Lewis acidic platinum(II) complexes as catalysts for the hetero Diels–Alder reaction

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Dedicated to Professor Renato Ugo in occasion of his 65th birthday

Abstract

Bis-triflate diphosphine complexes of Pt(II) can be used as catalysts for the hetero Diels–Alder reaction (DA) between simple dienes (isoprene, 2,3-dimethylbutadiene) and glyoxylate esters or simple aldehydes (benzaldehyde, terephthalaldehyde) to yield a variety of substituted dihydropyrans under mild conditions. The reactions produces also hetero-ene products, but the selectivity to hetero Diels–Alder is always high (75–100%). Chiral catalysts based on R-binap yield only low e.e.'s.
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1. Introduction

Over the past few years, a great interest has arisen on the use of cationic, square planar, diphosphine based Pd(II) and Pt(II) Lewis acid catalysts for selective carbon–carbon bond-forming reactions [1–13]. Among these, the Diels–Alder reaction (DA) stands as one of the most powerful methods of C–C bond construction in synthetic organic chemistry [14–19]. The softness of Pd(II) and Pt(II) metal centers that increases their carbophilicity with respect to oxophilicity [20] makes them particularly attractive as unusual reaction pathways are in principle possible [12,13].

In a previous paper [2], we have reported the use of a variety of solvento and chloro complexes of Pd(II) and Pt(II) for the ordinary and the enantioselective DA reaction using simple dienophiles like, e.g.

acrolein. Complexes of the type $[(P–P)M(solv)_2]^{2+}$, $[(P–P)M(OTf)_2]$ and $[(P–P)M(\mu\text{-Cl})]_2^{2+}$ (P–P = diphosphine; M = Pd, Pt; solv = MeCN, THF; OTf = triflate) have been employed as catalysts. It was observed that bis-solvento species or species bearing poorly coordinating anions such as TfO^- are the most active catalysts, however they are unable to exert a sufficient stereochemical control in enantioselective transformations because the presence of two vacant coordination sites does not allow the necessary stereochemical rigidity to the intermediate M (dienophile) adduct (Scheme 1). This observation, which applies to simple dienophiles, contrasts with many examples reported in the literature ([12,13] and references therein) where chelating dienophiles like, e.g. acryloyl-*N*-oxazolidinone (Scheme 1) ensure the formation of a rigid template. This issue has been clearly defined by Kündig and Saudan as two-point binding versus one-point binding [21]. With simple dienophiles, it was therefore necessary to switch to less Lewis acidic (and less active) $[(P–P)M(\mu\text{-Cl})]_2^{2+}$

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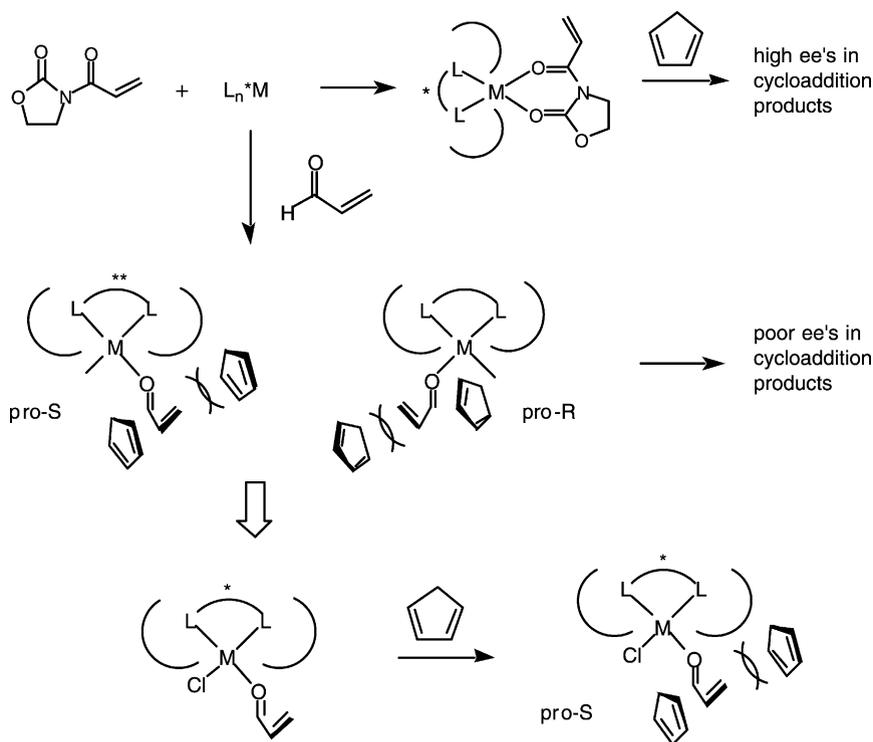
Scheme 1.

