NUS National University of Singapore | Faculty of Science

Advances in Science

Volume 23 Number 2 December 2018

A special issue on Green & Sustainable Chemistry II

FEATURES

- Understanding catalysis
- Catalysts for water splitting reactions
- Waste to value conversions
- Economical and non-toxic metals for catalysis
- Visible light enhanced green synthesis

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On the cover: Green chemistry reduces environmental impact by developing scientific expertise that eliminates the use or generation of hazardous substances in the design, manufacture and application of products for sustainable development.

Understanding catalysis

Ligand properties important for achieving high catalytic activities are revealed using a stereoelectronic map, facilitating the design of improved and tailor-made catalysts.

Introduction

As a major pillar of green chemistry, catalysis is extremely important to modern society. Most materials we encounter and use on a daily basis rely on it. This becomes even more apparent if one considers that a significant fraction of the nitrogen in our body originates from the catalytic Haber-Bosch process. This is an industrial nitrogen fixation process which uses a catalyst to combine nitrogen and hydrogen into ammonia for fertilizers to enable food production. Without a catalyst, this seemingly simple process would not be possible. Also, more than 80% of all fine chemicals are catalytically produced.

Many (homogeneous) catalysts comprise transition metals bound to (usually) organic molecules, which are known as ligands. These ligands activate and stabilise the catalysts. However, the identification of the optimal metal/ligand combination for a given chemical transformation is extremely difficult. Much of the current research relies on combinatorial-like approaches where numerous ligands and metals are tediously screened. Although this approach can identify good catalytic systems, it is also highly time-consuming and labour-intensive. In addition, many ligands are very expensive and difficult to prepare, which adds significantly to the overall cost. Also, this approach provides very little understanding of the structure-activity relationship (SAR) of the catalyst.

Stereoelectronic map

Ligands control the reactivity of metal catalysts by electron donation and steric control. While the size (steric bulk) of a ligand can be easily estimated by its structure, it is much more difficult to evaluate its electron donating power. Although many electronic parameters have been proposed for this purpose, a number of them have severe limitations in terms of safety, resolution and accuracy [1]. We have developed a new, unified and accurate electronic parameter, known as the Huynh Electronic Parameter (HEP). This parameter is based on the carbon-13 nuclear magnetic resonance (NMR) spectroscopy, which is a general spectroscopic tool available in most research institutions. Our team, as well as other researchers, have measured the donor strengths of more than 100 mono- and bidentate ligands. For the steric bulk, a recent measure, known as the “percent Volume buried” (%V_{bur}) has been introduced by NOLAN and CAVALLO [2]. Intuitively, a larger %V_{bur} value is obtained for a more bulky ligand. By plotting the HEP values of ligands against their steric bulk, a stereoelectronic map can be obtained. This is used to understand the factors affecting catalytic activity (Figure 1).

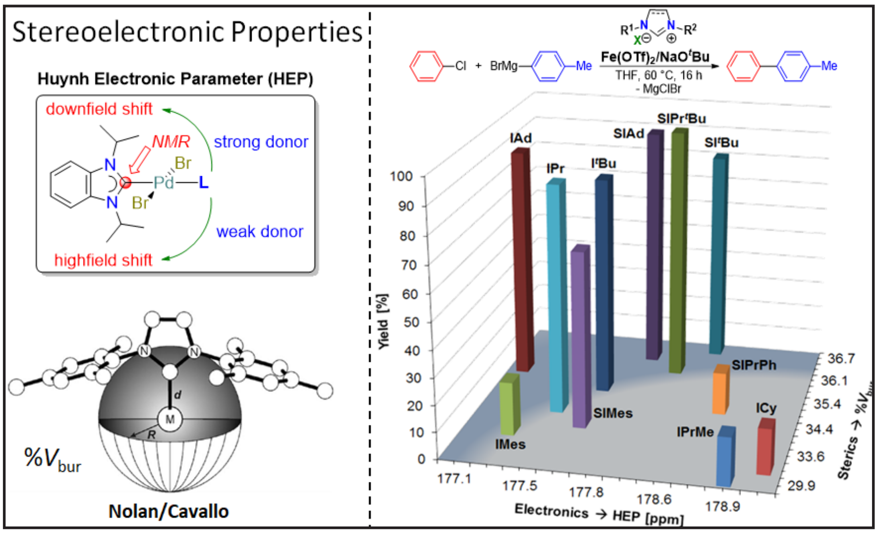

Figure 1: HEP and %V_{bur} stereoelectronic parameters and the first stereoelectronic map of NHCs.

Iron catalysed Kumada coupling

In collaboration with the Institute of Chemical and Engineering Sciences (ICES), a research institute under the Agency for Science, Technology and Research (A*STAR), we have used this plot to evaluate the catalytic activities of 11 classical N-heterocyclic carbenes (NHCs) used in the iron-catalysed Kumada-coupling reaction (Figure 1). By mass, iron is one of the most common elements on earth, and the development of iron-based catalysts would potentially lead to cost savings. This study has led to the conclusion that electronic factors are less important, while steric control is crucial for this type of reaction. The best performing ligands were found to have %V_{bur} greater than 35. More importantly, the understanding in SAR can lead to the development of a better catalytic system by selective choice of bulky NHCs [3].

The findings have also prompted us to study expanded-ring NHCs with six to eight membered heterocycles in iron catalysis. The larger ring size of these ligands has a larger steric bulk compared to their smaller five-membered classical analogues. Overall, the influences of ring sizes (five to eight) and different N-aryl substituents were explored in terms of spectroscopic structural features, which affect their $\%V_{bur}$ values. Notably, the best three performers with “optimal” steric bulk were found on the diagonal positions of the matrix diagram (Figure 2), which shows that the catalytic activity is sensitive to small changes in the NHC structure. Thus, a subtle increase or decrease in the steric effects away from the optimal systems leads to a significant loss of catalytic activity. To the best of our knowledge, this is the first study that systematically investigates the combined steric influences originating from N-substituents and carbene ring sizes.

Palladium-mediated Suzuki-Miyaura reaction

While the iron catalysed Kumada coupling is primarily controlled by the ligand’s steric bulk, we found that the palladium-mediated Suzuki-Miyaura reaction in water is more sensitive to the donating ability of the NHC ligand. In this study, four charge-tagged NHC ligands with different stereoelectronic profiles were tested (Figure 3). It was found that the most bulky and less electron rich ligands were poor performers (Mes-tazy-NEt_3 and Dipp-tazy-NEt_3), while the least bulky and most donating ones (Cy-tazy-NEt_3 and Ph-tazy-NEt_3) provided significantly better yields of the coupling products.

