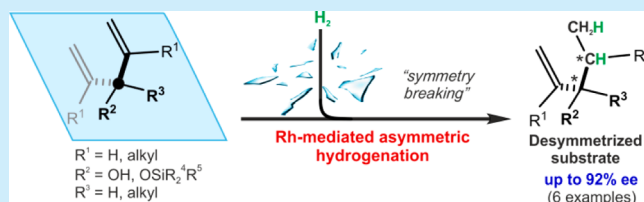


Stereoselective Rh-Catalyzed Hydrogenative Desymmetrization of Achiral Substituted 1,4-Dienes

Héctor Fernández-Pérez,^{†,§} Joan R. Lao,^{†,§} and Anton Vidal-Ferran^{*,†,‡,§}[†]Institute of Chemical Research of Catalonia (ICIQ), Av Països Catalans, 16, 43007 Tarragona, Spain[‡]Catalan Institution for Research and Advanced Studies (ICREA), P. Lluís Companys, 23, 08010 Barcelona, Spain[§]The Barcelona Institute of Science and Technology, Av Països Catalans, 16, 43007 Tarragona, Spain

Supporting Information

ABSTRACT: Highly efficient catalytic stereoselective hydrogenative desymmetrization reactions mediated by rhodium complexes derived from enantiopure phosphine–phosphite (P–OP) ligands are described. The highest performing ligand, which contains a TADDOL-derived phosphite fragment [TADDOL = (2,2-dimethyl-1,3-dioxolane-4,5-diyl)bis-(diphenylmethanol)], presented excellent catalytic properties for the desymmetrization of a set of achiral 1,4-dienes, providing access to the selective formation of a variety of enantioenriched secondary and tertiary alcohols (six examples, up to 92% ee).



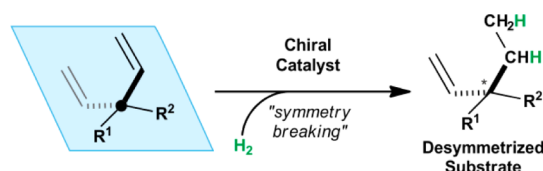
The stereoselective desymmetrization of achiral and *meso* compounds has proved to be a powerful synthetic entry for the preparation of more elaborate optically enriched molecules.¹ This transformation implies breaking the symmetry of the molecule by a synthetic operation, in which two enantiotopic groups of an achiral or *meso* compound are differentiated: the choice of one enantiotopic group (or face) over the other is provided by a chiral reagent or an enantioselective catalyst. Compared to other asymmetric catalytic methodologies, desymmetrization offers several advantages,² such as allowing the concurrent generation of multiple stereogenic centers in a single synthetic step.³ The potential of this synthetic method has been demonstrated by its application in a wide range of catalytic asymmetric transformations.¹ However, catalytic stereoselective desymmetrizations by reductive methods have been less studied,^{1c} and for certain transformations, no satisfactory solution in terms of efficiency or chemo- and stereoselectivity has yet been developed.⁴ For instance, the catalytic hydrogenative desymmetrization of achiral 1,4-dienes (Scheme 1) can be considered an example of understudied desymmetrization. Several challenges need to be addressed when developing efficient stereoselective catalysts for this transformation: (i) selectivity

control in terms of obtaining the monohydrogenation product of the achiral 1,4-diene and (ii) the ability of the catalyst to differentiate two enantiotopic vinyl groups. Notable progress in this topic was made by Brown et al., who paved the way for desymmetrizing a set of achiral 1,4-dienes through enantioselective hydrogenation. These authors used enantiopure Rh bisphosphine complexes as catalysts and demonstrated the feasibility of this hydrogenative desymmetrization, though without complete control of the chemoselectivity of the reaction and with only moderate enantioselectivities (up to 53% ee).⁵

Following our efforts in developing highly efficient catalytic systems derived from phosphine–phosphite (P–OP) ligands for asymmetric hydrogenations⁶ and kinetic resolutions,^{6k} we became interested in developing enantioselective catalysts for the hydrogenative desymmetrization of achiral 1,4-dienes (Tables 1 and 3), as the resulting products can be considered versatile building blocks for the construction of more complex molecules. Herein, we describe the optimization studies toward the identification of the lead enantioselective catalyst and development of optimal reaction conditions, together with their application in the desymmetrization of a set of structurally diverse achiral 1,4-dienes.

