Development of Highly Efficient Platinum Catalysts for Hydroalkoxylation and Hydroamination of Unactivated Alkene

Yali Zhou
Southern University of Science and Technology
Xingjun Xu
Southern University of Science and Technology
Hongwei Sun
Southern University of Science and Technology
Guanyu Tao
Southern University of Science and Technology
Xiaoyong Chang
Southern University of Science and Technology
Xiangyou Xing
Southern University of Science and Technology
Bo Chen
Southern University of Science and Technology
Chen Xu (✉ xuc@sustech.edu.cn)
Southern University of Science and Technology https://orcid.org/0000-0002-3222-459X

Article

Keywords: platinum catalysts, hydroalkoxylation, hydroamination, unactivated alkenes

Posted Date: October 6th, 2020

DOI: https://doi.org/10.21203/rs.3.rs-82534/v1

Version of Record: A version of this preprint was published at Nature Communications on March 29th, 2021. See the published version at https://doi.org/10.1038/s41467-021-22287-w.

Abstract

Hydrofunctionalization, the direct additon of an X–H (e.g., X = O, N) bond across an alkene, is a desirable strategy to make heterocycles that are important structural components of naturally occurring molecules. Described here is the design and discovery of “donor–acceptor”-type platinum catalysts that are highly effective in both hydroalkoxylation and hydroamination of unactivated alkenes over a broad range of substrates under mild conditions. A number of alkene substitution patterns were accommodated, including tri-substituted, 1,1-disubstituted, (E)-disubstituted, (Z)-disubstituted and even mono-substituted double bonds. Detailed mechanistic investigations suggest a plausible pathway that includes an unexpected dissociation/re-association of the electron-deficient ligand to form an alkene-bound *“donor–acceptor”*-type intermediate. These mechanistic studies help understand the origins of the high reactivity exhibited by the catalytic system, and provide a foundation for the rational design of chiral catalysts towards asymmetric hydrofunctionalization reactions.

Background

Aliphatic or aromatic ethers and amines are often significant structural components of biologically active natural products[1-2]. Of the methods to generate these prevalent motifs, the most straightforward and atom-economical route would involve the direct addition of an O–H and a N–H bond across an alkene, commonly referred to as hydroalkoxylation and hydroamination, respectively. In the past decade, there have been a growing number of reports for novel catalysts that can facilitate hydroalkoxylation[3-14] and hydroamination[15-29]. To the best of our knowledge, the most frequently used methods are metal catalyzed conditions, which have been primarily enabled by the activation of either the nucleophile (OH or NH group)[6, 8-9, 14, 16] or the electrophile (C=C bond)[4-5, 19-20, 23] with varying degrees of efficiency (Figure 1A). Of the metals that are able to catalyze hydroalkoxylation and hydroamination, platinum catalysts attracted considerable attention for its unique Lewis acidity towards C=C double bonds[30-31]. Platinum-based complexes that can selectively activate simple C=C double bonds could fall into the following three categories (Figure 1B)[32]. (1) Anionic systems, such as the famous Zeise’s salt ($K[PtCl_3(C_2H_4)]\cdot H_2O$) and Chojnacki’s salt ($K[PtBr_3(C_2H_4)]$). (2) Neutral systems[33-34], such as $[PtCl_2(C_2H_4)_2]_2$ that have been introduced by Widenhoefer[4, 19, 33-34]. (3) Cationic systems, with diamine[35-38], bisphosphine[39-40], carbine[41-43] or pincer ligands[44-46]; in particular, Gagné discovered a series of elegant cationic Pt(II) complexes, such as $(PPP)Pt^{2+}$ and $(PP)PPt^{2+}$, which efficiently inhibit *β*-H elimination as a competing decomposition pathway[31, 40, 46]. Among the three activation modes, coordination to the cationic Pt derivatives renders the multiple bonds more electrophilic and thus susceptible to nucleophilic attack[47-48].

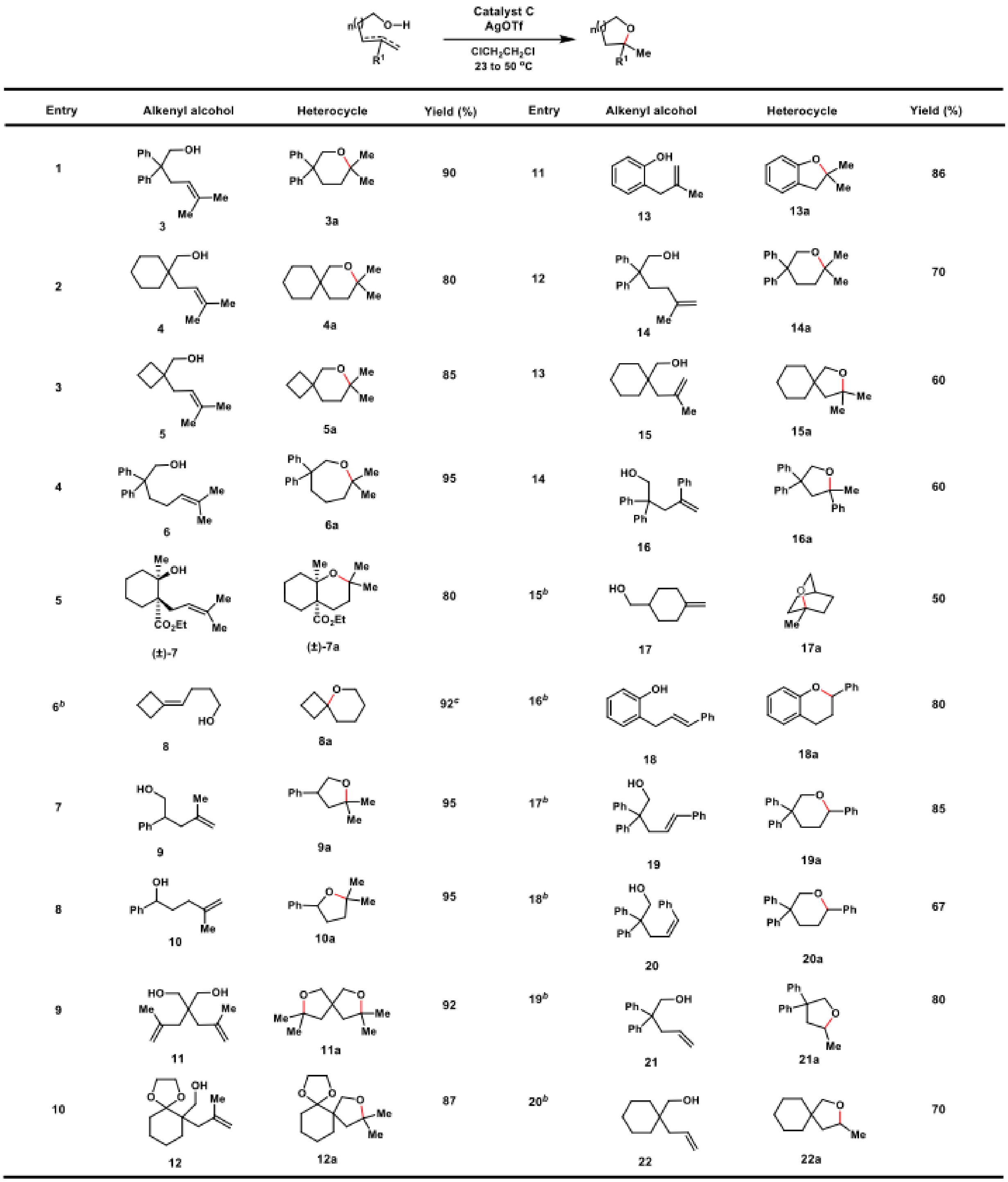
Recently, Grubbs described the design and synthesis of novel “*donor–acceptor*”-type platinum catalysts by introducing electron-rich bisphosphine and electron-deficient dimethylphosphine oxide on the platinum center, and these catalysts have been demonstrated to be highly effective in hydration of nitriles and cyanohydrins at ambient temperature[49]. We envisioned that this catalyst design concept may be suitable for the cationic, electrophilic activation of olefins: introducing both electron-rich “*donor*” ligand and electron-deficient “*acceptor*” ligand to the Pt center would make a soft and stable cationic system[50-51], thus leading to a more effective activation of soft Lewis bases, such as C-C multiple bonds. Herein, we disclose readily accessible “*donor–acceptor*”-type platinum catalysts that are highly active in both hydroalkoxylation and hydroamination, along with mechanistic studies that reveal the origins of the high reactivity of the catalytic system. The hydroalkoxylation and hydroamination reactions catalyzed by the new Pt-complexes typically proceed at mild temperatures (23 –50 ^{o}C), and encompass a remarkably broad substrate scope, including alkenes with various substitution patterns (Figure 1C). Mechanistic data reveals an unusual dissociation/re-association of the electron-deficient mono-phophine, and that a polarizable alkene-bound “*donor-acceptor*”-type intermediate could be formed, thus facilitating activation of simple alkenes[52]. In addition, chiral platinum catalysts bearing (*R*)-BINAP or (*R*)-Difluorphos and an electron-deficient monodentate ligand with hydrogen-bonding site allows the asymmetric hydroalkoxylation and hydroamination with enantioselectivities, likewise supporting that a more complex metal catalyst than triflic acid is involved[53-56].