Overall, the examples reported demonstrate that stereoelectronic parameters constitute an important toolbox for chemists. They can be used to understand the often complex nature of SARs of chemical applications. We believe that such SAR studies could be extended beyond the realm of catalysis and possibly inspire future research.

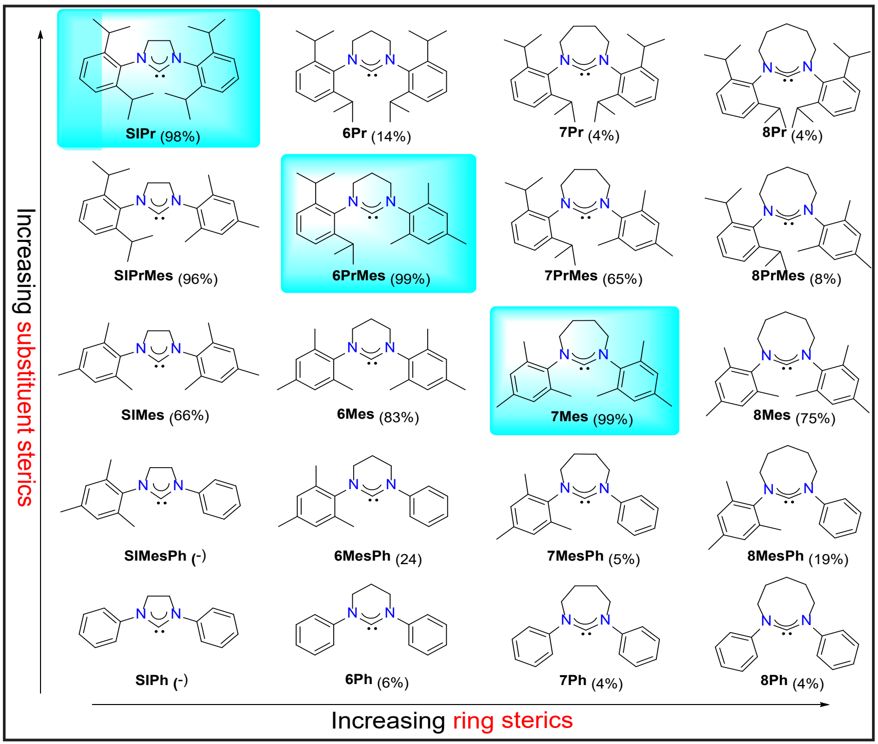

Figure 2: SAR of expanded-ring NHCs in the iron-catalysed Kumada coupling reaction.

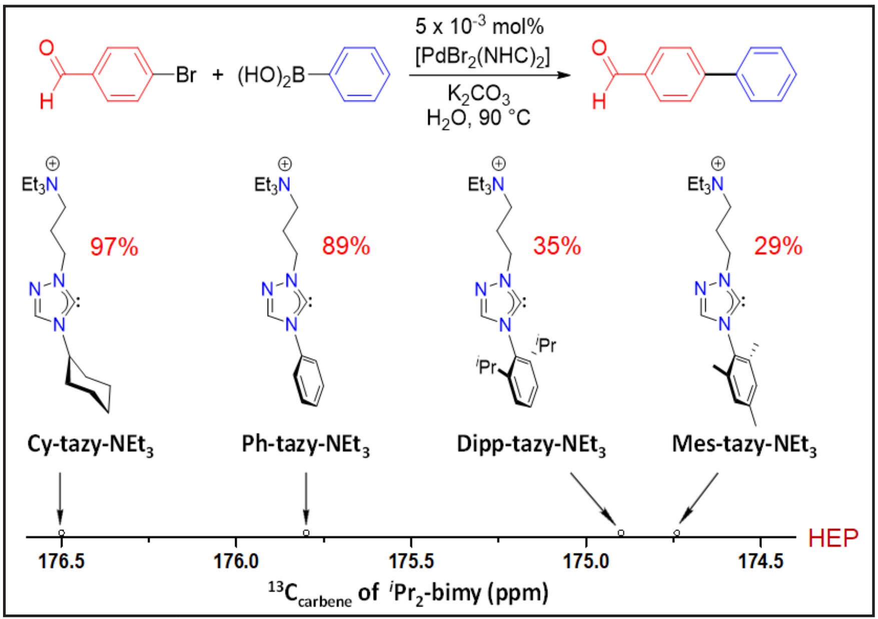

Figure 3: SAR of charge-tagged NHCs in the palladium-catalysed Suzuki-Miyaura reaction in water.

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Catalysts for water splitting reactions

The search for a robust and inexpensive catalyst to transform acids into hydrogen gas for green fuel

Introduction

Over the past decades, there has been increased interest in alternative and renewable energy sources to reduce our reliance on fossil fuels such as coal and oil. Most of the energy needed to cater to our demands comes from burning fossil fuels. These fuels increase carbon dioxide levels in the atmosphere, leading to greenhouse effects and climate changes.

Hydrogen gas, which can be produced from water, has often been touted as a clean and environmentally friendly energy source to replace fossil fuels. The process to obtain hydrogen gas from water is known as water splitting. It comprises two parts: (i) proton reduction to hydrogen gas ($2H^+ + 2e^- \rightarrow H_2$) and (ii) water oxidation to oxygen gas ($H_2O \rightarrow ½O_2 + 2H^+ + 2e^-$).

