Institution: The Open University (OU)		
Unit of Assessment: B12 Engineering		
Title of case study: Improving purity, reproducibility and mass production of organosilicon compounds and related materials for Industry		
Period when the underpinning research was undertaken: 2000-2020		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s):	**Role(s) (e.g. job title):**	**Period(s) employed by submitting HEI:**
Prof Peter Taylor	Professor of Organic Chemistry	1978-2019
Dr James Bruce	Senior Lecturer	2001- present
Prof Alan Bassindale	Professor of Organometallic Chemistry	1976 – 2017
Dr Simon Collinson	Senior Lecturer	2014 - present
Period when the claimed impact occurred: 2014-2020		
Is this case study continued from a case study submitted in 2014? N		

1. Summary of the impact

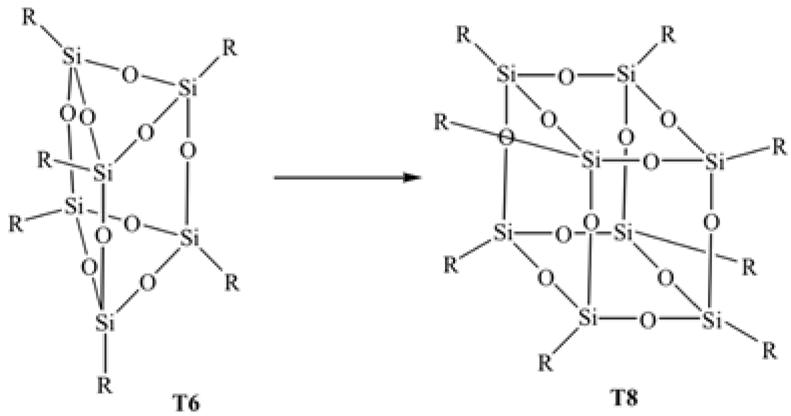
Organosilicon compounds contain carbon–silicon bonds whose properties, including stability, water repellent abilities, and colourlessness make them widely used in commercial applications. OU research has resulted in new organosilicon compounds for industry using new routes, in high purity, on large scale and reproducibly. One of the high performance liquid chromatography (HPLC) columns produced as part of a knowledge transfer protocol (KTP) with Hichrom has been selected by the U.S.A Food and Drug Administration (FDA) as an official FDA analytical protocol, because of its unique selectivity, reliability and reproducibility. This is used to test the purity of a commonly used over the counter drug – Zantac, to reduce risk of carcinogenic impurities and enable sales of the drug. Hichrom has only been able to do this as a result of OU research, and sold around 22,000 columns with income over GBP12,000,000. This subsequently led to a development of new products with chemicals company Cornelius Specialities, road markings specialists WJ Group, technology membership organisation TWI and global chemicals company Johnson Matthey.

2. Underpinning research

A group at the Open University has been undertaking research in Organosilicon chemistry for over 40 years in a range of areas, including mechanistic and hypervalent silicon chemistry, biological silicon chemistry, synthetic organosilicon chemistry and the synthesis and properties of silsesquioxane cages (silicon-oxygen colourless solids with polymeric structures). The key area of underpinning work related to the impact in the REF period has been the synthesis of organosilicon compounds selectively, in high purity, reproducibly and potentially on a large scale.

The organosilicon chemistry developed by the OU group in an academic context can be used to solve a range of specific problems within Industry. Companies have come to the OU to investigate specific problems outside the academic research but with relevant applications. The element silicon is a semimetal and when combined with carbon forms organosilicon compounds. The presence of the silicon atom in the organosilicon compounds leads to unique physical and chemical properties for example, organosilicon compounds (e.g. silicones) are used in applications ranging from bath sealants to cupcake trays, as well as body implants, sealants, adhesives, lubricants, personal care products (Methicone) and contact lens additives. Their unique chemical reactivity has led to a separate field of study and OU organosilicon chemists have a deep understanding of how these compounds behave chemically and can thus synthesise new organosilicon compounds in high yield and purity. The OU group are world leaders in organosilicon chemistry and have used their knowledge to produce a new class of compound known as silsequioxanes researched hypervalent silicon compounds and developed new chemical transformations using organosilicon compounds. Armed with this unique knowledge of how to make and use organosilicon compounds, the OU group have been able to help a large number of companies develop their products.

