

Tailored Catalysis for the F&F Industry

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Dedicated to the memory of Dr. Hubert Mimoun who contributed strongly to Firmenich industrial success stories in catalysis

Abstract: Over the past decades, scientists at Firmenich have focused their efforts on continuously improving chemical transformations for the production of F&F ingredients in order to make them safer, cleaner, more efficient and consequently cost effective, through the implementation of the Green Chemistry principles. Numerous examples of innovative catalytic technologies could be cited, particularly in the field of homogeneous and heterogeneous catalytic hydrogenation. Nevertheless, we chose here to provide a rare insight into the industrial application of some very useful and atom-economic carbon–carbon bond forming reactions. We selected two examples among others as a good illustration of how catalysis makes the difference compared to conventional stoichiometric approaches. The first example deals with catalysed cross-aldol condensation and the second example concerns catalysis of cross-coupling reactions.

Keywords: Catalysis · Flavour & Fragrance ingredients · Green Chemistry · Sustainability



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development of catalytic processes for F&F ingredients.

1. Introduction

It is now obvious that one top F&F industry priority, like any other chemical industry, is the improvement of its chemical processes in term of carbon footprint, impact on environment, energy saving, health and safety. Chemical transformations have to be more and more efficient in order to at least compensate for the continuous growth of the worldwide production.

If, in a tough context of competition, cost and also quality of the finished products obviously remain key objectives, most of the time, they point in the same direction as safety and respect for the environment.

Green Chemistry and sustainability are not just pretty words but they are made of measurable principles clearly designed to maximize chemistry efficiency and minimize its hazardous effect on human health and the environment.^[1] The substitution of conventional chemical processes using large amounts of hazardous reagents, toxic solvents, stoichiometric protective groups and generating huge amounts of gaseous, aqueous or organic wastes, by cleaner and safer catalytic technologies are under continuous development. In addition, the implementation of efficient catalysis often implies a decrease in the quantity used, the replacement or even the total suppression of solvent as well as the increase of reaction selectivity and yield. As a result the chemical process is

simplified and its productivity increased resulting in significant savings of energy and CO₂ release.

Over the past decades, scientists at Firmenich have focused their efforts on taking up the Green Chemistry challenges. The chemical processes to manufacture F&F ingredients have become more and more efficient. Catalysis was successfully applied in most of the chemical transformations. For instance, catalytic hydrogenation was industrially applied for the reduction of a wide range of functionalities including selective hydrogenation of 1,4-dienes, unsaturated aldehydes or ketones, lactones and esters, advantageously replacing the use of the hazardous hydride reagents.^[2]

However, it is worth noting that catalysis is not exempted from its own ‘green principles’. Indeed, most catalysts are composed of metal. Most of the metals must be totally removed from the finished product and a clear process should be defined for waste treatment. Moreover the catalyst used must be reasonably air stable to be safely handled and reasonably resistant towards potential traces of impurities to ensure industrial robustness. Highly toxic elements such as mercury, lead, chromium, selenium are totally banned.

Another important aspect that we should be particularly aware of nowadays is the constraint regarding the use of precious metals as catalysts. They are widely used in many industrial processes such as hydrogenation, hydroformylation, isomerisation, cross-coupling reactions to cite some of them. Due to their low abundance, the energy needed for their mining and purification, the growing use in increasing number of applications (electronics, automotive, industrial boom of emerging countries, *e.g.* India...), the unavoidable speculation, the commercial availability of precious metals has become more problematic and their price has drastically increased over the last years. This concerns most precious metals, particularly the very useful palladium, ruthenium, iridium with a special record for rhodium whose price skyrocketed from 30'000 USD/kg to 900'000 USD/kg within 5 years.

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Needless to say that the catalyst turnover number as well as the efficiency of a recycling and refining process have become critical aspects for precious metal catalysis.

In such a context, a Green Chemistry approach consists of focusing catalysis on the use of earth-abundant metals wherever possible. In this regard, a very interesting and unusual classification of transition metals was done on the basis of their abundance and their industrial availability in a recent paper in *Science*.^[3]

Like other chemical industries, including pharmaceuticals,^[4] we anticipated this situation a long time ago by prioritising non-precious metal catalysis for the development of many industrial processes. Elements such as titanium, zirconium, manganese, iron, nickel, copper, tungsten, zinc are widely used in a broad range of chemical transformations including oxidations, reductions, isomerisations, and carbon-carbon bond-forming reactions.

In this paper, we present, as a first example, a new homogeneous catalytic cross-aldol condensation transformation for the manufacture of Delta Damascone, a key floral ingredient of the perfumery palette, and we point out the impact of catalysis comparing the results obtained to those from conventional chemistry to perform the same transformation.

In a second example, we present a new nickel-catalysed reaction for highly sensitive cross-coupling transformation in the manufacture of Galbanum ingredients.

2. Cross-aldol Catalysis

2.1 The case of Delta Damascone

Delta Damascone is an important member of the Rose Ketones, one of the prestigious families of fragrance ingredients from the Firmenich palette. It offers a very complex fruity and rosy profile with plum undertone. It is a very diffusive note exhibiting a unique floral effect.

Delta Damascone was patented by IFF in 1977^[5] and in the patent the special role of the *trans*-E Delta isomer was pointed out.