species, having only one vacant coordination site, that allow a certain degree of stereochemical control. From this point of view the switch to the hetero DA reaction, that deals with more functionalized substrates (e.g. see in Eq. (1) the synthesis of dihydropyrans) capable of binding the metal in a potentially chelating mode, may allow the successful use of the more coordinatively unsaturated and hence more Lewis acidic species.

In this work, we report the use of diphosphine Pt-triflate complexes as catalysts for the synthesis of substituted dihydropyrans starting from isoprene or 2,3-dimethylbutadiene and a series of glyoxylate esters (which in principle should be two-point binding systems) via hetero DA cycloaddition.

2. Experimental

2.1. General

IR spectra were taken on a Nicolet FTIR Magna 750 and on a Digilab FTS 40 interferometers either in solid (KBr pellets) or in CH_2Cl_2 solution using CaF_2 win-

dows. ^1H and $^{31}P\{^1H\}$ NMR spectra were recorded on a Bruker AC 200 spectrometer operating in FT mode, using as external references TMS and 85% H_3PO_4, respectively. Negative chemical shifts are upfield from the reference. Unless otherwise specified CD_2Cl_2 was used as the solvent. Conductivity measurements were performed on a Radiometer instrument using 10^{-3} M solutions at 25 °C. GC measurements were taken on a Hewlett-Packard 5790A gas chromatograph equipped with a 3390 automatic integrator. The following commercial columns were used: HP-5 and HP-FFAP (from Hewlett-Packard), Lipodex E (from Macherey-Nagel). GC–MS measurements were performed on a Hewlett-Packard 5971 mass selective detector connected to a Hewlett-Packard 5890 II gas chromatograph. Identification of products was made with GC or GC–MS by comparison with authentic samples.

2.2. Materials

Solvents were dried and purified according to standard methods. 1,2-Bis-diphenylphosphinobutane

(dppb, from Strem), R-binap (from Fluka) and most of the synthetic reagents were commercial products and used without purification.

The synthesis of glyoxylate esters was performed according to the method outlined by Wolf and Weijlard [22]. The following complexes were prepared according to literature procedures: [(COD)PtCl$_2$] [23], [(COD)PtMe$_2$] [24]. The preparation of [(dppb)Pt(OTf)$_2$] and [(R-binap)Pt(OTf)$_2$] was accomplished according to a new method outlined below. It should be noticed that both triflate complexes were identified as cationic in [2], where at least one of the TfO$^-$ was recognized to be present as non-coordinating anion. However, being the extent of the interaction strongly dependent on temperature, for a simpler notation complexes will be indicated as above.