For example, one of the key intermediates industry has been interested in are trialkoxysilanes, that are often used to coat silica particles. These are the types of compounds used to make the HPLC columns described in the impact statement. Expertise in making such compounds has been developed though making a wide range of trialkoxysilanes for the synthesis of silsesquioxane cages, regular three-dimensional structures such as cubes and prisms made out of R-Si(O-)$_3$ units as shown below **[O1, O2]**:



The OU researchers developed a simple route to these compounds from trialkoxysilanes (RSi(OEt)$_3$) using tetrabutyl ammonium fluoride **[O2]**. The pendant R groups provide the materials with a range of properties such as liquid crystals, metal complexing and protein binding **[O3]**. So, in order to make a wide range of different silsesquioxanes the OU group have had to develop a wide range of routes to trialkoxysilanes which can be very water sensitive. Synthesising a new trialkoxysilane requires careful planning through a knowledge of the way these organosilicon compounds react, what to avoid, how to maximise the yield and how to purify the products. For example, one of the key reactions used is known as hydrolsilylation which requires a platinum catalyst. Knowing which type of platinum catalyst to use, which solvent and the reaction conditions is essential to ensure high yields and purity **[O6]**. The OU group have developed a toolbox of key reactions used to synthesise trialkoxysilanes with a wide range of R groups, in the high purity required for the synthesis of silsesquioxanes, which also has wide application in industry. The OU team supplied the characterisation of new materials and analysed their properties on instrumentation not available at the companies. Feedback of this data further improved the synthesis and the properties of these novel materials.

The team have gone on to synthesise and characterise a new class of compound where a fluoride ion is trapped in the centre of the cage **[O4]**. Again, they have had to synthesise different alkoxysilanes, this time with electron withdrawing groups, which provided new insights into the way alkoxysilanes are made, handled and reacted **[O5]**.

As part of the research into hypervalent silicon compounds and organosilicon compounds in organic synthesis, the researchers have had to carry out other types of reaction such as hydrosilylation, Suzuki coupling and organolithium and Grignard methodologies **[O6]**. The expertise in using these reactions to make organosilicon compounds was the basis of KTPs with three different companies, albeit with very different target compounds. For example, whilst Hichrom were focussed on trialkoxysilanes, Cornelius Specialities wanted routes to organosilicon intermediates for use in the contact lens and personal care industries. This led to a toolbox of reactions, based on couplings and organometallics that we had developed as part of our research, which Cornelius Specialities could use to make their targets. WJ needed our methodology and expertise to develop new alterative materials for road marking.

3. References to the research

O1. **A R Bassindale**, I A MacKinnon, M G Maesano and **P G Taylor** (2003) The Preparation of Hexasilsesquioxane (T$_6$) cages by "Non Aqueous" Hydrolysis of Trichlorosilanes, *Chem. Commun*., 1382-1383 ISSN 1359-7345. https://doi.org/10.1039/b302556j. Blind peer reviewed.

O2. **A R Bassindale**, Z Liu, I A MacKinnon, **P G Taylor**, Y Yang, M E Light, P N Horton and M B Hursthouse (2003) A higher yielding route for T_8 silsesquioxane cages and X-ray crystal structures of some novel spherosilicates, *J. Chem. Soc., Dalton Trans.*, 2945-2949 ISSN 1477-9226. https://doi.org/10.1039/b302950f. Blind peer reviewed.

O3. **Bruce, J**., O'Connell, Patrick J.; **Taylor, P G**.; Smith, David P.T.; Adkin, Roy C. and Pearson, Victoria K. (2020) Synthesis of Organosilicon Ligands for Europium (III) and Gadolinium (III) as Potential Imaging Agents. *Molecules*, 25(18) e4253. https://doi.org/10.3390/molecules25184253. Blind peer reviewed.

O4. **P. G. Taylor**, **A. R. Bassindale**, Y. El Aziz, M. Pourny, M. Hursthouse and S. J.Coles (2012) Further studies of fluoride ion entrapment in octasilsesquioxane cages; X-ray crystal structure studies and factors that affect their formation, *J. Chem. Soc., Dalton Trans.*, 41(7), 2048–2059 ISSN 1477-9226. https://doi.org/10.1039/c1dt11340b. Blind peer reviewed.

O5. Y. El Aziz, **P. G. Taylor**, **A. R. Bassindale**, S. J. Coles and M. B. Pitak (2016) Synthesis and Structures of Novel Molecular Ionic Compounds Based on Encapsulation of Anions and Cations, *Organometallics*, 35 (24), 4004–4013 https://doi.org/10.1021/acs.organomet.6b00565. Blind peer reviewed.

