Hz, 2H, -N_3CH_2-), 5.23 (s, 2H, -OCH_2-), 6.95 (d, *J* = 8.7 Hz, 2H, H9, H11), 7.23 (d, *J* = 8.2 Hz, 1H, H2), 7.34 (s, 1H, H6), 7.44 (s, 1H, Tz-H), 7.48 (d, *J* = 15.6 Hz, 1H, Hα), 7.62-7.68 (m, 4H, H3, H4, H8, H12), 7.79 (d, *J* = 15.6 Hz, 1H, Hβ). ^{13}C NMR (101 MHz, $CDCl_3$, 25 °C): δ 12.5 ($SiCH_2$), 25.5 (C**C**H_2C), 49.7 (CH_2**C**H_2N), 52.2 (N_3CH_2), 54.4 (OCH_3), 56.3 (O**C**H_2CH_2), 60.9 (OCH_2), 113.2 (C6), 113.4 (C9, C11), 118.4 (C2), 118.6

(C4), 120.1, 141.6 (Tz-C), 122.4 (Cα), 126.4 (C8, C12), 128.7 (C7), 129.4 (C3), 138.7 (C5), 143.5 (Cβ), 157.5 (C10), 160.7 (C1), 188.6 (C=O). Anal. Calcd. for $C_{28}H_{34}N_4O_6Si$: C, 61.07; H, 6.22; N, 10.17. Found: C, 61.04; H, 6.13; N, 10.07.

3.1.6.17. (E)-1-(3-((1-(3-(silatranyl)propyl)-1H-1,2,3-triazol-4-ylmethoxyphenyl-3-(2-methoxyphenyl)prop-2-en-1-one (**9c**)

The quantities used were as **6c** (1.0 g, 3.4 mmol), 3-AzPSa (0.88 g, 3.4 mmol). Yellow solid, Yield: 1.69 g, 3.1 mmol, 90 %. IR (neat, cm^{-1}): 585 (N→Si), 766, 1095 (Si-O), 1654 (C=N), 2921 (C=C-H). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 0.42 (m, 2H, -$SiCH_2$-), 2.00 (m, 2H, -CCH_2C-), 2.80 (t, *J* = 5.8 Hz, 6H, -CH_2N-), 3.75 (t, *J* = 5.8 Hz, 6H, -O*CH$_2$*CH_2-), 3.92 (s, 3H, -OCH_3), 4.34 (t, *J* = 7.5 Hz, 2H, -N_3CH_2-), 5.26 (s, 2H, -OCH_2-), 6.94 (d, *J* = 8.3 Hz, 1H, H11), 7.00 (t, *J* = 7.5 Hz, 1H, H9), 7.21 (d, *J* = 6.5 Hz, 1H, H2), 7.36-7.43 (m, 3H, Hα, H8, H10), 7.58 (s, 1H, Tz-H), 7.61-7.66 (m, 2H, H3, H4), 7.69 (s, 1H, H6), 8.12 (d, *J* = 15.9 Hz, 1H, Hβ). ^{13}C NMR (101 MHz, $CDCl_3$, 25 °C): δ 13.2 ($SiCH_2$), 26.3 ($C\mathbf{C}H_2C$), 51.0 ($CH_2\mathbf{C}H_2N$), 53.4 (N_3CH_2), 55.6 (OCH_3), 57.5 ($O\mathbf{C}H_2CH_2$), 62.3 (OCH_2), 111.2 (C6, C11), 114.4 (C7), 119.4 (C9), 120.8 (C2), 121.4, 140.5 (Tz-C), 122.9 (Cα), 123.9 (C4), 128.3 (C8), 129.3 (C10), 131.8 (C3), 139.9 (C5), 143.0 (Cβ), 158.6 (C12), 158.8 (C1), 190.8 (C=O). Anal. Calcd. for $C_{28}H_{34}N_4O_6Si$: C, 61.07; H, 6.22; N, 10.17. Found: C, 60.98; H, 6.13; N, 10.14.

3.1.6.18. (E)-1-(3-((1-(3-(silatranyl)propyl)-1H-1,2,3-triazol-4-ylmethoxyphenyl-3-(2,4-dimethoxyphenyl)prop-2-en-1-one (**9d**)

The quantities used were as **6d** (1.0 g, 3.1 mmol), AzPSa (0.80 g, 3.1 mmol). Yellow solid, Yield: 1.65 g, 2.8 mmol, 92 %. IR (neat, cm^{-1}): 579 (N→Si), 764, 1096 (Si-O), 1655 (C=N), 2925 (C=C-H). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 0.42 (m, 2H, -$SiCH_2$-), 2.00 (m, 2H, -CCH_2C-), 2.80 (t, *J* = 5.8 Hz, 6H, -CH_2N-), 3.75 (t, *J* = 5.8 Hz, 6H, -O*CH$_2$*CH_2-), 3.85 (s, 3H,

-OCH_3), 3.90 (s, 3H, -OCH_3), 4.33 (t, *J* = 7.5 Hz, 2H, -N_3CH_2-), 5.25 (s, 2H, -OCH_2-), 6.47 (s, 1H, H11), 6.53 (d, *J* = 8.6 Hz, 1H, H9), 7.19 (d, *J* = 8.6 Hz, 1H, H2), 7.35-7.47 (m, 2H, Tz-H, H8), 7.52 (d, *J* = 15.8 Hz, 1H, Hα), 7.58 (d, *J* = 8.6 Hz, 1H, H4), 7.61-7.64 (m, 1H, H3), 7.68 (s, 1H, H6), 8.05 (d, *J* = 15.8 Hz, 1H, Hβ). ^{13}C NMR (101 MHz, $CDCl_3$, 25 °C): δ 13.2 ($SiCH_2$), 26.3 (C**C**H_2C), 51.0 (CH_2**C**H_2N), 53.4 (N_3CH_2), 55.5 (OCH_3), 55.6 (OCH_3), 57.5 (O**C**H_2CH_2), 62.3 (OCH_2), 98.5 (C11), 100.0 (C9), 105.4 (C7), 114.3 (C6, C11), 119.2 (C2), 120.4, 140.6 (Tz-C), 121.3 (Cα), 122.9 (C4), 129.6 (C8), 131.0 (C3), 140.3 (C5), 143.1 (Cβ), 158.5 (C12), 160.5 (C10), 163.1 (C1), 190.8 (C=O). Anal. Calcd. for $C_{29}H_{36}N_4O_7Si$: C, 59.98; H, 6.25; N, 9.65. Found: C, 59.83; H, 6.05; N, 9.63.