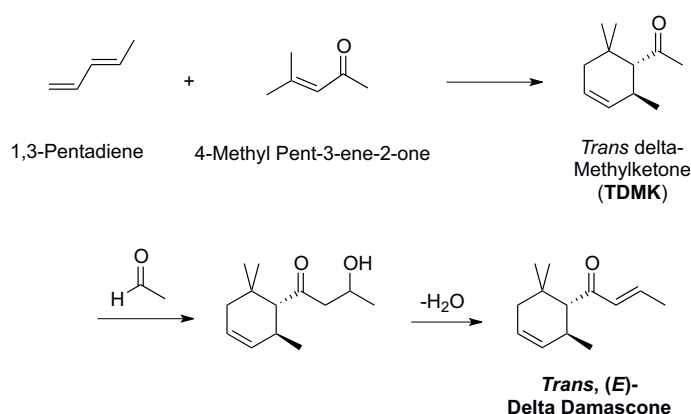
Given the straightforward access of its precursor (see Scheme 1), *trans* delta methylketone (TDMK), by Diels Alder condensation of inexpensive raw material, piperylene (1,3-pentadiene) and mesityloxide (4-methylpentenone) followed by a base-catalysed epimerisation, Delta Damascone has become a cost effective and large volume ingredient with a current worldwide market of more than 1'000 MT/y.

On the synthetic side, apart from the quite challenging Diels-Alder condensation, the key step is obviously the cross-aldol condensation of TDMK with acetaldehyde. As a result, in spite of some apparently straightforward access, the production of Delta Damascone is indeed greatly dependent on the performance of the chemical transformation technology used.

While the cross-aldol condensation has been known for 150 years,^[6] and it is certainly the most practical way for carbon-carbon bond formation, promoted by a wide range of catalysts including metal hydroxides, metal oxides, or carbonates, organocatalysts to cite a few,^[7] it can be in fact much more challenging depending on the nature of the substrates to be reacted.

When the substrates (ketones or aldehydes) are poorly reactive or, to the contrary, are highly reactive, the self-aldol pathway for one of the two partners is then favoured over the cross-condensation reaction. It is also quite frequent that both the substrates and the products are poorly stable under the reaction conditions. Lastly, the use of unsymmetrical ketones as the substrates may result in selectivity issues. In these scenarios, traditional aldol catalysis results in very low reaction yield along with the formation of a complex mixture of isomers and organic residues.

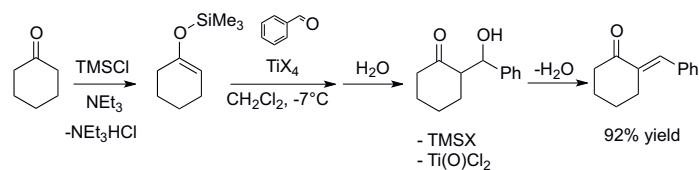
In order to overcome this problem, non industrially viable solutions are generally proposed. A pre-activation of the ketone



Scheme 1. Global synthetic route to Delta Damascone.

partner into a metal enolate or a silylenol ether followed by a catalysed condensation and a final deprotection and dehydration usually affords the desired product in good yield.

As an illustration, the Mukaiyama reaction is particularly well documented.^[8] Out of many other examples, the regioselective condensation of the highly reactive cyclohexanone to benzaldehyde is shown in Scheme 2.



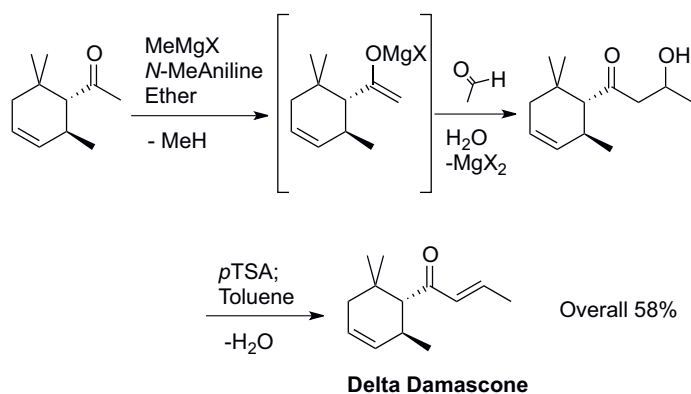
Scheme 2. Example of the 'Mukaiyama' cross aldol reaction.

However, this approach presents several serious drawbacks. It is a multi-step process, requiring the use of protective groups, of stoichiometric quantities of strong bases or hazardous reagents (e.g. LDA, Grignard reagents...), high dilution in unfriendly solvents (e.g. tetrahydrofuran, diethylether, dichloro methane...), and generates large amounts of wastes, hence being far from adequate for industrial purposes, particularly for the manufacture of large volume ingredients.

Unfortunately, the cross-aldol reaction of TDMK with acetaldehyde is a perfect illustration of the 'worst case scenario' for such a condensation process. TDMK is indeed a very hindered and poorly reactive ketone whereas acetaldehyde is probably the most reactive aldehyde in organic chemistry, readily available for oligomerisation or polymerisation reactions. In addition, the final 'enone' fragment of the formed Delta Damascone is not very stable, particularly in alkaline medium. Consequently, traditional aldol catalysis including metal alcoholates, metal hydroxides or metal oxides, strong protic acids, metal triflates, acid or base supported catalysts, is totally ineffective.