O6. R. Panisch , **A. R. Bassindale**, A. A. Korlyukov, M. B. Pitak, S. J. Coles, and **P. G. Taylor** (2013) Selective Derivatization and Characterization of Bifunctional "Janus-type" Cyclotetrasiloxanes, Organometallics, 32 (6), 1732–1742. https://doi.org/10.1021/om301158w. Blind peer reviewed.

Other authors are PhD students, Post-Doctoral researchers, Industry collaborators, analysts providing expertise in X-Ray crystallography or colleagues from other Universities providing biological expertise.

4. Details of the impact

OU research into the creation and function of organosilicon compounds has created benefit for chemicals companies supplying markets as diverse as pharmaceuticals, personal care, road markings and industrial consultancy for the offshore industry.

A collaboration with Hichrom, underpinned by this research, led to the development of High Performance Liquid Chromatography (HPLC) columns which are used to demonstrate the safety of the world's best-selling drug. Zantac, generically known as ranitidine, is one of the world's leading treatments of excess stomach acid production. In 2018 nearly 25 million prescriptions were written for ranitidine in the USA and Sanofi, who sell under brand name Zantac, made USD124,000,000 sales in the USA. In September 2019, the USA's Food and Drug Administration (FDA) became aware that an impurity present in some formulations known as *N*-nitrosodimethylamine (NDMA) had potential carcinogenic properties which led to the withdrawal of Zantac from the market **[C1]**. In order for pharmaceutical companies to reintroduce Zantac they needed to show that the levels of NDMA were low enough to reduce the risk of cancer.

The FDA developed a (HPLC) – Mass Spectrometry (MS) technique for the analysis of NDMA in ranitidine samples **[C2]**. This technique involves separating the individual compounds present in a sample and then analysing them. At the heart of the separation process is an HPLC column, a long column of very small silica particles coated with specific material that promotes the separation of the compounds in the sample. The column chosen by the FDA for their crucial analysis of ranitidine is the Ace C18-AR column which researchers at the OU created as part of a KTP with Hichrom **[C2,** line 22 of p.2 and **C3]**. The column was chosen by the FDA because of its remarkable properties, its stability and its reproducibility. Hichrom was able to produce this novel column as a result of the OU's expertise in synthesising new organosilicon compounds such as trialkoxysilanes that can be bound to the silica particles and in particular the method of making them in a very pure form, which can be reproduced on a large scale (with high yields) without dependence upon a single raw materials supplier **[O5, O6]**. This synthetic expertise has been developed over many years of making organosilicon compounds as a result of the research described in section 2.

Hichrom had an excellent record of manufacturing reliable and reproducible columns but in 2010 they lacked the expertise to be able to synthesise organosilicon compounds and had to rely on what was commercially available. They approached OU to enter a partnership to produce a new range of HPLC columns and create compounds that their competitors could not. First, they funded a Post-Doctoral worker for a year to work at the OU and this grew into a three-year KTP worth GBP200,000 (2010 – 2014), which was subsequently classified as outstanding by Innovate UK. The KTP's aim was to develop new columns that have orthogonal selectivity, that is they have different mechanisms for separating the materials, and thus together create a toolkit for analysis of any mixture. This was successful in that five new columns were produced **[C4]** and Hichrom have sold about 22,000 of these columns over the last six years **[C5**, p.1**]**. This has greatly increased in recent years at an average of GBP540 giving a sales value of over GBP12,000,000 **[C5,** p.2, **C6]**. The partnership between the OU and Hichrom has continued up to the present day and a Hichrom employee now works on synthesis within the OU group/laboratories. As the then CEO stated in the final KTP report "*new agile development techniques have speeded up the development of silanes from one every 20 months before the KTP to successfully commercialising 5 in three years*" **[C7,** p.9**]**. In addition, Hichrom's improved reputation for innovation and reliability has led to acquisition by VWR, part of Avantor **[C8]**.