2.3. [(dppb)Pt(OTf)$_2$]

In a round-bottomed flask, dppb (255 mg, 0.599 mmol) and benzene (10 ml) were introduced under N$_2$, followed by [(COD)PtMe$_2$] obtaining a yellow solution that was stirred for 2 h. The initially clear solution became turbid with time because [(dppb)PtMe$_2$] is slightly soluble in benzene. Then HOTf (0.105 ml, 1.198 mmol) was added in four aliquots (one every 30 min) venting from time to time to eliminate CH$_4$. After the addition was completed, the mixture was reacted for 40 min, then brought to dryness and the residue was treated with 10 ml Et$_2$O. The white solid was filtered, washed with Et$_2$O and dried in vacuo. The IR and NMR spectroscopic characteristics and conductivity data were identical to the solid obtained according to the method outlined in [2]. Yield: 95%.

2.4. [(R-binap)Pt(OTf)$_2$]

This complex was prepared following an identical procedure starting from [(COD)PtMe$_2$] and R-binap. The spectroscopic characteristics were identical to the solid obtained according to the method outlined in [2]. Yield: 55%.

2.5. Catalytic reactions

These were carried out in a 25 ml round-bottomed flask equipped with a stopcock for vacuum/N$_2$ operations and a side-arm fitted with a screw-capped silicone septum to allow sampling. Constant temperature (± 0.1 °C) was maintained by water circulation through an external jacket connected with a thermostat. Stirring was performed by a Teflon-coated bar driven externally by a magnetic stirrer.

The following general procedure was followed: the catalyst (0.01 mmol) was placed solid in the reactor which was evacuated and filled with N$_2$. Purified, N$_2$ saturated CH$_2$Cl$_2$ (3 ml) was added followed by 3A molecular sieves (50 mg). After thermostatting at the required temperature for a few minutes, the dienophile (1 mmol) and the diene (1 mmol) were sequentially injected through the septum and time was started.
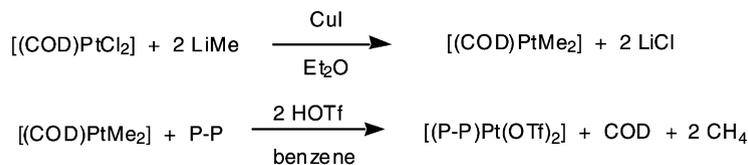
All reactions were monitored with GC by direct injection of samples taken periodically from the reaction mixtures with a microsyringe. Separation of the products was performed on 25 m HP-5 capillary column using a thermal conductivity detector. Conversion % was determined through the use of calibration curves between the individual substrates and toluene as internal standard.

Where applicable, the extent of the asymmetric induction (e.e. %) was determined with GC with the use of Lipodex E chiral column.

3. Results and discussion

The complexes used as catalysts were synthesized according to a new method outlined in Scheme 2. The previous synthetic method reported in [2] starting from the diphosphino dichloro complex and AgOTf was found less reliable as, depending on the (unavoidable) amount of water retained by the highly hygroscopic AgOTf, mixtures of the desired [(P–P)Pt(OTf)$_2$] and [P–P)Pt(µ-OH)]$_2^{2+}$ are obtained. These are very difficult to separate. We then devised a new approach which avoids possible contamination with water (Scheme 2). The complexes isolated in this way are spectroscopically identical to those previously described [2].
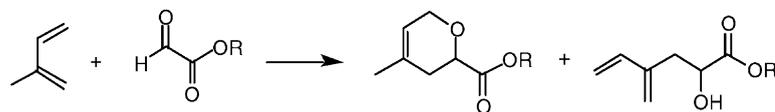
The reaction between isoprene and glyoxylates was studied first (Eq. (1)). In principle, two hetero DA products are possible (Fig. 1) depending on the regioselectivity of the cycloaddition. As shown in Eq. (1), also a hetero-ene product is generally observed arising from the transfer of an allylic hydrogen to the

$$[(COD)PtCl_2] + 2\,LiMe \xrightarrow[\text{Et}_2\text{O}]{\text{CuI}} [(COD)PtMe_2] + 2\,LiCl$$

$$[(COD)PtMe_2] + P\text{-}P \xrightarrow[\text{benzene}]{2\,\text{HOTf}} [(P\text{-}P)Pt(OTf)_2] + COD + 2\,CH_4$$

HOTf = triflic acid

Scheme 2.

carbonyl. These reactions do not occur in the absence of catalyst even heating at 70 °C for 24 h. A further complication of this reaction is the possible polymerization of isoprene promoted by the presence of the Lewis acid. In the literature, hetero DA reactions with these substrates catalyzed by transition metals in which polymer content may be as high as 90% of the total products have been reported [25].

cycloaddition product (A or B in Fig. 1) can be isolated from the reaction mixture by flash chromatography and identified by NMR. Comparison with the literature [29] indicates that all cycloaddition products are of type A.