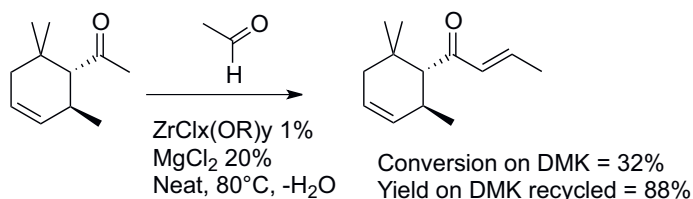
Unsurprisingly, the original IFF synthesis was clearly inspired by the Cookson method and since then we were unable to find any significant modification of this protocol.^[5,9] It is a stepwise process consisting of the pre-activation of TDMK as a magnesium enolate by using a metal amide *in situ* generated from a Grignard reagent and a hindered secondary amine (*N*-methylaniline) in diethylether or tetrahydrofuran as the solvent and low temperature.

The next steps are as follows: introduction of acetaldehyde, hydrolysis of the resulting ketoalcohol intermediate and a final acid-catalysed dehydration affording Delta Damascone. The overall reaction scheme is given in Scheme 3.



Scheme 3. Original industrial process to Delta Damascone.

This process was probably optimised over the years. Nevertheless this approach will surely suffer from some of the above-mentioned drawbacks. This was the reason why we decided to search for a straightforward and fully catalytic alternative that led us to the discovery of an unprecedented cross aldol catalytic process^[10] (Scheme 4)



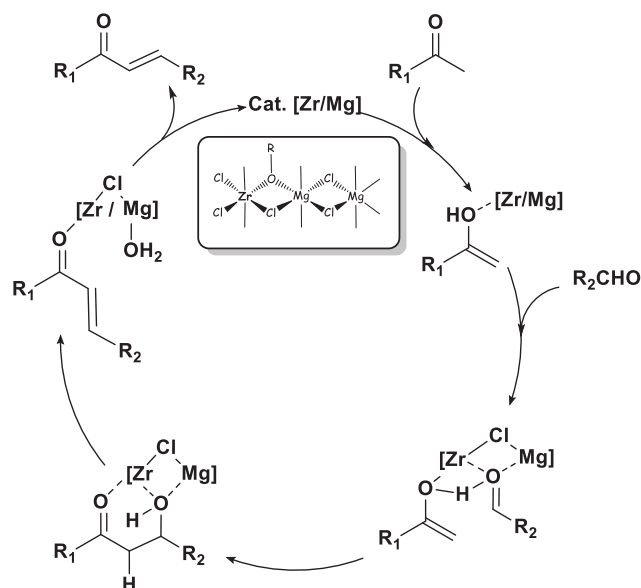
Scheme 4. Unprecedented catalytic process to the manufacture of Delta Damascone.

The main concept was to revisit the Mukaiyama methodology but make it much more sustainable.

Titanium and zirconium were selected as earth-abundant and inexpensive metals and the strong acidity of their halide complexes was modulated by the generation of mixed alkoxy metal chlorides with $x = 1$ to 3 and $y = 4 - x$. Moreover, it is possible to adapt x and y values to the reactivity of the ketonic or aldehydic substrates. Such heteroleptic complexes are readily available from different routes^[11] which exploit the ability of these metals for anionic exchange reactions.

A very important aspect of the cross-aldol transformation, if we want to render the system catalytic, is the resistance of the metal complex used towards water as one equivalent of water is released during the process. If we can't achieve this key point, the use of stoichiometric reagents is mandatory otherwise the catalyst is rapidly deactivated. Ti and Zr complexes exhibit enough acidity to trigger both the enolic activation of TDMK and the aldehydic activation but they are unfortunately also rapidly hydrolysed into their inert hydroxide or oxide species.

Therefore, a notable step forward in the development of the catalytic system was the co-use of an additive like anhydrous magnesium chloride enabling the formation of a stable heterobimetallic complex in which the Mg partner has the ability to extract water from the titanium or zirconium metallic sphere, making the whole catalytic system water resistant and providing an assistance to the dehydration of the aldol intermediate. Consequently, the method becomes truly catalytic at a level as low as 1% molar with zirconium as the metal. The catalytic cycle is depicted in Scheme 5.



Scheme 5. Proposed mechanism for the cross aldol reaction catalysed by the heterobimetallic Zr/Mg complex.

This novel catalytic process is notably attractive on different levels. It is a single-step process including the activation of the substrates and the dehydration to the finished product. It is base free and no protective group is required. The metal 'cocktail' is inexpensive and environmentally benign. It is a neat process, TDMK being used as both the solvent and the reactant. The conversion of Delta Damascone on TDMK was optimised to about 27–34% in order to reach 85–89% selectivity and the unreacted TDMK is readily recycled through a distillation process.

2.2 Green Score of the Aldol Process

As set out by P.T. Anastas and J.C. Warner^[1] green chemistry consists of measurable principles. We are prompted to define relevant metrics so that we can evaluate and compare the performance of the chemical processes, not only in term of cost effectiveness but also in term of safety and carbon footprint.

Several years ago, we developed the Grignard process, including a laboratory optimisation and a pilot campaign, in order to evaluate its potential. Therefore, we were able to perform a comparative analysis with the previously described catalytic process. In Fig. 1, we outlined the material flux necessary to produce a same quantity of Delta Damascone from both approaches, adjusting the different values to 100% from the Grignard process (Fig. 1).