3.1.6.19. (E)-1-(3-((1-(3-(silatranyl)propyl)-1H-1,2,3-triazol-4-ylmethoxyphenyl-3-(2,3,4-trimethoxyphenyl)prop-2-en-1-one (**9e**)

The quantities used were as **6e** (1.0 g, 2.8 mmol), AzPSa (0.72 g, 2.8 mmol). Yellow solid, Yield: 1.54 g, 2.5 mmol, 91 %. IR (neat, cm^{-1}): 583 (N→Si), 763, 1092 (Si-O), 1655 (C=N), 2930 (C=C-H). ^{1}H NMR (400 MHz, $CDCl_3$, 25°C): δ 0.43 (m, 2H, -$SiCH_2$-), 2.01 (m, 2H, -CCH_2C-), 2.81 (t, *J* = 5.8 Hz, 6H, -CH_2N-), 3.75 (t, *J* = 5.8 Hz, 6H, -O*CH*$_2CH_2$-), 3.89 (s, 3H, -OCH_3), 3.92 (s, 3H, -OCH_3), 3.95 (s, 3H, -OCH_3), 4.33 (t, *J* = 7.5 Hz, 2H, -N_3CH_2-), 5.26 (s, 2H, -OCH_2-), 6.74 (d, *J* = 8.8 Hz, 1H, H9), 7.21 (d, *J* = 8.8 Hz, 1H, H8), 7.36 (s, 1H, Tz-H), 7.42 (d, *J* = 7.0 Hz, 1H, H2), 7.54 (d, *J* = 15.8 Hz, 1H, Hα), 7.62 (d, *J* = 7.7 Hz, 1H, H4), 7.65 (m, 1H, H3), 7.69 (s, 1H, H6), 8.01 (d, *J* = 15.8 Hz, 1H, Hβ). ^{13}C NMR (101 MHz, $CDCl_3$, 25 °C): δ 13.2 ($SiCH_2$), 26.3 (C**C**H_2C), 51.0 (CH_2**C**H_2N), 53.4 (N_3CH_2), 56.1 (O**C**H_2CH_2), 60.9 (OCH_3), 61.5 (OCH_3), 62.3 (OCH_2), 107.3 (C9), 107.7 (C7), 114.4 (C6), 119.4 (C8), 121.3, 142.5 (Tz-C), 122.0 (C2), 122.9 (Cα), 123.9 (C4), 129.6 (C3), 140.0 (C5), 140.2 (C11), 143.1 (Cβ), 153.9 (C12), 155.8 (C10), 158.6 (C1), 190.5 (C=O). Anal. Calcd. for $C_{30}H_{38}N_4O_8Si$: C, 59.00; H, 6.27; N, 9.17. Found: C, 58.87; H, 6.17; N, 9.08.

3.1.6.20. (E)-1-(3-((1-(3-(silatranyl)propyl)-1H-1,2,3-triazol-4-ylmethoxyphenyl-3-p-tolyl-prop-2-en-1-one (**9f**)

The quantities used were as **6f** (1.0 g, 3.6 mmol), AzPSa (0.93 g, 3.6 mmol). Yellow solid, Yield: 1.73 g, 3.2 mmol, 90 %. IR (neat, cm^{-1}): 581 (N→Si), 756, 1091 (Si-O), 1664 (C=N), 2931 (C=C-H). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 0.28 (m, 2H, -$SiCH_2$-), 1.93 (m, 2H, -CCH_2C-), 2.39 (s, 3H, CH_3), 2.83 (t, *J* = 5.9 Hz, 6H, -CH_2N-), 3.71 (t, *J* = 5.9 Hz, 6H, -O*CH*$_2CH_2$-), 4.30 (t, *J* = 7.3 Hz, 2H, -N_3CH_2-), 5.24 (s, 2H, -OCH_2-), 7.24 (d, *J* = 8.0 Hz, 2H, H9, H11), 7.32 (d, *J* = 15.6 Hz, 1H, Hα), 7.44 (t, *J* = 7.9 Hz, 1H, H3), 7.60-7.66 (m, 3H, Tz-H, H2, H4), 7.68 (s, 1H, H6), 7.73 (d, *J* = 15.6 Hz, 1H, Hβ), 7.89 (d, *J* = 7.9 Hz, 2H, H8, H12). ^{13}C NMR (101 MHz, $CDCl_3$, 25 °C): δ 13.1 ($SiCH_2$), 20.9 (CH_3), 26.1 (C**C**H_2C), 50.0 (CH_2**C**H_2N), 52.6 (N_3CH_2), 56.7 (O**C**H_2CH_2), 61.3 (OCH_2), 113.7 (C6), 119.0 (C2), 120.5, 141.9 (Tz-C), 120.7 (Cα), 123.2 (C4), 128.2 (C8, C12), 129.1 (C9, C11), 129.2 (C3), 131.5 (C7), 139.0 (C10), 140.4 (C5), 144.0 (Cβ), 158.0 (C1), 188.9 (C=O). Anal. Calcd. for $C_{28}H_{34}N_4O_5Si$: C, 62.90; H, 6.41; N, 10.48. Found: C, 62.82; H, 6.34; N, 10.43.

