Transition-Metal Catalysis of the Michael Reaction of 1,3-Dicarbonyl Compounds and Acceptor-Activated Alkenes

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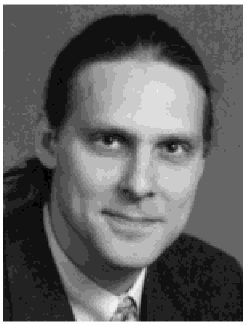
Transition-metal catalysis of the Michael reaction of 1,3-dicarbonyl compounds with acceptor-activated alkenes is introduced as a valuable alternative to the classic base catalysis of this reaction. Owing to the mild, neutral reaction conditions, the chemoselectivity of these processes is superior to that offered by the base catalysis, since the latter suffers from various unwanted side- and subsequent reactions, such as aldol cyclizations and ester solvolyses. The most efficient transition-metal catalysts do not require inert or anhydrous conditions, even solvents are unnecessary in some cases, and quantitative conversions can be achieved at room temperature. Furthermore, the development of transition-metal catalysts on solid supports has allowed very simple work-up procedures. Despite the extraordinary chemoselectivity, in terms of diastereoselectivity transition-metal catalysis gives better results than base catalysis only in a very few special cases. Also, in terms of enantioselectivity, results recently achieved with basic rare-earth metal catalysts cannot be reproduced by transition metals. Nevertheless, with transition-metal catalysis, even new reactivities can be observed, which have hitherto been unknown for base-catalyzed systems. For example, Michael donor molecules have been found to react in an unprecedented vinylogous fashion.

Introduction

The Michael addition reaction of 1,3-dicarbonyl compounds **1** to acceptor-activated olefins **2** is widely recognized as one of the most important carbon−carbon bond-forming reactions in organic synthesis. Traditionally, these reactions are catalyzed by strong bases such as alkali metal alkoxides or hydroxides.[1] Although base catalysis of the Michael reaction is commonly known as a very efficient and high-yielding process, the strongly basic conditions are often a limiting factor since they can lead to a number of side- and subsequent reactions. Scheme 1 outlines some typical drawbacks of a base-catalyzed Michael reaction of a β-dicarbonyl compound **1** with methyl vinyl ketone (MVK, **2a**): First of all, to avoid ester solvolysis (X = alkoxy, pathway a), conversions have to be carried out under exclusion of moisture in anhydrous solvents. Moreover, in some cases, the Michael acceptor itself tends to undergo side-reactions; e.g. enones might form dimers **6** in hetero Diels-Alder reactions (pathway b). More commonly, intermediate enolates **4** bearing other enolizable CH moieties are usually consumed in subsequent aldol processes, leading to cyclic by-products **7** (pathway c). In cases of steric congestion at the quaternary carbon center (R′ ≠ H) in the



Jens Christoffers was born in 1966 and grew up in northern Germany. He studied Chemistry in Marburg (Germany) and in 1992 he moved together with Prof. K. H. Dötz to Bonn (Germany), where he completed his doctorate in 1994 on carbene-complex-fuctionalized Pauson-Khand systems. After a postdoctoral stay with Prof. R. G. Bergman in Berkeley (USA), where he got in touch with zirconocene catalysis, he started his own projects for his habilitation in 1996 at the Technische Universität Berlin. His current research interests are in the field of transition-metal catalysis − with special respect to the Michael reaction − and the design of new polydentate chiral ligands.

MICROREVIEWS: This feature introduces the readers to the authors' research through a concise overview of the selected topic. Reference to important work from others in the field is included.

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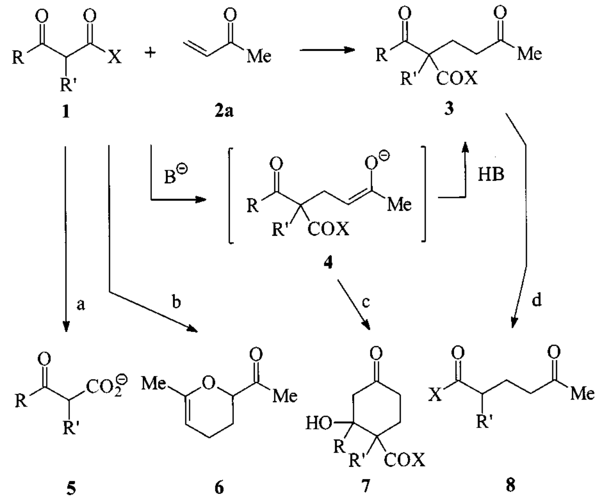
Michael reaction product **3**, retro-Claisen-type carbon−carbon bond cleavage leads to degradation products **8** under basic conditions.