A typical reaction profile is shown in Fig. 2, while Table 1 reports a summary of the catalytic reactions

$$\text{(1)}$$

With [(dppb)Pt(OTf)$_2$] as catalyst the reaction can be conveniently carried out at room temperature in CH$_2$Cl$_2$ as the solvent and in the presence of 3A molecular sieves. The latter are known to frequently improve the enantioselectivity in Lewis acid catalyzed DA and ene reactions [26–28]. In the present case, it was observed that their presence in the reaction mixture leads to better cycloaddition product yields and lower amounts of undesired products.

GC analyses of our reaction mixtures always evidence the presence of a major product and two minor products. MS analysis allows to conclude that the major component is always the cycloaddition product, while, of the two minor products, one is the hetero-ene product and the other is an isoprene dimer. Notably, the latter forms also in the absence of dienophile. The
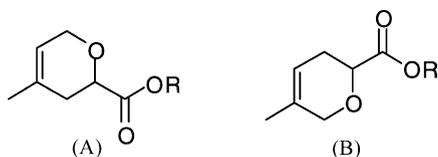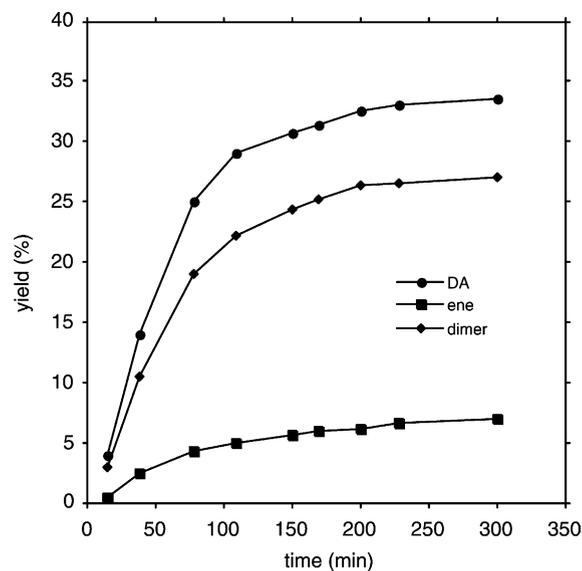
Fig. 2. A typical reaction profile for the hetero Diels–Alder reaction between isoprene and methylglyoxylate. Circles: the hetero Diels–Alder product; squares: the hetero-ene product; diamonds: the isoprene dimer.
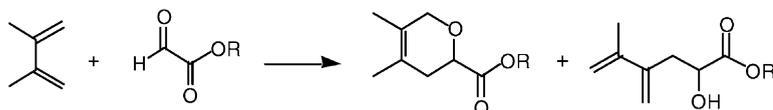
Fig. 1. The possible isomers arising from hetero Diels–Alder reaction between isoprene and glyoxylate esters.