Compounds 1a–c were selected for the initial studies, as these substrates had already been hydrogenatively desymmetrized by Brown et al.⁵ After some experimentation, efficient desymmetrization conditions involving low temperature (–40 °C), 1 bar of H₂ in CH₂Cl₂, and the Rh complex derived from ligand L1 as the catalyst were identified (Table 1).⁷

Scheme 1. Stereoselective Hydrogenative Desymmetrization of a General Achiral 1,4-Diene



Received: April 14, 2016

Table 1. Preliminary Studies of the Desymmetrization of Substrates 1a–c^a

$ \begin{array}{c} \text{OR} \\ \\ \text{CH}_3\text{CH}=\text{CHCH}_3 \\ \text{1a (R = H)} \\ \text{1b (R = SiMe}_2^t\text{Bu)} \\ \text{1c (R = SiMe}_2\text{Ph)} \end{array} \xrightarrow[\text{CH}_2\text{Cl}_2, \text{H}_2 \text{ (1 bar), } -40^\circ\text{C, 23 h}]{[\text{Rh}(\text{nbd})_2]\text{BF}_4 \text{ (1.0 mol \%), (R,S,S_a)\text{-L1 (1.1 mol \%)}}} \begin{array}{c} \text{OR} \\ \\ \text{CH}_3\text{CH}^*\text{CH}_2\text{CH}_3 \\ \text{2a-c} \end{array} + \begin{array}{c} \text{OR} \\ \\ \text{CH}_3\text{CHCH}_2\text{CH}_3 \\ \text{3a-c} \end{array} $				
entry	substrate	conv ^b (%)	2:3 ^b	ee of 2 (%) ^c (S) ^d
1	1a	>99	>99:1	46
2	1b	>99	>99:1	62
3	1c	>99	>99:1	66

^a[Substrate] = 0.1 M. ^bDetermined by ¹H NMR. ^cDetermined by chiral HPLC analysis after derivatization into the corresponding benzoyl derivatives 4.⁸ ^dThe absolute configuration of 2a was established by comparison with reported optical rotation values for 4a. The absolute configuration of 2b and 2c was tentatively assigned by analogy with the stereochemical outcome of the reaction leading to 2a.

As summarized in Table 1, the rhodium complex derived from ligand L1 afforded products 2a–c with full conversion and perfect chemoselectivity (2:3 ratio >99:1) in the three substrates assessed (entries 1–3, Table 1). Moreover, products 2a–c were obtained with moderate ee values (from 46 to 66% of ee; entries 1–3, Table 1). The best result in this screening was achieved for substrate 1c, where the desymmetrized product 2c was selectively obtained with complete conversion and with 66% ee (entry 3, Table 1). Further studies were aimed at improving the enantioselectivity of the desymmetrization of 1c by screening a library of structurally diverse P–OP ligands (Figure 1).⁹ The assayed conditions and results are listed in

Table 2. Ligand Screening for Substrate 1c^{a,b}

<div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>1c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>3c</div></div></div></div> <div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div><div>OSiMe₂Ph</div><div>2c</div></div><div><div><div><div><div><div></div><div></div></div><div><div></div><div></div></div></div><div><div></div><div></div></div><div><div></div><div></div></div></div></div></div></div>			
---	--	--	--

^aSee footnotes a–d in Table 1. ^bFull conversion was achieved, unless otherwise stated. ^c74% of conversion was obtained. ^dThis result has been already shown in Table 1.

