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Conjugation reactions of hybrid organosilanes for nanoparticle and surface modifications

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ABSTRACT

Hybrid Molecules with incorporation of heteroatoms and different domains and properties could be achieved by the use of Silanes, Organosilanes, and chemically functionalized Organosilanes. These chemical agents are versatile reagents that could be covalent linked to other types of molecules such Organics by covalent and non-covalent linking. In this way, in this Research communications was summarized and discussed the use of a set of modified Organosilanes based on different experimental reactions for targeted objectives. Different conjugation reactions were involucrated based on optimized current Organic chemical reactions. By this manner, it was showed the chemical modifications of Organosilanes with Fluorescent dye reporters. As example, it was afforded the use of these bi-functional chemical species, with hydrolysable hetero-atom bonds accompanied with Laser dyes sensitizer properties. Thus, it was showed their applications for design and synthesis of Nanoparticle s and chemical surface modifications.

Keywords: Laser dye reporters, Organosilanes, Bioconjugation, conjugation reactions, Covalent and non-covalent bonding.

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Introduction

Silicon as the second most abundant element on earth after oxygen with a similar electronic configuration as Carbon (Smith, 1972) showed to be largely used and developed in Chemistry by Silane compounds and derivatives (Petkowski, 2020). From these groups of compounds then it was developed modified Silanes such as Organosilanes (Thames, 1996) that today are as well applied in a huge number of studies and developments within Chemistry, Biochemistry, Nano-technology, Biotechnology, etc. For example, Organosilanes showed a high impact on Polymerization reactions with incorporation of different types of molecules (Tau, 2011), Bio-molecules, formation of porous structures (Maria Chong, 2004), and Functionalities (Liu, 2018). Moreover, the capability to polymerize lead to the formation from variable small chemical oligomeric structures, to modified Polymers that in controlled conditions formed Nanoparticles (Ab Rahman, 2012 and Fernandes, 2019).

In similar manner, Organosilanes were applied for Chemical surface modifications (Brehm, 2020) that leaded to further Chemical functionalization for different types of studies and applications (Nejhad, 2015). In this way, in literature it could be found a lot of studies and developments with the use of Organosilanes that in combination of other types of reactions could generate functional materials with a wide view of uses, interests and applications depending of the modifications achieved.

Thus, it was afforded the use of Organosilanes, and modified Organosilanes for Hibrid Organic and Inorganic Nanomaterials synthesis with incorporation of Fluorescent Laser dyes. In this manner, based in designs and synthesis reported by us as well from other authors it was showed the versatility of these Luminescent Nanomaterials. In this context, it was discussed the main Organic chemical reactions used for covalent linking and Bioconjugation in the design of Nanomaterials and functional modified surfaces.

Classical conjugations reactions based organic chemistry

There are a larger types reactions that it could be applied for covalent bonding; however not so many within aqueous solutions and Colloidal dispersions. The reactions should be compatible as well for the targeted applications. In this way, as for example for Bio-applications it is highly desired biocompatible conditions to avoid problems in their use. Thus, within these groups of reactions, there are many types of reactions developed in variable polar media, with organic, aqueous and mixed solvents. For example there were many chemical reactions based on differences in the electronic densities of heteroatoms and Organic functional groups. In this manner, nucleophilic reactions by the use of nucleophiles such amines, thiols, hydroxyls groups in presence of organic groups with electronic deficiencies showed covalent bonding between heteroatoms (Fig 1a). By this manner, as for example alkoxides could lead to oxidation as well as to nucleophilic reactions depending of the conditions. Thus, by as for example with activated carboxylic groups with the right esters formations or similar could be easily replaced by other nucleophiles with variables secondary chemical structures (Fig. 1b). By this manner, it could be mentioned the carboxylic activation with *N*-Hydroxysuccinimide (Knight, 2001) in aqueous media, the *EDC*(1-ethyl-3-(3-dimethylaminopropyl) carbodiimide) in intermediate solvent polarities or mixed solvents with a high reactivity for inter-cross linking (Kumar, 2016); and the use of N, N′-Dicyclohexylcarbodiimide (*DCC*/DCCD) in apolar solvents (Albert, 2017).

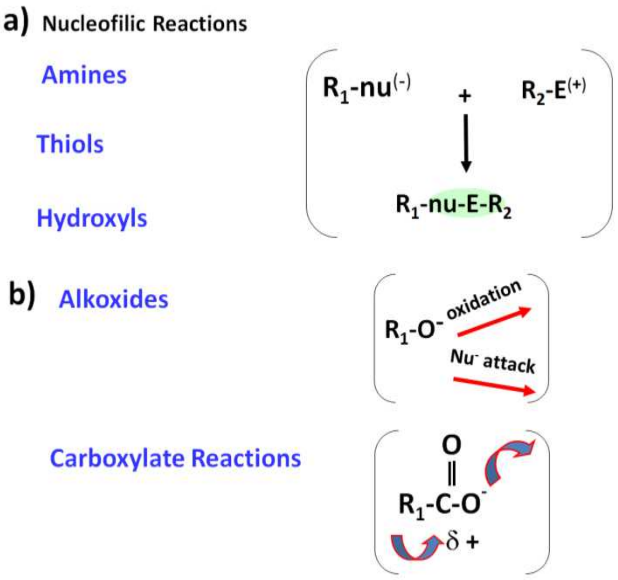

Fig 1. Scheme of conjugation reaction by covalent bonding: a) by Nucleophilic reactions with varied types of nucleophiles such as Amines, Thiols, Hydroxyl groups; b) further reactions occurred by alkoxides and carboxylic groups.

All the mentioned reagents activated carboxylic groups lowering the Energy of activation of the concerted nucleophilic attack and leaving group in a Substitution Nucleophilic reaction 2 or SN2 (McMurry, 1992).