Scheme 1. Base-catalyzed Michael reaction of donors **1** and MVK (**2a**); side- and subsequent reactions: a) ester solvolysis (X = alkoxy), b) hetero Diels-Alder dimerization, c) aldol cyclization, d) retro-Claisen C−C bond cleavage



In order to circumvent strongly alkaline conditions, several alternatives have been developed in recent years that make use of weak Brønsted bases [e.g. $Ba(OH)_2$[2] or alkali metal fluorides][3] or employ mild reaction conditions (e.g. basic zeolites,[4] alumina,[5] phase-transfer catalysis,[6] solid-phase catalysis[7]). However, the most valuable alternatives should be able to proceed under neutral reaction conditions.[8] Most notably, the application of transition-metal compounds as catalysts is a mild and efficient alternative to base catalysis of the Michael reaction.[9] Likewise, lanthanide compounds, which have become very popular for a number of carbon−carbon bond-forming reactions in the past few years,[10] were reported to catalyze the Michael reaction with high efficiency. Catalysis of the Michael reaction of 1,3-dicarbonyl compounds **1** and acceptor-substituted olefins **2** is the subject of this review.

Transition-metal or lanthanide compounds also represent potential catalysts for enantioselective Michael reactions, since they can bear additional chiral coligands. The breakthrough in this field was the discovery of hetero-bimetallic alkali-lanthanide-binolate catalysts by Shibasaki et al.,[11] which facilitate highly efficient catalytic asymmetric Michael reactions with excellent enantioselectivities. However, Shibasaki's work will not be included in this paper for two reasons: First, it has recently been reviewed elsewhere,[12] and secondly, Shibasaki's reaction conditions are not Brønsted-neutral but basic, since anionic binaphtholate ligands are required to deprotonate the Michael donor.

Transition-Metal and Lanthanide Catalysis

The catalysis of transition metals in the Michael reaction was first reported in 1972. Saegusa et al.[13] treated malonates **1a**, **b** and diketones **1c**, **d** (Figure 1) with acceptors such as methyl acrylate (**2b**), acrylonitrile (**2c**), and ethyl propiolate (**2d**) using Cu^I−isonitrile complexes **9a**, which were prepared in situ from Cu_2O (Table 1). In 1980, the first systematic studies were published by Watanabe and coworkers[14] and by Nelson et al.[15]; Ni^{II}− and Co^{II}−bipyridine complexes **9c** and **9d**, as well as $Ni(acac)_2$ (**9e**), were reported to catalyze conversions of a number of donors (malonates like **1a**, diketones like **1c**, and oxo esters and amides like **1e** and **1f**) with various acceptor molecules (**2a**−**c**, **2e**−**k**). In most cases, elevated temperatures (up to

Figure 1. List of Michael donors **1** and acceptors **2** (incomplete)

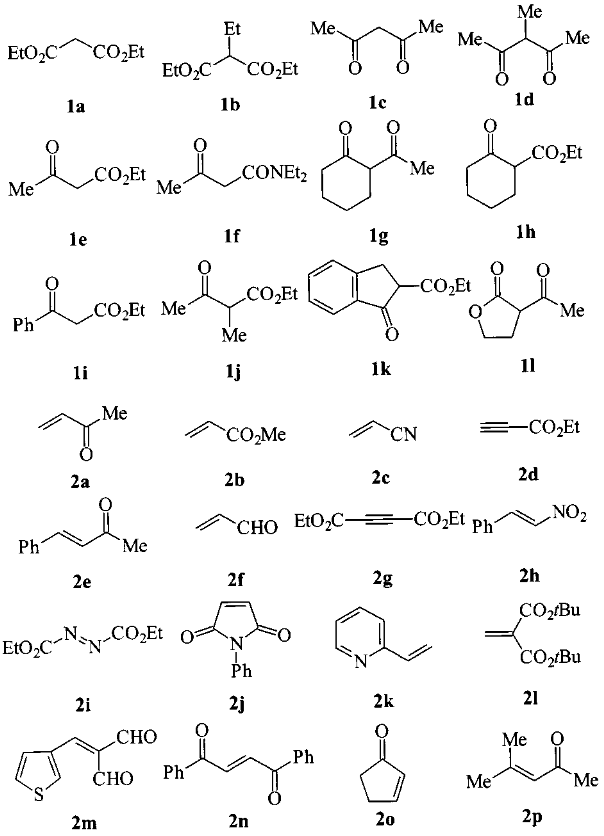


Table 1. Catalytic systems (chronological order)