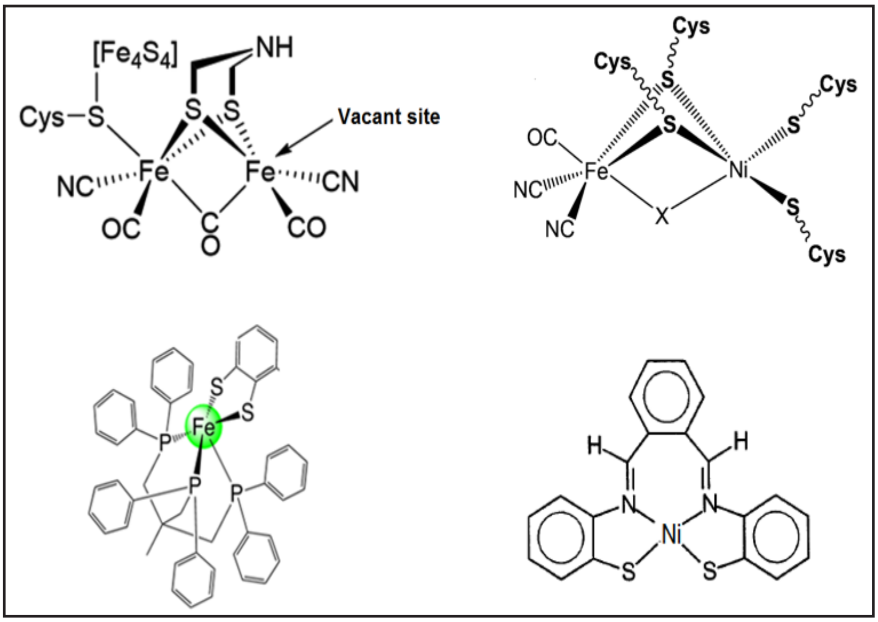


Figure 1: (Top from left) Structures of the [Fe-Fe] and [Ni-Fe] hydrogenase which are enzymes able to catalyse the reversible oxidation of molecular hydrogen (Cys: Cysteine; X can be an oxide, sulphur, hydroperoxide, or a hydroxide). (Bottom from left) Structures of the synthetic iron and nickel complexes developed in our laboratory for potential use as catalyst for proton reduction reactions, (bdt) triphosFe^{II} complex and Ni(II) complex.

Proton reduction process

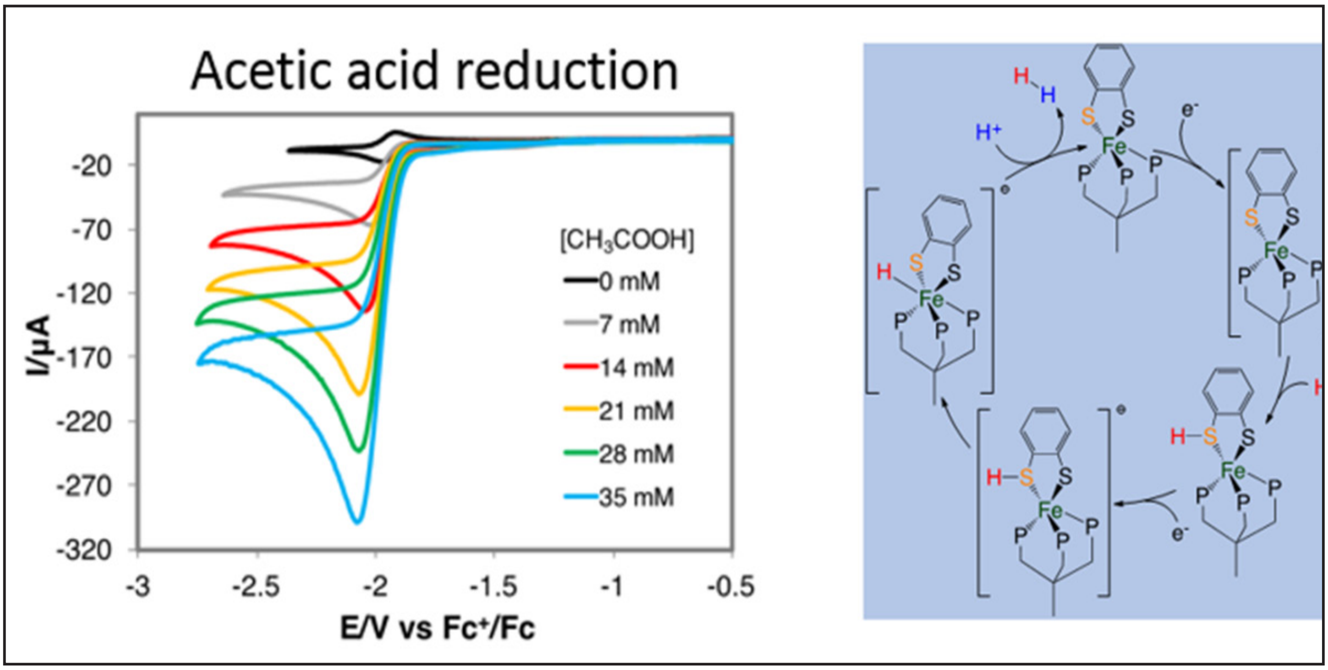
My research laboratory at the Department of Chemistry, NUS, focuses on the proton reduction process. This is a very challenging chemical process because of the high energy input required to produce the hydrogen gas. To make this process more viable, chemists are searching for suitable catalysts which can reduce its energy consumption. A catalyst is a chemical compound that can lower the energy barrier for a chemical reaction, allowing it to proceed with less activation energy. There have been ongoing research efforts to find inexpensive, earth-abundant catalysts to make this a more efficient process. Fortunately, some guidance can be drawn from nature. There is a remarkable class of iron- and nickel-containing enzymes known as hydrogenases present in certain bacteria and small organisms. These hydrogenases catalyse the proton reduction process efficiently, allowing the bacteria and small organisms to use hydrogen as an energy source for their own growth. The [Fe-Fe] hydrogenase (Figure 1) is one such example that is able to convert protons to hydrogen gas at a very low energy barrier, with high turnover rates (number of chemical conversions which a catalytic site can perform).

Our research team is fascinated by how these enzymes are able to carry out this challenging reaction without requiring high temperatures or pressure conditions. We have analysed the structure and bonding of the active sites of the [Fe-Fe] and [Ni-Fe] hydrogenase and used them to guide our research in developing synthetic catalysts to mimic the efficiency of hydrogenases occurring naturally in microorganisms in the proton reduction process. However, these enzymes cannot be extracted and used directly for clean energy applications. A key issue is that these hydrogenases become unstable and their proton reduction ability is reduced when they are removed from their natural biological environment. Instead of looking at ways to stabilise them, our research focus is on developing synthetic catalysts that are able to mimic the ability of these hydrogenases.

Our research team has been carrying out proton reduction studies in the laboratory and has explored many different chemical compounds as potential catalysts. The following paragraphs highlight an iron-based catalytic system that we have developed and a nickel-based system which we are currently exploring.

Iron-based catalytic system

The iron-based catalytic system involved a compound known as (bdt)



Credit: *Inorganic Chemistry 2017.*

Figure 2: (Left) Cyclic voltammogram showing proton reduction using (bdt)triphosFe^{II} as the electrocatalyst in a solution of acetic acid. (Right) Proposed proton reduction mechanism which illustrate how the catalysis might have taken place.

triphosFe^{II} complex (Figure 1). The design of the iron compound was modelled after the structural motif of one of the iron centres in the natural [Fe-Fe] hydrogenase. The iron centre is in the +2 oxidation state and it has a vacant site for a possible proton binding reaction. We synthesised this chemical compound and evaluated its proton reduction property using an electrochemical method called cyclic voltammetry. This method was chosen because it is able to give a fast and accurate determination of the efficiency of the compound in terms of the energy barrier and turnover rates. These are the two most important parameters required in the experiments to gauge the performance of the catalyst.