With just only this example, it could be designed homo-functional, or bi-functional linkers cite formed by variable short molecular spacers cite, and polymeric chains cite that could be chemically modified or inter-crossed with varied reactive agents for targeted reactions involucrated. In this way it could be noted as example; the use of functionalized PEGylated chains; modified hydrocarbons, modified benzene rings, modified lipids, and functional oligomers (Smith, 2005). In addition to the mentioned nucleophiles it could be used di-thianes (Yus, 2003), di-thiols, thio-amines, etc. In similar manner, other types of strong non-covalent interactions such as adamantane with cyclodextrins macrocycles (Weber and Ohlendorf, 1989) and Biotin-Streptavidin (Chivers, 2011). Interactions could be applied to graft or link chemical structures. Other types of reactions such click chemistry could be developed as well with potential uses in design of new drugs, materials and Nanotechnology (Ha, 2019).

Modified Organosilanes

Actually there are many Nanomaterials in current development; where the chemical manipulation from atomic towards higher sized structures is main challenge to afford targeted properties. However, for all the cases were required to achieve covalent and non-covalent bonds by the application of varied chemical reaction types such as the previous ones discussed. In this communication, it was of our interest to communicate some of the most used reactions to design and synthesize Optical Nanoplatforms for multiple applications as Nanotechnology, Biotechnology, Biophotonics and Life Sciences. Therefore, it was developed typical organic chemical reactions between Laser dyes with different functional groups and modified Organosilanes. As it is known, Laser dyes showed to be chemical structures with high Quantum Yields properties that could be affected for their media and close surrounding (Ghazya R, 2004). For this reason, the synthesis and controlled modification of their structures to improve emission efficiencies still being a challenge due to their high sensitivity to media modifications (Hua and Chung, 2016). In addition, their emitter properties could be joined to other ones within

Hybrid Nanomaterials and Metamaterials to design new Nano-emitters and Meta-fluorophores (Woehrstein, 2017) Thus, the use Silica based Nanomaterials provided excellent dielectric properties, optical transparent characteristics that could lead to variable design, study and fabricate devices of variable sizes from the Nano-, to Micro-scale (Soref, 1987). In this way, it should be noted the use of the Störber methodology by sol-gel synthesis for organo-modified silica nanoparticles (Rahman, 2011). However, due to the large application of Silanized materials; motivated to the development of new synthetic methodologies of Nanostructured Silica as well that it should be highlighted (Mcheik, 2018).

In this manner, new Luminescent emitters from the Nano-scale were designed from the molecular control of covalent bonding with the right Laser dyes (Rampazzo, 2017). For example, it was assayed by us the activation of the carboxylic group of Lasers dyes with NHS, EDC, with combination of both; and DCC to react with (3-Aminopropyl) trimethoxysilane (APS) to form fluorescent modified organosilanes (Fig. 2).

So, in controlled conditions it was added to single Organosilane Fluorescent properties. But, it should be mentioned the versatility of these reaction that could be achieved in different condition media depending of the activation agent such aqueous solutions with NHS, intermediate organic polar media for EDC as well as for EDC combined with NHS; and organic solvents with DCC. These were just only few examples that could be applied depending of external conditions required as for Nanotechnology or Life Sciences developments. Moreover, the combinations of reagents as NHS and EDC enhance the activation via the nucleophilic attack of the APS due to a faster kinetics of EDC reaction with the carboxylic group that activate the entrance of the NHS with a global faster and improved nucleophilic substitution of the amine group.

Other example, it was the use of bifunctional modified Laser dyes with Isocyanate groups to react with APS and other types of amined hydrocarbons and other chemical structures adding by this manner varied properties. Moreover the hydroxyls groups could form ester bonds modifying reagents and conditions used when it is need it (Figure 3).

The Isocyanate reactions were achieved in organic solvents; while ester formation in buffer aqueous solutions to obtain the targeted covalent bonds. In this manner, it could be added a Luminescent Laser dye emitter joined to a hydrolysable Organosilane. So, these types of chemical structures could be polymerized based on concerted SN2 reactions in acid and basic media (Fig. 4a). These reactions could be controlled kinetically and thermodynamically in order to control the stop of the reaction in 2 and 3 dimensions forming films, Nano-, and Micro-structures (Fig 4b). These varied structures are managed modifying organized media, concentrations, pH, etc. Therefore, it was achieved modified surfaces and reduced sized Silica Nanoparticles (Suteewong, 2012 and Ma, 2015).

For surface modifications, it could be used different modified Organosilanes such as with amine, isocyanate, hydroxyl, epoxy-, groups that could afford the chemical modification with Laser dyes, Biomolecules, Nanoparticles, Enzymes, Biostructures and further functionalization (Fig 5). It should be noted that the surface could be as for example on deposed metallic films, Nano-surfaces of Nanoparticles and Micro-particles. By this manner, it could be mentioned many developments as for example; patterning self-assembled monolayers with microcontact printing: for new Biosensing methodologies (Mrksich, 1995), Organosilane deposition for microfluidic application (Glass, 2011), Bio-assays for Biostructures and Endotoxins detections (Tinker-Kulberg, 2020); and Smart Molecular responsive surfaces (Siafaka, 2016).

Hybrid Organic and Inorganic Nanocomposites

It is of high interest the creation of new Hybrid Nanocomposites joining Organic and Inorganic materials with an accurate control of sizes, lengths molecular positions, within the Nanoscale, below and beyond for the study of new matter properties from their interactions. From literature, Organosilanes with their capability to be modified by different Organic reactions and strategies could afford to target Functionalities. For example based on Bioconjugates technique with the incorporation of organic chemical reactions Silica cargo loaded Nanoparticles for Drug Delivery were reported (Werengowska-Ciećwierz, 2015). But, Silica not only showed the capability of 3D chemical structure formation; as well it permitted the modification of Nano-surfaces within Colloidal dispersion for Bioconjugation and functionalization (Sperling, 2010).