Catalyst		ref.
Cu_2O−isonitrile	(**9a**)	[13]
$Cu(acac)_2$	(**9b**)	[13]
$Co(OAc)_2$−bpy[a]	(**9c**)	[14]
$Ni(OAc)_2$−bpy[a]	(**9d**)	[14]
$Ni(acac)_2$	(**9e**)	[15]
$Ni(acac)_2$−polymer-bound	(**9f**)	[16]
$Fe(acac)_3$−polymer-bound	(**9g**)	[16]
$Cu(OAc)_2 \bullet H_2O$	(**9h**)	[17]
$Co(acac)_2$	(**9i**)	[18]
$M(acac)_n + Et_2O \bullet BF_3$	(**9j**)	[21]
$Ru(PPh_3)_4H_2$	(**9k**)	[19]
$Ni(acac)_2$ on solid support + $FeCl_3$	(**9l**)	[22]
$EuCl_3$	(**9m**)	[23]
$RhH(CO)(P_2)$[b]	(**9n**)	[20]
$Yb(OTf)_3$	(**9o**)	[25]
$EuCl_3 \bullet 6\ H_2O$ (microwave oven)	(**9p**)	[24a]
$FeCl_3 \bullet 6\ H_2O$	(**9q**)	[26]

[a] bpy = bipyridyl. − [b] (P_2) = chiral diphosphane.

100 °C) and inert solvents were required in order to achieve satisfactory conversions (50−90% yield). In the following years, numerous other catalytic systems (**9f−i**, **k**, **n**) were described (see Table 1) and, although these did not actually introduce any significant improvements, they did broaden the range of types of Michael donors and acceptors that could be applied (**1g−1l**, **2l−2o**).[16][17][18][19][20] It is worthy of mention that the application of catalytic amounts of an additional Lewis acid either BF_3 (**9j**)[21] or anhydrous $FeCl_3$ (**9l**)][22] besides the transition-metal compound allowed a reduction of the reaction temperatures.

In 1993, Scettri and co-workers[23] reported $EuCl_3$ (**9m**) in anhydrous CCl_4 to be an efficient catalyst for the Michael reaction, which was an interesting discovery in two respects: It was the first lanthanide salt to be applied in this field, and it also broke the previous unwritten rule that either the catalyst had to be a complex bearing dionato ligands, or that the anion had to be a Brønsted base such as acetate, so that dionato species would be readily generated in situ from the 1,3-dicarbonyl compounds. There have been some improvements on Scettri's procedure since the original report.[24] For example, Feringa and Keller[25] reported Michael reactions in aqueous media at room temperature by employing $Yb(OTf)_3$ (**9o**) as catalyst. Although a threefold excess of the acceptor and 10 mol-% of the Yb salt were required in order to achieve satisfactory conversions, the efficiency of this procedure was outstanding at the time. The work-up procedure was reported to be extraordinarily simple and the catalyst could be reused.

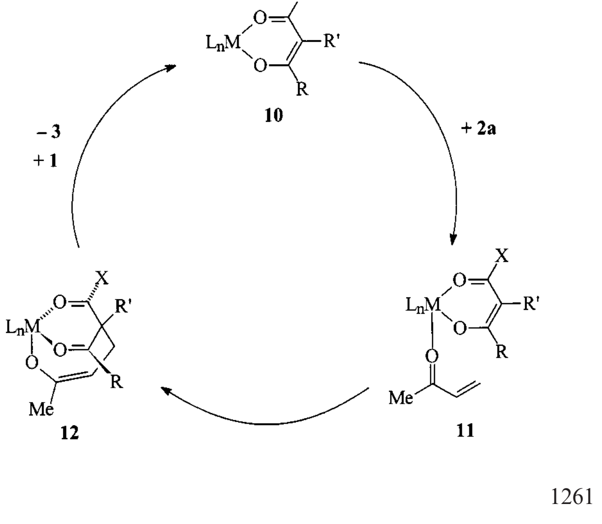
Further improvement of the Feringa protocol was reported in 1997 through the introduction of $FeCl_3 \bullet 6\ H_2O$ (**9q**) as the catalyst.[26] β-Diketones or β-oxo esters and MVK (**2a**) were cleanly converted to the corresponding Michael reaction products within a few hours at room temperature, with quantitative yields being achieved in most cases. No significant excess of the Michael acceptor was required, and the amount of **9q** employed was as low as 1 mol-%. Importantly, as long as the product and the starting materials were liquid at room temperature, solvents were unnecessary. Moreover, the reactions were performed without any need for anhydrous or inert conditions. Since no side-reactions were observed, work-up was very simple: Filtration through a short column of silica gel removed all iron-containing materials. Considering also the environmentally friendly nature[27] of **9q**, the Fe^{III} catalysis represents the most important alternative to the classic base catalysis of the Michael reaction reported to date. The strong tendency of Fe^{III} to form 1,3-dionato complexes under neutral and even under acidic conditions, which has been known since the beginning of this century,[28] is thought to be the underlying reason for the outstanding efficiency of the Fe^{III} catalysis. However, only $FeCl_3 \bullet 6\ H_2O$ seems to be a very active catalyst, possibly due to its kinetic lability and vacant coordination sites at the iron center. $Fe(acac)_3$[16][21] and anhydrous $FeCl_3$[22] are significantly less active than the hexahydrate **9q**. However, not all donors or acceptors can be converted with **9q**, and some substituted acceptors require elevated temperatures (50 °C).[26b]

