ORGANOMETALLICS

Arene-Ruthenium Chemistry and Brønsted Acid Catalysis of a Chiral Phosphane-Hydroxyl Ligand

Daniel Carmona,^{*,†} M. Pilar Lamata,^{*,†} Pilar Pardo,[†] Ricardo Rodríguez,^{*,†} Fernando J. Lahoz,[†] Pilar García-Orduña,[†] Ibon Alkorta,[‡] José Elguero,[‡] and Luis A. Oro[†]

[†]Instituto de Síntesis Química y Catálisis Homogénea (ISQCH), Departamento de Química Inorgánica, CSIC-Universidad de Zaragoza, Pedro Cerbuna 12, E-50009 Zaragoza, Spain

[‡]Instituto de Química Médica, CSIC, Juan de la Cierva, 3, E-28006 Madrid, Spain

Supporting Information

ABSTRACT: The phosphane-hydroxyl ligand (S_{C1},R_{C2}) -Ph₂PC(Ph)HC-(OH)HCH₂OMe (**POH**) displays $\kappa^1 P$, $\kappa^2 P$,O, $\kappa^3 P$,O,O', and anionic deprotonated $\kappa^3 P$,O,O' coordination modes toward the metallic (η^6 -*p*-MeC₆H₄*i*Pr)Ru moiety. The hydroxyl group in $[(\eta^6$ -*p*-MeC₆H₄*i*Pr)Ru-($\kappa^3 P$,O,O'-**POH**)][SbF₆]₂ (**3**) has strong acidic properties. This complex catalyzes the Diels–Alder reaction between cyclopentadiene and *trans-β*nitrostyrene or methacrolein as well as the Friedel–Crafts reaction between indole and methyl 3,3,3,-trifluoropyruvate or *trans-β*-nitrostyrene. Solution studies strongly indicate that complex **3** acts as a metallic Lewis acid assisted Brønsted-acid catalyst.







ring metallacycles (see complex 2, Scheme 2). Furthermore, the acidic properties of the OH group would be enhanced by coordination to metallic cations, resulting in potential LBA catalysts.

bond donating ability of the catalysts is usually increased by means of electron-withdrawing organic substituents. In principle, this role can also be played by metallic Lewis acids, giving rise to Lewis acid assisted Brønsted acid catalysts (LBA).⁴ Brønsted acid catalysts of this type are scarce. Among them, it has been reported that coordination of binols^{4,5} or a hydroxyl-phosphane ligand derived from binol⁶ to SnCl₄ or to La(OTf)₃, respectively, enhances the acidity of the ligand OH groups, rendering active LBA catalysts for the enantioselective protonation of silyl enol ethers and biomimetic cyclization of polyprenoid. Toste et al. have successfully applied to the former process chiral Brønsted acids obtained by activation of the OH group of EtOH or *i*PrOH by coordination to gold diphosphane complexes,⁷ and it has been recently reported⁸ that the hydroxyl group of a water ligand participates in the redox isomerization of allylic alcohols in aqueous medium by Ru(IV) based complexes.

The use of weakly acidic small organic molecules as

electrophile activators through either hydrogen bond or Brønsted acid catalysis constitutes an important branch of organocatalysis that over the last years has grown at a dramatic pace. Diols,¹ (thio)ureas,^{1a,b,d,e,2} and phosphoric acids^{1a,c-e,3} are

the most representative organocatalysts of this class. The H-

In 2008, Vidal-Ferran et al. reported the regioselective and stereospecific preparation of the BH₃-protected phosphanohydroxyl compound (S_{C1},R_{C2}) - $(BH_3)Ph_2PC(Ph)HC(OH)$ -HCH₂OMe $(BH_3$ -**POH**) by ring opening of the corresponding (R_{C1},R_{C2}) -epoxide with potassium diphenylphosphanide (Scheme 1).⁹ We anticipate that **POH** can act as a bidentate $\kappa^2 P$,O chelate ligand through the phosphane and hydroxyl functionalities, giving rise to stable unstrained five-membered-



Received: December 19, 2013 Published: January 24, 2014 In the present communication, we report on (i) the preparation, characterization, and reactivity of *p*-cymene– ruthenium compounds (*p*-cymene = η^6 -*p*-MeC₆H₄*i*Pr) containing a variety of coordination modes of the phosphano–hydroxyl ligand **POH**, (ii) the application of one of these complexes, namely [(η^6 -*p*-MeC₆H₄*i*Pr)Ru($\kappa^3 P,O,O'$ -**POH**)]-[SbF₆]₂ (3), as a catalyst in examples of Diels–Alder (DA) and Friedel–Crafts (FC) reactions, and (iii) NMR spectroscopic evidence for the Brønsted acid activation of the electrophilic substrates involved in the catalytic reactions.