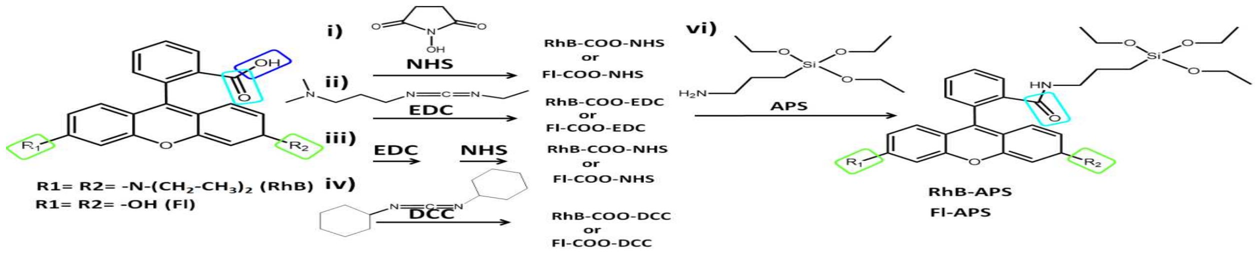

Fig 2.Scheme of conjugation reaction of Laser dyes based on Xanthene derivatives by activation of the carboxylic group for nucleophilic reaction with Aminopropyltriethoxysilane (APS).

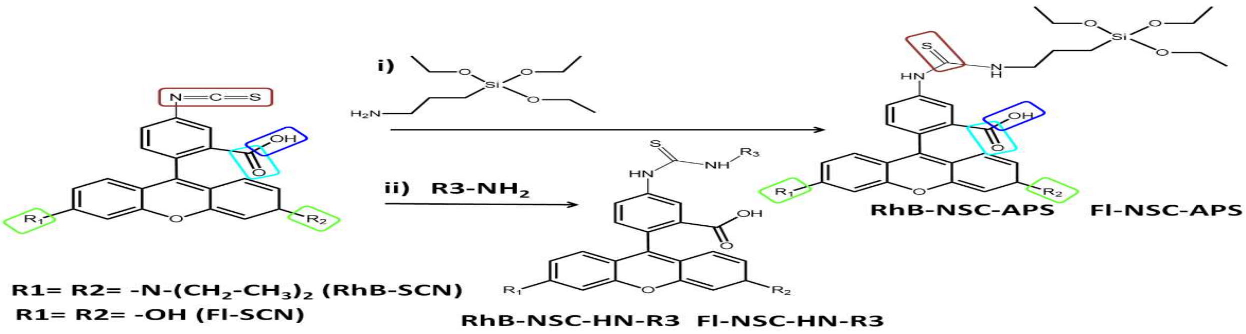

Fig 3. Scheme of conjugation reaction of Laser dyes based on Xanthene by nucleophilic reaction between the Isothicyanate derivative and Aminopropyltriethoxysilane (APS).

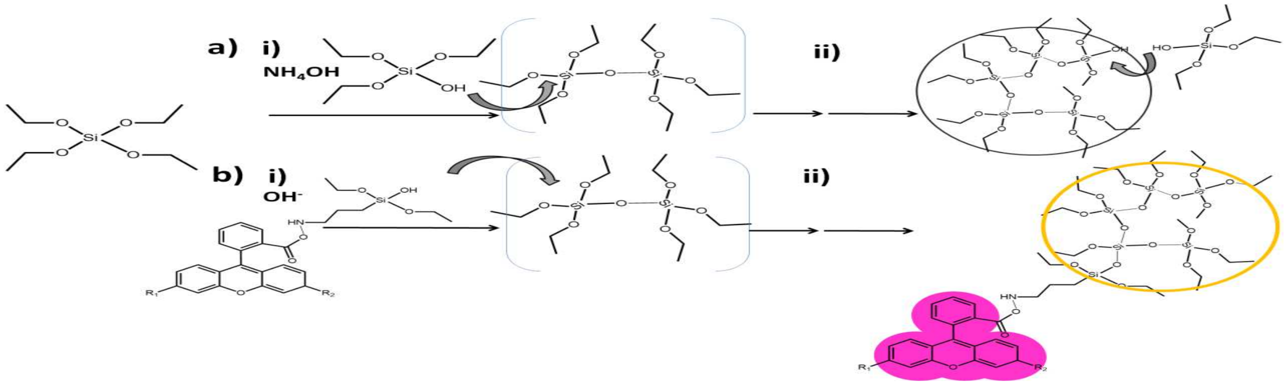

Fig. 4.Scheme of hydrolysis reactions of modified Organosilanes: a) Tetraethyl Orthosilicate (TEOS) in basic media; b) TEOS and APS conjugated with Laser dyes.