For a comparable consumption of TDMK and acetaldehyde, the catalytic process demonstrates a huge improvement in the use of raw material, particularly hazardous chemicals and solvent such as Grignard reagent, methylaniline, tetrahydrofuran and consequently a real drop in the generation of wastes. As a result, the E factor of the catalytic process is a third of that of the Grignard route.

The solvent-free process is also a big advantage compared to the conventional Grignard reaction using unfriendly solvents like tetrahydrofuran or diethylether.

To conclude this part, the substitution of the standard process by a catalytic version provides a quantum jump to the safety and the sustainability of the manufacture of Delta Damascone, enabling to save the generation of thousand tons of wastes a year. We can assume that the catalytic process to Delta Damascone is a step forward to the ideal concept of the green chemistry principles as illustrated in Scheme 6.

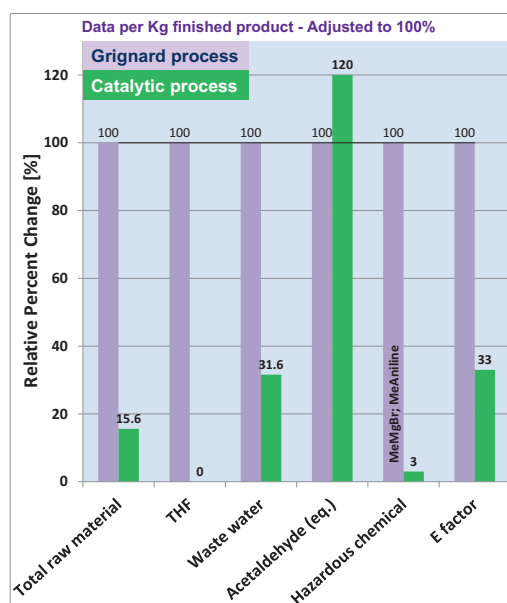
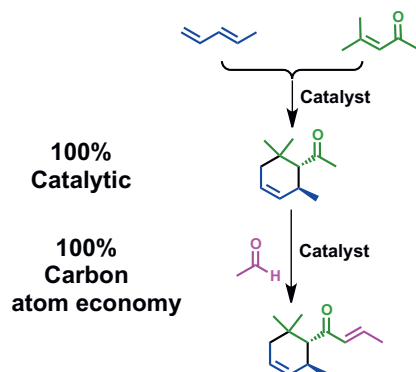


Fig. 1. Comparative analysis of the Grignard vs the catalytic industrial processes in term of environmental performance.



Scheme 6. Carbon efficiency of the catalytic process.

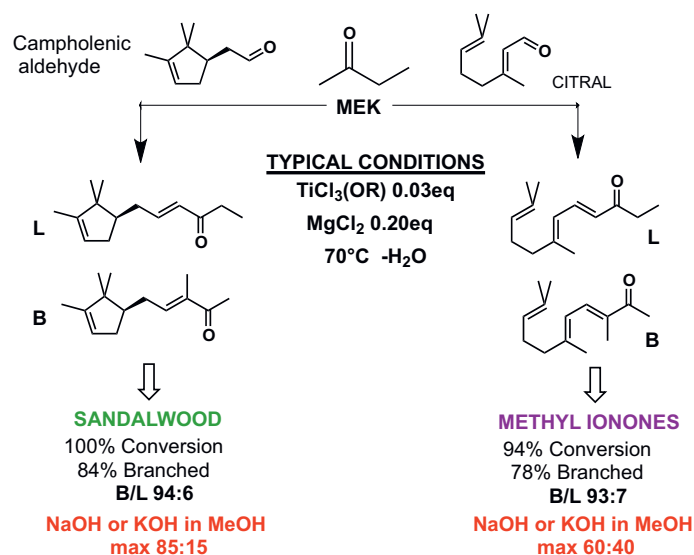
2.3 Chemoselectivity of the New Aldol Catalysis

Before closing this chapter, we present an interesting extension of the new catalysis regarding the chemoselectivity of the cross aldol reaction of unsymmetrical ketones or ketones comprising a methylene alkyl chain on both sides.

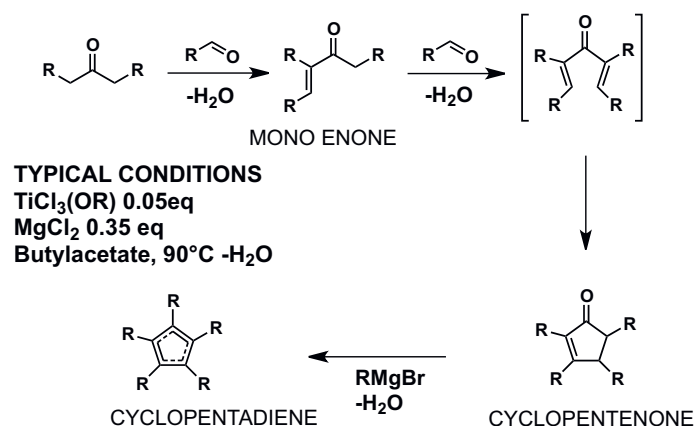
In a first example we are displaying the chemoselectivity achieved in cross-aldol transformation using methylethylketone and aldehydes as reaction partners. When conventional catalysis using bases like sodium or potassium hydroxide or methoxide is applied, a mixture of the 'linear' and 'branched' regioisomers is usually obtained. In contrast, the use of $\text{TiCl}_3(\text{OiPr})$ together with MgCl_2 leads to some noticeably higher selectivity towards the 'branched' isomer. As an illustration, we report the condensation of methylethylketone to campholenic aldehyde affording a 'high-branched' quality of a key precursor of Sandalwood ingredients (Scheme 7). Using Citral as the aldehyde partner, we also accessed the challenging 'high-branched' quality of a key precursor of methyl-ionones (Scheme 7).