3.1.6.21. (E)-1-(3-((1-(3-(silatranyl)propyl)-1H-1,2,3-triazol-4-ylmethoxyphenyl-3-(4-chlorophenyl)prop-2-en-1-one (**9g**)

The quantities used were as **6g** (1.0 g, 3.4 mmol), AzPSa (0.87 g, 3.4 mmol). Yellow solid, Yield: 1.63 g, 2.9 mmol, 87 %. IR (neat, cm^{-1}): 584 (N→Si), 762, 1093 (Si-O), 1661 (C=N), 2917 (C=C-H). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ 0.19 (m, 2H, -$SiCH_2$-), 1.86 (m, 2H, -CCH_2C-), 2.81 (t, *J* = 5.9 Hz, 6H, -CH_2N-), 3.65 (t, *J* = 5.9 Hz, 6H, -O*CH*$_2CH_2$-), 4.26 (t, *J* = 7.2 Hz, 2H, -N_3CH_2-), 5.24 (s, 2H, -OCH_2-), 7.30 (d, *J* = 8.1 Hz, 1H, H2), 7.34 (s, 1H, Tz-H), 7.44-7.48 (m, 4H, H9, H11, H3, Hα), 7.70-7.77 (m, 3H, H4, H8, H12), 7.84-7.88 (m, 2H, Hβ, H4). ^{13}C NMR (101 MHz, $CDCl_3$, 25 °C): δ 13.1 ($SiCH_2$), 20.9 (CH_3), 26.1 (C**C**H_2C), 50.0 (CH_2**C**H_2N), 52.6 (N_3CH_2), 56.7 (O**C**H_2CH_2), 61.3 (OCH_2), 113.7 (C6), 119.0 (C2), 120.5, 141.9 (Tz-C), 120.7 (Cα), 123.2 (C4), 128.2 (C8, C12), 129.1 (C9, C11), 129.2 (C3), 131.5

(C7), 139.0 (C10), 140.4 (C5), 144.0 (Cβ), 158.0 (C1), 188.9 (C=O). Anal. Calcd. for $C_{27}H_{31}ClN_4O_5Si$: C, 58.42; H, 5.63; N, 10.09. Found: C, 58.28; H, 5.53; N, 10.03.

3.2. X-ray crystallography

Measured crystals were prepared under inert conditions immersed in perfluoropolyether as protecting oil for manipulation. Then the crystals were mounted on a MiTeGen Micromounts^{TM} and this sample was used for data collection. Data were collected with a Bruker D8 Venture diffractometer. Data were processed with APEX2 [80] and corrected for absorption using SADABS [81]. The structures were solved by direct methods [82], which revealed the position of all non-hydrogen atoms. These atoms were refined on F^2 by a full-matrix least-squares procedure using anisotropic displacement parameters [82]. All hydrogen atoms were located in difference Fourier maps and included as fixed contributions riding on attached atoms with isotropic thermal displacement parameters 1.2 times those of the respective atom. Drawings were produced with Olex2 [83].

3.3. Biological assays

3.3.1. In vitro antiparasitic assay

Antigiardial and antitrichomonal activity of the newly synthesized compounds was tested by MTT assay against Portland 1 strain of *Giardia lamblia* and *Trichomonas vaginalis* culture (*Trichomonas symptomatic 162 strain*) respectively [84]. The newly synthesized purified compounds and standard drug metronidazole were initially dissolved in dimethyl sulphoxide (DMSO). IC_{50} was calculated by serial two-fold dilutions (0.9-15 μg/ cm^3) and all the tests were performed in duplicate with three sets of independent experiments in triplicates. Culture of Trichomonas and Giardia were first grown in 96-well U-bottom plates (Greiner) at 37 °C for 24 h and then serially diluted compounds and reference drug metronidazole were added into the microtitre plates for checking the antiparasitic activity. After 48 h of incubation,

colorimetric assay was used to check the viability of the parasites by mitochondrial oxidation of MTT [3-(4,5-dimethylthiazol-2-yl)-2,5 diphenyl tetrazolium bromide] [84,85]. Briefly, MTT was prepared freshly by dissolving in PBS (5 mg/ cm^3) and sterilized by using filter of 0.22 µm. After adding MTT (0.25 µg /cm^3) to each well, micro-titre plate was incubated for 4 h at 37 °C in dark. Parasites grown in culture were detached from the micro-titre plate by adding 100% DMSO and were kept at room temperature on Gel Rocker for 30 min. ELISA reader was used to measure the absorbance at 570 nm and correlated with blank and controls. DMSO at a concentration of 0.5% was used in cultures as a control to check the inhibitory effect of DMSO on parasites and this was considered as 100% growth for comparison. The IC_{50} after 48 h of incubation was calculated with a sigmoid dose response curve using the following equation:

Percentage of inhibition = [(O.D. of Blank – O.D. of Test) / O.D. of Blank] X 100

3.3.2. Cytotoxicity test

The cytotoxicity of the six compounds (**7e**, **7f**, **8a**, **8d**, **9c** and **9e**) with superior antiparasitic activities was determined using MTT assay (3-(4, 5)-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide) against Human embryonic kidney cell 293 (Hek-293) and cancer cells (HeLa). Briefly, the cells (5 x 10^4/well) were cultured in RPMI-1640 medium supplemented with 10% fetal bovine serum in 96-well microtiter plates at 37 °C for overnight. The next day, all six compounds at concentrations ranges (100 µM to 1.56 µM) were added to the cells in separate wells and incubated at 37 °C for 18 h. Untreated cells are taken as negative control. The MTT solution (20 µl, 5 mg/ml) in phosphate buffer saline (PBS) was added, and the cells were further incubated at 37 °C for 3-4 h. Supernatant (120 µl) was removed, 100 µl Dimethylsulfoxide (DMSO) was added, and the resulting suspension was mixed to dissolve the formazan crystals [86]. The CC_{50} was defined as the concentration of compounds which

result in the 50% inhibition of growth compare to untreated cells. The selective index (SI) was calculated based on the ratio between CC_{50} and IC_{50} values.

4. Conclusion

A variety of triazole and silatrane clubbed chalcones have been synthesized with a motive to generate such system that incorporates bioactivities of these three moieties. Computer based screening publicized the compounds to show admirable physicochemical properties essential for drug bioavailability. All the synthesized compounds have been evaluated for their giardial and trichomonal activities. SAR revealed that the compounds with o/p-substitution on ring A of chalcone with tri-methoxy or chloro substitution on ring B rendered good activities. Further exploration of the chalcone template may produce more potent antiparasitic compounds.