Results

Screening of the optimal catalysts. In Grubbs’ previous studies on hydration of nitriles and cyanohydrins, more electron-rich groups in the “*donor*” moiety was discovered to increase the activity of the catalysts[49]. Therefore, we take the electron-rich 1.1’-[bis(5-methyl-2-furanyl)phosphine]ferrocene “*donor*” ligand and modulate the electronic nature of the monodentate “*acceptor*” ligands. As shown in Figure 2, five Pt-catalysts **A**-**E** were synthesized via the reaction of 1.1’-[bis(5-methyl-2-furanyl)phosphine]ferrocene platinum dichloride (dmfpfPtCl$_2$) with the corresponding monodentate phosphine ligands (in blue) in the presence of silver triflate, respectively (See Supporting Information). Then the activity of the newly synthesized platinum catalysts was evaluated by performing hydroalkoxylation of **1** and hydroamination of **2** (Figure 2). The results show that catalyst **A**, with triphenylphosphine as the monodentate ligand, has the worst reactivity for both hydroalkoxylation of **1** and hydroamination of **2**. Catalyst **B** that bears electron-deficient monodentate tris(4-(trifluoromethyl)phenyl)phosphine slightly improved the reactivity for both hydroalkoxylation and hydroamination. Catalyst **C** harbouring the more electron-deficient monodentate tris(3,5-bis(trifluoromethyl)phenyl)phosphine displays noticeably increased catalytic activity, providing hydroalkoxylation product **1a** and hydroamination product **2a** in 46% and 44% yields, respectively. The observation that more electron-deficient tri-aryl phosphine ligand in the “*accept*or” moiety resulted in higher catalytic activity as demonstrated by the improved performance of catalysts **A**, **B** and **C** supports Grubbs’ “*donor–acceptor*” catalyst design[49]. Catalysts **D** and **E** bearing other two different electron-deficient monodentate ligands, tris(3,4,5-trifluorophenyl)phosphine and tris(3,5-difluoro-4-(trifluoromethyl)phenyl)phosphine, also show good reactivity for both hydroalkoxylation and hydroamination, and have their own advantages for different substrates. The trend that more elelctron-rich group in the “*donor*” part and/or the more electron-deficient group in the “*acceptor*” part increased the activity of the Pt-catalysts could be explained: the cationic Pt(II) was stabilized by the strong σ donating from the electron-rich bidentate ligand, while the electron-deficient monodentate ligand which acts as weak σ donor but strong π acceptor makes the Pt(II) center more electrophilic towards multiple bonds4[7-48, 51].

Scope for hydroalkoxylation. we next investigated the scope of intramolecular hydroalkoxylation with catalyst **C**, which contains the commercially available and inexpensive tris(3,5-bis(trifluoromethyl)phenyl)phosphine as the monodentate ligand (Table 1). All the reactions were conducted under mild conditions (either at 23 or 50 °C). The catalytic protocol displays excellent generality with Markovnikov regioselectivity, and is notably applicable to the synthesis of sterically hindered ethers with fused-, bridged- and spiro-ring systems (Table 1, entries 5; 15; 2, 3, 6, 9, 10, 13 and 20). Various hydroxyl groups such as primary, secondary, tertiary alcohols and phenols serve as good nucleophiles. Different olefins with various substitution patterns including trisubstituted (Table 1, entries 1 to 6), 1,1-disubstituted (Table 1, entries 7 to 15), 1,2-disubstituted (both *cis* and *trans*) (Table 1, entries 16 to 18), and even mono-substituted (Table 1, entries 19 and 20) double bonds work well in this reaction. Good to excellent yields were obtained in all cases reported.

Table 1. Substrate scope for intramolecular hydroalkoxylation[a].

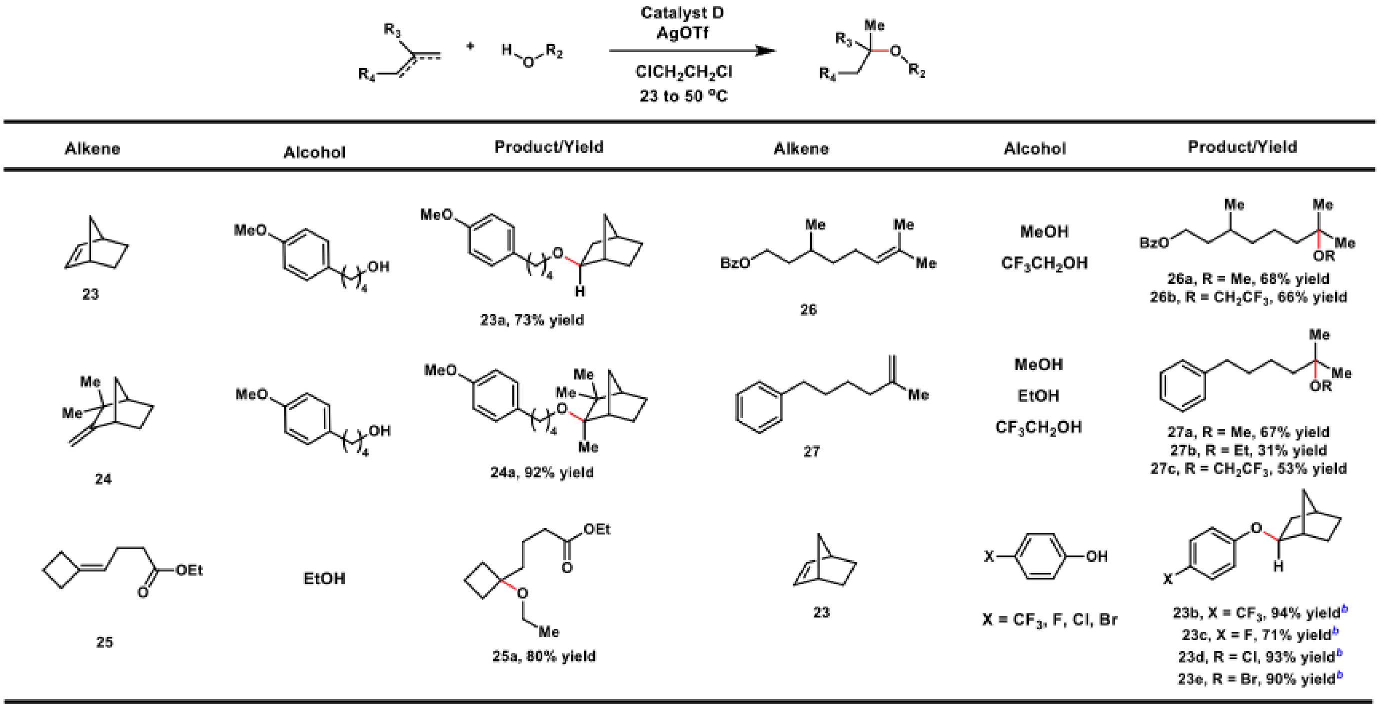


Entry	Alkenyl alcohol	Heterocycle	Yield (%)	Entry	Alkenyl alcohol	Heterocycle	Yield (%)
1	3	3a	90	11	13	13a	86
2	4	4a	80	12	14	14a	70
3	5	5a	85	13	15	15a	60
4	6	6a	95	14	16	16a	60
5	(±)-7	(±)-7a	80	15[b]	17	17a	50
6[b]	8	8a	92[c]	16[b]	18	18a	80
7	9	9a	95	17[b]	19	19a	85
8	10	10a	95	18[b]	20	20a	67
9	11	11a	92	19[b]	21	21a	80
10	12	12a	87	20[b]	22	22a	70

[a] General conditions: Catalyst **C** (1 mol%), AgOTf (2 mol%), $ClCH_2CH_2Cl$, 23 °C, 24 h. Yields of isolated products are given.
[b] Catalyst **C** (2 mol%), AgOTf (4 mol%), $ClCH_2CH_2Cl$, 50 °C, 48 h. [c] Determined by ^1H NMR analysis using 4,4'-di-*tert*-butyl-1,1'-biphenyl as an internal standard.

Expanding our investigation to intermolecular hydroalkoxylation, we discovered that catalyst **D** was the optimal catalyst whereas **C** gave slightly reduced yields over a range of different substrates (Table 2). Higher catalyst loadings (5 mol%) and slightly elevated temperatures are required for optimal conversion of the intermolecular reactions reported here. Alkenes with ring strain such as norbornene (**23**), comphene (**24**), and four-membered carbocycles (**25**) all productively undergo intermolecular hydroalkoxylation reactions with alcohols. Acyclic alkenes such as **26** and **27** that are less reactive substrates than their cyclic counterparts were coupled with alcohols in moderate yields. These reactions generally stalled at 30 to 70% conversions depending on the nature of the nucleophile used; longer reaction times or higher catalyst loadings do not help to convert the reactions further. Intermolecular hydroalkoxylation of norbornene (**23**) with *para*-substituted phenols were also investigated. Phenols have a potential to engage in hydroarylation reactivity[57]; however, we only observed hydroalkoxylation products (ethers) when *para*-substituted phenols (CF_3, F, Cl, Br) and norbornene (**23**) were treated with **D**/AgOTf at either room temperature or 50 °C. In contrast, bis-*ortho*-hydroarylation products were exclusively generated when triflic acid (TfOH) alone was used as the catalyst (See the Supporting Information for further details). These results suggest a distinct mechanistic pathway for our catalytic system, different from that of a Brønsted acid-catalyzed hydroalkoxylation.

Table 2 Substrate scope for intermolecular hydroalkoxylation[a].