The ruthenium dimer $[\{(\eta^6 \cdot p \cdot \text{MeC}_6 H_4 i \text{Pr}) \text{RuCl}\}_2(\mu \cdot \text{Cl})_2]$ reacts with **POH**, rendering the mononuclear compound $[(\eta^6 \cdot p \cdot \text{MeC}_6 H_4 i \text{Pr}) \text{RuCl}_2(\kappa^1 P \cdot \text{POH})]$ (1), which in turn reacts with AgSbF₆ to afford $[(\eta^6 \cdot p \cdot \text{MeC}_6 H_4 i \text{Pr}) \text{RuCl}(\kappa^2 P, O \cdot \text{POH})]$ -[SbF₆] (2) (Scheme 2). Compound 2 was isolated as a 65/ 35 ratio mixture of the two epimers at metal. Subsequent treatment of 2 with 1 equiv of AgSbF₆ gives $[(\eta^6 \cdot p \cdot \text{MeC}_6 H_4 i \text{Pr}) \text{Ru}(\kappa^3 P, O, O' \cdot \text{POH})]$ [SbF₆]₂ (3). Even in the presence of good coordinating ligands such as pyridine, PPh₃, and P(OMe)₃ the η^3 coordination of the ligand induces the diastereopure formation of the *R* at ruthenium epimer of complex 3.

Complexes 1–3 have been characterized by analytical and spectroscopic means as well as by the determination of the crystal structures of 2 and $3 \cdot \text{Et}_2\text{O}$ (see the Supporting Information). In particular, $\delta(\text{OH})$ shifts downfield on going from 1 to 3 ($\delta(\text{OH})$ 3.84 (1), 5.96 (2), 7.95 ppm (3)), indicating that, as a consequence of the coordination with the metal and the increase of the formal charge of the cation, hydrogen acidity increases in the same direction.

As expected, the molecular structure of 3 reveals that the configuration at the metal is R^{10} Due to the polarization of the OH bond, in the crystal, the oxygen atom of a molecule of Et₂O is hydrogen-bonded to the OH group of the cation (Figure 1).



Figure 1. Molecular representation of the cation of 3 showing the H-bonded Et_2O molecule.

Accordingly, complex 3 reacts with $NaHCO_3$ to render the deprotonated monocation 4 (Scheme 3), which has been isolated and spectroscopically characterized (see the Supporting Information).

Scheme 3. Deprotonation of Complex 3



We have calculated the acidity of compound 3, defined as its energy difference with 4, as $\Delta H^{\circ} = 751.7$ kJ mol⁻¹ at the B3LYP/LANL2DZ level,¹¹ using the facilities of the Gaussian 09 package.¹² This value corresponds to a very strong acid. According to the NIST database,¹³ neutral acids have values in the range 1456 (CH₃CO₂H)–1278 kJ mol⁻¹ (CF₃SO₃H), all of which are much weaker than 3. However, compound 3 is a dication which by losing a proton yields the monocation 4, while the reported compounds are neutral molecules. To find closer acidity values, it is necessary to search for cations that on loss of a proton became neutral molecules:¹³

$$C_6H_7^+ \rightarrow C_6H_6 \text{ (benzene)} \quad 750.5 \text{ kJ mol}^{-1}$$

 $H_3SiOH_2^+ \rightarrow H_3SiOH \text{ (silanol)} 746.4 \text{ kJ mol}^{-1}$

On the other hand, complex 3 catalyzes the DA reaction between cyclopentadiene and *trans-\beta*-nitrostyrene or methacrolein as well as the FC reaction between indole and methyl 3,3,3,-trifluoropyruvate or between different indoles and substituted *trans-\beta*-nitrostyrenes (Scheme 4).

Scheme 4. Catalytic Reactions



In general, good conversions were achieved and activation was shown to be efficient even in the case of the DA reaction involving a *trans* dienophile (reaction 1). Catalytic reactions proceed with enantioselectivity indicating that complex 3, the only possible source of chirality, plays a key role in the process. In particular, under the conditions indicated in reaction 4 and Table 1, around 80% ee was obtained for the reaction between indoles and substituted *trans-β*-nitrostyrenes (Table 1).