Table 1
Hetero Diels–Alder reaction between isoprene and alkyl-glyoxylates catalyzed by [(dppb)Pt(OTf)$_2$]

Alkyl	Time (min)	Conv. dienophile (%)	Conv. diene (%)	Selectivity (%)		
				DA	ene	Dimer
Me	200	39	66	50	11	39
Et	180	50	72	72	4	24
i-Pr	180	10	13	60	17	23
n-Bu	200	11	13	65	20	15

Table 2
Hetero Diels–Alder reaction between 2,3-dimethylbutadiene and alkyl-glyoxylates catalyzed by [(dppb)Pt(OTf)$_2$]

Alkyl	Time (min)	Conv. dienophile (%)	Conv. diene (%)	Selectivity (%)		
				DA	ene	Dimer
Me	205	40	76	39	13	48
Et	190	38	71	41	12	47
i-Pr	190	9	22	33	9	58
n-Bu	210	10	16	50	15	35

between isoprene and the different glyoxylates (Me-, Et-, *i*-Pr-, *n*-Bu-). As can be seen different conversions can be observed depending on whether the dienophile or the diene are considered. This is a consequence of the fact that the latter is consumed also to produce the isoprene dimer. Table 1 indicates also that moderate amounts of ene product are formed. This seems to demonstrate an interesting selectivity of the [(dppb)Pt(OTf)$_2$] complex towards hetero DA, a feature that is not very common as in current literature on transition metal catalyzed hetero DA reaction the hetero DA and ene products are usually produced in similar amounts (see, for example [29]). In the present case DA/ene ratios as high as 18 are observed in the case of ethylglyoxylate. This ratio, however, never drops below 3 (*i*-propylglyoxylate). Another observation is that the reaction seems to show a maximum conversion for ethylglyoxylate, then, as the size of the alkyl group increases, some steric congestion may slow down the activity of the catalyst.

Similar considerations apply to the reaction between 2,3-dimethylbutadiene and the different glyoxylates (Table 2). In this case, only one hetero DA product is possible (Eq. (2)). Dimer formation is slightly higher than in the case of isoprene, but again the hetero DA/ene products ratio never drops below 3 and the same reactivity order with the respect to the ester alkyl group is observed.

products. A summary of the results obtained in the Pt catalyzed reactions is reported in Table 3. The reactivity observed is similar to the other cases (see Tables 1 and 2) and even in this case the catalyst promotes also the dimerization of dienes. Additionally, only the hetero DA products are formed in these reactions. These results are interesting as in the literature simple aromatic aldehydes are generally reported to react with activated dienes bearing oxygenated groups that make them more reactive [30,31] or, viceversa, simple dienes are reported to react with aromatic aldehydes containing electron-withdrawing groups capable of lowering the energy of the dienophile's LUMO, thereby favoring the reaction [32].

A comment on the unusual selectivity towards hetero DA products displayed by these catalysts seems in order. The Lewis acid catalyzed Diels-Alder and ene reaction are mechanistically related [33], they both involve catalyst activation of the (di)enophile to lower the energy of its LUMO, they can be concerted and proceed through cyclic transition states involving six electrons. This is why catalysts capable of promoting the DA reaction generally promote also the ene reaction (if possible). However, the activation energy for the ene reaction is generally higher thereby requiring strong Lewis acids and higher temperatures than in a

The hetero DA reaction was extended to the case of simple aldehydes (benzaldehyde and terephthalaldehyde) and dienes. As indicated by Scheme 3, in principle this reaction can also give hetero-ene

$$(2)$$
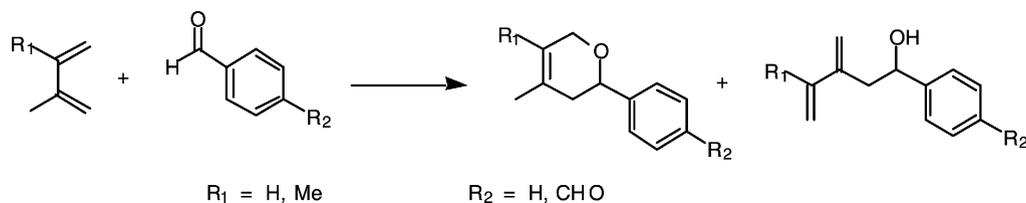
comparable Diels–Alder [33]. It seems therefore reasonable that softer transition metal centers would result in a better discrimination between the two reactions.