In our experiments in which the iron complex is used as a catalyst with an organic acid such as acetic acid serving as the proton source, cyclic voltammetry studies showed that the above complex is able to reduce the energy barrier significantly for proton reduction with a high turnover rate (Figure 2). Also, the iron complex demonstrated a high degree of robustness by being able to generate hydrogen gas over many hours without severe decomposition. We have also proposed a mechanism for the proton reduction process involving this catalyst, incorporating the salient features observed in our experiments [1].

Nickel-based catalytic system

We also have an ongoing study on nickel complexes modelled after the [Ni-Fe] hydrogenase for proton reduction reactions. We have begun to incorporate nitrogen and sulphur ligands into Ni(II) ions, which are found to be linked to sulphur moieties in the hydrogenase. Our team has developed a neutral Ni(II) complex with free binding sites (Figure 1) [2]. Using cyclic voltammetry, this complex has been shown to be able to catalyse proton reduction reactions with a moderate energy barrier and efficiency over a sustained period.

We believe that these nickel-based complexes have the potential as robust proton reduction catalysts. There are plans to study them more extensively in my laboratory.

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Waste to value conversions

Selective carbon-fluorine activation for recycling of polyfluorocarbons

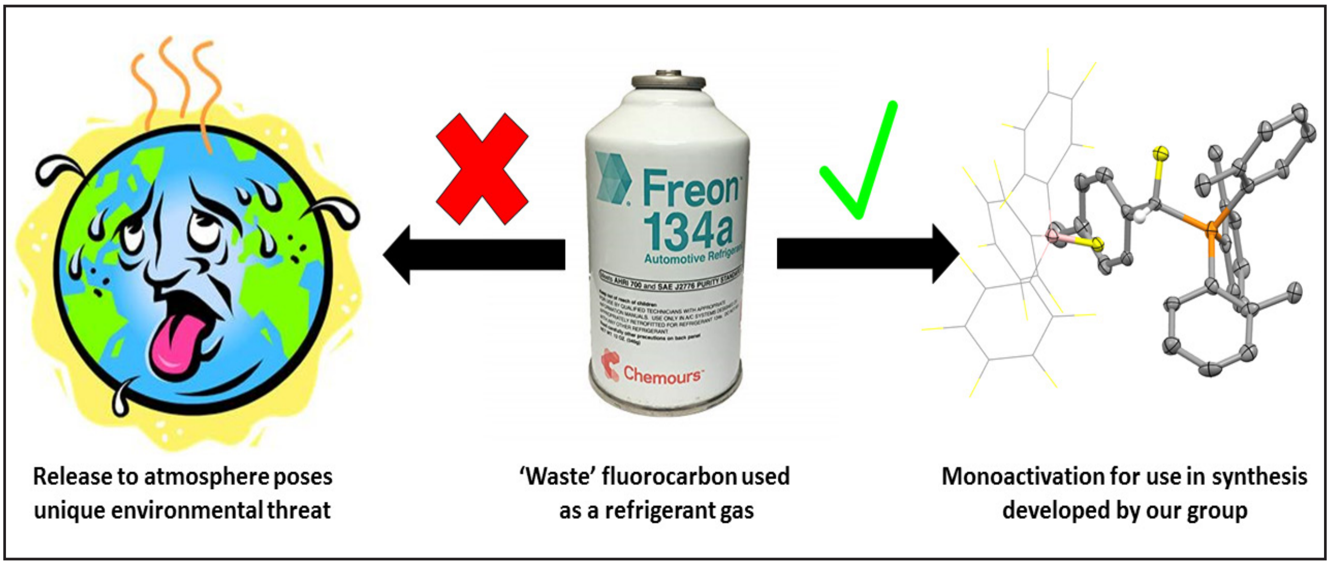

Figure 1: Fluorocarbons present a unique environmental threat given their high global warming potential. However, such compounds can be of synthetic utility if selective carbon-fluorine activation can be achieved.

Introduction

Organic molecules that contain fluorine can be found in agrochemicals, polymers, pharmaceuticals, surfactants, refrigerants, fine chemicals and many other applications. Fluorine is incorporated into these molecules to enhance solubility, chemical and biological activity, chemical resistivity and thermal stability. It is also found in hydrofluorocarbon (HFC)-based refrigerant gases which have global warming potential that is thousands of times that of carbon dioxide (Figure 1).

Given that HFCs generally contain multiple fluorine atoms, there exists an opportunity to convert these waste HFC gases (and their fluorine containing chemical groups) into more complex molecules, transforming them into valuable chemicals. However, this requires the selective activation of carbon-fluorine bonds, a process that has remained challenging in the field of organic chemistry over the past few decades.

Frustrated Lewis Pairs

For the functionalisation of HFCs, our research group uses Lewis acid catalysts as "electron pair acceptors" that coordinate with the fluorine atom's electrons before extracting the electrons from the substrate molecule as a fluoride anion (having residual negative charge). This then allows another atom or molecule to be substituted in its place. As fluorine is generally deactivating, when a fluorine atom in polyfluorocarbons is substituted, it leads to more reactive products that subsequently "over-react" and result in multiple fluorine substitutions (as opposed to a desired single substitution).

Our team envisaged that the "over-reaction" effect could be avoided by having the resulting products as cations. As cations have a residual positive charge, they would be less inclined to react with the Lewis acids, thereby "protecting" the entire molecule from further fluorine extraction. This could be a viable generic strategy for the activation of carbon-fluorine bonds in polyfluorocarbon compounds, regardless of the relative fluorine positions.

For this strategy to work, a neutral nucleophile (electron pair donor) is introduced to "trap" the resulting chemical product as a cation after the (negative) fluorine anion is extracted. However, nucleophiles, being electron pair donors, can also interact with the Lewis acids used in the process. In order to avoid this side-reaction, nucleophiles with large bulky substituents are selected. The combination of these Lewis acids and nucleophiles is known as "Frustrated Lewis Pairs". Using these "trapped" cations as intermediates, further functionalisation methods can be used to access a wide range of valuable compounds.

Wittig reaction: Generating alkene products

One of the most widely studied "Frustrated Lewis Pair" systems is the combination of bulky phosphine nucleophiles with borane Lewis acid $B(C_6F_5)_3$. Using this as the starting point, our team managed to demonstrate the generation of cationic monofluorocarbon (phosphonium) products from simple difluorocarbons (compounds in which two of the hydrogen atoms in a hydrocarbon is replaced with fluorine atoms). Further functionalisation of these cationic phosphonium products can take many directions, but our team showed that they could be utilised in a well-established carbon-carbon (C-C) bond, forming a Wittig reaction (Figure 2).