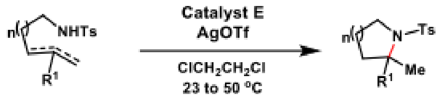


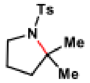
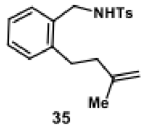
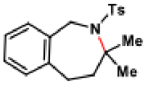
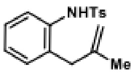
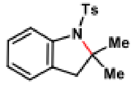
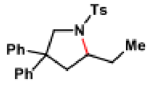
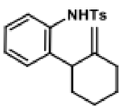
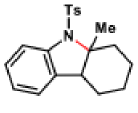
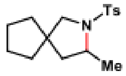
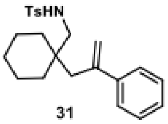
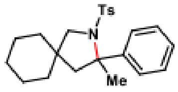
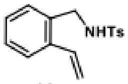
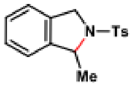
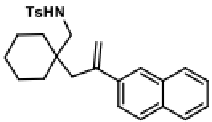
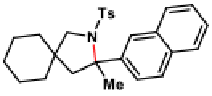
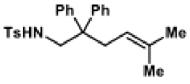
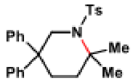
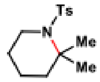
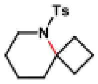
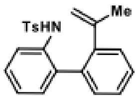
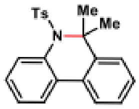
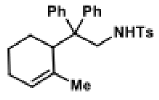
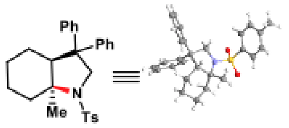
Alkene	Alcohol	Product/Yield	Alkene	Alcohol	Product/Yield
23		23a, 73% yield	26	MeOH CF_3CH_2OH	26a, R = Me, 68% yield 26b, R = CH_2CF_3, 66% yield
24		24a, 92% yield	27	MeOH EtOH CF_3CH_2OH	27a, R = Me, 67% yield 27b, R = Et, 31% yield 27c, R = CH_2CF_3, 53% yield
25	EtOH	25a, 80% yield	23	X = CF_3, F, Cl, Br	23b, X = CF_3, 94% yield[b] 23c, X = F, 71% yield[b] 23d, R = Cl, 93% yield[b] 23e, R = Br, 90% yield[b]

[a] General conditions: Catalyst **D** (5 mol%), AgOTf (6 mol%), 50 °C, 16 to 24 h. Yields of isolated products were given. [b] Catalyst **D** (2 mol%), AgOTf (3 mol%), 23 °C, 24 h.

Substrate scope for hydroamination. The "*donor–acceptor*"-type Pt-catalysts not only are capable of catalyzing hydroalkoxylation, but can also effect hydroamination of unactivated alkenes in generally good yields. As complied in Table 3, the catalyst **E**, even used at lower loading of 1 mol%, was shown to be capable of effecting intramolecular alkene hydroamination with sulfonamides at ambient temperatures, providing various nitrogen-heterocycles that are important structraul motifs in naturally occuring and pharmaseuticals. A wide range of alkene substitution patterns are tolerated, including 1,1-disubstitutied (Table 3, entries 1 to 8), 1,2-disubstituted (Table 3, entry 9), mono-substituted (Table 3, entries 10 and 11) and trisubstituted alkenes (Table 3, entries 12 to 14). The relative stereochemistry of **41a** was unambiguously confirmed by X-ray crystallography (Table 3, entry 14). Next, we examined the viability of more difficult intermolecular alkene aminations with *p*-toluenesulfonamide, (*p*-tolylsulfonyl)methylamine, *N*-tosyl-4-methoxyaniline and methanesulfonamide (Table 4). A number of alkene substitution patterns were accommodated, including trisubstituted (Table 4, entries 1 to 4), terminal (Table 4, entries 5 to 7) and 1,2-disubstituted alkenes (Table 4, entries 8 and 9). Both cyclic and acyclic alkene partners can be aminated successfully. The structure of **23f** was verified by X-ray crystallogrphy.

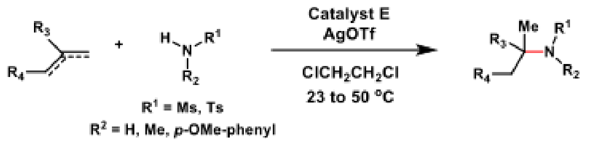
Table 3. Substrate scope for intramolecular hydroamination[a].

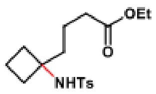
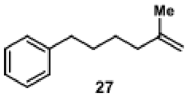
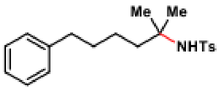
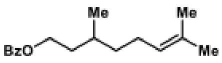
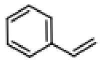
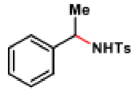
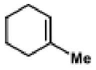
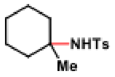
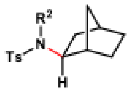
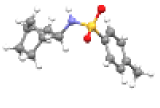
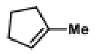
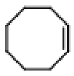
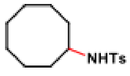
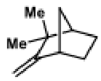
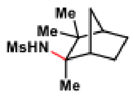


Entry	Alkenyl amine	Heterocycle	Yield (%)	Entry	Alkenyl amine	Heterocycle	Yield (%)
1	 28	 28a	84	8	 35	 35a	78
2	 29	 29a	85	9[b]	 36 (E/Z = 8:1)	 36a	62
3	 30	 30a	63	10[b]	 37	 37a	97
4	 31	 31a	96	11	 38	 38a	93
5	 32	 32a	94	12	 39	 39a	50
6	 33	 33a	88	13	 40	 40a	80
7	 34	 34a	79	14	 41	 41a X ray of 41a	85

[a] General conditions: Catalyst **E** (1 mol%), AgOTf (2 mol%), 23 °C, 24 h. Yields of isolated products were given. [b] Catalyst **E** (5 mol%), AgOTf (6 mol%), 50 °C, 48 h.

Table 4. Substrate scope for intermolecular hydroamination[a].



Entry	Alkenes	Products	Yields (%)	Entry	Alkenes	Products	Yields (%)
1	 25	 25b	77	6	 27	 27d	86
2	 26	 26c	92	7	 44	 44a	97
3	 42	 42a	86	8	 23	 23f, R^2 = H, 98% yield; 23g, R^2 = Me, 90% yield; 23h, R^2 = p-OMe-phenyl, 97% yield	 *X ray* of 23f
4	 43	 43a	95	9[b]	 45	 45a	65
5	 24	 24b	98				

[a] General conditions: Catalyst **E** (2 mol%), AgOTf (4 mol%), 23 C, 8 to 24 h. Yields of isolated products were given. [b] Catalyst **E** (5 mol%), AgOTf (6 mol%), 50 C, 48 h.

Mechanistic Studies. Recently, several groups have independently demonstrated that triflic acid can catalyze the additions of oxygen- and nitrogen-based nucleophiles to simple alkenes with comparable efficiency/selectivity as some metal triflates[53-56]. The aforementioned reports raised the question of a competitive acid-catalyzed pathway when metal triflates are employed. Therefore, we elected to perform a detailed analysis of the possible mechanistic pathways for the "*donor– acceptor*" Pt-catalyzed hydroalkoxylation of alkenes.

The mechanistic study commenced with monitoring the reaction of norbornene and 4-trifluromethylphenol catalyzed by **D** and AgOTf in deuterated dichloromethane at 23 °C by ^{31}P, ^{19}F and ^{1}H NMRs (Figure 3 and please also see Supporting Information). When equal molar of AgOTf was added into catalyst **D** in deuterated dichloromethane, ^{31}P NMR revealed the appearance of a new peak at *d* -22.5 (s, $^{1}J_{Pt\text{-}P}$ = 4022 Hz) ppm (Figure 3c). This peak was confirmed to be complex **G** that can be generated independently by mixing 1 equivalent of 1,1'-[bis(5-methyl-2-furanyl)phosphine]ferrocene platinum dichloride (dmfpfPtCl$_2$) with 2 equivalents of AgOTf (Figure 3b). It is worth to note that when the chloride ion in the catalyst **D** was abstracted by AgOTf, a more electron-deficient Pt(II) center was formed; as a result, the monodentate phosphine ligand was dissociated from the Pt center and coordinated with Ag(I) ion to form new complexes such as [(Ar$_3$P)$_x$AgOTf]$_n$ (**H**) with ^{19}F signals at *d* -131.2 (d, *J* = 21.3 Hz) and -154.2 (t, *J* = 21.0 Hz) ppm (please see ^{19}F NMR in Supporting Information)[58].

4 equivalents of norbornene were then added to the above solution which led to rapid disappearance of complexes **G** and **H**, and ^{1}H NMR analysis revealed that diagnostic alkene peaks move downfield (Figure 3d and also see ^{19}F and ^{1}H NMRs in Supporting Information). These results together indicate that the mono-phosphine ligand re-combined to the Pt center when the alkene was coordinated to the Pt. Finally, when 4-trifluoromethylphenol was added, ^{1}H NMR confirmed that the hydroalkoxylation product **23b** was formed with the concurrent regeneration of complexes **G** and **H** (Figure 3e and also see Supporting Information).