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Table Captions

Table 1. Predicted physicochemical properties calculated by using molinspiration software for oragnosilatranes **7a-7g**/**8a-8g**/**9a-9g**.

Table 2. Crystallographic data for compounds **7a** and **7c**.

Table 3. Selected bond lengths and bond angles for compounds **7a** and **7c**.

Table 4. In vitro antiparasitic bioactivity of organosilatranes **7a-7g**/**8a-8g**/**9a-9g**.

Table 5. Cytotoxicity activities of organosilatranes against Hek 293 cells and HeLa cells.

	7a-7g					8a-8g					9a-9g				
	clogP	PSA	HBD	HBA	nRotB	clogP	PSA	HBD	HBA	nRotB	clogP	PSA	HBD	HBA	nRotB
a	3.54	87.96	0	9	10	3.49	87.96	0	9	10	3.52	87.96	0	9	10
b	3.60	97.20	0	10	11	3.55	97.20	0	10	11	3.57	97.20	0	10	11
c	3.37	97.20	0	10	11	3.32	97.20	0	10	11	3.35	97.20	0	10	11
d	3.40	106.43	0	11	12	3.35	106.43	0	11	12	3.38	106.43	0	11	12
e	3.19	115.67	0	12	13	3.14	115.67	0	12	13	3.17	115.67	0	12	13
f	3.99	87.96	0	9	10	3.94	87.96	0	9	10	3.97	87.96	0	9	10
g	4.22	87.96	0	9	10	4.17	87.96	0	9	10	4.19	87.96	0	9	10

Table 1.

Crystal data	**7a**	**7c**
Empirical formula	$C_{27}H_{32}N_4O_5Si$	$C_{28}H_{34}N_4O_6Si$
Formula weight	520.66	550.68
Temperature (*K*)	300	100
Wavelength (Å)	1.54178	1.54178
Crystal system	Monoclinic	Monoclinic
Space group	$P12_1/c1$	$C12/c1$
Unit cell dimensions (Å)	a = 15.859(2)	a = 30.875(12)
	b = 14.195(2)	b = 6.930(2)
	c = 11.773(17)	c = 25.810(10)
	β = 92.416(7)°	β = 109.458(2)°
Volume (Å^3)	2648.2 (7)	5207.7(3)
Z	8	8
Density (calculated), mg/m^3	1.306	1.405
Absorption coefficient, mm^{-1}	1.153	1.233
F(000)	1104	2336
Crystal size (mm^3)	0.10 x 0.08 x 0.08	0.12 x 0.12 x 0.08
Theta range for data collection	2.79 to 33.25°	15.16 to 68.58°
Index ranges	-17<=h<=18,	-36<=h<=25,
	-16<=k<=11,	-8<=k<=7,
	-13<=l<=14	-30<=l<=25
Reflections collected	4545	4518
Independent reflections	3643 [R(int) = 0.0409]	4006 [R(int) = 0.0231]
Completeness to theta	97.7	98.0
Absorption correction	Multi-scan	Multi-scan
Max. and min. transmission	0.7528 and 0.6665	0.7528 and 0.6803
Refinement method	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2
Data / restraints / parameters	4545 / 0 / 334	4518 / 0 / 353
Goodness-of-fit on F^2	1.140	1.055
Final R indices [I>2sigma(I)]	R_1 = 0.0789,	R_1 = 0.0385,
	wR_2 = 0.2469	wR_2 = 0.0965

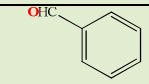
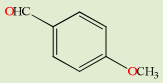
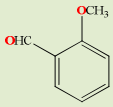
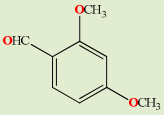
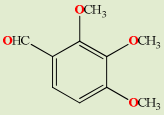
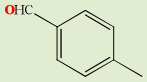
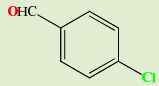
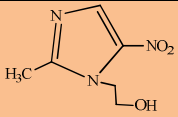
R indices (all data)	R_1 = 0.0903,	R_1 = 0.0444,
	wR_2 = 0.2550	wR_2 = 0.1010

Table 2.

7a		**7c**	
Bond lengths [Å]			
Si(1)- O(1)	1.646(4)	Si(1)- O(1)	1.6746(14)
Si(1)- O(3)	1.646(3)	Si(1)- O(3)	1.6673(13)
Si(1)- C(7)	1.883(4)	Si(1)- C(7)	1.8745(19)
O(2)- C(4)	1.427(6)	O(2)- C(4)	1.420(2)
O(4)- C(12)	1.430(5)	O(4)- C(12)	1.434(2)
O(5)- C(19)	1.224(5)	O(5)- C(19)	1.234(2)
N(1)- C(3)	1.464(7)	O(6)- C(28)	1.419(2)
N(2)- N(3)	1.327(5)	N(1)- C(3)	1.471(3)
N(2)- C(10)	1.338(5)	N(2)- N(3)	1.342(2)
N(4)- C(11)	1.352(5)	N(2)- C(10)	1.344(2)
C(3)- C(4)	1.451(9)	N(4)- C(11)	1.356(2)
C(7)- C(8)	1.529(5)	C(3)- C(4)	1.503(3)
		C(7)- C(8)	1.525(2)
		C(10)- C(11)	1.369(2)
		C(20)- C(21)	1.337(3)
Bond angles [°]			
O(1)- Si(1)- O(2)	117.4(2)	O(1)- Si(1)- N(1)	82.48(6)
O91)- Si(1)- N(1)	82.92(17)	O(2)- Si(1)- O(1)	119.61(7)
O(2)- Si(1)- N(1)	83.05(18)	O(2)- Si(1)- N(1)	82.23(6)
O(3)- Si(1)- O(2)	119.0(2)	O(3)- Si(1)- O(1)	115.50(7)
O(3)- Si(1)- C(7)	96.5(2)	O(3)- Si(1)- C(7)	97.45(8)
C(2)- O(1)- Si(1)	123.3(4)	C(2)- O(1)- Si(1)	122.83(12)
C(6)- O(3)- Si(1)	122.9(4)	C(6)- O(3)- Si(1)	122.80(13)
C(1)- N(1)- Si(1)	104.4(4)	C(27)- O(6)- C(28)	117.05(15)
C(3)- N(1)- C(1)	112.7(6)	C(1)- N(1)- C(3)	113.60(16)
C(5)- N(1)- C(1)	114.9(6)	C(5)- N(1)- Si(1)	103.68(12)
N(3)- N(2)- C(9)	120.7(3)	C(5)- N(1)- C(3)	114.19(16)