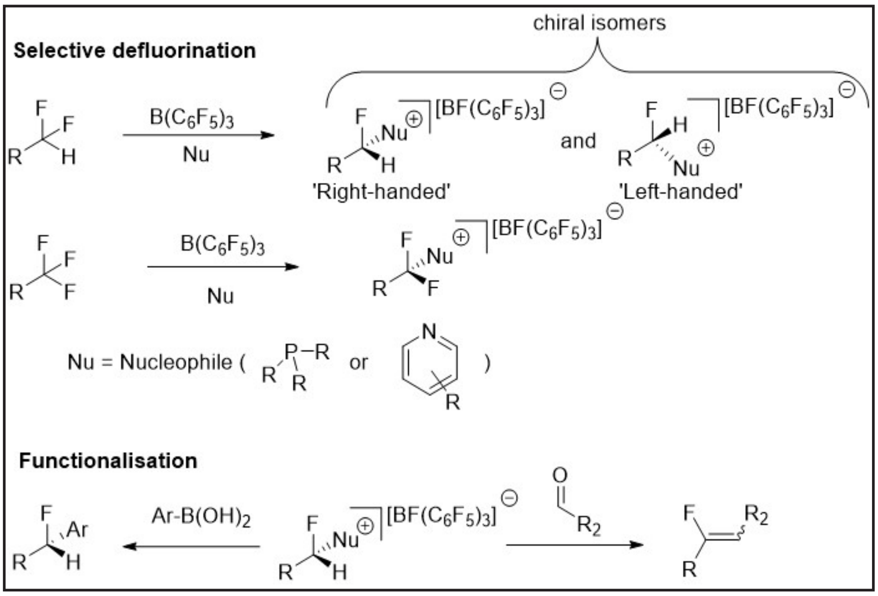

Figure 2: Selective monodefluorination of di- and trimethyl groups and subsequent functionalisation (R, R_2 = alkyl or aryl group).

Wittig reactions combine phosphonium and carbonyl starting materials to generate alkene products (formation of a carbon-carbon double bond). Monofluoroalkenes (alkenes with a single fluorine atom) are important synthons in organic and materials chemistries, and are present in a number of agrochemicals, synthetic materials and pharmaceuticals. Thus, being able to access such compounds directly from polyfluorides is a highly desirable process. As such molecular groups are difficult to access using known methods, our methodology provides a way of recycling difluorocarbons and also to access this class of difficult-to-synthesise molecules.

After successful development of this concept, we extended it in several directions. Compared to difluoromethyl groups ($-CF_2H$), trifluoromethyl groups ($-CF_3$) are generally much more commonly found in chemical products. The selective activation of $-CF_3$ groups to generate difluoride products is a way of increasing the chemical complexity of the compound. Despite their desirability, there are only very limited methods for the single functionalisation of $-CF_3$ groups. Our team discovered that the mono-functionalised cationic difluorocarbon products can be obtained under optimised processing conditions. In this example, the team utilised pyridine based nucleophiles as the subsequent C-C single bond functionalisation is more established for pyridinium cations when compared to phosphonium cations. This represents a general approach for the selective functionalisation of $-CF_3$ positions.

Chiral chemical products

Our team also explored the generation of chiral products from difluorocarbon starting materials. Some chemical products (such as those in the top right of Figure 2) have non-superimposable (chiral) mirror images. This is similar to the way our hands are mirror images of each other, but are non-superimposable. The spatial configuration of molecules in space is important for their reactivity, especially in biological settings. Using commonly available and inexpensive sulphur-based chiral nucleophiles, our team was able to generate a single chiral selectivity (consisting of only a right-handed or left-handed molecule). This chirality property was retained in subsequent single C-C bond functionalisation reactions for creating different biologically important molecules.

Our research on catalytic chemical transformations not only allows the reuse of waste fluorocarbons (e.g. refrigerants), but it also provides a way to access difficult-to-synthesise fluorine containing molecules. These contribute to a greener future.

Rowan YOUNG is an Assistant Professor with the Department of Chemistry, NUS. He received his Ph.D. from the Australian National University, where he was awarded the Director's Prize in Chemical Sciences. He joined NUS in 2014 after his postdoctoral research at the University of Oxford and the University of Edinburgh.

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Economical and non-toxic metals for catalysis

Cobalt catalysts for organic transformations to synthesise value-added chemicals

Introduction

A catalyst is a substance that increases the rate of a chemical reaction without itself being consumed during a chemical process. Transition metals play an indispensable role as catalysts in the chemical and pharmaceutical industries. Approximately 90% of commercially produced chemicals involve catalysts at some stage of their manufacturing process. These catalytic chemical processes rely heavily on the use of precious metals, such as ruthenium, osmium, rhodium, iridium, palladium and platinum. However, there are drawbacks associated with their use:

(a) These metals have limited production and only dozens of tons of the materials are produced a year;

(b) They are highly toxic to human beings and their trace residues must be reduced to very low levels (parts per million), especially for the production of pharmaceutical products;

(c) They are harmful to the natural ecosystem and wastes from the production process have to be properly treated; and

(d) Their reserves in the Earth's crust are being depleted and this could pose an issue for long-term sustainability.

Catalytic transformations using base metals

New catalytic chemical processes for the industry are expected to be practical, inexpensive and environmentally friendly. These requirements would mean that the development of catalytic processes involving earth-abundant and non-toxic base metals, such as iron (Fe) and cobalt (Co) are getting increasingly important. However, a transition from the more established catalytic processes (using precious metals) to less established ones (using base metals) is not straightforward. In recent years, there have been on-going research efforts in the development of catalysts using suitable base metals that can play the catalytic role of precious metals in chemical transformations.

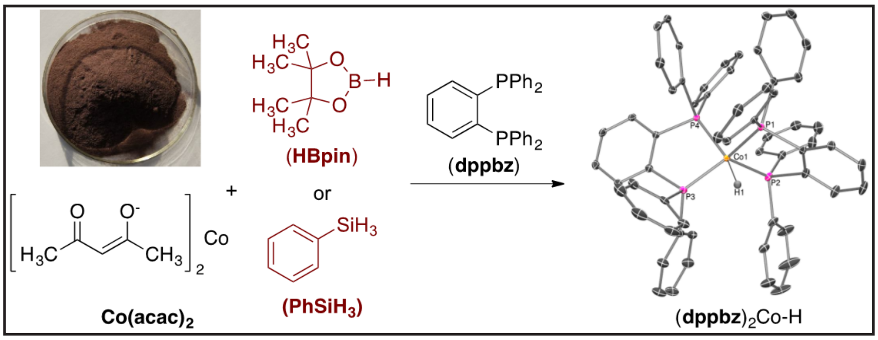

Figure 1: Activation of $Co(acac)_2$ with hydrosilanes or hydroboranes ($Co(acac)_2$: cobalt(II) acetylacetonate; HBpin: pinacolborane; $PhSiH_3$: phenylsilane; dppbz: 1,2-Bis(diphenylphosphanyl)benzene; $(dppbz)_2Co$-H: Co(I)-H complex); The photo shows the appearance of $Co(acac)_2$.