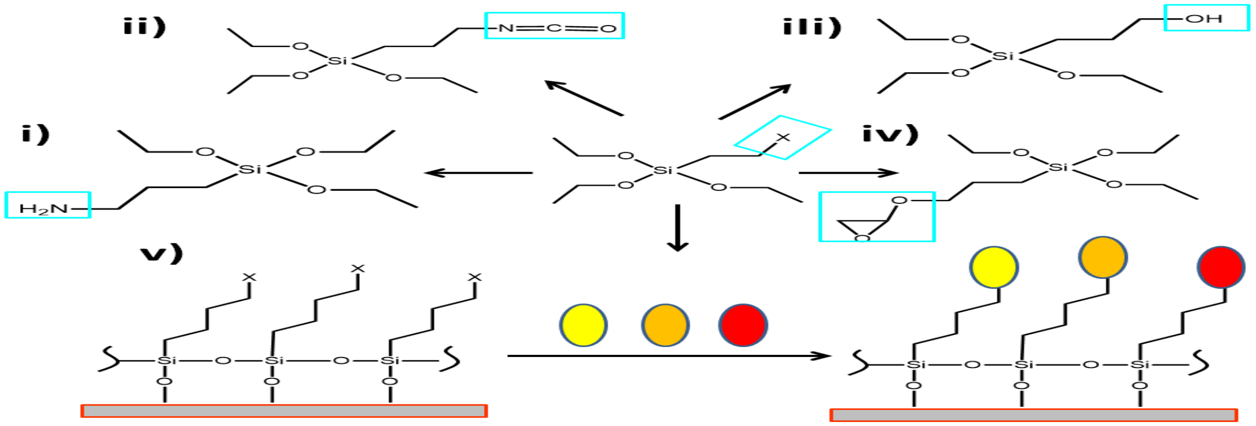

Fig. 5. Scheme of chemical versatility of modified Organosilaneswith different organic groups. Modified Tetraethyl Orthosilicate (TEOS) with *i)* amine groups, *ii)*Isothiocyanate group, *iii)* hydroxyls, *iv)* epoxies; and v) chemical surface modification by the use of modified Organosilanes and conjugation with other types of molecules such as Optical active structures (represented with coloured ovals).

In this way, it was developed grafted gold Nanoparticles with antibodies for ultrasensitive detection of 17β-estradiol (Pinto Oliveira, 2019); the application of click chemistry in nanoparticle modification and its targeted delivery (Yi, 2018); and Maleimide-Based thiolated Nanoparticleto Control Cellular Interactions (Lee, 2020). Moreover, it could be tuned the surface of Nanoparticles with Polyhedral Oligomeric Silsesquioxane Porphyrin Derivatives for targeted Photodynamic Therapy (Siano, 2020). And, it should be highlighted the control of the Nanoscale leading to new structures accompanied with potential functionalities such as porous Silica materials (Hong, 2020) obtained by modifying the media of reaction of the Organosilanes involucrated (Mishra, 2019). Actually, these versatile materials are available on the market with large chemical structure modifications ready to targeted new designs and properties developments. Thus, in the workflow the desired design and study is more accessible.

In this way the design and fabrication of Nano-tools such as Lab.-On-particles (Burns, 2006) is of high interest. In this Research field the Nano-Optics should be well developed based on varied material, Metamaterials by the right selection and tuning of Optical active Nanomaterials (Bracamonte, 2020). These optical properties could be joined to Optical active and non-active Biostructures developing by this manner new Nano-Bio-Optics platforms; which could be applied for the detection of Unicellular organisms, Virus towards Higher sized Biostructures, and Single cells (Ame, 2020). For these type of developments the Nano-scale control, composition, and Nano-surface modification, Bioconjugation, and functionalization is required. Therefore, in the different steps of synthesis it should control matter, and molecular compositions. For example, functional organic groups and molecules incorporated within Nanomaterials; such as quantification of amino groups on halloysite surfaces using the Fmoc-method (Fidecka, 2020); and Laser dyes incorporated within tuned silica Nanophotonic platforms based on fluorescence resonance energy transfer (FRET)(Salinas, 2020).

In these Nanoplatforms were incorporated variable Laser dyes in order to tune non-classical light emissions based on FRET. For these Nano-emitters was quantified the Laser dyes incorporation within a large varied concentrations from Nano-Molar to Micro-Molar interval. Different ways of emitter quantifications should be applied accurately in order to optimize emissions from single emitters to controlled inter-molecular dyes. For the quantification should be considered in the different steps of reactions, centrifugations and re-dispersions for cleaning (Fig. 6).

Thus, free dyes could be collected; and from the difference between the total concentrations added and unreacted free conjugated dyes were quantified. In this manner, as for example by Static Fluorescence could be prepared Calibration curves for the quantifications (Fig. 7). From the control of added Lasers dyes Enhanced Luminescent Nanoplatforms based on FRET for targeted non-classical light delivery applications were developed (Salinas, 2020).

The Luminescence emissions recorded from Single Nanoplatforms by Laser Fluorescence Microscopy, showed proportional intensities and variable wavelength intervals depending of concentrations added, related Quantum Yields, and activation of FRET phenomena. The Silica Nanoparticles obtained were well dispersible in Colloidal dispersion, and well spherical shapes defined (Fig. 8a). The Mono-coloured Silica Nanoplatforms with Rhodamine B (RhB) showed well defined Luminescent Nanoparticles (Figure 8.b); but by the use of Fluorescein (Fl) was augmented the emission intensity due to its higher Quantum Yield (Fig. 8c and 8d). However, by the addition of both Laser dyes Enhanced emissions non-explained by the sum of both individual contributions were collected (Fig 8e and 8f). Thus, it was controlled the non-classical emissions from well-defined Luminescent Nanoparticles towards higher emissions that generated bigger diameters accompanied with diminished photobleaching properties. Then, these Silica Nanoplatforms showed tide interactions with Bio-membranes such as Optical active Unicellular organisms based on non-covalent interactions. In this point it is important to note that polar interactions, hydrogen bridges; and additional interaction with particular Biomolecules of membranes are involucrated (Gammoudi, 2013). Therefore, sizes of Nanoparticles, chemical modification of Nanosurfaces and membranes compositions showed varied resolutions by Laser Fluorescence Microscopy. In addition, it should be contemplated additional non-classical light