To ascertain whether the nucleophile is reacting or coordinating with the Pt center, we changed the sequence of adding 4-trifluoromethylphenol and norbornene (Figure 4). When 4 equivalents of 4-trifluoromethylphenol were added into the solution of **D** and AgOTf, there was no change in ^{1}H, ^{19}F and ^{31}P NMRs (Figure 4b and also see Supporting Information). Next, 4 equivalents of norbornene were added and the resulting solution was immediately analyzed: ^{31}P and ^{19}F NMRs revealed that both the ^{31}P signal for complex **G** and ^{19}F signals for complex **H** decreased (Figure 4c and see Supporting Information). These results suggest that both the mono-phosphine ligand and norbornene were coordinating to the Pt center. As the reaction proceeds for 1 hour, the hydroalkoxylation product **23b** was formed, and both complexes **G** and **H** were generated again (Figure 4d, and also see ^{1}H and ^{19}F NMRs in Supporting Information).

Based on the NMR experiments, we propose a plausible mechanism for "*donor–acceptor*"-type Pt-complex catalyzed hydroalkoxylation of unactivated alkenes (Figure 5). Catalyst **D** reacts with AgOTf to form Pt(II) species **F** and precipitates AgCl. Since complex **F** is more electron-deficient and unstable, the monodentate phosphine ligand dissociates from the Pt center and reacts with an additional equivalent of AgOTf to generate complexes **G** and **H**. Then complex **G** coordinates with the alkene to form complex **I**. Due to its s-donating nature, the alkene makes the Pt center in complex **I** more electron-rich than in complexes **F** and **G**. Therefore, the electron-deficient mono-phosphine re-associates to form a 16-electron, "*donor-acceptor*"-type Pt complex **J**, thus further activating the alkene. Nucleophilic attack on the bound alkene by a free alcohol provides complex **K**. Proton transfer thereafter provides the hydroalkoxylation product and regenerates complexes **G** and **H**.

Finally, we explored the catalytic asymmetric hydroalkoxylation[14, 5][9-63] and hydroamination6[4-69] with the "*donor–acceptor*" catalytic system (Figure 6). Various chiral Pt-complexes generated in situ from chiral bisphosphine platinum dichlorides with electron-deficient tris(3,4,5-trifluorophenyl)phosphine were examined in the reaction of **21** and **2** under standard conditions. Disappointingly, none of the chiral Pt-catalysts produced enantioselectivities (See Supporting Information). We envisioned that a bi-functional catalysis where the monodentate ligand has a basic group that can form a hydrogen-bonding with the nucleophile would assist recognition of prochiral faces of the alkenes[61, 70]. To our delight, catalysts **N** and **M** bearing (*R*)-BINAP and (*R*)-Difluorphos as "*donor*" ligands and the monodentate "*acceptor*" ligand with a hydrogen bonding site induced moderate enantioselectivities in both hydroalkoxylation of **21** and hydroamination of **2**. The observed enantioselectivity strongly supports our proposed mechanism that "*donor-acceptor*" Pt-catalyzed hydroalkoxyations and hydroaminations are true metal-catalyzed processes[53-56].

Conclusion

In summary, we have described herein the newly synthesized "*donor–acceptor*"-type platinum catalysts that are superior in effecting both hydroalkoxylation and hydroamination with respect to mild reaction conditions and generality in substrate scope. Mechanistic studies suggested a plausible pathway that includes an unusual dissociation/re-association of the electron-deficient mono-phosphine ligand to generate an alkene bound "*donor–acceptor*" type intermediate. Efforts to improve the reactivity and enantioselectivity of the chiral platinum catalysts based on bi-functional catalysis for asymmetric hydrofunctionalization will be the subject of future studies.

Methods

General procedure for preparing "*donor-acceptor*" Pt catalyst. In an argon filled glovebox, to a 4 mL vial with a magnetic stir bar were added (dmfpf)$PtCl_2$ (100 mg, 0.12 mmol), silver trifluoromethanesulfonate (31 mg, 0.12 mmol, 1.0 equiv.), monophosphine ligand (0.13 mmol, 1.05 equiv.) and CH_2Cl_2 (2 mL). Then the vial was taken outside of the glovebox and was stirred at 23 ^{o}C for 12 h. The orange solution was filtered and CH_2Cl_2 was evaporated to provide orange solid, which was recrystallized in CH_2Cl_2 and hexane to give yellow precipitate.

General procedure for intramolecular hydroalkoxylation. In an argon filled glovebox, to a 4 mL vial with a magnetic stir bar were added catalyst **C** (0.001 mmol, 1 mol%), silver trifluoromethanesulfonate (0.002 mmol, 2 mol%), the substrate (0.1 mmol), and $ClCH_2CH_2Cl$ (1 mL). Then the vial was taken outside of the glovebox and stirred at 23 ^{o}C for 24 h. The mixture was diluted with CH_2Cl_2, filtered through a pad of celite and concentrated. The residue was purified by silica gel chromatography to give the desired product.

General procedure for intermolecular hydroalkoxylation. In an argon filled glovebox, to a 4 mL vial with a magnetic stir bar were added catalyst **D** (0.01 mmol, 5 mol%), silver trifluoromethanesulfonate (0.012 mmol, 6 mol%), alkenes (0.2 mmol), alcohols (0.3 mmol, 1.5 equiv.) and $ClCH_2CH_2Cl$ (1 mL). Then the vial was taken outside of the glovebox and stirred at 50 ^{o}C for 16 h. THe reaction mixture was cooled to room temperature (23 ^{o}C) and diluted with CH_2Cl_2, filtered through a pad of celite and concentrated in vacue. The residue was purified by silica gel chromatography to give the desired product.

General procedure for intramolecular hydroamination. To a 4 mL vial equipped with a magnetic stir bar were added the catalyst **E** (0.001mmol, 1 mol%), silver trifluoromethanesulfonate (0.002 mmol, 2 mol%) and $ClCH_2CH_2Cl$ (1.0 mL) in an argon filled glovebox. The mixture was stirred at 23 °C for 1 h. Then to the mixture was added a solution of **37** (30.7 mg, 0.1 mmol) in $ClCH_2CH_2Cl$ (0.5 mL). The vial was taken outside of the glovebox and stirred at 23 ^{o}C for 24 h. The mixture was diluted with CH_2Cl_2 and concentrated under reduced pressure. The residue was purified by flash chromatography to afford the desired product.

General procedure for intermolecular hydroamination. In an argon filled glovebox, to a 4 mL vial with a magnetic stir bar were added catalyst **E** (0.002 mmol, 2 mol%), silver trifluoromethanesulfonate (1.0 mg, 0.004 mmol, 4 mol%), alkenes (0.1 mmol), sulfonamide (0.15 mmol, 1.5 equiv.) and $ClCH_2CH_2Cl$ (0.7 mL). Then the vial was taken outside of the glovebox and stirred at 23 °C or 50 °C for 6 to 48 h. The reaction mixture was diluted with CH_2Cl_2, filtered through a pad of celite and concentrated. The residue was purified by silica gel chromatography to afford the desired product.

Data availability

The data that support the findings of this study are available within the paper and its supplementary information files. Raw data are available from the corresponding author on reasonable request. Materials and methods, experimental procedures, characterization data, ^{1}H, ^{13}C, ^{19}F, ^{31}P NMR spectra and mass spectrometry data are available in the Supplementary Materials. Crystallographic data are available free of charge from the Cambridge Crystallographic Data Centre (https://www.ccdc.cam.ac.uk/) under reference number CCDC 1942024 (catalyst **E**), CCDC 1945616 (**41a**), CCDC 1942471 (**23f**), CCDC 2021353 (catalyst **M**), respectively.

Declarations

Acknowledgments

We wish to thank Shenzhen Nobel Prize Scientists Laboratory Project (Grant No. C17783101), Shenzhen Science and Technology Program (Grant No. KQTD20180411143514543) and the National Natural Science Foundation of China (Grant No. K18211006) for financial support. Prof. Robbert H. Grubbs is acknowledged for helpful discussions and valuable suggestions.

Author Contributions

Y. Z., X. X., H. S., G. T. developed and conducted the reactions. X-Y. C. conducted the experiment for X-ray crystallography and did structure determination. C. X., B. C. and X. X. designed and directed the investigations. C. X. and B. C. wrote the paper.

Competing interests

The authors declare no competing interests.