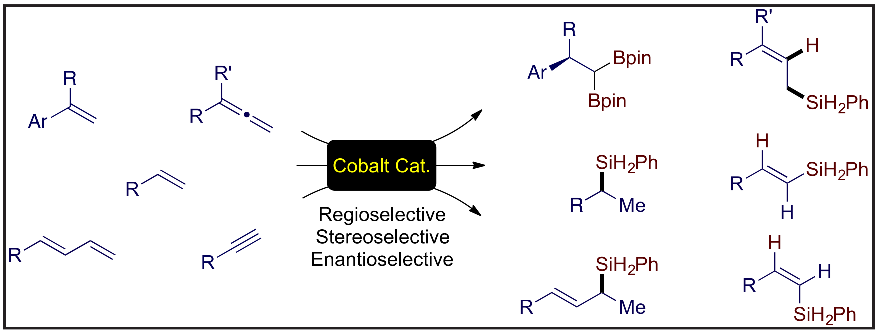

Figure 2: Cobalt-catalysed selective hydrosilylation and hydroboration reactions (R, R' = alkyl or aryl group).

Compared with catalysis using precious metals, catalysis using base metals is still in its infancy stage. The major challenges associated with the design of the base metal catalysts include the lack of the following:

(a) Ligand libraries that allow systematic evaluation to identify effective ligand/metal combinations;

(b) Metal precursors that can be readily and effectively activated to generate catalytically active compounds; and

(c) Mechanistic insights that can guide further improvement in the performance of base metal catalysts.

Over the past few years, our research group has been working on cobalt catalysts that are able to transform readily available starting materials into value-added chemicals. Our team has discovered that cobalt(II) acetylacetonate ($Co(acac)_2$), a commercially available and non-toxic cobalt(II) salt, can be made active by reacting it with hydroboranes or hydrosilanes to form a cobalt(I) hydride species "Co(I)-H". This chemical species can form stable Co(I)-H complexes (Figure 1) [1]. In addition, our team has also shown that these Co(I) hydride complexes can function as catalysts for a series of hydrofunctionalisation reactions for unsaturated organic molecules.

Cobalt-catalysed selective hydrosilylation and hydroboration of alkenes and alkynes

Organosilanes and organoboronates are stable and biocompatible compounds which contain active carbon-silicon and carbon-boron bonds. These chemical bonds can readily undergo diverse chemical reactions to produce new chemical compounds. Thus, these organosilane and organoboron compounds are very useful building blocks for the synthesis of biologically active natural products and pharmaceuticals. One of the most direct synthetic approaches to access these organosilane and organoboron compounds is to add a hydrogen-silicon (H-Si) or hydrogen-boron (H-B) bond to an unsaturated carbon-carbon double (C=C) or triple (C ≡ C) bond. This process is known as the “hydrosilylation” or “hydroboration” reaction. In general, precious metal catalysts are required to drive these chemical reactions.

By using cobalt catalysts, our team has developed several selective hydrosilylation and hydroboration reactions involving alkenes, alkynes and allenes to make organosilane and organoboron compounds with high yield (Figure 2) [2]. These reactions which are simple to process with a high tolerance towards reactive functional groups, can potentially be extended to a broader range of chemical compounds.

Cobalt-catalysed asymmetric hydroboration/cyclization of enynes

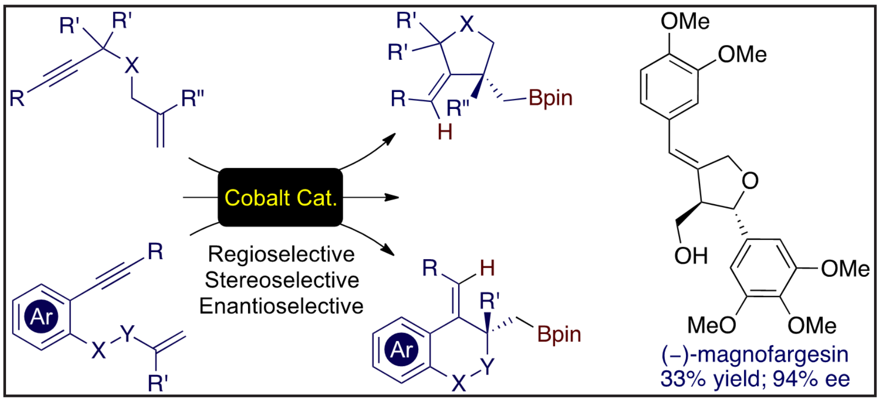

Figure 3: (Left) Cobalt-catalysed asymmetric hydroboration/cyclisation of enynes. (Right) Enantioselective (-)-magnofargesin product obtained from cobalt-mediated asymmetric catalysis.

Chiral molecules exist in pairs (called enantiomers) and are mirror images of each other, similar to the relationship between our left and right hands. Asymmetric catalysis is a type of catalytic process to selectively produce one of these molecular pairs in the presence of a chiral catalyst. In general, the two enantiomers have different bioactivity, and the selective production of one enantiomer is of importance for the development of drugs in medicinal chemistry. Therefore, our team is very interested in the development of chiral cobalt catalysts for use in asymmetric organic transformations.

Chiral five-membered carbocyclic and heterocyclic structural motifs are present in numerous natural products which are active ingredients in traditional medicine. Examples include burseran (an anti-tumour compound present in *Bursera microphylla*) and magnofargesin (an antagonist of platelet-activating factor present in *Magnolia fargesii*). During the development of cobalt-catalysed hydroboration of unsaturated organic molecules, our team found that 1,6-enynes (a functional group in organic chemistry comprising both an alkene and an alkyne) underwent asymmetric cyclisation, in addition to the hydroboration reaction, to form chiral boron-containing five-membered cyclic compounds (Figure 3) [3]. By using this methodology, we achieved an enantioselective synthesis of (-)-magnofargesin, an active ingredient of *materia medica* found in China and Japan. Our team has also developed an enantioselective hydroboration/cyclisation of 1,7-enynes to produce chiral six-membered cyclic compounds.