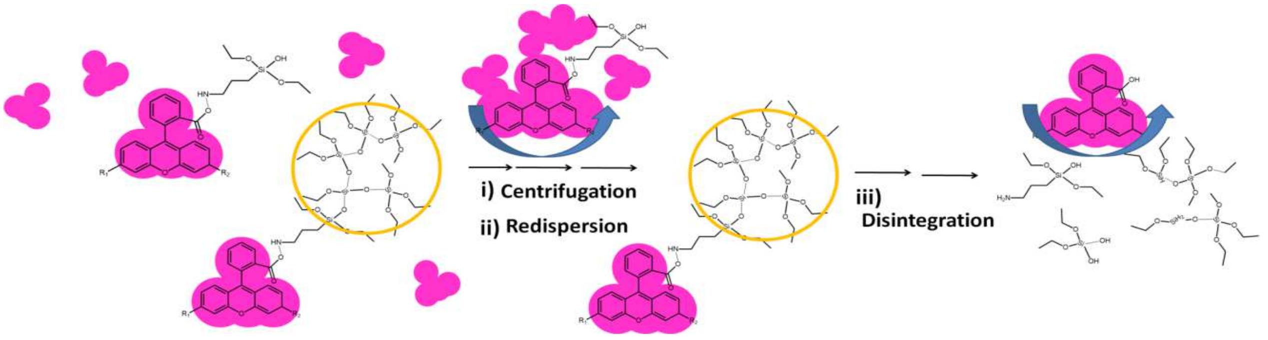

Fig. 6. Scheme of hydrolysis and polymerization of modified conjugated Tetraethyl Orthosilicate (TEOS) withAminopropyltriethoxysilane (APS) linked to Laser dyes, to form Luminescent Nanoarchitectures. Step i) centrifugation, ii) re-dispersion of the Nanoarchitectures obtained and collection of the supernatant with non-reactive APS-Laser dye, iii) disintegration of the Nanoarchitecture and collection of the incorporated APS-Laser dye by covalent linking.

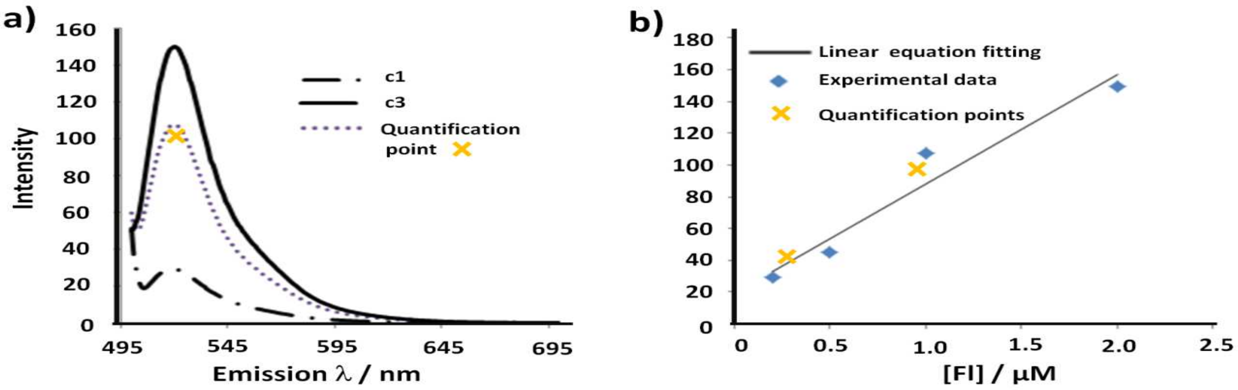

Fig 7. Quantification of APS-Laser dye incorporated within the Nanoarchitecture of Luminescent Nanoparticles: a) Fluorescence emissions of two calibration curve points made, and from the sample collected from the supernatant after conjugation; b) Representative calibration curve with quantification points at different levels of concentrations with highlighted yellow cross.

pathways and coupling phenomena depending of the Optical activity of the Biostructure and Nanoemitters used. By this manner, it was showed by us the targeted delivery of Synthetic non-classical luminescence by Enhanced Silica Nanophotonics on Cyanobacteria. Thus, it was generated Higher augmentations of Nano-Bio-luminescence based on Nano-Bio-FRET (Salinas, 2020) pathways. These additional increases were recorded by controlling the light delivered on targeted natural photo systems known as PS I and PS II. of Cyanobacteria (Yamazaki, 1984). Just to mention; the mentioned phenomena in volucrated are related with high impact Research related with Living Lasers (Meech, 2011), Biolasers (Gather, 2011), and new Laser Nano-Biostructures (Salinas, 2020); as well as for the development of new strategies of Single Molecule Detection (SMD) (Nie, 1994 and Veglia, 2019).

In addition, these Optical active Enhanced Luminescent Nanoplatforms were evaluated fordesign of Smart Opto-responsive substrates. In this way, the Multi-coloured Nano-emitters were deposed on modified silanized cover glass slides. The multi-deposition of the Nanoparticles controlling their colloidal dispersion concentrations permitted the controlled Multi-layered Nanoparticle depositions. In optimal conditions, it was possible to activate varied emissions by switching the Laser excitation wavelength; such as from 543.0 nm to optimally excite just only the Fluorescence Energy acceptor (Fig. 9a); while by 488.0 nm excitation the Fluorescence Energy donor (Fig. 9b). Thus, it was showed the coupled FRET pathways that generated substrates with improved materials properties such as; i) higher emission intensities; ii) larger Ultraluminescent surfaces; iii) wider transmission of non-classical light across the modified substrate within the micrometer scale; and iv) absence of photobleaching properties. It should be noted that these Nanostructured surfaces could afford to further chemical modifications for functionalization and 3D hierarchical bottoms up fabrications (Kumar, 2017).

So, it was showed how from the molecular covalent bonding with functional building blocks as Organosilanes could be designed versatile Nanoplatforms with potential implications in Nanotechnology and Functional devices.