In a second example, we report an unprecedented cross-aldol of symmetrical long chain ketones to aldehydes.^[12] The application of the same catalytic cocktail $\text{TiCl}_3(\text{OiPr})/\text{MgCl}_2$ to dialkylketones and various aldehydes led to the unexpected one-pot formation of 2,3,4,5-tetraalkylcyclopentenone through a tandem double aldol and Nazarov cyclisation according to Scheme 8.

This is obviously an attractive method to directly access polysubstituted cyclopentenones and cyclopentadienes, such as the widely used ligand 1,2,3,4,5 pentamethyl cyclopentadiene (Cp Star).



Scheme 7. Selectivity of cross-aldol transformations from unsymmetrical ketones.

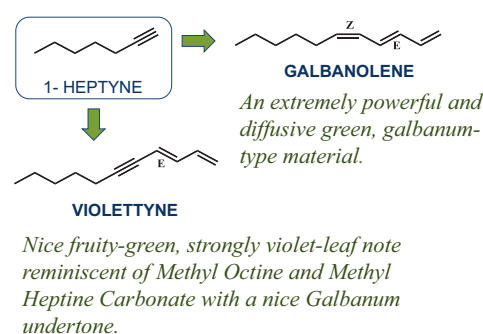


Scheme 8. Straightforward access to tetrasubstituted cyclopentenones.

3. Nickel-catalysed Cross-coupling Processes

3.1 A Green Chemistry for Green Fragrances

Violetteyne and Galbanolene are prestigious green ingredients for perfumery.^[13] Just by looking at their conjugated trienic or diene-yne structure, it is easily deduced that their synthesis from 1-heptyne will be a real challenge (Scheme 9). Most of the synthesis intermediates and the final products exhibit low stability and, in addition, the stereochemistry of the internal double bonds are essential to match the desired olfactory properties.



Scheme 9. Challenging access to Galbanum ingredients from 1-heptyne.

Violettene and Galbanolene are stored and delivered as a highly diluted and stabilised solutions, but the synthetic transformations remain very delicate and require a special mastery of the cross-coupling processes on industrial scale.

The original industrial syntheses^[14] were operated over several decades (Scheme 10). Nevertheless they were suffering from several defects hardly compliant with the principles of green chemistry. Indeed, the first step was a deprotonation of heptyne using hexylGrignard in THF releasing hexane. The Galbanolene route consisted of a coupling reaction using the highly sensitising propargyl tosylate. The next step was an aminomethylation followed by a Lindlar hydrogenation, a quarternisation of the resulting dieneamine and a final elimination. The access to Violettene was shorter from the condensation of heptyne magnesium chloride to crotonaldehyde but due to the poor stability of the product, the use of a strong acid in the final dehydration implied a very high dilution in toluene.

In order to better align the chemistry to the ecological requirements, we searched the literature for cross-coupling catalysts whereby homogeneous palladium displays an undisputed supremacy.

However, in the field of cross coupling of terminal alkynes, among the non-precious metal catalysts, copper and nickel may be attractive alternatives.

In spite of the numerous examples of CuX-catalysed allylations of alkynes using allylhalides together with a large amount of strong base,^[15] we were particularly interested by a paper from M. Catellani who reported a base-free allylation with allylacetate using a Ni(0)tetrakis phosphite complex.^[16] In fact the only drawback of this approach is the need for the highly air sensitive and expensive Ni(1,5-COD)₂ as the catalyst precursor, clearly unsuitable for industrial purposes.

3.2 In Search of a 'Green' Nickel Complex

An important piece of work consisted of finding an industrial alternative to Ni(COD)₂. Among various possibilities, we focused on the Vinal and Reynolds^[17] methodology which offers the advantage of starting from the widely available, inexpensive and air stable nickel(II) chloride hexahydrate salt NiCl₂(H₂O)₆ (Fig. 2).

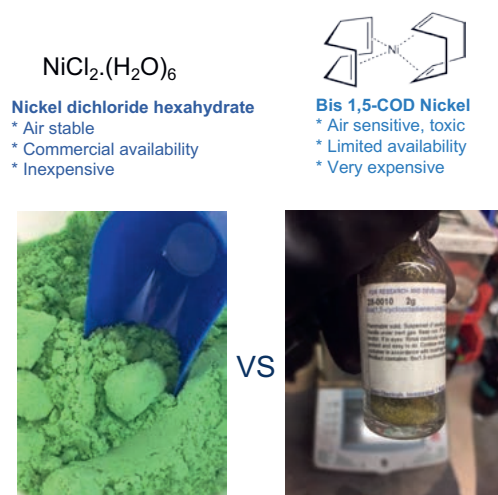


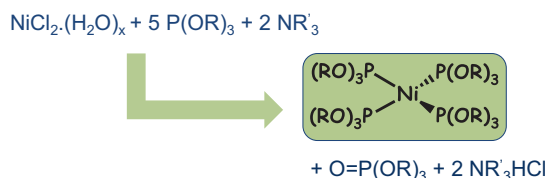
Fig. 2. Choice of nickel precursors for industrial purpose.