References

1. DeSimone, R. W., Currie, K. S., Mitchell, S. A., Darrow, J. W. & Pippin, D. A. Privileged Structures: Applications in Drug Discovery. *Chem. High Throughput Screening* **7**, 473–494 (2004).
2. Elliott, M. C. & Williams, E. Saturated oxygen heterocycles. *J. Chem. Soc., Perkin Trans. 1* 2303–2340 (2001).
3. Hintermann, L. *Recent Developments in Metal-Catalyzed Additions of Oxygen Nucleophiles to Alkenes and Alkynes. In C-X Bond Formation*; Vigalok, A., Ed.; Springer Berlin Heidelberg: Berlin, Heidelberg, **2010**; pp 123–155.
4. Qian, H., Han, X. & Widenhoefer, R. A. Platinum-catalyzed intramolecular hydroalkoxylation of *γ*- and *δ*-hydroxy olefins to form cyclic ethers. *J. Am. Chem. Soc.* **126**, 9536–9537 (2004).
5. Yang, C.-G. & He, C. Gold(I)-catalyzed intermolecular addition of phenols and carboxylic acids to olefins. *J. Am. Chem. Soc.* **127**, 6966–6967 (2005).
6. Seo, S., Yu, X. & Marks, T. J. Intramolecular hydroalkoxylation/cyclization of alkynyl alcohols mediated by lanthanide catalysts. Scope and reaction mechanism. *J. Am. Chem. Soc.* **131**, 263–276 (2009).
7. Hamilton, D. S. & Nicewice, D. A. Direct catalytic anti-markovnikov hydroetherification of alkenols. *J. Am. Chem. Soc.* **134**, 18577–18580 (2012).
8. Sevov, C. S. & Hartwig, J. F. Iridium-catalyzed, intermolecular hydroetherification of unactivated aliphatic alkenes with phenols. *J. Am. Chem. Soc.* **135**, 9303–9306 (2013).
9. Haibach, M. C. et. al. Olefin hydroaryloxylation catalyzed by pincer–iridium complexes. *J. Am. Chem. Soc.* **135**, 15062–15070 (2013).
10. Shigehisa, H., Aoki, T., Yamaguchi, S., Shimizu, N. & Hiroya, K. Hydroalkoxylation of unactivated olefins with carbon radicals and carbocation species as key intermediates. *J. Am. Chem. Soc.* **135**, 10306–10309 (2013).
11. Lohr, T. L., Li, Z. & Marks, T. J. Thermodynamic strategies for C–O bond formation and cleavage via tandem catalysis. *Acc. Chem. Res.* **49**, 824–834 (2016).
12. Marcyk, P. T. & Cook, S. P. Iron-catalyzed hydroamination and hydroetherification of unactivated alkenes. *Org. Lett.* **21**, 1547–1550 (2019).
13. Discolo, C. A., Touney, E. E. & Pronin, S. V. Catalytic asymmetric radical–polar crossover hydroalkoxylation. *J. Am. Chem. Soc.* **141**, 17527–17532 (2019).
14. Schluter, J., Blazejak, M., Boeck, F. & Hintermann, L. Asymmetric hydroalkoxylation of non-activated alkenes: titanium-catalyzed cycloisomerization of allylphenols at high temperatures. *Angew. Chem. Int. Ed.* **54**, 4014–4017 (2015).
15. 15. Müller, T. E. & Beller, M. Metal-initiated amination of alkenes and alkynes. *Rev.* **98**, 675–704 (1998).
16. Hong, S. & Marks, T. J. Organolanthanide-catalyzed hydroamination. *Acc. Chem. Res.* **37**, 673–686 (2004).

17. Müller, T. E., Hultzsch, K. C., Yus, M., Foubelo, F. & Tada, M. Hydroamination: direct addition of amines to alkenes and alkynes. *Chem. Rev.* **108**, 3795–3892 (2008).
18. Brunet, J. J. et. al. The first platinum-catalyzed hydroamination of ethylene. *Organometallics* **23**, 1264–1268 (2004).
19. Bender, C. F. & Widenhoefer, R. A. Platinum-catalyzed intramolecular hydroamination of unactivated olefins with secondary alkylamines. *J. Am. Chem. Soc.* **127**, 1070–1071 (2005).
20. Johns, A. M., Utsunomiya, M., Incarvito, C. D. & Hartwig, J. F. A highly active palladium catalyst for intermolecular hydroamination. Factors that control reactivity and additions of functionalized anilines to dienes and vinylarenes. *J. Am. Chem. Soc.* **128**, 1828–1839 (2006).
21. McBee, J. L., Bell, A. T. & Tilley, T. D. Mechanistic studies of the hydroamination of norbornene with electrophilic platinum complexes: the role of proton transfer. *J. Am. Chem. Soc.* **130**, 16562–16571 (2008).
22. Dub, P. A. & Poli, R. The Pt-catalyzed ethylene hydroamination by aniline: a computational investigation of the catalytic cycle. *J. Am. Chem. Soc.* **132**, 13799–13812 (2010).
23. Liu, Z., Yamamichi, H., Madrahimov, S. T. & Hartwig, J. F. Rhodium phosphine–π-arene intermediates in the hydroamination of alkenes. *J. Am. Chem. Soc.* **133**, 2772–2782 (2011).
24. Zhu, S., Niljianskul, N. & Buchwald, S. L. Enantio- and regioselective CuH-catalyzed hydroamination of alkenes. *J. Am. Chem. Soc.* **135**, 15746–15749 (2013).
25. Nyuyen, T. M. & Nicewicz, D. A. Anti-markovnikov hydroamination of alkenes catalyzed by an organic photoredox system. *J. Am. Chem. Soc.* **135**, 9588–9591 (2013).
26. 26. Huang, L., Arndt, M., Gooßen, K., Heydt, H. & Gooßen, L. J. Late transition metal-catalyzed hydroamination and hydroamidation. *Rev.* **115**, 2596–2697 (2015).
27. Ensign, S. C., Vanable, E. P., Kortman, G. D. & Weir, L. J. & Hull, K. L. Anti-markovnikov hydroamination of homoallylic amines. *J. Am. Chem. Soc.* **137**, 13748–13751 (2015).
28. 28. Musacchio, A. J. et al. Catalytic intermolecular hydroaminations of unactivated olefins with secondary alkyl amines. *Science* **355**, 727–730 (2017).
29. Aaron, T., Scarlett, M. W. & Matthew, J. G. New strategies for the transition-metal catalyzed synthesis of aliphatic amines. *Chem. Rev.* **120**, 2613–2692 (2020).
30. Fürstner, A. & Davies, P. W. Catalytic carbophilic activation: catalysis by platinum and gold π acids. *Angew. Chem. Int. Ed.* **46**, 3410–3449 (2007).
31. Chianese, A. R., Lee, S. J. & Gagné, M. R. Electrophilic activation of alkenes by platinum(II): so much more than a slow version of palladium(II). *Angew. Chem. Int. Ed.* **46**, 4042–4059 (2007).
32. Cao, P. et. al. Hydroamination of unactivated alkenes catalyzed by novel platinum(II) *N*-heterocyclic carbene complexes. *Organometallics* **31**, 921–29 (2012).
33. Liu, C., Bender, C. F., Han, X. & Widenhoefer, R. A. Platinum-catalyzed hydrofunctionalization of unactivated alkenes with carbon, nitrogen and oxygen nucleophiles. *Chem. Commun.* 3607–3618 (2007).

34. Bender, C. F., Brown, T. J. & Widenhoefer, R. A. Mechanism of the platinum(II)-catalyzed hydroamination of 4-pentenylamines. *Organometallics* **35**, 113–125 (2016).
35. McBee, J. L. & Tilley, T. D. Nucleophilic attack of amides onto coordinated ethylene in platinum complexes supported by a chelating pyridyl−pyrrolide ligand: azaplatinacyclobutane and vinylamine complexes. *Organometallics* **29**, 184–192 (2010).
36. Figg, T. M., Cundari, T. R. & Gunnoe, T. B. Non-redox oxy-insertion via organometallic baeyer-villiger transformations: a computational hammett study of platinum(II) complexes. *Organometallics* **30**, 3779–3785 (2011).
37. Hoover, J. M., DiPasquale, A., Mayer, J. M. & Michael, F. E. Platinum-catalyzed intramolecular hydrohydrazination: evidence for alkene insertion into a Pt-N bond. *J. Am. Chem. Soc.* **132**, 5043–5053 (2010).
38. McKeown, B. A. et. al. Mechanistic studies of ethylene hydrophenylation catalyzed by bipyridyl Pt(II) complexes. *J. Am. Chem. Soc.* **133**, 19131–19152 (2011).
39. Lavery, C. B., Ferguson, M. J. & Stradiotto, M. Platinum-catalyzed alkene cyclohydroamination: evaluating the utility of bidentate P,N/P,P ligation and phosphine-Free catalyst systems. *Organometallics* **29**, 6125–6128 (2010).
40. Feducia, J. A., Campbell, A. N., Doherty, M. Q. & Gagné, M. R. Modular catalysts for diene cycloisomerization: rapid and enantioselective variants for bicyclopropane synthesis. *J. Am. Chem. Soc.* **128**, 13290−13297 (2006).
41. Zhang, R., Xu, Q., Mei, L.-Y., Li, S.-K. & Shi, M. A *N*-heterocyclic carbene (NHC) platinum complex as pre-catalyst for the intramolecular hydroamination of olefins with secondary alkylamines and oxidative amination of ω-alkenic amines *Tetrahedron* **68**, 3172–3178 (2012).
42. Cao, P. et. al. Hydroamination of unactivated alkenes catalyzed by novel platinum(II) N-heterocyclic carbene complexes. *Organometallics* **31**, 921–929 (2012).
43. Rios, P. et. al. Isolation of a cationic platinum(II) σ-silane complex. *Angew. Chem. Int. Ed.* **57**, 3217–3221(2018).
44. Hahn, C., Cucciolito, M. E. & Vitagliano, A. Coordinated olefins as incipient carbocations: catalytic codimerization of ethylene and internal olefins by a dicationic Pt(II)-ethylene complex. *J. Am. Chem. Soc.* **124**, 9038–9039 (2002).
45. Geier, M. J. & Gagné, M. R. Diastereoselective Pt catalyzed cycloisomerization of polyenes to polycycles *J. Am. Chem. Soc.* **136**, 3032–3035 (2014).
46. Felix, R. J., Leighton, C. M. & Gagné, M. R. Electrophilic Pt(II) complexes: precision instruments for the initiation of transformations mediated by the cation−olefin reaction. *Acc. Chem. Res.* **47**, 2319–2331 (2014).
47. Hahn, C. Enhancing electrophilic alkene activation by increasing the positive net charge in transition-metal complexes and application in homogeneous catalysis. *Chem. Eur. J.* **10**, 5888–5899 (2004).
48. Ríos, P., Rodríguez, A. & Conejero, S. Enhancing the catalytic properties of well-defined electrophilic platinum complexes. *Chem. Commun.*, **56**, 5333−5349 (2020).