Catalysis of the Michael reaction of 1,3-dicarbonyl compounds and α,β-unsaturated carbonyl compounds is a property not only shown by the compounds listed in Table 1: Several transition and main-group metal ions, which have at least some tendency to form 1,3-dionato complexes, also show catalytic activity, e.g. Cr^{III}, Mn^{II}, Ag^{I}, Zn^{II}, Pb^{II}, and Sn^{II}.[29] However, the most efficient compound is $FeCl_3 \bullet 6\ H_2O$ (**9q**), which is followed by Ni^{II}, Co^{II}, and Cu^{II} species.

Mechanism

Although it is rather unlikely that all the different catalytic systems listed in Table 1 induce reactions of 1,3-dicarbonyl compounds **1** with acceptors **2** according to the same mechanism, a number of authors has made proposals to this effect. At least for Ni^{II},[15] Cu^{II},[17] Co^{II},[18] and Fe^{III},[26a] as well as for the lanthanides,[23][25] it is well understood that under the reaction conditions 1,3-diketonato species **10** (Scheme 2) are formed [on the other hand, Ru^{II} [19] and Rh^{I} [20] might follow a completely different mechanism]. Starting from complexes **10**, in which the ligand is planar and is particularly stabilized by π-delocalization, the enone **2a** is proposed to coordinate at a vacant coordination site to form species **11** (Scheme 2). Subsequently, the central carbon atom of the dionato ligand is thought to be alkylated by the coordinated enone, but only if the enone is in the *s-cis* conformation. The latter is obviously impossible for cyclopentenone (**2o**) and is strongly disfavored in mesityl oxide (**2p**), and indeed, little or no reactivity was reported for these acceptors **2o**[26a] and **2p**.[21] Likewise, propiolate **2d** cannot achieve an *s-cis*-like conformation; the α-carbon atom of the donor and the β-carbon atom of the acceptor cannot get close enough to each other if coordinated to the same metal center, and so **2d** cannot be converted according to the mechanism outlined in Scheme 2.[25] However, once intermediate **12** is formed, product **3** is liberated readily and complex **10** can be regenerated through ligand exchange. The central carbon atom of

Scheme 2. Proposed mechanism for the transition-metal-catalyzed Michael reaction



the dione ligand in **12** is tetrahedral, thus π delocalization is impossible, and the compound is destabilized compared to compounds **10** and **11**.

Overall, the transition-metal catalysis of the Michael reaction outlined in this section is a template reaction in the classical sense: Both reactants are coordinated to and activated by the same metal center. In fact, Fe(acac)$_3$, which offers no vacant coordination site to an enone, does not catalyze the Michael reaction at all by itself; in this case, activation of the acceptor by an additional Lewis acid is required.[21]

Chemoselectivity

As outlined in Scheme 1, there are a number of disadvantages associated with base catalysis of the Michael reaction, including side-reactions of the starting materials **1** and **2** and subsequent reactions of the products **3**. Incompatibilities with base-sensitive groups, ester solvolyses, aldol processes leading to cyclic products, or retro-Claisen-type decompositions can in some cases significantly decrease the yields of the base-mediated Michael reactions. As a representative example, the formation of **3a** from acetylacetone (**1c**) and MVK (**2a**) is discussed here in detail. The reaction shown in Scheme 3 is known as a notorious worst-case scenario, since the product bears three enolizable acetyl moieties, each of which is capable of undergoing subsequent aldol cyclizations. Indeed, the classical procedure employing 2 mol-% NaOMe in absolute MeOH yielded only 45% of the product **3a**, which had to be separated from various by-products.[30] In Table 2, this result is compared with a number of transition-metal- and lanthanide-catalyzed procedures. By virtue of the neutral reaction conditions, in the latter cases aldol reactions are avoided, and thus yields of product **3a** are significantly improved. The optimal conditions, which employ either Nelson's[15] Ni(acac)$_2$ catalyst or Laszlo's[22] bimetallic system, give 90% isolated yields of the target molecule **3a**.