Vinal and Reynolds report an elegant and smooth access to nickel tetrakis phosphite complexes by simply reacting the Ni(II) chloride salt in the presence of trialkylphosphite and exactly two equivalents of an amine, with respect to nickel. Interestingly, in this process, trialkylphosphite plays a double role toward nickel, acting both as the ligand and the reducing reagent. In this redox process, phosphite is oxidised to phosphate and the resulting HCl is captured by the amine according to Scheme 11.

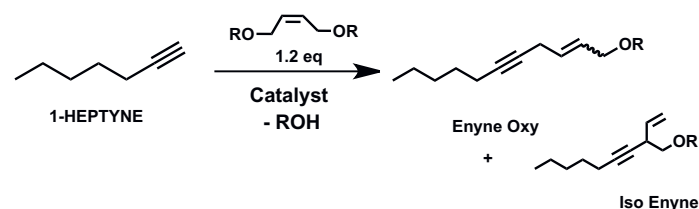
Furthermore, it is worth noting that in this preparation we don't need a strong reducing reagent such as the pyrophoric AlEt_3 , which is generally used to perform the reduction of Ni(II) salts to the Ni(0) active species.^[18]

3.3 'Green' Nickel-catalysed Cross-coupling Reactions

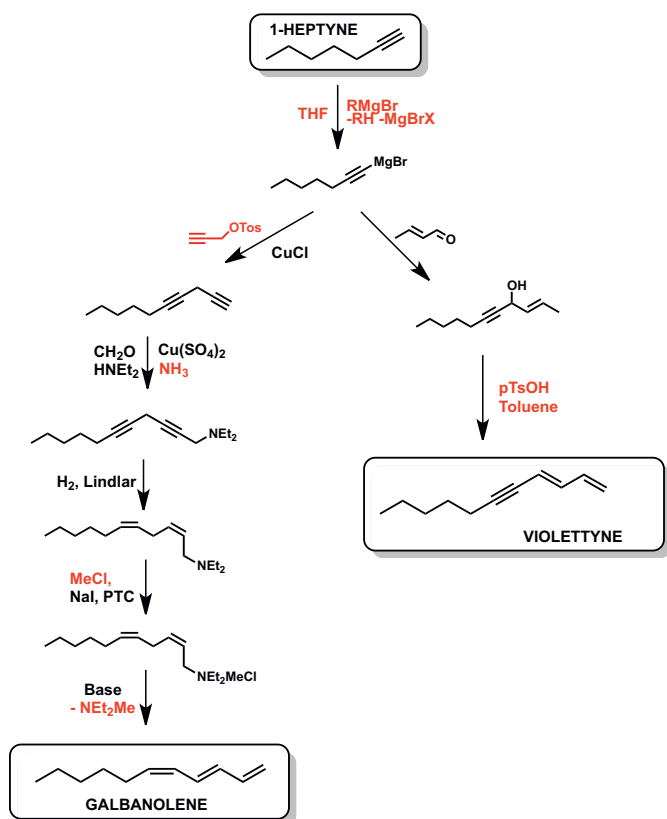
We were pleased to successfully apply this 'green' generation of Ni(0) catalysts to our substrates, namely 1-heptyne and several derivatives of 1,4-butenediol (dioxybutene) as shown in Scheme 12.



Scheme 11. Attractive access to nickel(0) tetrakis phosphite.



Scheme 12. Base free nickel catalysed cross coupling of 1-heptyne to butene 1,4-diol derivatives.



Scheme 10. Original industrial synthesis to both Violettene and Galbanolene.

We were able to adapt the catalyst protocol to our application, still using nickel dichloride hexahydrate as the nickel source, triisopropylphosphite (TIPP) as the ligand and reducing reagent and triethylamine as the catalytic base. The resulting tetrakis(TIPP) Ni(0) was prepared *in situ* and engaged as such, without any further purification, in the cross-coupling process. This protocol was applied to different derivatives of butene 1,4-diol, particularly butene 1,4-diacetoxy (diacetoxybutene). In most of the cases, as expected, we got a mixture of SN₂/SN₂' coupling products. However the desired linear isomer (enyne oxy) was predominant. The most relevant examples are given in Table 1.

We could confirm that the industrial generation of Ni(0) catalyst worked in exactly the same way as the reference process using Ni(COD)₂ and we could even replace tetrahydrofuran by isopropylacetate as the solvent. We also tested some usual cross-coupling catalysts based on copper or palladium, including the Sonogashira catalyst, but all of them proved to be unsuccessful.