49. Xing, X., Xu, C., Chen, B., Li, C., Virgil, S. C. & Grubbs, R. H. Highly active platinum catalysts for nitrile and cyanohydrin hydration: catalyst design and ligand screening via high-throughput techniques. *J. Am. Chem. Soc.* **140**, 17782–17789 (2018).
50. Frenking, G. & Frohlich, N. The nature of the bonding in transition-metal compounds. *Chem. Rev*. **100**, 717–774 (2000).
51. Clarke, M. L. et. al. The electron-poor phosphines $P\{C_6H_3(CF_3)_2\text{-}3,5\}_3$ and $P(C_6F_5)_3$ do not mimic phosphites as ligands for hydroformylation. A comparison of the coordination chemistry of $P\{C_6H_3(CF_3)_2\text{-}3,5\}_3$ and $P(C_6F_5)_3$ and the unexpectedly low hydroformylation activity of their rhodium complexes. *Dalton Trans.* 1294–1300 (2005).
52. Prout, C. K. & Wright, J. D. Observations on the crystal structures of electron donor-acceptor complexes. *Angew. Chem. Int. Ed. Engl.* **7**, 659–667 (1968).
53. Rosenfeld, D. C., Shekhar, S., Takemiya, A., Utsunomiya, M. & Hartwig, J. F. Hydroamination and hydroalkoxylation catalyzed by triflic acid. Parallels to reactions initiated with metal triflates. *Org. Lett.* **8**, 4170–4182 (2006).
54. Taylor, J. G., Adrio, L. A. & Hii, K. K. Hydroamination reactions by metal triflates: Brønsted acid vs. metal catalysis? *Dalton Trans*. **39**, 1171–1175 (2010).
55. Dang, T. T., Boeck, F. & Hintermann & L. Hidden Brøsted acid catalysis: pathways of accidental or deliberate generation of triflic acid from metal triflates. *J. Org. Chem.* **76**, 9353–9361 (2011).
56. Chen, J., Goforth, S. K., Mckeown, B. A. & Gunnoe, T. B. Brønsted acid-catalysed intramolecular hydroamination of unactivated alkenes: metal triflates as an *in situ* source of triflic acid. *Dalton Trans.* **46**, 2884-2891 (2017).
57. Bentley, J. N. & Captuo, C. B. Catalytic hydroarylation of alkenes with phenols using $B(C_6F_5)_3$. *Organometallics* **37**, 3654–3658 (2018).
58. Lettko, L., Wood, J. S. & Rausch, M. D. Synthesis of (phosphine)silver(I) trifluoromethanesulfonate complexes and the molecular structure of di-*μ*-trifluoromethylsulfonate-(tetrakis-triphenylphosphine)disilver(I). *Inorganica Chimica Acta* **308**, 37–44 (2000)
59. Murayama, H., Nagao, K., Ohmiya, H. & Sawamura, M. Copper(I)-catalyzed intramolecular hydroalkoxylation of unactivated alkenes. *Org. Lett.* **17**, 2039–2041 (2015).
60. Shigehisa, H. et. al. Catalytic synthesis of saturated oxygen heterocycles by hydrofunctionalization of unactivated olefins: unprotected and protected strategies. *J. Am. Chem. Soc.* **138**, 10597–10604 (2016).
61. Tsuji, N. et. al. Activation of olefins via asymmetric Brønsted acid catalysis. *Science* **359**, 1501–1505 (2018).
62. Ebisawa, K. et. al. Catalyst- and silane-controlled enantioselective hydrofunctionalization of alkenes by cobalt-catalyzed hydrogen atom transfer and radical-polar crossover. *J. Am. Chem. Soc.* **142**, 13481–13490 (2020).

63. Chen, D., Berhane, I. A. & Chemler, S. R. Copper-catalyzed enantioselective hydroalkoxylation of alkenols for the synthesis of cyclic ethers. *Org. Lett.* https://dx.doi.org/10.1021/acs.orglett.0c01691 (2020).
64. Hannedouche, J. & Schulz, E. Asymmetric hydroamination: a survey of the most recent developments. *Chem. Eur. J.* **19**, 4972–4985 (2013).
65. Reznichenko, A. L. & Hultzsch, K. C. *Asymmetric Hydroamination,* Chapter 11, p342–372.
66. Chen, J., Guo, H.-M., Zhao, Q.-Q., Chen, J.-R. & Xiao, W.-J. Visible light-driven photocatalytic generation of sulfonamidyl radicals for alkene hydroamination of unsaturated sulfonamides. *Chem. Commun*. **54**, 6780–6783 (2018).
67. Gao, P. et. al. Chiral NHC-iridium complexes and their performance in enantioselective intramolecular hydroamination and ring-opening amination reactions. *Organometallics* **39**, 556–573 (2020).
68. Roos, C. B., Demaerel, J., Graff, D. E. & Knowles, R. R. Enantioselective hydroamination of alkenes with sulfonamides enabled by proton-coupled electron transfer. *J. Am. Chem. Soc.* **142**, 5974–5979 (2020).
69. Shen, X. et. al. Ligand-promoted cobalt-catalyzed radical hydroamination of alkenes. *Nat. Commun.* **11**, 783 (2020).
70. Paull, D. H., Abraham, C. J., Scerba, M. T., Alden-Danforth, E. & Lectka, T. Bifunctional asymmetric catalysis: cooperative lewis acid/base systems. *Acc. Chem. Res.* **41**, 655–663 (2008).

Figures

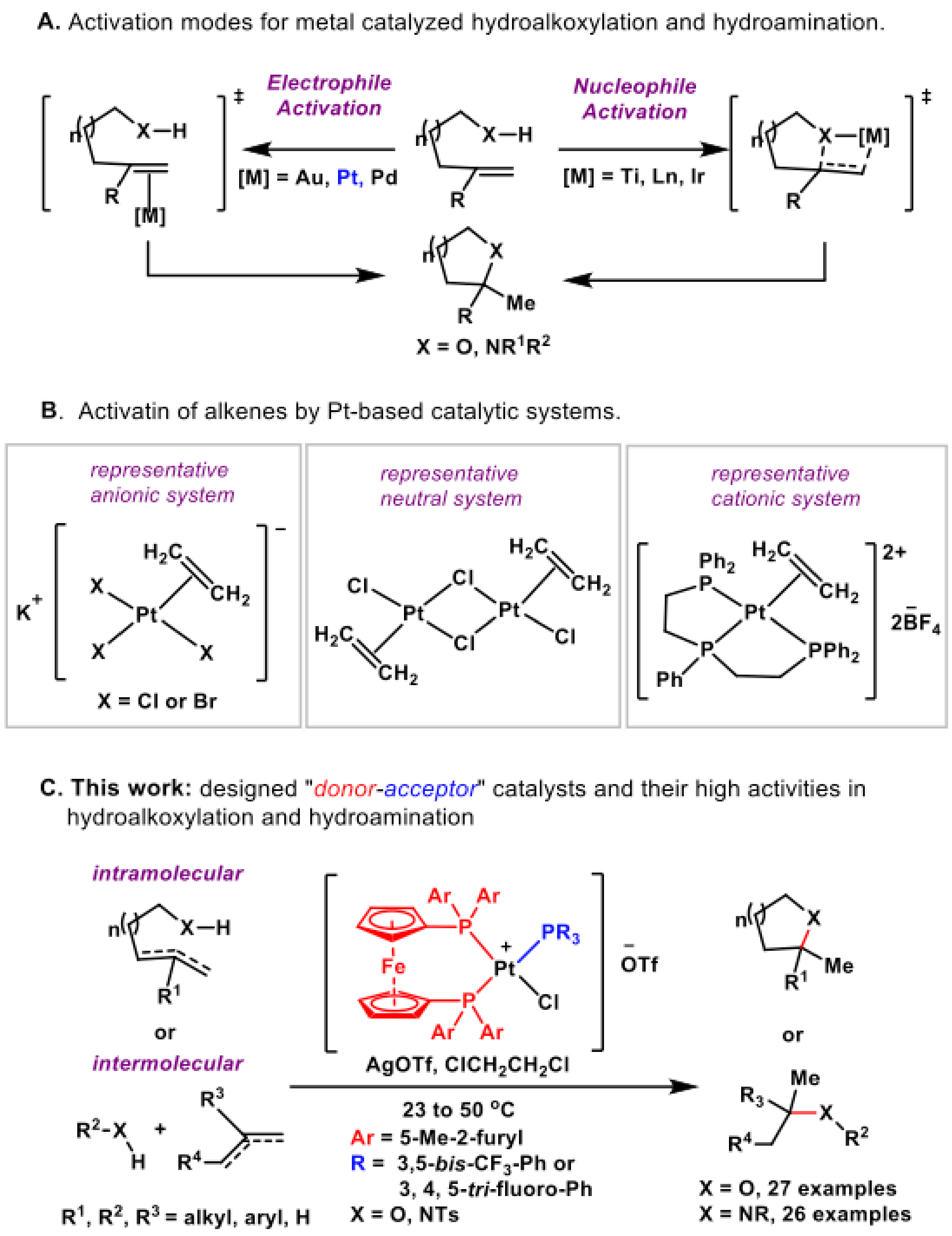


Figure 1

Pt catalyzed hydroalkoxylation and hydroamination of unactivated alkenes.