To shed light on the catalytic systems, solutions containing catalyst **3** and methacrolein were monitorized by NMR

Table	1.	Cataly	rtic	Results	for	Reaction	4 ^a
I abie	1.	Cataly	/uc	Acounts	101	Reaction	т.

entry	\mathbb{R}^1	R ²	R ³	conversn $(\%)^b$	ee (%) ^c
1	Н	Н	Н	93	75
2	Н	Н	2-OMe	68	78
3	Н	Н	4-Me	43	81
4	Н	Н	2-Cl	>99	81
5	Н	Н	4-Br	78	79
6	Н	Me	Н	>99	28
7	Me	Н	Н	94	15
8	Me	Me	Н	>99	35

^{*a*}Reaction conditions: catalyst 0.03 mmol (5.0 mol %), indole 0.60 mmol, *trans-β*-nitrostyrene 0.90 mmol, in 2 mL of CH₂Cl₂. ^{*b*}Based on indole. Determined by NMR. ^{*c*}Determined by HPLC.

¹H NMR СНО Ru-OMe Ru-OH Ru-OH Ru-OH Ru-OF Ru-OF 55 85 8.0 75 70 65 6.0 50 4.0 ppm 10.0 95 90 45

spectroscopy. Figure 2 shows the evolution of a selected region of the ¹H NMR spectrum, by successive addition of



methacrolein to a CD_2Cl_2 solution of 3. All proton resonances of 3 remain essentially unchanged except for that of the hydroxyl group.¹⁴ This resonance undergoes a gradual downfield displacement from 7.95 (trace a, δ value in the absence of methacrolein) to 9.84 ppm (trace e, 20 equiv of methacrolein added). Notably, the ¹H NMR OMe singlet appears invariably at 4.25 ppm and the ³¹P{¹H} NMR spectrum consists of one singlet that methacrolein addition only shifts 0.55 ppm, from 54.83 to 55.38 ppm. All these data strongly support that, in solution, the metallic cation is an 18-electron coordinatively saturated species with the four groups, i.e. pcymene, PPh₂, OMe, and OH, remaining bonded to it in the presence of excess methacrolein. Therefore, methacrolein does not interact directly with the metal. Similar trends in the NMR spectra were observed with progressive addition of *trans-\beta*nitrostyrene or methyl 3,3,3-trifluoropyruvate to complex 3 (see the Supporting Information).¹⁵

The spectroscopic data can be accounted for by assuming that an equilibrium between complex **3** and adduct **5**, in which methacrolein is hydrogen-bonded to the hydroxyl group of **3**, is established in solution (Scheme 5). Such an equilibrium

Scheme 5. Equilibrium between Complex 3 and Methacrolein



between 3 and the electrophile would be responsible for activation in all of the tested DA and FC catalytic reactions. Therefore, the aforementioned DA and FC processes can be considered as examples of Brønsted acid catalysis mediated by a Lewis acid assisted Brønsted acid (LBA) catalyst.⁴

In summary, in this communication we have reported on the richness of ruthenium coordination chemistry that the **POH** ligand displays. Examples of $\kappa^1 P$, $\kappa^2 P$,O, and $\kappa^3 P$,O,O' as well as anionic deprotonated $\kappa^3 P$,O,O' coordination modes have been described (Scheme 6). From theoretical, crystallographic, and





spectroscopic data, it can be concluded that complex **3** is an active metallic Brønsted acid catalyst for DA and FC reactions through the OH coordinated group. Brønsted acid activation of carbonyl- and nitro-containing substrates occurs with asymmetric induction. Optimization and further development of enantioselective catalytic processes mediated by complex **3**, as well as other related M–OH-containing species, are currently under investigation in our laboratory.

ASSOCIATED CONTENT

S Supporting Information

Text, figures, tables, and CIF files giving experimental procedures and spectroscopic and analytical characterization data of the new complexes and DA and FC catalytic results, X-ray crystallographic data for complexes 2 and $3 \cdot \text{Et}_2O$, and Cartesian coordinates of compounds 3 and 4. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Author

*E-mail: dcarmona@unizar.es (D.C.); plamata@unizar.es (M.P.L.); riromar@unizar.es (R.R.) Tel: 34-976-762027. Fax: 34-976-761187.