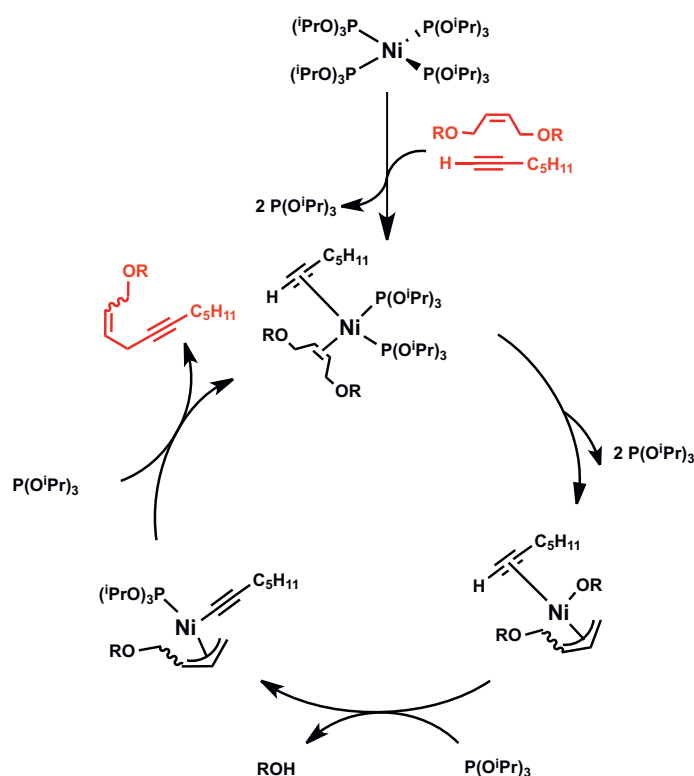
It is worth noting that, in contrast to the traditional cross-coupling catalysis using stoichiometric amount of strong bases, we did not observe the formation of allenic side products. This is another advantage of this attractive base-free methodology.

To close this chapter, we propose a mechanism mainly based on the traditional metal oxidative addition of allylic substrates followed by the alkyne activation then reductive elimination liberating the cross-coupled product (Scheme 13)

3.4 'Green' Nickel-catalysed Elimination

The final elimination reaction of enyneoxy intermediate turned out to be another challenging step as the stereochemistry of the formed double bonds has to meet the product specifications. While the conversion of enyneoxy to dieneoxy (see Tables 2 and 3) was perfectly *Z*-selective by successfully applying a Lindlar-catalysed hydrogenation, the stereochemistry of the consecutive elimination of both substrates was disappointing upon traditional elimination catalysis, DBU or Pd(PPh₃)₄, regardless of the nature of the oxo leaving group.

In the best cases we achieved a *E/Z* mixture with a prevalence of the non-desired *Z* isomer. Luckily, we discovered that *E*-selectivity was favoured by using the 'green nickel' as the catalyst, leading to Violetyne and Galbanolene with an *E*-elimination



Scheme 13. Proposed mechanism for the Ni-catalysed cross coupling of 1-heptyne to allyloxy derivatives.

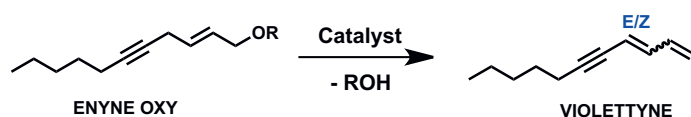
selectivity of 72% and 98% respectively (Tables 2 and 3).

Therefore we could report the first nickel-catalysed *trans* stereoselective allylic elimination. This unexpected *E*-selectivity of the Ni catalysis may be explained by a fast *E/Z* π -allyl isomerisation in contrast to the Pd elimination catalysis, unless this isomerisation is influenced by an extra coordination of the metal to the triple bond (Scheme 14).

Table 1. Cross-coupling catalysis of 1-heptyne to 1,4-diacetoxybutene.

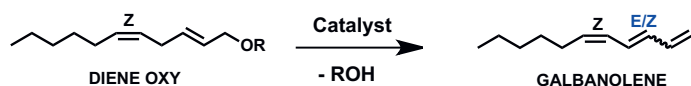
Catalyst Ingredients			Solvent %wt	Conditions	% Yield (isolated)		
Pre Catalyst n.eq.	Ligand n.eq.	Co catalyst n.eq.			Dioxy butene	Enyne oxy	Iso enyne
Ni(COD) ₂ 0.025 eq.	P(OiPr) ₃ 0.1 eq.		THF 300%	8 h, 20 °C	6	42	17
NiCl ₂ (H ₂ O) ₆ 0.025 eq.	P(OiPr) ₃ 0.125 eq.	NEt ₃ 0.05 eq.	THF 100%	16 h, 20 °C	14	50	19
NiCl ₂ (H ₂ O) ₆ 0.025 eq.	P(OiPr) ₃ 0.125 eq.	NEt ₃ 0.05 eq.	iPAcetate 100%	16 h, 20 °C	23	47	17
Pd(OAc) ₂ 0.01 eq.	P(OiPr) ₃ 0.05 eq.	NEt ₃ 0.25 eq.	iPAcetate 100%	16 h, 20 or 70 °C	No reaction		
Pd(PPh ₃) ₄ 0.01 eq.		NEt ₃ 0.25 eq.	THF 400%	16 h, 20 or 70 °C	No reaction		
PdCl ₂ (PPh ₃) ₂ 0.02 eq.	iPr ₂ NH 2 eq.	CuI 0.04 eq.	THF 400%	16 h, 20 or 70 °C	No reaction		
CuI 0.04 eq.		K ₂ CO ₃ 1 eq.	toluene 400%	16 h, 20 or 70 °C	No reaction		

Table 2. Selectivity of the elimination to Violettyne.