C(10)- N(2)- C(9)	129.2(4)	N(3)- N(2)- C(10)	110.93(14)
N(3)- N(4)- C(11)	108.5(3)	N(4)- N(3)- N(2)	107.29(14)
C(4)- C(3)- N(1)	107.7(5)	N(1)- C(1)- C(2)	106.62(14)
C(8)- C(7)- Si(1)	113.5(3)	N(1)- C(3) -C(4)	106.77(16)
C(9)- C(8)- C(7)	112.1(3)	N(1)- C(5)- C(6)	106.41(16)
N(2)- C(10)- C(11)	105.8(4)	C(8)- C(7)- Si(1)	115.13(13)
N(4)- C(11)- C(10)	107.8(3)	N(2)- C(9)- C(8)	111.87(14)
C(10)- C(11)- C(12)	131.3(4)	N(4)- C(11)- C(10)	108.73(15)
		C(10)- C(11)- C(12)	127.98(16)
		O(4)- C(13)- C(14)	125.10(15)
		O(5)- C(19)- C(16)	119.68(17)
		O(6)- C(27)- C(22)	115.28(16)

Table 3.

	R-CHO	7a-7g				8a-8g				9a-9g			
		Yield (%)	M.P. (°C)	IC_{50} (µM) *G. lamblia*	IC_{50} (µM) *T. vaginalis*	Yield (%)	M.P. (°C)	IC_{50} (µM) *G. lamblia*	IC_{50} (µM) *T. vaginalis*	Yield (%)	M.P. (°C)	IC_{50} (µM) *G. lamblia*	IC_{50} (µM) *T. vaginalis*
a		92	177	59.695	27.24	86	110	28.08	23.26	93	161	80.96	65.595
b		90	141	54.855	21.605	88	152	32.16	26.69	91	157	NS	30.275
c		89	172	40.94	22.69	88	164	NS	23.81	90	170	43.73	43.125
d		91	149	31.945	22.855	91	161	35.395	22.125	92	150	43.885	43.805
e		90	144	30.175	18.245	89	183	NS	21.265	91	161	19.58	42.095
f		90	210	33.245	24.82	87	160	47.995	50.025	90	181	131.2	101.265
g		88	190	33.08	21.925	87	189	33.935	22.27	87	180	78.45	55.68
Met		**62.48 µM** (for *G. lamblia*)				**55.85 µM** (for *T. vaginalis*)							

NS: Not Significant

Table 4.

S. No.	Organo silatranes	CC_{50} (µM) Hek 293 cells	CC_{50} (µM) HeLa cells	*G. lamblia*			*T. vaginalis*		
				IC_{50} (µM)	SI (for Hek cells)	SI (for HeLa cells)	IC_{50} (µM)	SI (for Hek cells)	SI (for HeLa cells)
1.	7e	269.68	227.27	30.175	8.94	7.53	18.245	14.78	12.46
2.	7f	197.78	188.96	33.245	5.95	5.68	24.82	7.97	7.61
3.	8a	208.07	237.98	28.08	7.41	8.48	23.26	8.94	10.23
4.	8e	284.73	232.34	-	-	-	21.265	13.39	10.92
5.	9b	266.80	203.00	-	-	-	30.275	8.81	6.70
6.	9e	327.86	339.90	19.58	16.74	17.36	42.095	7.79	8.07

Table 5.

Figure Captions

Figure 1. Commonly used drugs for giardiasis and trichomoniasis.

Figure 2. General structure of the synthesized chalconyl blended 1,2,3-triazole encapped silatranes.

Figure 3. Ortep plots of compounds **(A) 7a** and **(B) 7c**. Thermal ellipsoids drawn at 50% probability.

Figure 4. Ball and stick model **(A)**, lattice figure **(B-left)** and sketch lattice model **(B-right)** for compound **7a**.

Figure 5. Ball and stick model **(A)**, lattice figure **(B-left)** and sketch lattice model **(B-right)** for compound **7c**.

Figure 6. Comparative antitrichomonal activity of organosilatranes **7a-7g**/**8a-8g**/**9a-9g**.

Figure 7. Comparative antigiardial activity of organosilatranes **7a-7g**/**8a-8g**/**9a-9g**.

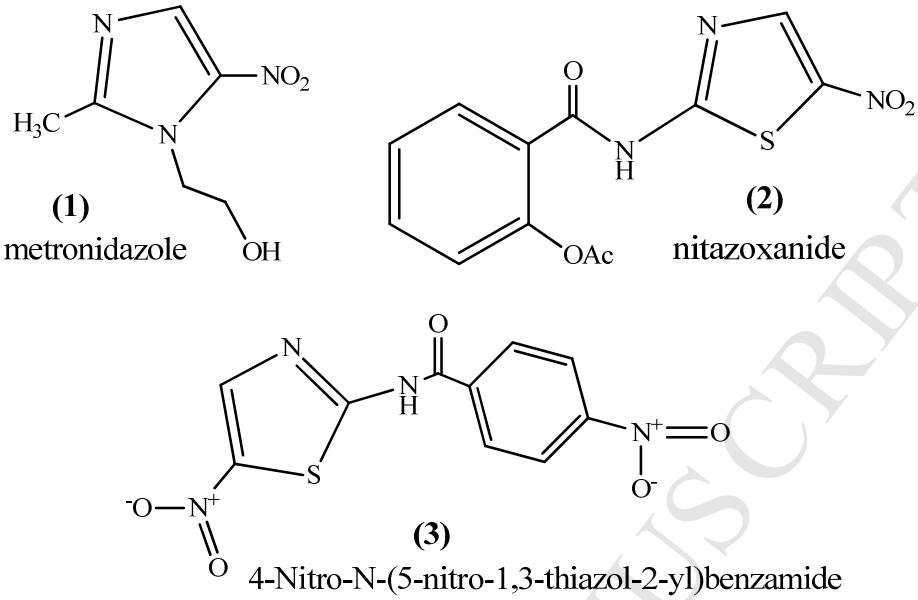


Fig. 1.