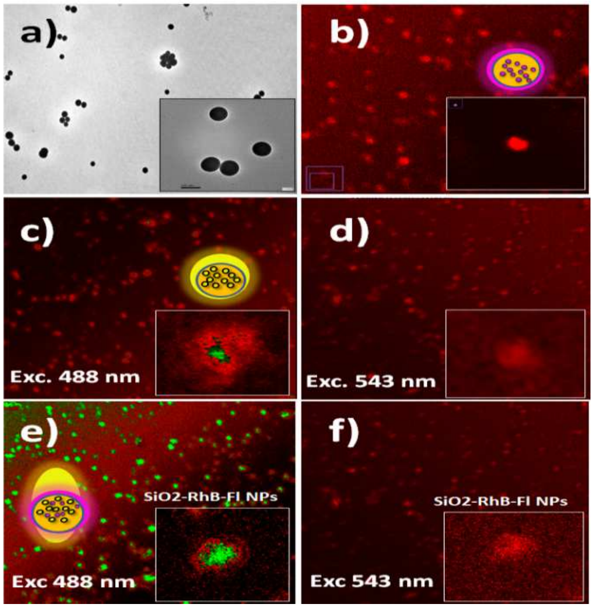

Fig 8. Nanoimaging of Luminescent Nanoparticles based on conjugated Tetraethyl Orthosilicate (TEOS) with Aminopropyltriethoxysilane (APS) linked to varied Laser dyes: a) representatite TEM image of Nanoparticles obtained. Inset image corresponded to 250 nm Nanoparticle diameters; b) Laser Fluorescence Microscopy (LFM) of Mono-coloured Nanoparticles by incorporation of Rhodamine B (RhB) as Laser dye. Laser excitation at 543.0 nm; c) and d) LFM of Mono-coloured Nanoparticles by incorporation of Fluorescein (Fl).Laser excitation at 488.0 nm and 543.0 nm respectively; e) and f) LFM of Multi-coloured Nanoparticles by incorporation of RhB and Fl as Fluorescence Energy Transfer (FRET) pairs.Laser excitation at 488.0 nm and 543.0 nm respectively.

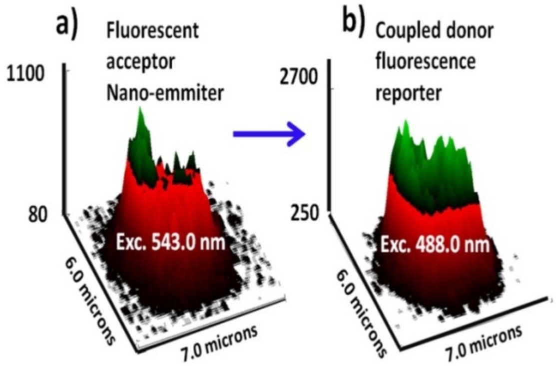

Fig 9. 3D fluorescence surfaces from deposed multi-colored nanoparticles on silica substrates: a) with only optimal excitationof Rh Basafluorescent energyacceptorat 543nm and b) only optimal excitation of Flasa fluorescent energy donor at 488 nm and coupling with RhB as a fluorescent energy acceptorvia FRET.

Conclusion

In this communication it was introduced some of the most used organic chemical reactions for covalent bonding of different fundamental molecular building blocks. Thus, controlled properties were generated by joining Laser Fluorescent dyes and polymerizable modified Organosilanes. In this context, it was discussed the applications of classical conjugations and Bioconjugations reactions based organic chemistry using variable solvents and chemical reagents that afforded to develop covalent bonding in different media depending of needs. Moreover, it was showed and discussed the versatility of the modified Organosilanes for different types of reactions. Therefore, it was permitted the modification of larger surface and substrate modifications, as well as to Nano-surfaces applications.

In addition, the chemical precursors obtained permitted the synthesis and design of controlled Luminescence emissions from Silica Nanoplatforms. In this manner it was developed Enhanced Luminescence based on FRET, and Bio-FRET controlling the Energy transference by Laser excitation.

Finally, it should be mentioned that further potential uses and applications could be developed by joining their molecular building block properties on varied Nano-matter composition and patterned surfaces to design new Opto-active Nanoplatforms and Organized systems. By this manner it could be mentioned Light responsive DNA detection (Brouard, 2011) by coupling FRET signaling with Metal Enhanced Fluorescence (MEF)(Brouard, 2013) based on modified silver Cores templates. Moreover, these strategies could be extended to hybrid Organic/Inorganic organized systems by FRET signaling (Gruber, 2010) as well for the detection of peptides related with thrombin and blood coagulation (Muller, 2014). So, there is high potential for the design of versatile and Functional surfaces and Nanoplatforms.

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Reference

Albert JS, Hamilton AD, Hart AC, Feng X, Lin L and Wang Z (2017). 1,3-Dicyclohexylcarbodiimide, EEROS, 1–9. doi:10.1002/047084289X.rd146.pub3

Ame M and Bracamonte AG (2020). Advances in Nano-Bio-Optics: detection from Virus towards Higher sized Biostructures, Frontiers Drug Chem.y Clinical Res., 3: 1-7. doi: 10.15761/FDCCR.1000148

Bracamonte AG (2020). New Matter Properties and Applications based on Hybrid Graphene-based Metamaterials, Special Issue: Design and Synthesis of Graphene based Metamaterials, Current Graphene Science, Bentham Sci. Pub., 4: 1-4.

Brehm M, Scheiger JM, Welle A and Levkin PA (2020). Reversible Surface Wettability by Silanization, Adv. Mater. Interfaces, 7 (1902134): 1-8.

Brouard D, Lessard VM, Bracamonte AG and Boudreau D (2011). Label-free biosensing based on multilayer fluorescent nanocomposites and a cationic polymeric transducer., ACS Nano, 5: 1888-1896.

Brouard D, Ratelle O, Bracamonte AG, St-Louis M and Boudreau D (2013). Direct molecular detection of SRY gene from unamplified genomic DNA by metal-enhanced fluorescence and FRET, Analytical Methods, 5: 6896 - 6899.

Burns A, Ow H and Wiesner U (2006). Fluorescent core–shell silica nanoparticles: towards "Lab on a Particle" architectures for nanobiotechnology, Chem. Soc. Rev., 35: 1028-1042.