Catalyst			Solvent %wt	Conditions	% GC (isolated)	
Catalyst n.eq.	Ligand n.eq.	Co catalyst n.eq.			Violettyne	E/Z (E>70)
DBU 0.1 eq.			toluene	2 h, 80 °C	72%	25/75
Pd(PPh ₃) ₄ 0.05 eq.			THF 200%	5 h, 50 °C	97%	15/85
Ni(COD) ₂ 0.025 eq.	P(OiPr) ₃ 0.1 eq.		MeCN 200%	5 h, 50 °C	98%	72/28
NiCl ₂ (H ₂ O) ₆ 0.025 eq.	P(OiPr) ₃ 0.125 eq.	NEt ₃ 0.05 eq.	MeCN 200%	5 h, 50 °C	97% (79)	72/28

Table 3. Selectivity of the elimination to Galbanolene.



Catalyst			Solvent %wt	Conditions	% GC (isolated)	
Catalyst n.eq.	Ligand n.eq.	Co catalyst n.eq.			Galbanolene	E/Z (E>90)
DBU 0.1 eq.			toluene	2 h, 80 °C	81%	33/67
Pd(PPh ₃) ₄ 0.05 eq.			THF 200%	5 h, 50 °C	97%	33/67
Ni(COD) ₂ 0.025 eq.	P(OiPr) ₃ 0.1 eq.		MeCN 200%	5 h, 50 °C	98%	98/2
NiCl ₂ (H ₂ O) ₆ 0.025 eq.	P(OiPr) ₃ 0.125 eq.	NEt ₃ 0.05 eq.	MeCN 200%	5 h, 50 °C	97% (85)	98/2

3.5 New Industrial Process

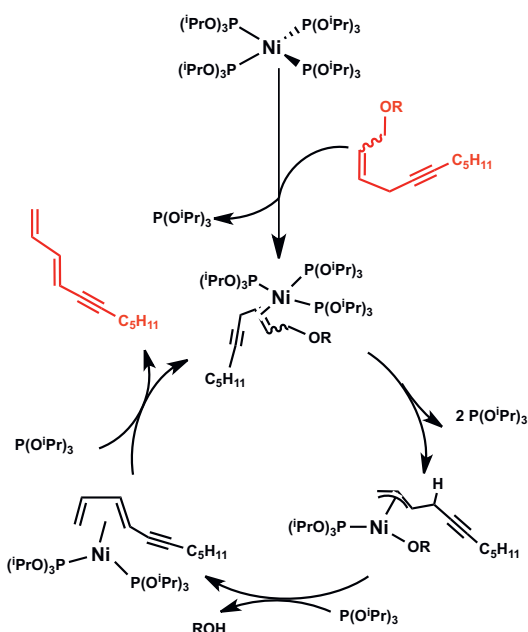
As a consequence of this work, we provided a major improvement of the industrial processes to both Violettyne and Galbanolene (Scheme 15). The whole synthetic scheme has become straightforward, catalytic on all steps, cost effective, safer, and with a *E* factor less than a third compared to the original process. While special care was dedicated to develop the safest and easy handling nickel precatalyst, we also implemented different options for the treatment of nickel-containing water wastes such as burning in a furnace or metal recovery through electrolysis process working with an external partner.

We also optimised the process in order to ensure a full removal of nickel from the finished products.

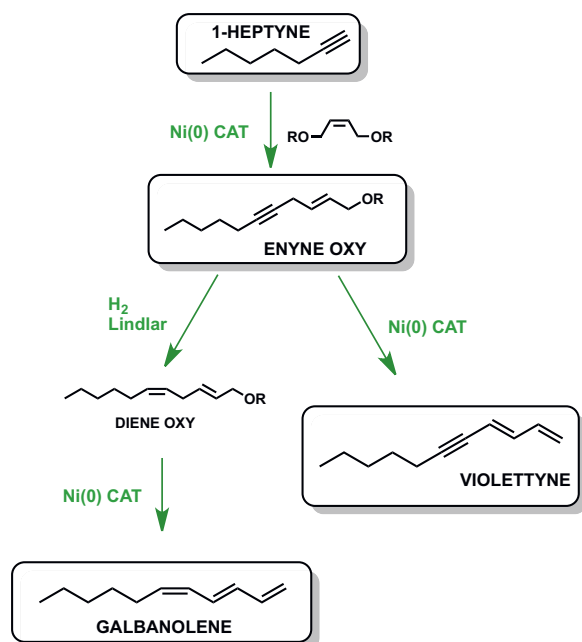
4. Conclusions

To conclude, we can assume that catalysis, and particularly transition metal catalysis, remains one of the cornerstones of modern chemistry to sustain the F&F industry for the upcoming years, together with other relevant areas like biotechnology or renewable carbon sourcing.

As an illustration, we have been pleased to report those examples coming from an extensive research at Firmenich with a view to continuously improve the sustainability of the chemical



Scheme 14. Proposed mechanism for the 'green' nickel-catalysed allylic elimination.



Scheme 15. The new synthesis of Galbanum ingredients.

processes wherever they are operated.

Nowadays, non-precious metal catalysis is experiencing a new momentum, providing cost effective, high yielding and environmentally friendly transformations from earth abundant and inexpensive transition elements.

Non-precious metals often provide a ratio cost vs catalytic turnover clearly advantageous compared to precious elements like palladium and they can provide new reactivity modes towards organic synthesis as it was shown in the titanium or zirconium-catalysed cross-aldol reaction or in the nickel-catalysed chemistry of Galbanum ingredients.

To end with, we would assume that, beyond the big complexity which governs our technological universe, there are still many simple and valuable processes to be discovered, this principle being particularly true in the chemical industry.

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