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

We thank the Ministerio de Economía y Competitividad of Spain (CTQ2012-32095) and Gobierno de Aragón (Grupo Consolidado: Catalizadores Organometálicos Enantioselectivos) for financial support. This work was supported by the CONSOLIDER INGENIO 2010 program under the project "Factoría de Cristalización" (CSD2006-0015). R.R. and P.P. acknowledge the CSIC and European Social Fund for JAE grants. I.A. and J.E. thank the Ministerio de Economía y Competitividad of Spain (Project CTQ2012-13129-C02-02) and the Comunidad Autónoma de Madrid (Project MADRI-SOLAR2, ref S2009/PPQ-1533) for financial support. Dedicated in memory of María Pilar García Clemente.

REFERENCES

(1) (a) Akiyama, T.; Itoh, J.; Fuchibe, K. Adv. Synth. Catal. 2006, 348, 999–1010. (b) Taylor, M. S.; Jacobsen, E. N. Angew. Chem., Int. Ed. 2006, 45, 1520–1543. (c) Akiyama, T. Chem. Rev. 2007, 107, 5744–5758. (d) Yu, X.; Wang, W. Chem. Asian J. 2008, 3, 516–532. (e) Brak, N.; Jacobsen, E. N. Angew. Chem., Int. Ed. 2013, 52, 534–561.

(2) (a) Takemoto, Y. Org. Biomol. Chem. 2005, 3, 4299-4306.
(b) Connon, S. J. Chem. Eur. J. 2006, 12, 5418-5427. (c) Miyabe, H.; Takemoto, Y. Bull. Chem. Soc. Jpn. 2008, 81, 785-795. (d) Zhang, Z.; Schreiner, P. Chem. Soc. Rev. 2009, 38, 1187-1198.

Organometallics

(3) (a) Connon, S. J. Angew. Chem., Int. Ed. 2006, 45, 3909-3912.
(b) Terada, M. Chem. Commun. 2008, 4097-4112. (c) Terada, M. Bull. Chem. Soc. Jpn. 2010, 83, 101-119. (d) Rueping, M.; Nachtsheim, B. J.; Ieawsuwan, W.; Atodiresei, I. Angew. Chem., Int.

Ed. **2011**, *50*, 6706–6720. (e) Yu, J.; Shi, F.; Gong, L.-Z. *Acc. Chem. Res.* **2011**, *44*, 1156–1171. (f) Rueping, M.; Kuenkel, A.; Atodiresei, I. *Chem. Soc. Rev.* **2011**, *40*, 4539–4549.

(4) Yamamoto, H.; Futatsugi, K. Angew. Chem., Int. Ed. 2005, 44, 1924–1942.

(5) (a) Ishibashi, H.; Ishihara, K.; Yamamoto, H. Chem. Rec. 2002, 2, 177–188. (b) Ishihara, K.; Nakashima, D.; Hiraiwa, Y.; Yamamoto, H.

J. Am. Chem. Soc. **2003**, *125*, 24–25.

(6) Cheon, C. H.; Imahori, T.; Yamamoto, H. Chem. Commun. 2010, 46, 6980-6982.

(7) Cheon, C. H.; Kanno, O.; Toste, F. D. J. Am. Chem. Soc. 2011, 133, 13248-13251.

(8) Díez, J.; Gimeno, J.; Lledós, A.; Suárez, F. J.; Vicent, C. ACS Catal. 2012, 2, 2087–2099.

(9) Fernández-Pérez, H.; Pericàs, M. A.; Vidal-Ferran, A. Adv. Synth. Catal. 2008, 350, 1984–1990.

(10) Priority sequence η^6 -*p*-MeC₆H₄iPr > P > OMe > OH: Lecomte, C.; Dusausoy, Y.; Protas, J.; Tirouflet, J. *J. Organomet. Chem.* **1974**, 73, 67–76.

(11) Hay, P. J.; Wadt, W. R. J. Chem. Phys. 1985, 82, 270-283.

(12) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, N. J.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. Gaussian 09, Revision A.1; Gaussian, Inc. Wallingford, CT, 2009.

(13) Linstrom, P. J., Mallard, W. G., Eds. NIST Chemistry Webbook; NIST Standard Reference Database No. 69; National Institute of Standards and Technology, Gaithersburg, MD, 2003; available from http://webbook.nist.gov.

(14) A small upfield shift of about 0.1 ppm is observed for the nearest to the OH group C*H proton that, in complex 3, resonates as a doublet centered at 4.66 ppm (see Scheme 2).

(15) Addition of *trans-\beta*-nitrostyrene to complex **3**, in addition to affecting the OH proton, affects the aromatic protons of the *p*-cymene ring as well as the vicinal proton cited in ref 14. Probably, the presence of two NO₂ oxygen atoms accounts for this behavior.