Scheme 3. Catalyzed formation of **3a**

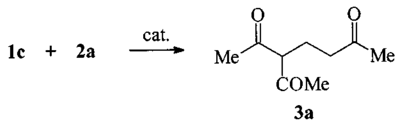


Table 2. Catalyzed formation of **3a**

Catalyst (mol-%)	Conditions	**3a**, Yield (%)	ref.
MeONa (2)	30°C, 24 h	45	[30]
9e (1)	85°C, 18 h	90	[15]
9h (1)	100°C, 72 h	77	[17a]
9l	20°C, 24 h	90	[22]
9p (2)	100 W[a], 10 min	82	[24a]

[a] Microwave power.

Diastereoselectivity

Diastereoselectivity in transition-metal-catalyzed Michael reactions has only rarely been reported.[26b][31] Two general cases have to be distinguished: In the first, the newly formed stereocenter, the former C−H-acidic α-center of the donor, is a quaternary carbon atom. In the second case, this carbon center is a tertiary one.

For the first case, as far as diastereoselectivity is concerned, transition-metal catalysis has never been reported to offer an improvement on the results obtained with base catalysis. Stereoselectivities achieved are either not very different,[26b] or base catalysis is found to be more selective than transition-metal catalysis (Scheme 4 and Table 3, products **3b** and **3c**).[31]

Scheme 4. Diastereoselective Michael reactions

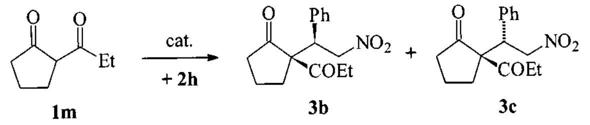


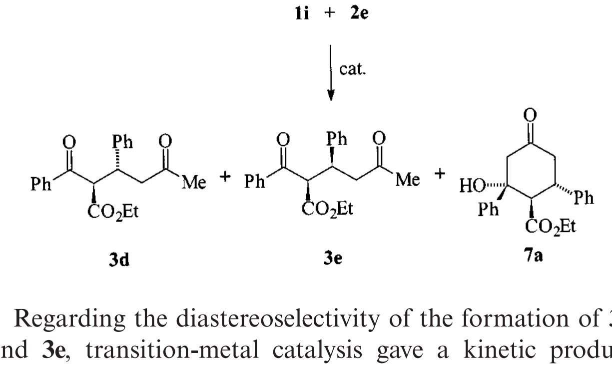
Table 3. Diastereoselective Michael reactions; comparison of base and transition-metal catalysis

Catalyst (mol-%)	Conditions	Product	Yield (%)	d.r.[a]
DMAP[b] (7)	toluene, 20°C, 1 d	**3b**/**3c**	90	88:12
Ni(acac)$_2$ (3.5)	toluene, 80°C, 1 d	**3b**/**3c**	50	48:52
Ni(acac)$_2$ (3.5)	toluene, 20°C, 70 d	**3b**/**3c**	45	59:41
EtOK (5)	EtOH, 23°C, 1 d	**3d**/**3e** (**7a**)	48 (12)	39:61
FeCl$_3$ (1)	CH$_2$Cl$_2$, 50°C, 1 d	**3d**/**3e** (**7a**)	85 (0)	84:16

[a] Diastereomeric ratio. − [b] 4-(Dimethylamino)pyridine

More interesting is the second case (Scheme 5): Products **3d** and **3e** still bear a β-oxo ester moiety with a formally acidic C−H bond, thus one might expect them to be in constant thermodynamic equilibrium through the corresponding enol form. However, compounds **3d** and **3e** fail to equilibrate, and they can even be separated by chromatography. The inability of the isomers **3d** and **3e** to interconvert under neutral conditions seems to be closely related to the 1,3-diphenyl structure of these products. Presumably, the enol form, which would be the intermediate species in an equilibrium of the two diastereoisomers, cannot be stabilized by H-bonding because of allylic 1,3-strain.[32]

Scheme 5. Diastereoselective Michael reactions



Regarding the diastereoselectivity of the formation of **3d** and **3e**, transition-metal catalysis gave a kinetic product mixture in an 84:16 ratio.[26b] In contrast, base catalysis led to a thermodynamic mixture (**3d**/**3e** = 39:61) (Table 3) since the isomers were of course in equilibrium in the basic medium. In other words, transition-metal catalysis can yield a kinetic product distribution even in cases where base catalysis would lead to a thermodynamic mixture. These kinetic and thermodynamic ratios can be significantly different, as shown for compounds **3d** and **3e** (Table 3).