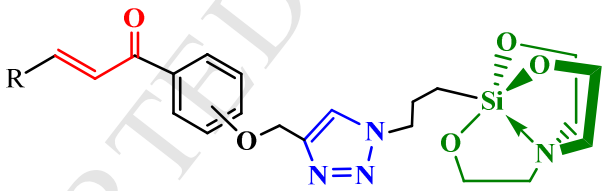


Fig. 2.

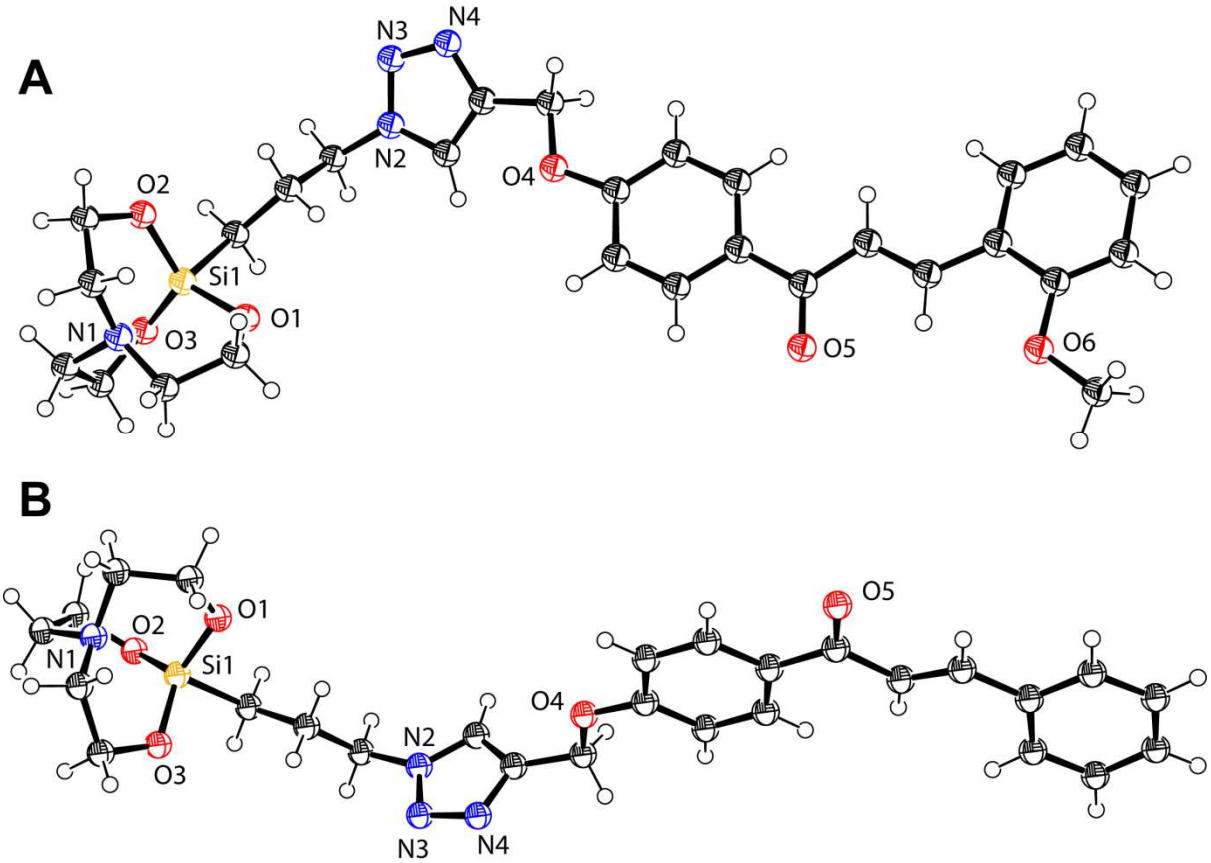

A
N3
N4
N2
O4
O2
Si1
O1
N1
O3
O5
O6
B
O1
O2
N1
Si1
O5
O4
N2
O3
N3
N4

Fig. 3.