Apart from these practical and cost effective hydrosilylation and hydroboration reactions of unsaturated organic molecules using cobalt catalysts, we plan to further develop cobalt-catalysed asymmetric transformations and to apply our methodology in the synthesis of more complex drug molecules.

GE Shaozhong is an Assistant Professor with the Department of Chemistry, NUS. He received his Ph.D. degree from the University of Groningen in 2009. After his postdoctoral work at University of Illinois at Urbana-Champaign and University of California, Berkeley, he joined NUS in 2015. His research interests lie in transition metal catalysis, green chemistry, organometallic chemistry and medicinal chemistry.

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Visible light enhanced green synthesis

Using visible light to catalyse cost-effective and environmentally friendly chemical transformations

Introduction

Over the past few years, my research group has been involved in two main research fields in organic synthesis: continuous-flow synthesis and photocatalysis. Continuous-flow synthesis includes reactions which occur in continuously flowing fluids using micro-tubing reactors. Compared to traditional batch reactors, continuous-flow synthesis can be more efficient and offers better control of the reaction parameters, especially for reactions involving gas and liquids. This makes it attractive for the production of chemicals and pharmaceuticals. Photocatalysis is a catalytic process that relies on the absorption of light energy by one or more reacting species/catalysts as the driving force in chemical transformations.

Development of stop-flow reactors

Although continuous-flow reactors are effective for industrial processes, there are limitations when they are used in the development of new processes which involve screening of reaction parameters (e.g. reagents, catalysts, solvents, etc). For example, a typical continuous-flow system usually does not allow for more than one reaction to be investigated at a time. This can therefore be time consuming.

By combining elements from both continuous-flow and conventional batch reactors, our group has developed a "stop-flow" micro-tubing (SFMT) reactor platform which is suited as an efficient and effective platform for gas/liquid reaction screening. The SFMT platform uses sealed micro-tubings, which can be made from perfluoroalkoxy alkane (PFA) or stainless steel as the reactor. Instead of flowing the reaction mixture continuously, the SFMT platform allows for the flow to be paused by shutting off two valves at each end of the micro-tubing. This sealed micro-tubing is disconnected at high pressure and the reaction is allowed to proceed till its desired reaction time. A new micro-tubing can then be attached to the system to explore a different set of reaction parameters. The SFMT has proven to be efficient for the screening of gas/liquid and light-mediated reactions (Figure 1).

Visible light-mediated fine chemical synthesis using natural gas feedstocks

Feedstocks derived from natural gas such as carbon dioxide, acetylene, ethylene and ethane which are inexpensive, non-toxic and highly available are becoming increasingly attractive as highly affordable starting materials in chemical synthesis. However, research into their potential application for the development of fine chemicals remains challenging and is constrained by the use of complex laboratory apparatus, especially for processes involving high pressure and phototransformations. The SFMT reactor is particularly suitable to evaluate chemical reactions involving gases and those which are catalysed by light. This is because of its high gas/liquid surface-to-volume ratio associated with the micro-tubing reactors and its increased light penetration properties.

Since 2017, our group has developed several new fundamental reactions that can directly convert inexpensive gaseous feedstocks into value-added chemicals in the presence of visible light using the SFMT reactors (Figure 2). Example of reactions affording desirable chemicals include:

(i) Vinylation of aryl halogen compounds using acetylene gas under photoredox conditions;

(ii) Visible light driven hydrocarboxylation and carbocarboxylation of alkynes with carbon dioxide to synthesise various pharmaceutically important compounds such as coumarins, quinolones and hydroxybutenolides;

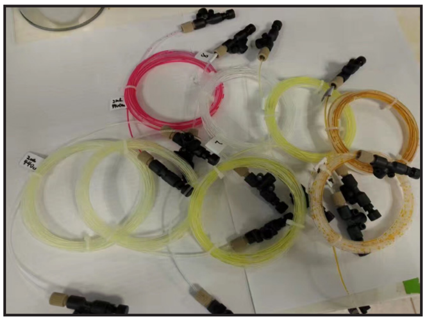

Figure 1: The micro-tubing of the SFMT reactors are sealed and maintained at high pressure. These are made of PFA and obtained commercially from IDEX Corporation.

(iii) A photo-mediated divergent ethylene difunctionalisation via modulating oxidation states of the nickel catalyst by using different photoredox catalysts;

(iv) A visible light promoted metal-free difunctionalisation of alkenes using carbon dioxide and readily available Si-H and C(sp^3)-H bonds as feedstocks; and

(v) Utlisation of ethane as the ethylating reagent to react with electron deficient alkenes by merging a photoredox catalyst and hydrochloric acid as the hydrogen atom transfer catalyst.

Visible light mediated C-H and Si-H activation

Direct carbon-hydrogen (C-H) bond transformations, or the replacement of "H" in C–H bonds with other atoms or substituents, is one of the most coveted ways to create new and useful molecules. However, while the C-H bond can be found in most organic molecules, it is considered inactive and therefore difficult to functionalise. C-H bond functionalisation refers to the substitution of the hydrogen atom in the C-H bond with another functional group. Although direct C-H bond transformations have attracted continuous interest since the early 1970s, the majority of the research work has focused on the activation of the C(sp^2)-H bonds to develop new ways of making chemical compounds. There are limited routes associated with the catalytic activation of C(sp^3)-H bonds (Figure 3).

Our group has contributed to C(sp^3)-H activations via three different strategies:

(i) C(sp^3)-H activations via photoredox reactions. Our team developed an allylic/benzylic alkylation using only an organo-photoredox catalyst. This reaction enables a broad range of alkenes/arenes and electron-deficient alkenes to form new organic compounds in an atom and redox-economic manner. The benzylic alkylation reaction was further extended to less electron deficient enones (a type of organic compound) for the development of complex bioactive molecules.

(ii) C(sp^3)-H activations via direct hydrogen atom transfer (HAT) photocatalysis. Our team found that a chemical dye, neutral eosin Y, when activated under visible light can be used as a HAT photocatalyst to effectively catalyse a wide range of C-H bonds. HAT is one of the most fundamental chemical reactions (A-H + B → A + H-B) and is a key step in many chemical processes. A variety of synthons can be easily achieved by this method, which will likely find wide industrial application.