$R_1 = H, Me$ $R_2 = H, CHO$

Scheme 3.

Indeed, both the hetero DA and ene products indicated in Eqs. (1) and (2) are formed as a pair of enantiomers. Therefore, we considered the possibility to carry out some asymmetric reactions using [(R-binap)Pt(OTf)$_2$] as the catalyst. Results are summarized in Table 4.

As a catalyst [(R-binap)Pt(OTf)$_2$] appears to be even better than [(dppb)Pt(OTf)$_2$] as good conversions are observed also with the bulkiest dienophiles. Moreover, dimerization of the diene is more limited and also the hetero DA/ene products ratio is generally better. All together these features increase the yields in hetero DA products. Quite disappointingly, the e.e.'s observed in the different reactions are al-

most negligible. Reducing the reaction temperature to −20 °C does not seem to improve the situation: reaction rates are drastically decreased while the e.e.'s are only slightly improved.

These results are partly in contrast with those obtained by Oi et al. [4] in the same hetero DA reactions using [(S-binap)Pd(PhCN)$_2$](BF$_4$)$_2$ as the catalyst where, in the case of 2,3-dimethylbutadiene, e.e.'s exceeding 95% in the hetero DA product and 30% in the ene product were observed (in the case of isoprene, e.e.'s are similar to ours). Additionally, Gagné and coworkers [34] observed 74% e.e. in the ene reaction between ethylglyoxylate and methylenecyclohexane catalyzed by [(MeO-biphep)Pt(OTf)$_2$] generated

Table 3
Hetero Diels–Alder reaction between aromatic aldehydes and simple dienes catalyzed by [(dppb)Pt(OTf)$_2$]

Diene	Aldehyde	Time (min)	Conv. aldehyde (%)	Conv. diene (%)	Selectivity (%)	
					DA	Dimer
Isoprene	Benz	230	28	58	48	52
Isoprene	Terephthal	240	38	60	63	37
Dimethylbutadiene	Benz	230	32	60	54	46
Dimethylbutadiene	Terephthal	240	41	66	62	38

Table 4
Asymmetric hetero Diels–Alder reaction between different dienes and alkyl-glyoxylates catalyzed by [(R-binap)Pt(OTf)$_2$]

Diene	Alkyl	Time (min)	Conv. dienophile (%)	Conv. diene (%)	Selectivity (%)		
					DA (e.e.)	ene (e.e.)	Dimer
Isoprene	Me	180	38	54	64 (4)	6 (3)	30
	Et	195	51	68	65 (7)	10 (6)	25
	i-Pr	180	50	59	68 (5)	17 (4)	15
	n-Bu	200	33	42	50 (8)	30 (1)	20
Dimethylbutadiene	Me	200	29	48	52 (14)	8 (8)	40
	Et	200	48	80	49 (10)	10 (2)	41
	i-Pr	195	51	76	54 (7)	13 (1)	33
	n-Bu	210	24	31	50 (8)	29 (2)	21

in situ by reaction between the dichloro complex and AgOTf. Given the close similarities between the catalysts used by the above authors and the present one, a rationale for the observed different behaviors in the enantioselective reaction remains obscure.

4. Conclusions

In this work, we have demonstrated that [(P–P)Pt (OTf)$_2$] catalysts can effectively catalyze the hetero DA reaction between simple non-activated dienes and glyoxylates or simple aromatic aldehydes. Given the unsatisfactory e.e.'s observed in the enantioselective transformation when R-binap is the diphosphine, the major advantage of using these catalysts seems to be in the always observed high ratio between the hetero DA products and products arising from the undesired, but in some cases avoidable (with aldehydes), hetero-ene reaction. This may be related to the (probably) milder Lewis acid character of Pt(II) complexes with respect to early transition metals and the first row late metals (Cu(II) and Zn(II)) that may favor the hetero DA reaction over the hetero-ene reaction.

Acknowledgements

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