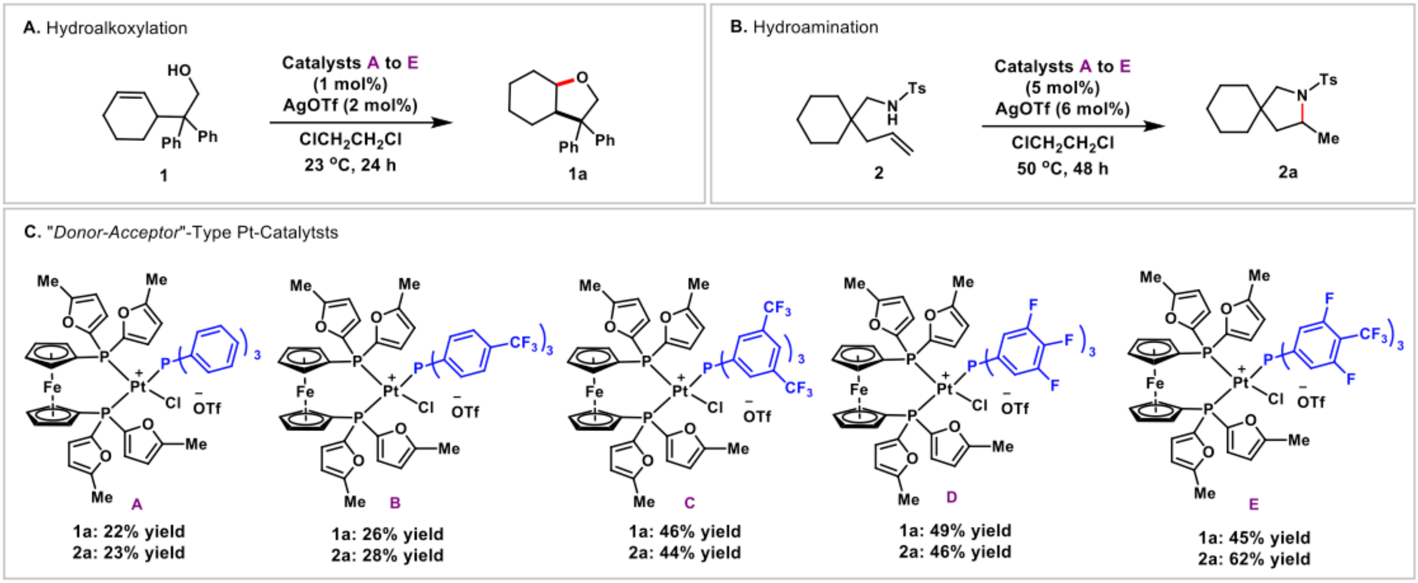


Figure 2

Development of “donor-acceptor” type Pt-catalysts for hydroalkoxylation and hydroamination.

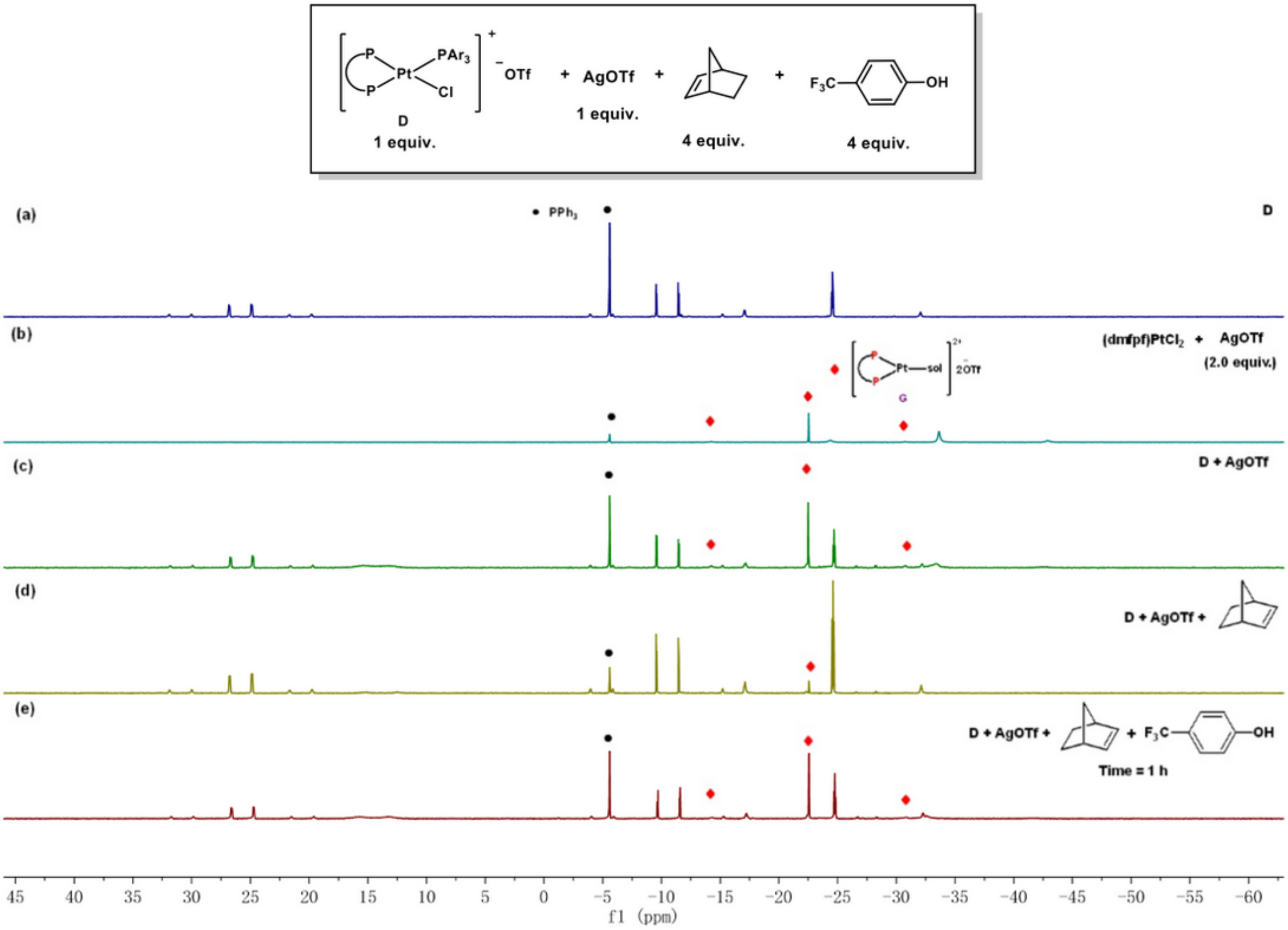


Figure 3

31P NMR spectra for monitoring the reaction of catalyst D + AgOTf + norbornene + 4-trifluromethylphenol (PPh3 was used as an external standard).

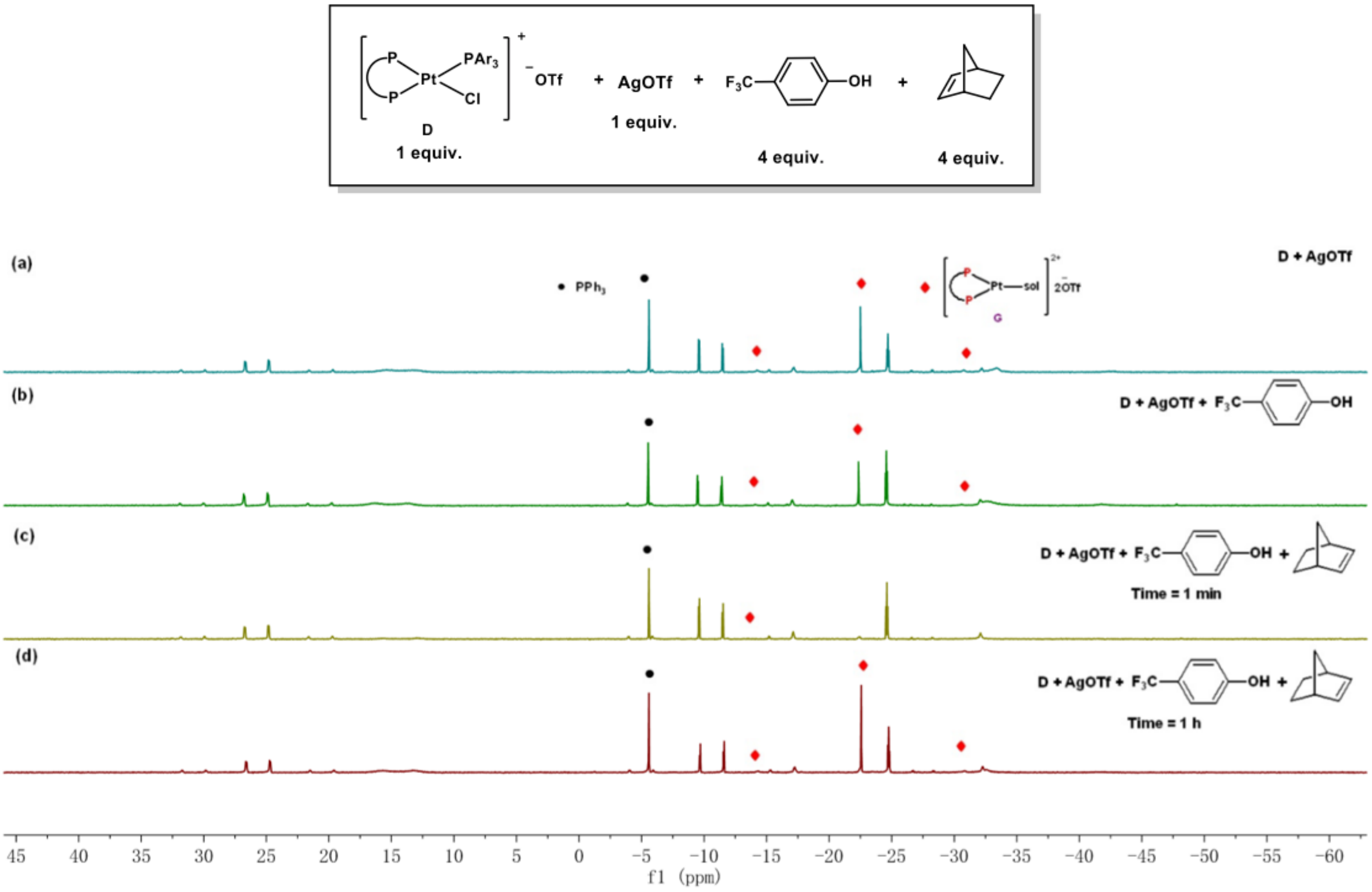


Figure 4

31P NMR spectra for monitoring the reaction of catalyst D + AgOTf + 4-trifluromethylphenol + norbornene (PPh3 was used as an external standard).