Enantioselectivity

A number of authors have reported on enantioselective base-catalyzed Michael reactions.[33] For example, cinchona alkaloids[34] or derivatives of natural amino acids[35] have often been mentioned as chiral bases. A breakthrough in this area was the discovery of the hetero-bimetallic alkali rare-earth metal catalysts with binolate ligands by Shibasaki et al.[11] For example, a catalyst derived from one equivalent La^{III}, three equivalents Na^{I}, and three equivalents of binaphtholate was reported to catalyze the Michael reaction of 1,3-dicarbonyl compounds **1** and enones **2** with high efficiency (yields up to 91%) and with excellent enantioselectivity (*ee*'s up to 93%).[11]

However, as already mentioned in the introduction, Shibasaki's reaction conditions are not neutral but basic, and thus this work will not be reviewed in this article in more detail. Moreover, Shibasaki's work has recently been reviewed elsewhere.[12b]

The first enantioselective example of transition-metal catalysis was reported by Brunner and Hammer,[18] who applied Co(acac)$_2$ and a C_2-symmetrical diamine (**13a**, Figure 3) as the chiral ligand. The product **3f** (Figure 2) was formed with 66% *ee* (Table 4), a value which was subsequently improved[36] up to 75% *ee* (for **3f**).[37] In the latter case, Desimoni et al. employed Cu^{II} complexes with chiral salicylimine ligands derived from chiral amino alcohols (**13b**,**c**).

Other groups have also reported asymmetric Michael reactions with chiral diamines,[36b][38] chiral diphosphanes,[39] and chiral salicylimines[40] (see Table 4 for details). Interestingly, the chiral NMR shift reagent Eu(tfc)$_3$ (**13g**) [tfc = 3-(trifluoromethylhydroxymethylene)-D-camphor] has also been reported to catalyze Michael reactions enantioselectively.[23]

Figure 2. List of products in asymmetric Michael reactions (incomplete)

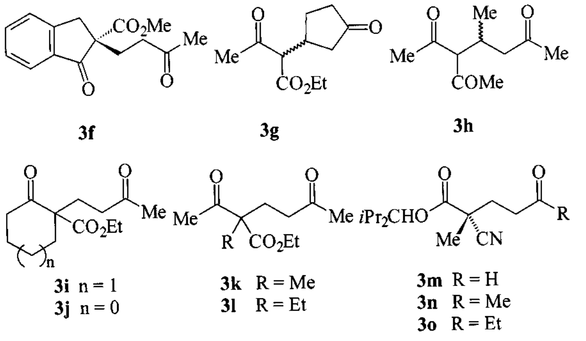


Figure 3. List of chiral catalysts (incomplete)

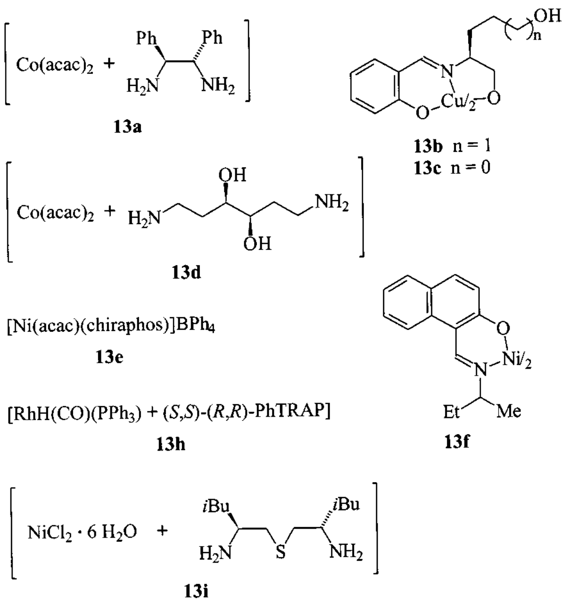


Table 4. Asymmetric Michael reactions

Product	Catalyst	*ee* [%] (yield [%])	ref.
3f	**13a**	66 (59)	[18]
3f	**13b**	70 (quant.)	[36a]
3f	**13d**	38 (91)	[36b]
3f	**13c**	75 (quant.)	[37]
3g	**13e**	≠ 0 (19)	[39]
3h	**13e**	≠ 0 (15)	[39]
3i	**13a**	39 (41)	[41]
3k	**13f**	6 (71)	[40]
3l	Eu(tfc)$_3$ (**13g**)	36 (50)	[23]
3m	**13h**	92 (88)	[42]
3n	**13h**	93 (99)	[42]
3o	**13h**	91 (99)	[42]
3j	**13i**	17 (90)	[38]