Chivers CE, Koner AL and Lowe ED (2011). Howarth M, How the biotin–streptavidin interaction was made even stronger: investigation via crystallography and a chimaeric tetramer, Biochem J, 435(1): 55–63.

Fernandes RS, Raimundo Jr IM and Pimente MF (2019). Revising the synthesis of Stöber silica nanoparticles: A multivariate assessment study on the effects of reaction parameters on the particle size, Colloids and Surfaces A, 577: 107-109.

Fidecka K, Giacoboni J, Picconi P, Vago R and Licandro E (2020). Quantification of amino groups on halloysite surfaces using the Fmoc-method, RSC Adv., 10: 13944-13948.

Gammoudi I, Rokhaya FN, Moroté F, Moynet D, Grauby-Heywang C and Cohen-Bouhacina T (2013). Characterization of Silica Nanoparticles in Interaction with Escherichia coli Bacteria, International Journal of Chemical, Molecular, Nuclear, Materials and Metallurgical Engineering, 7(7): 520-526.

Gather MC and Yun SH (2011). Single cell biological lasers, Nature Photonics, 5: 406-410.

Ghazya R, Azimb SA and Shaheena M (2004). El-Mekawey F, Experimental studies on the determination of the dipole moments of some different laser dyes, Spectrochimica Acta Part A, 60: 187–191.

Glass NR, Tjeung R, Chan P, Yeo LY and Friend JR (2011). Organosilane deposition for microfluidic application, BIOMICROFLUIDICS 5, 036501: 1-7.

Gruber B, Stadlbauer S, Spath A, Weiss S, Kalinina M and Konig B (2010). Modular Chemosensors from Self-Assembled Vesicle Membranes with Amphiphilic Binding Sites and Reporter Dyes, Angew. Chem. Int. Ed., 49: 7125–7128.

Ha SYY, Wong RCH, Wong CTT and Ng DKP (2019). An integrin-targeting glutathione-activated zinc(II) phthalocyanine for dual targeted photodynamic therapy. Eur. J. Med. Chem., 174:56–65.

Hong X, Zhong X, Du G, Hou Y, Zhang Y, Zhang Z, Gong T, Zhang L and Sun X (2020). The pore size of mesoporous silica nanoparticles regulates their antigen delivery efficiency, Sci. Adv. 6 (eaaz4462): 1-13.

Hua Chung P, Tregidgo C and Suhling K (2016) Determining a fluorophore's transition dipole moment from fluorescence lifetime measurements in solvents of varying refractive index, Methods Appl. Fluoresc. 4 (045001): 1-10.

Jurand PJ, Bains W and Seager S (2020). On the Potential of Silicon as a Building Block for Life, Life, 10(84):1-47.

Knight DW (2001). Encyclopedia of Reagents for Organic Synthesis, *N*-Hydroxysuccinimide, 1-3. https://doi.org/10.1002/047084289X.rh069

Kumar S, Bhushan P and Bhattacharya S (2017). Fabrication of Nanostructures with Bottom-up Approach and Their Utility in Diagnostics, Therapeutics, and Others, In: Bhattacharya S., Agarwal A., Chanda N., Pandey A., Sen A. (eds) Environmental, Chemical and Medical Sensors. Energy, Environment, and Sustainability.Springer, Singapore. https://doi.org/10.1007/978-981-10-7751-7_8

Kumar S, Raj S, Sarkar K and Chatterjee K (2016). Engineering a multi-biofunctional composite using poly (ethylenimine) decorated graphene oxide for bone tissue regeneration, Nanoscale**,** 8: 6820-6836.

Lee JC, Donahue ND, Mao AS, Karim A, Komarneni M, Thomas EE, Francek ER, Yang W and Wilhelm S (2020). Exploring Maleimide-Based Nanoparticle Surface Engineering to Control Cellular Interactions, ACS Appl. Nano Mater., 3 (3): 2421–2429.

Liu J**,** Ren J, Xie Z, Guan B, Wang J, Ikeda T and Jiang L (2018). Multi-functional organosilane-polymerized carbon dot inverse opals, Nanoscale, 10: 4642-4649.

Ma K, Mendoza C, Hanson M, Werner-ZwanzigerU, Zwanziger J and Wiesner U (2015). Control of Ultrasmall Sub-10 nm Ligand-Functionalized Fluorescent Core−Shell Silica Nanoparticle Growth in Water, Chem. Mater. 27: 4119−4133.

Maria Chong AS, Zhao XS and Qiao SZ (2004). Functionalization of large-pore mesoporous silicas with organosilanes by direct synthesis, Microporous and Mesoporous Materials, 72 (1–3): 33-42.

Mcheik A, Jacques L, Gibaud A, Berthie S and Lopez PJ (2018). Optical Properties of Nanostructured Silica Structures From Marine Organisms, Frontiers in Marine Science, 5 (123): 1-11.

McMurry JE (1992). Organic Chemistry (3rd ed.), Belmont: Wadsworth, ISBN0-534-16218-5

Meech S (2011). Biophotonics. Living lasers, Nature Photonics, 5:387–388.

Mishra R, Militky J and Venkataraman M (2019). 7 - Nanoporous materials, Nanotechnology in Textiles, Theory and Application, The Textile Institute Book Series, 311-353.

Mrksich M and Whitesides G M (1995). Patterning self-assembled monolayers using microcontact printing: a new technology for biosensors, TibTech, Elesevier, 13:228-235.

Muller A and Konig B (2014). Vesicular aptasensor for the detection of thrombin, Chem. Commun., 50: 12665-12668.

Nejhad MNG (2015). Multifunctional hierarchical nanocomposite laminates for automotive/aerospace applications, Multifunctionality of Polymer Composites, Challenges and New Solutions, 491-526.

Nie S, Chiu DT and Zare RN (1994). Probing individual molecules with confocal fluorescence microscopy, Science, 266 (5187): 1018-1021.