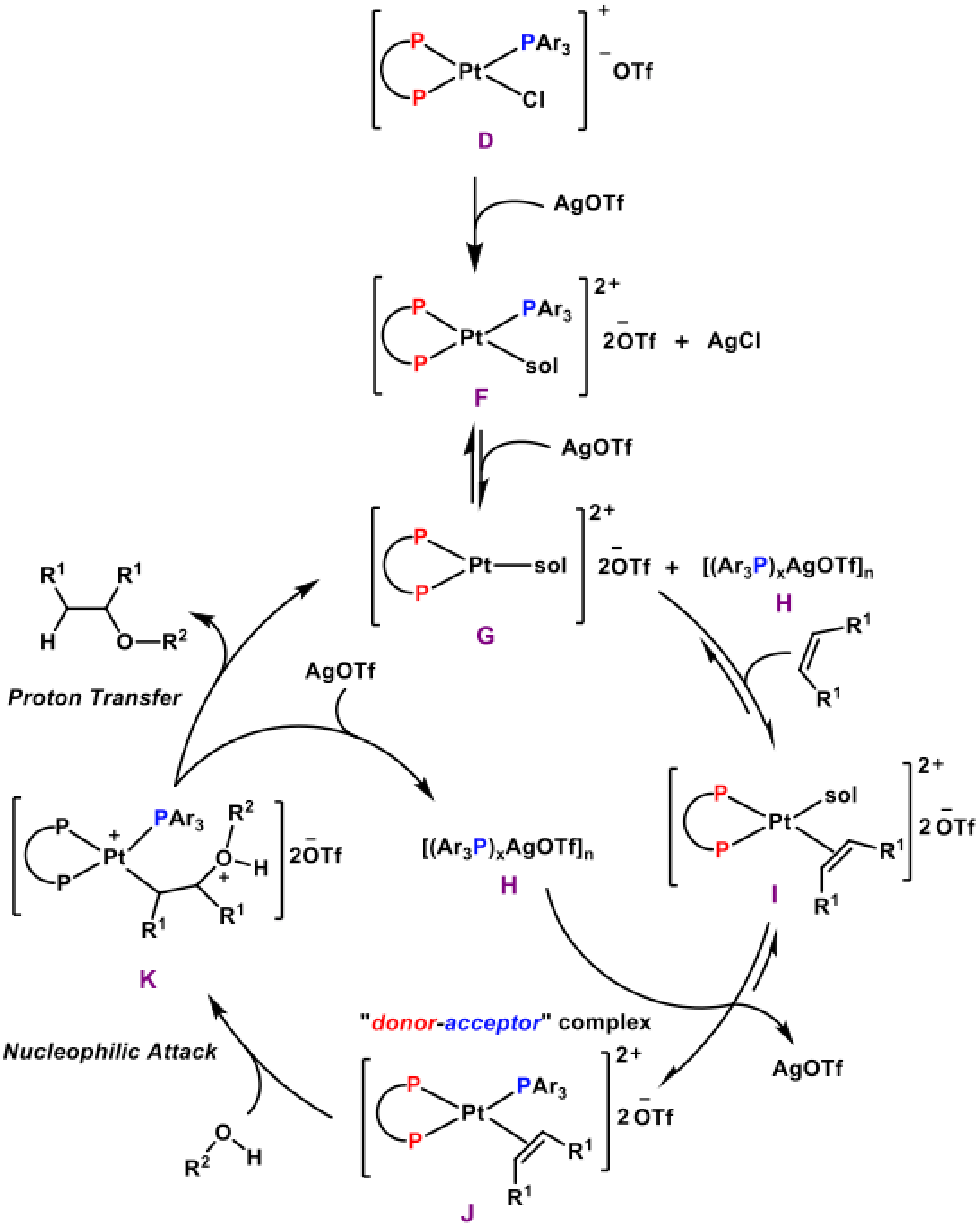


Figure 5

Proposed mechanism for “donor-acceptor” Pt-complex catalyzed hydroalkoxylation of unactivated alkenes. Asymmetric hydroalkoxylation and hydroamination.

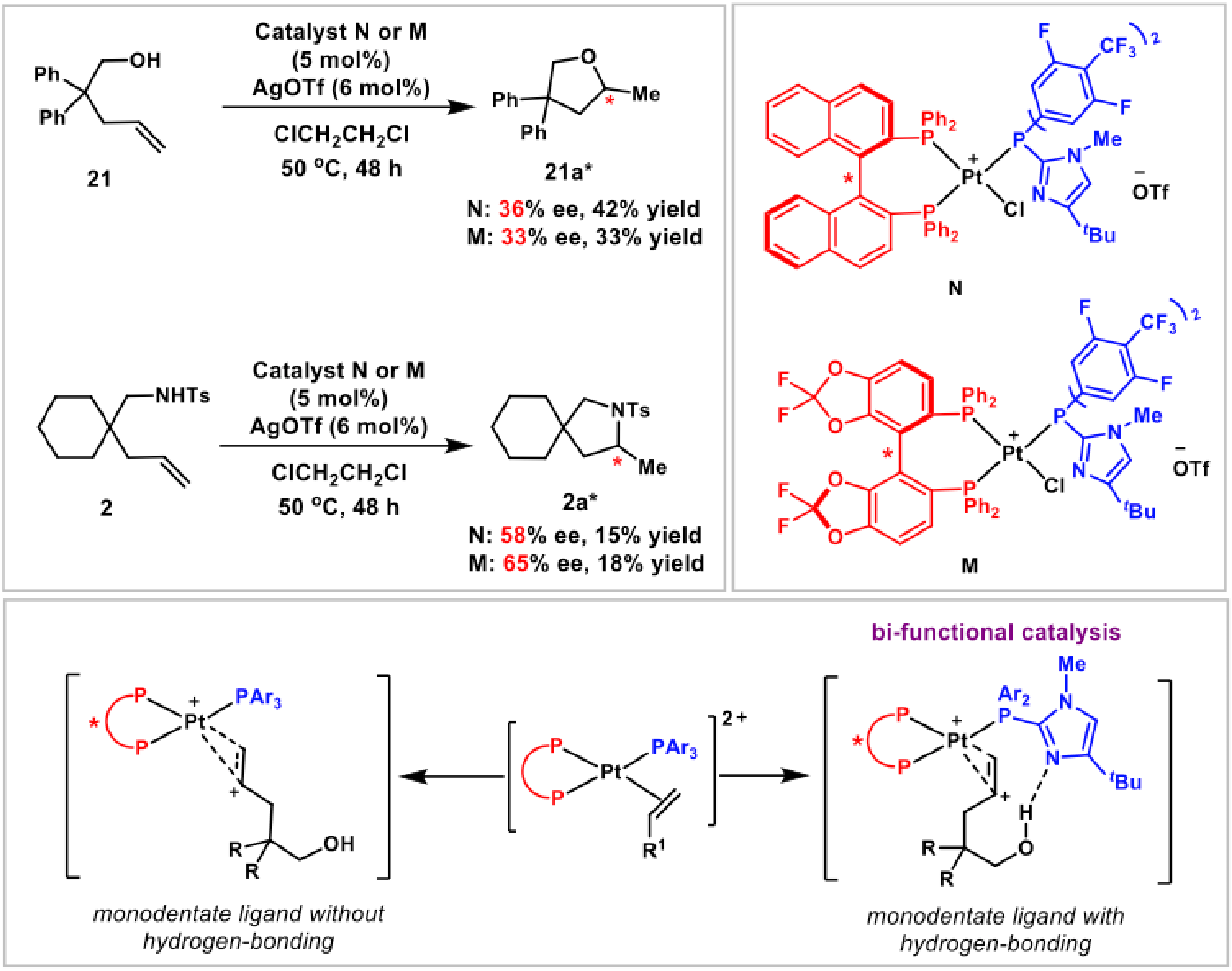


Figure 6

Development of bi-functional catalysis for catalytic asymmetric hydroalkoxylation and hydroamination.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- SupportingInformation.pdf
- catalystM.cif
- catalystE.cif
- 41a.cif
- 23f.cif