To date, best results with regard to asymmetric transition-metal catalyzed Michael reactions have been those of Ito and co-workers,[20] who reported *ee*'s up to 93% together with very good yields (up to 99%), using an Rh^{I} catalyst **13h**. The ligand in this case was a chiral diphosphane, abbreviated as PhTRAP {2,2''-bis[1-(diphenylphosphanyl)ethyl]-1,1''-biferrocene}, which was designed and synthesized to form transition-metal complexes in a *trans*-chelating manner.[42]

Supported Catalysts

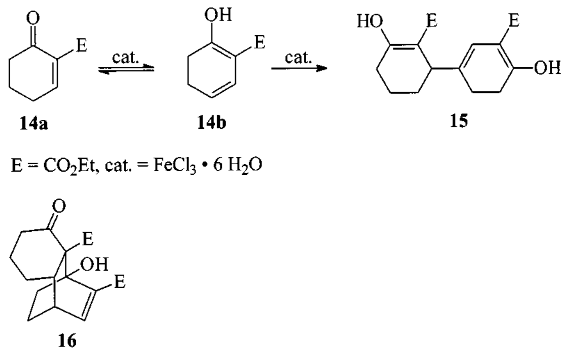
Commonly, homogeneous catalysis is assumed to be superior to heterogeneous catalysis, because catalytically active species are often well defined, thus resulting in better selectivities compared with heterogeneous systems. However, the main disadvantage of homogeneous catalysis is the catalyst-product separation following the reaction, which is obviously very simple in the case of heterogeneous systems. For this reason, polymer-supported transition-metal catalysts were developed very soon after the first reports of Nelson's Ni(acac)$_2$ catalysis of the Michael reaction.[16] Chan and Fei prepared a polymer-bound Ni system by simple reaction of Ni(acac)$_2$ with a chloromethylated macroporous polystyrene resin. In neutral media, the polymer-anchored dionato groups formed kinetically stable Ni complexes. Analogous Fe^{III} complexes have been prepared by ligand-exchange reactions. Results of Ni-catalyzed Michael reactions achieved with homogeneous systems were more or less reproducible with these supported catalysts, but the work-up procedure was of course significantly simpler in the heterogeneous case. Besides organic polymers,[39] Michael reaction catalysts supported on inorganic oxides have also been reported. For example, Laszlo's clay-supported nickel bromide[22] succeeded in reproducing Nelson's initial results in most cases, but additional Lewis acid activation (by anhydrous $FeCl_3$) was required, and in terms of chemoselectivity, subsequent aldol cyclizations were unavoidable for some substrates.

Kotsuki and co-workers[24b] recently introduced an important improvement by the application of $Yb(OTf)_3$ supported on silica gel. Highly efficient conversions, even of acceptors such as **2o**, which cannot be brought to reaction using $Yb(OTf)_3$ in homogeneous solution,[25] were achieved simply by mixing solutions of the starting materials **1** and **2** with the $Yb(OTf)_3/SiO_2$ catalyst. After evaporation of the solvent, the Michael reaction proceeded without solvent on the silica gel surface within 1−6 days at room temperature.