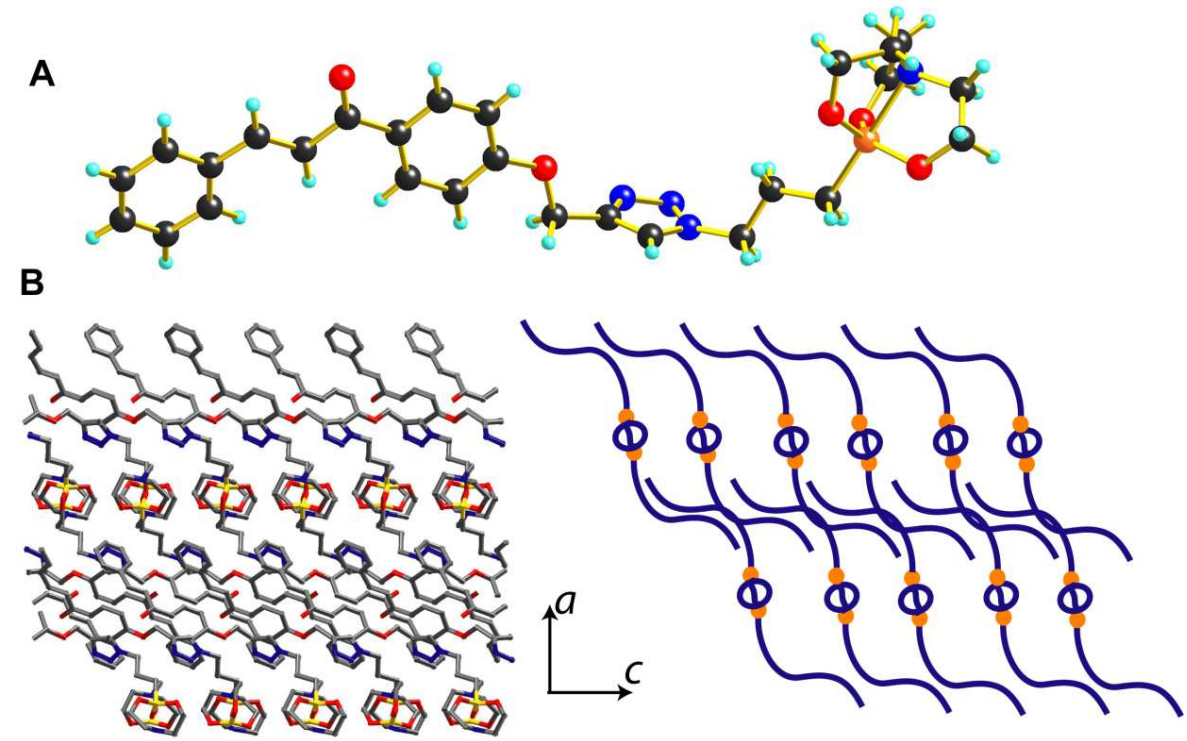

A
B
a
c

Fig. 4.

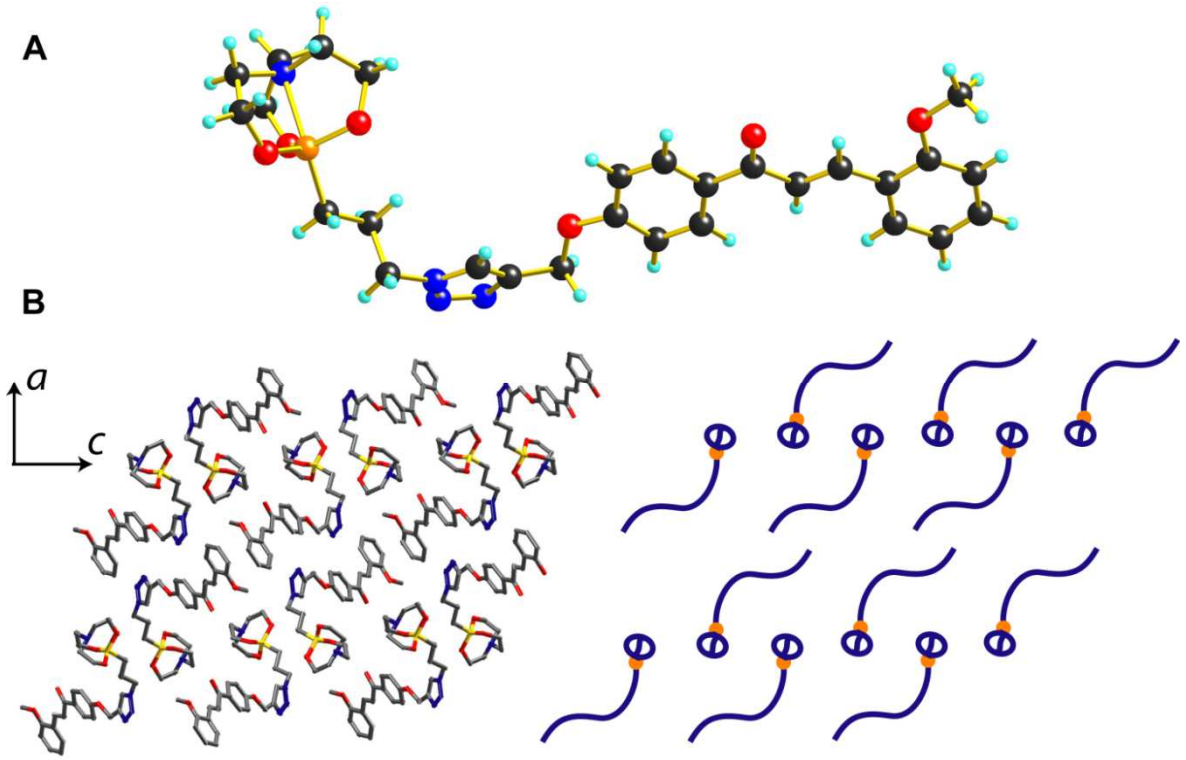

A
B
a
c

Fig. 5.