Pinto Oliveira J, Ribeiro Prado A, Juvencio Keijok W, Wagnner Pereira Antunes P, Ronald Yapuchura E and Cunegundes Guimarães MC (2019). Impact of conjugation strategies for targeting of antibodies in gold nanoparticles for ultrasensitive detection of 17β-estradiol, Scientific Reports, 9(13859): 1-8.

Rahman IA and Padavettan V (2012). Synthesis of Silica Nanoparticles by Sol-Gel: Size-Dependent Properties, Surface Modification, and Applications in Silica-Polymer Nanocomposites—A Review**.** Journal of Nanomaterials, 2012 (132424):1-15 doi:10.1155/2012/132424

Rahman IA, Jafarzadeh M, and Sipaut CS (2011). Physical and optical properties of organo-modified silica nanoparticles prepared by sol–gel. J Sol-Gel SciTechnol, 59**:** 63–72 https://doi.org/10.1007/s10971-011-2464-1

Rampazzo E, Prodi L, Petrizza L and Zaccheron N (2017). Luminescent Silica Nanoparticles Featuring Collective Processes for Optical Imaging, Light-Responsive Nanostructured Systems for Applications in Nanomedicine. Part of the Topics in Current Chemistry book series, TOPCURRCHEM, Springer International, Publishing AG. Part of Springer Nature 370: 1-28.

Salinas C, Amé M and Bracamonte AG (2020). Tuning silica nanophotonics based on fluorescence resonance energy transfer for targeted non-classical light delivery applications, J. Nanophoton, 14(4) 046007:1-19. DOI: 10.1117/1.JNP.14.046007

Salinas C, Valeria Ame M and Bracamonte AG (2020). Synthetic non-classical luminescence generation by Enhanced Silica Nanophotonics based on Nano-Bio-FRET, RSC Advances, 10:20620 – 20637.

Siafaka PI, Ustundag ON, Karavas E and Bikiaris DN (2016). Surface Modified

Multifunctional and Stimuli Responsive Nanoparticles for Drug Targeting: Current Status and Uses, Int. J. Mol. Sci., 17(1440): 1-40.

Siano P, Johnston A, Loman-Cortes P, Zhin Z and Vivero-Escoto JL (2020). Evaluation of Polyhedral Oligomeric Silsesquioxane Porphyrin Derivatives on Photodynamic Therapy, Molecules , 25(4965): 1-14.

Smith Andrew DK, Hirst R, Love CS, Hardy Sonia JG, Brignell V and Huang B (2005). Self-assembly using dendritic building blocks—towards controllable nanomaterials, Progress in Polymer Science, 30(3–4): 220-293.

Smith JD (1972). The chemistry of silicon. Science Progress, JSTOR, 60 (238):189-204.

Soref R and Bennett B (1987). Electrooptical Effects in Silicon, IEEE Journal of Quantum Electronics, 23(1): 123-129. doi:10.1109/JQE.1987.1073206

Sperling RA, and Parak WJ (2010). Surface modification, functionalization and bioconjugation of colloidal Inorganic nanoparticles, Philosophical Transactions of The Royal Society A Mathematical Physical and Engineering Sciences, 368, 1915: 1333-1383.

Suteewong T, Sai H, Bradbury M, Estroff LA, Gruner SM and Ulrich Wiesne (2012). Synthesis and formation mechanism of aminated mesoporous Silica Nanoparticles, Chem. Mater., 24: 3895−3905.

Tau TW, Chang, Smith RC, Regens CS, Bailey AD, Werner NS and Denmark SE (2011). Cross-Coupling with Organosilicon Compounds, Organic Reactions, Wiley, 1-10. doi.org/10.1002/0471264180.or075.03.

Thames SF and Panjnani KG (1996). Organosilane polymer chemistry: A review, Journal of Inorganic and Organometallic Polymers, 6: 59–94.

Tinker-Kulberg R, Dellinger K, Brady TE, Robertson L, Levy JH, Abood SK, LaDuca FM, Kepley CL and Dellinger AL (2020). Horseshoe Crab Aquaculture as a sustainable endotoxin testing source, Frontiers in Marine Science, 7 (153): 1-13.

Veglia AV and Bracamonte AG (2019). β-Cyclodextrin grafted gold nanoparticles with short molecular spacers applied for nanosensors based on plasmonic effects, Microchem J., 148: 277-284

Weber PC, Ohlendorf D, Wendoloski HJJ and Saleme FR (1989). Structural origins of high affinity Biotin binding to streptavidin, Science, 243: 85-88.

Werengowska-Ciećwierz K, Wiśniewski M, Terzyk AP and Furmaniak S (2015). The Chemistry of Bioconjugation in Nanoparticles-Based Drug Delivery System, Advances in Condensed Matter Physics, Hindawi Publishing Corporation, 198175 (2015):1-27. https://doi.org/10.1155/2015/198175

Woehrstein JB, Strauss MT, Ong LL, Wei B, Zhang DY, Jungmann R and Yin P (2017). Sub-100 nm metafluorophores with digitally tunable optical properties self-assembled from DNA, Sci. Adv. 3 (e1602128):1-12.

Yamazaki I, Mimuro M, Murao T, Yamazaki T, Yoshihara K and Fujita Y (1984). Excitation energy transfer in the light harvesting antenna system of the red alga Porphyridium cruenturn and the blue-green alga Anacystisnidulans: Analysis of time-resolved fluoresc- ence spectra. Photochem. Photobiol. 39: 233-240.

Yi G, Son J, Yoo J, Park C and Koo H (2018). Application of click chemistry in nanoparticle modification and its targeted delivery, Biomaterials Research, 22(13): 1-8.

Yus M, Najera C and Foubelo F (2003). The role of 1,3-dithianes in natural product synthesis, Tetrahedron, 59 (33): 6147-6212.

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