Vinylogous Donors

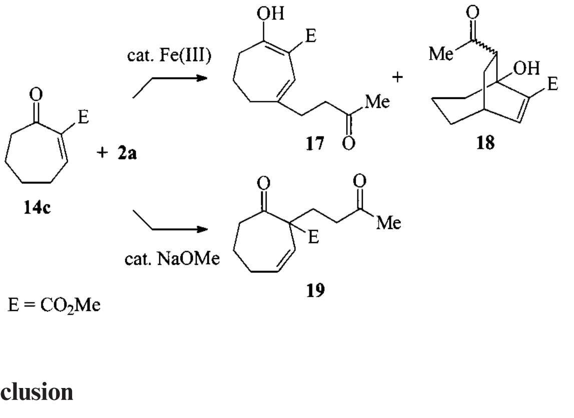
Cycloalkenone-2-carboxylates such as **14a** are valuable synthons in organic synthesis. For example, they can act as acceptors in Michael reactions[43] and they readily undergo Diels-Alder reactions with donor-functionalized dienes.[44] In the course of the author's investigations on Fe^{III}-catalyzed conversions of carbonyl compounds,[26] catalyzed tautomerization of **14a** to the dienol **14b** was observed.[45] The equilibration shown in Scheme 6 was achieved either by applying Brønsted acids (e.g. TFA) or by the use of a base (e.g. DMAP). However, this enone-dienol equilibration can also be achieved using a catalytic amount of iron(III) chloride hexahydrate in CH_2Cl_2 as solvent, although such mixtures are unstable and undergo conversion to a unique product **15** at room temperature.[45] Compound **15** was actually obtained as a mixture of tautomers; the constitution of the major isomer only is given in Scheme 6. At first glance, product **15** appears to be the dimer of the starting material **14a**, **b**. On closer inspection, the structure of **15** can be seen to be formally that of a Michael reaction product of the acceptor **14a** with the vinylogous donor **14b**. Vinylogous reactivity of Michael donor molecules, which is well known in aldol chemistry,[46] had previously been unprecedented in organic synthesis, but has now been observed for the first time in this Fe^{III}-catalyzed system. A mechanistic rationale for the formation of **15** might involve − after enone-dienol tautomerization − not a direct vinylogous Michael reaction, but a sequence of a [4 + 2] cycloaddition of **14a** and **14b** followed by a retro-aldol-type C−C bond cleavage of the intermediate **16**. Thus, the constitution of a formally vinylogous (with respect to the donor) Michael reaction product is generated by a sequence of enone-dienol tautomerization, Diels-Alder, and retro-aldol reactions.

Scheme 6. Fe^{III}-catalyzed dimerization of cycloalkenone-2-carboxylates



The dimerization reaction shown in Scheme 6 can be circumvented if the donor is treated with an excess of a different acceptor (Scheme 7). For example, Fe^{III}-catalyzed reaction of the seven-membered ring donor **14c** with **2a** furnished compound **17**, which again has the constitution of a formally vinylogous (with respect to the donor) Michael reaction product.[47] Moreover, the already postulated Diels-Alder intermediate **18** was obtained as a by-product in this case. The distinct effect of the iron(III) catalysis becomes particularly clear upon comparison with the base-catalyzed reaction of **14c** with MVK (**2a**), which yielded product **19** (Scheme 7). The latter can be regarded as the classic Michael reaction product, whereas iron(III) forces **14c** to react as a vinylogous Michael donor. This unprecedented behavior is another example of the novel selectivities that can be achieved by the application of transition metals as catalysts. Because of the particularly mild reaction conditions and the ecologically and economically friendly nature of the catalyst $FeCl_3 \bullet 6\,H_2O$, this novel vinylogous (with respect to the donor) Michael reaction can be regarded as an improvement on the classic Michael-type C−C bond-forming reactions.

Scheme 7.Fe^{III}-catalyzed Michael reaction of the vinylogous donor **14c**; base catalysis of a normal Michael reaction of **14c**



Conclusion

Catalysis of the Michael reaction of 1,3-dicarbonyl compounds with acceptor-substituted olefins by transition metals and lanthanides can be a valuable alternative to the classic base catalysis of this reaction. Since the reaction conditions are neutral and mild, a number of the side- and subsequent reactions usually associated with base catalysis, such as incompatibilities with base-sensitive groups, ester solvolyses, aldol cyclizations, or retro-Claisen-type processes, can be eliminated. The most efficient catalysts, such as $FeCl_3 \bullet 6\ H_2O$, do not require inert or anhydrous conditions, even solvents are unnecessary in some cases, and conversions are fast and clean at room temperature. Thus, high chemoselectivity can be achieved with transition-metal catalysts even in cases where base catalysis gives poor results or fails altogether. As far as diastereoselectivity is concerned, transition-metal catalysis can give kinetic product ratios even in cases where base catalysis leads to thermodynamic equilibrium mixtures, although these examples are somewhat special and cannot be generalized. In terms of enantioselectivity, transition-metal catalysis has not yet matched the results obtained with, e.g., basic rare-earth metal catalysts bearing binaphtholate ligands. Only in a very small number of cases have *ee*'s larger than 90% been achieved. However, with transition-metal catalysts, even some new reactivities have been observed, that were hitherto unknown for base-catalyzed systems. For example, $FeCl_3 \bullet 6\ H_2O$ causes some Michael donor molecules to react in an unprecedented vinylogous fashion, a result which can be regarded as a valuable addition to classic Michael-type C−C bond-forming chemistry.

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