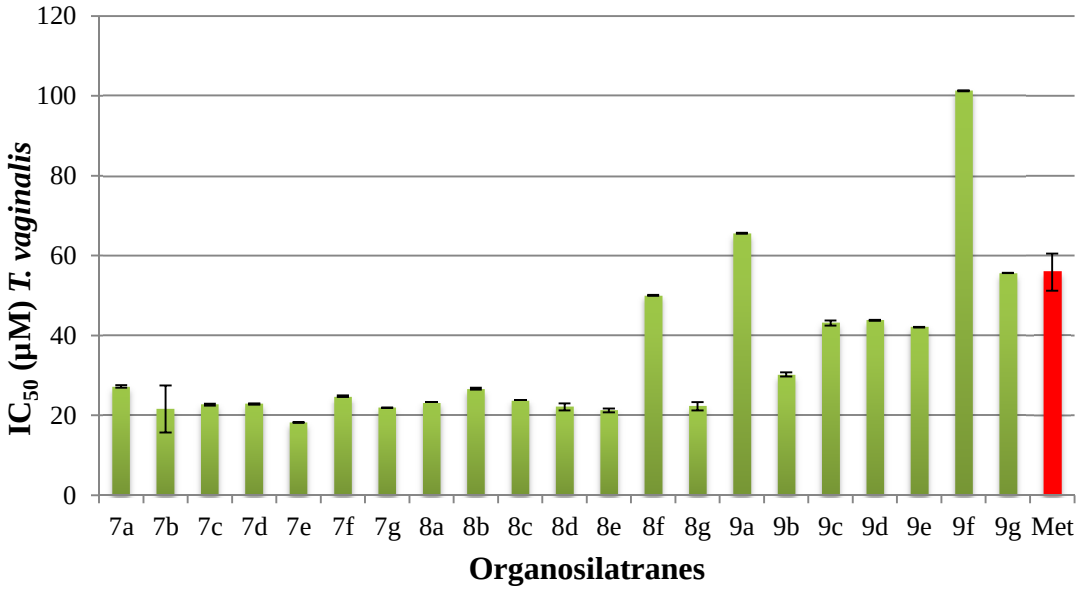

120
100
80
60
40
20
0
IC50 (µM) T. vaginalis
7a 7b 7c 7d 7e 7f 7g 8a 8b 8c 8d 8e 8f 8g 9a 9b 9c 9d 9e 9f 9g Met
Organosilatranes

Fig. 6.

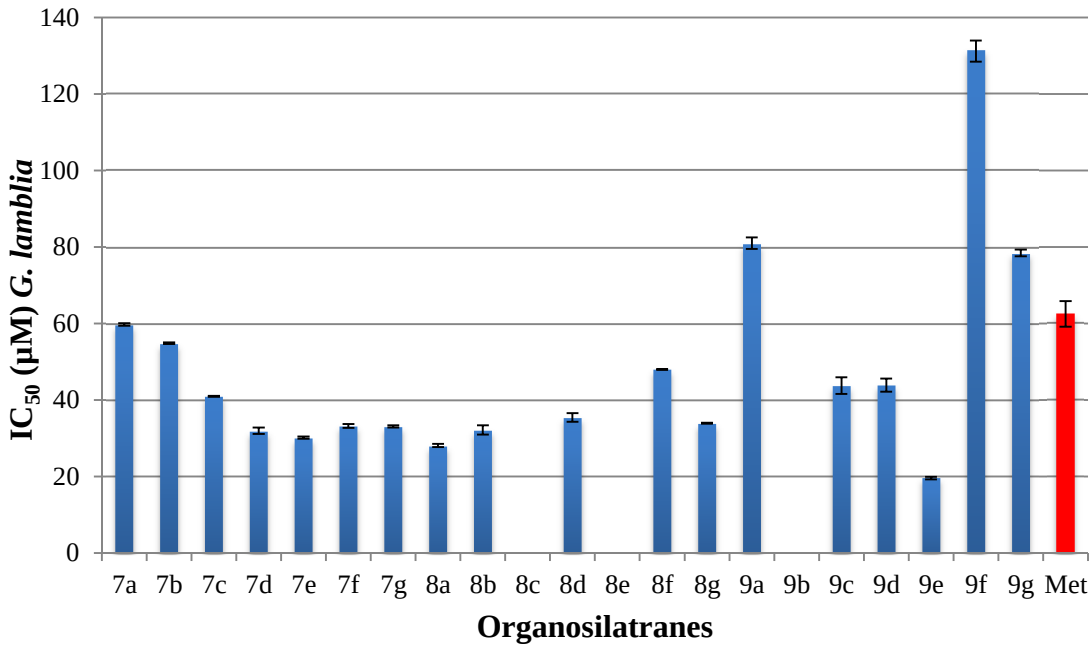
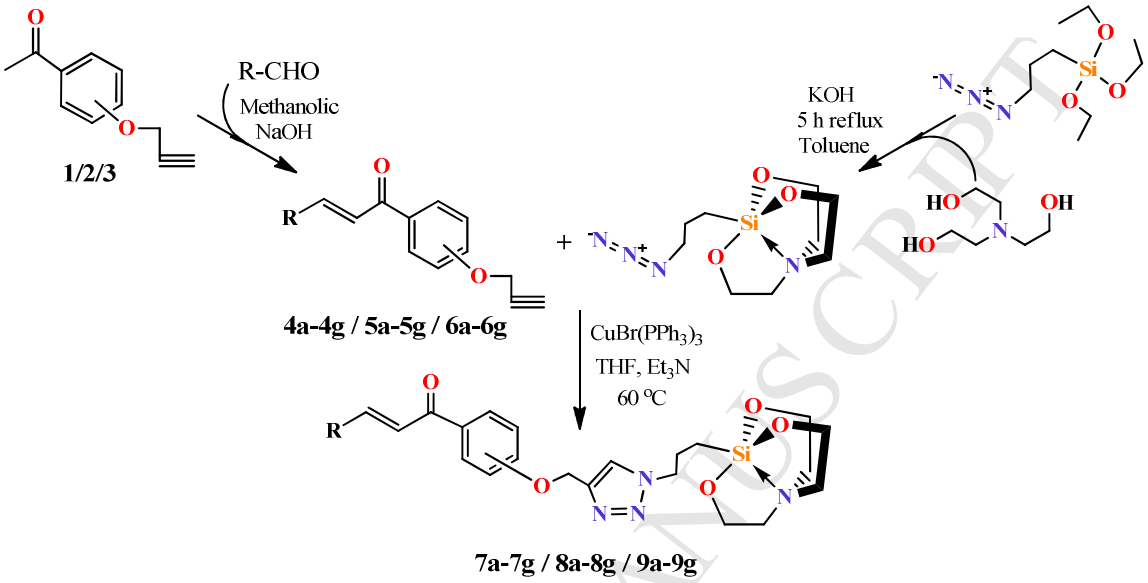


Fig. 7.

Scheme Caption

Scheme 1. Synthetic approach for the synthesis of chalcone substituted triazole allied orgaosilatranes.



Scheme 1.

Research Highlights

- A series of chalconyl blended triazole allied organosilatranes was synthesised.
- The hybrid molecules are passed through the computer based screening of their physicochemical properties.
- All the organosilatranes are investigated for their antigiardial and antitrichomonal activities.
- **9e** and **7e** were found to be most significant against *G. lamblia* and *T. vaginalis* respectively.
- Evaluated for their in vitro cytotoxicity against Hek-293 and HeLa cells.