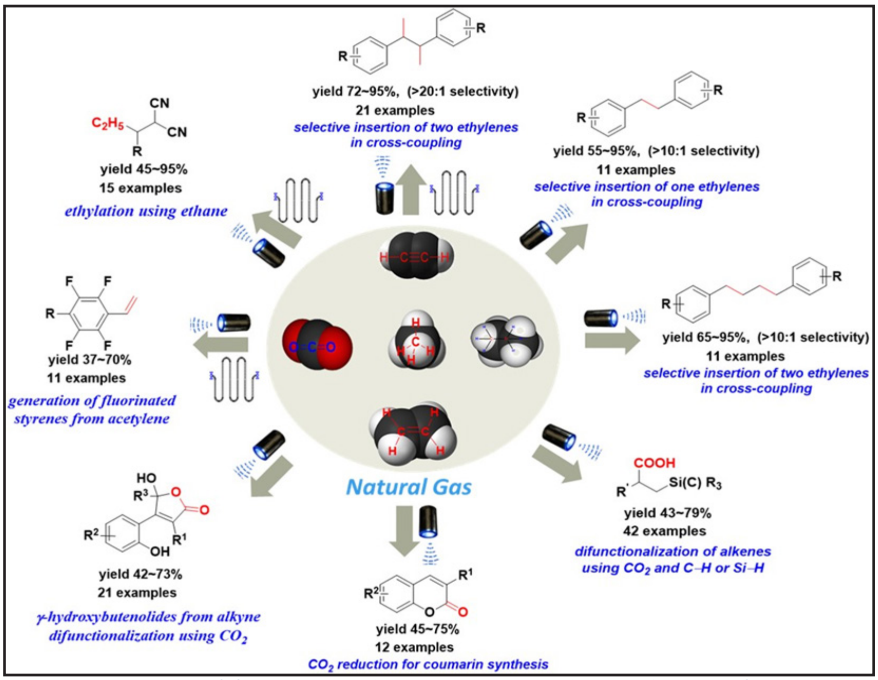

Figure 2: A range of fine chemical compounds can be synthesised from widely available natural gas feedstocks catalysed by visible light.

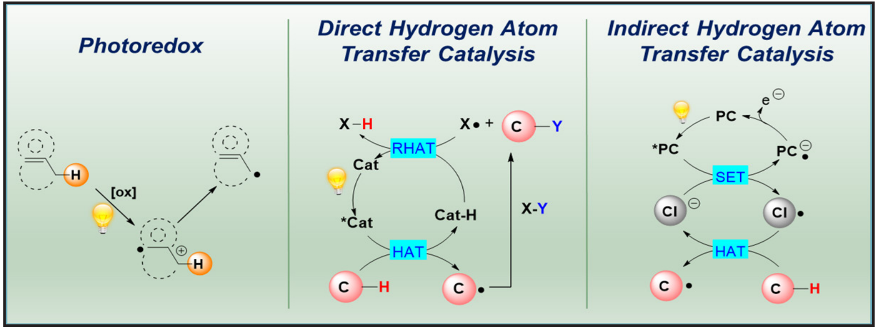

Figure 3: Mechanisms showing the three different types of activation modes for light catalysed C-H functionalisation reactions.

(iii) C(sp^3)-H activations via synergistic merging of photoredox and HAT catalysis (indirect HAT photocatalysis). Our team has developed a process that uses visible light and nickel catalysts for the hydroalkylation of alkynes with ether and amide C(sp^3)–H bonds. Ether and amide chemical groups are present in many pharmaceutically active agents. This new method provides an environmentally friendly way for pharmaceutical companies to produce pharmaceutical products involving the modification of these chemical groups.

Our team plans to continue developing green and sustainable visible light-promoted chemical transformations to enable direct C-H bond functionalisations of various types of organic compounds, which are useful for the chemical and pharmaceutical industries.

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Reference

Please visit https://www.wujiegroupnus.com/publications for more information about the research work of his group.

Launch of Applied Materials-NUS Advanced Materials Corporate Lab

Advances in semiconductor performance over the past decades have been led by improvements in transistor scaling. However, this is becoming more challenging as emerging applications based on artificial intelligence and big data require orders of magnitude improvements in chip performance and efficiency. Materials innovation will play an increasingly important role in achieving these improvements and advancing the semiconductor industry roadmap.

The lab combines Applied Materials' leading expertise in materials engineering and semiconductor technologies with NUS' world-class and multi-disciplinary research and development (R&D) capabilities that span applied chemistry, materials science and microelectronics processing techniques.

Researchers from the Faculty of Science and Faculty of Engineering, NUS are partnering Applied Materials, Inc. to establish the Applied Materials-NUS Advanced Materials Corporate Lab to accelerate discovery and commercialisation of new materials for manufacturing advanced semiconductors. This university-industry collaboration launched on 25 Oct 2018, will design, synthesise and test new materials and chemistries as well as develop processing techniques for the deposition and etching of advanced semiconductor manufacturing at the atomic scale. Prof Richard WONG from the NUS Faculty of Science and Prof Aaron THEAN from the NUS Faculty of Engineering will co-lead the lab with Applied Materials to steer greater teamwork and exchange between industry and academia.

The lab is expected to train over 50 researchers, engineers and doctoral students to support Singapore's next generation semiconductor manufacturing industry.

Urban biodiversity enhancement for better quality of life

The impact of rapid urbanisation and crowded cities on human health conditions, which include obesity, high blood pressure and depression are becoming more prevalent. Many of these health challenges can potentially be mitigated by increasing people's exposure to, and interaction with the natural environment. There are many research studies in temperate regions on the linkage between urban green spaces and human well-being. However, in tropical regions, there remains a knowledge gap to guide urban design which can translate to positive health outcomes of exposure to nature.

Prof Roman CARRASCO from the Department of Biological Sciences, NUS is collaborating with the National Parks Board (NParks), Singapore and the Centre for Biodiversity and Conservation Science at The University of Queensland, Australia to identify the causal links between biodiversity and subjective human well-being (perception of quality of life) in Singapore. NUS is leading the study using information from NParks. They will be supported by The University of Queensland which had conducted a similar study previously in Brisbane. This collaboration will study the relationship between the psychological impacts of the local population whose contact with nature is mostly through urban green spaces in their neighbourhoods and workplaces. It will measure and monitor a wide range of physical and psychological well-being indicators under different natural settings. The study is expected to provide recommendations on the minimum and optimal exposure to the natural environment for increasing well-being.

Walking and admiring nature in Windsor Nature Park, Singapore. Activities involving green spaces can help enhance people's well-being and contribute to positive health outcomes.

"The knowledge gleaned from this study will contribute to better management and enhancement of green spaces in Singapore, with the intent of improving subjective well-being. It will identify ecological characteristics of green spaces that could be enhanced to maximise well-being outcomes, and profile groups that would benefit significantly from contact with nature," said Prof Carrasco.

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