The OU team's research on the synthesis of organosilicon compounds described in Section 2 also led to an approach from Cornelius Specialities. This involved a further KTP (2013 – 2017, ~GBP200,000) to develop a toolkit of reactions that could be used to manufacture intermediates on a large-scale for the contact lens industry **[C9]**. Again, the OU's unique experience of synthesising organosilicon compounds was used to target new, cheaper routes to existing intermediates and to create new compounds - specifically reliably and in high purity. The company reported that: "*our novel silicon chemistry toolkit […] enabled us to make a range of existing and new products in high yield and with high purity. Our methodology was specifically designed to ensure we were competitive with price as well*" **[C8**, p.4**]**. Having successfully developed a toolkit for contact lens intermediates, the OU team worked with Cornelius to target the personal care industry as an alternative client base: "*This has led to a greater understanding of how organosilicon compounds can add value to a range of products such as personal care which will lead to a greater and more varied use of organosilicon compounds in the future*" **[C8**, p.5**]**.

As a result of the new opportunities opened up through developing new compounds, "*Cornelius Specialties Ltd (CSL) is manoeuvring itself to exploit other market opportunities from silicone materials that it is now able to develop as a result of this partnership*" **[C8**, p.6**]**. The company therefore required additional space to exploit its Engineered Silcones potential and invested GBP240,000 in new plant and machinery **[C8**, p.10**]**.

The Welding Institute (TWI) is a contract research organization that works for and on behalf of over 700 industrial members in over 4,500 locations world-wide. TWI and OU have been working together on the development of super hydrophobic coatings, that is surfaces that repel water, based on silica nanoparticles with a specific organosilicon coating. OU and TWI have been focussing on how they can control their processes and produce coatings that are more reproducible with a range of properties. TWI's Technology Fellow noted: "*As a result, we gained an insight into how the experimental conditions determined the final structure and material properties of our materials and coatings and we able to increase their hydrophobicity as a result. We were able to go further and apply the expertise developed in the partnership to control the synthesis of silica-based nanoparticles. This allowed us to control both the size and the surface of the nanoparticles which allows us to influence their material properties and more significantly incorporate the nanoparticles into some of our existing coating materials"* [**C9**]. The partnership with the OU continues to exploit the advances made in synthesising nanoparticles which are being applied to a new project funded by TWI. This applies the new knowledge to make composite materials recyclable through using nanoparticles to control the assembly and, more importantly disassembly. This has the potential to greatly enhance the ability of TWI industrial members to recover and recycle the composite materials they use **[C9]**.

WJ Group is the UK's leading specialist road marking business dedicated to permanent and temporary road markings, and other specialist road fixings and surfaces such as road studs, and high friction and safety surfacing. In 2014, OU and WJ Group embarked on a three-year KTP. As a result, WJ Group acquired a capability to apply road marking products all year round, along with the development of an R&D capability to continue producing high performing cold products with which to enter the GBP750m Northern European market **[C10,** p.2**]**. The KTP reinforced WJ Product's position as market leader and industry innovator from the sale of hot and cold state-of-the-art products **[C10,** p.2]. The Managing Director of WJ Product division noted that the work with the OU '*made a significant contribution to the WJ Groups expansion both in terms of commercial activity and R&D'* and transformed the way the company operates with a '*game-changing'* methodology for designing and testing new materials giving a rapid go/no go decision when developing new products **[C11]**. This has enabled the business to acquire new customers and as a result WJ Group now works with the Dutch equivalent to Highways England; 'Rijkswaterstaat'. The work has enabled WJ Group to become the 'go-to expert' in micro-plastics in road markings, enabling them to develop case studies for Highways England investment in more sustainable materials **[C11]**.

Further work building on this research with Johnson Matthey is developing techniques to recover metals from waste streams, acid mine drainage and wastewater, using silica materials modified with chelates for metals. This enables Johnson Matthey to meet its strategic aims to participate in the increasingly sustainable circular economy. So far, the work has led to novel and commercially applicable materials for which Johnson Matthey is applying for a patent and is also being deployed in the wider company **[C12]**.

5. Sources to corroborate the impact

C1. FDA news release on withdrawal of Ranitidine.
C2. FDA protocol for the analysis of Ranitidine.
C3. ACE C18-AR brochure.
C4. Brochure for four other new columns from Hichrom, resulting from KTP.
C5. Details of column sales by year from Hichrom.
C6. Testimonial from Andy Smith, UK Production Director, VWR International Ltd. (formerly Hichrom).
C7. Hichrom KTP final report.
C8. Cornelius Specialities KTP final report.
C9. Testimonial from Prof Alan Taylor, Technology Fellow, TWI Ltd.
C10. WJ Group KTP final report.
C11. Testimonial from Managing Director, WJ Products Ltd.
C12. Testimonial from Principal Scientist, Recycling and Separation Technology Group, Johnson Matthey.