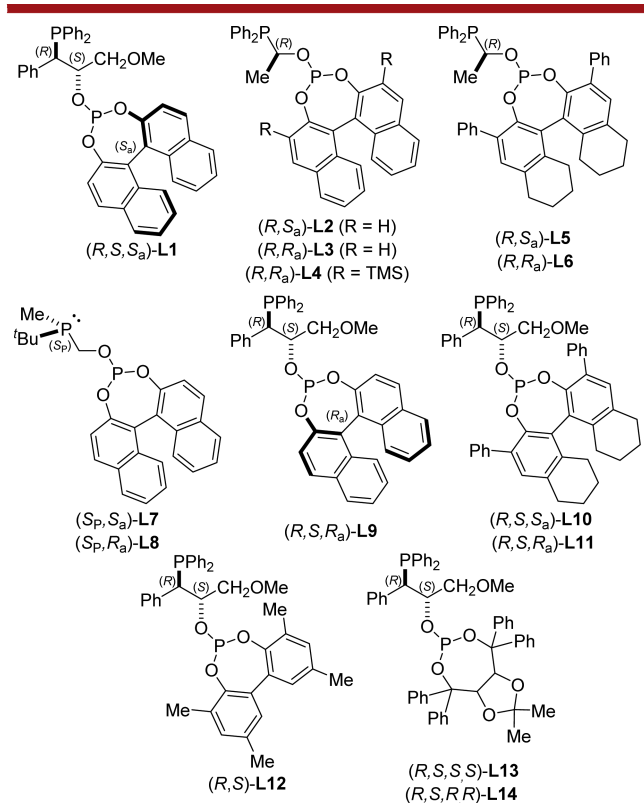


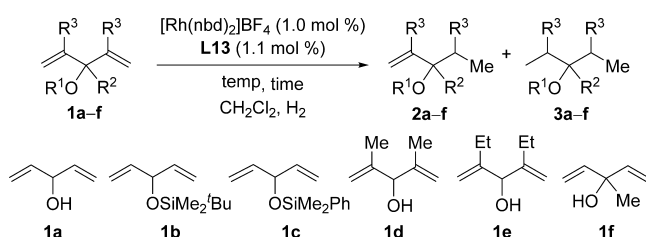
Figure 1. Library of P–OP ligands screened in the hydrogenative desymmetrization of substrate 1c.

Table 2. In general, and regardless of the nature of the set of P–OP ligands tested in these screening studies (L1–L14; Figure 1), their derived Rh catalysts efficiently mediated the desymmetrization of 1c with excellent values of activity (from 74 to 99% of conversion), perfect chemoselectivity (2c:3c ratios >99:1), and variable enantioselectivities, which strongly depended on the type of ligand used (see entries 1–14; Table 2). In a first series of experiments, geminal P–OP ligands L2–L8 (Figure 1) were tested. These narrow bite-angle ligands⁹ proved to be effective in the desymmetrization of 1c in terms of activity (conversion >99%) and chemoselectivity (2c:3c ratio >99:1), but not in terms of enantioselectivity (from null to 34% ee, entries 1–7, Table 2). Vicinal P–OP ligands⁹ L1 and L9–L14 were subsequently studied (Figure 1). The phosphite group in the ligand played a crucial role in the enantioselectivity of the reaction. As regards P–OP ligands with [1,1'-biaryl]-2,2'-diol-derived phosphite groups (i.e., L1 and L9–L12), as already discussed, ligand L1 containing a (S_a)-BINOL-derived phosphite fragment mediated the desymmetrization of 1c with moderately high ee (66% ee, entry 3 in Table 1). An inversion of the configuration of the phosphite fragment (ligand L9 with a (R_a)-BINOL group) was detrimental both for the catalytic activity and enantioselectivity (74% of conversion and 18% ee; entry 8, Table 2). Ligands bearing substituents at the 3 and 3' positions of the [1,1'-biaryl]-2,2'-diol unit (L10 and L11; Figure 1) were also assessed in the desymmetrization of 1c. Although complete conversions and chemoselectivities were observed with ligands L10 and L11 (entries 10 and 11; Table 2), no improvement on enantioselectivity was achieved with this modification in the ligand backbone (up to 36% ee; entries 10 and 11, Table 2). Ligand L12, which incorporates the 3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2,2'-diol-derived phosphite group, was also assessed in this transformation in order to study whether a conformationally adaptive biaryl group could be beneficial for the stereoselectivity of the reaction. As with the other ligands studied, this new ligand mediated the desymmetrization of 1c with perfect conversion and chemoselectivity but moderated enantioselectivity (49% ee; entry 12,

Table 2). In order to broaden the structural diversity of the catalyst, ligands containing the TADDOL-derived phosphite fragment [TADDOL = (2,2-dimethyl-1,3-dioxolane-4,5-diyl)-bis(diphenylmethanol)] were included in this study (L13 and L14; Figure 1).^{11,12} The use of these ligands in the desymmetrization of **1c** resulted in a considerable improvement in the enantioselectivities of **2c** (ranging from 77 to 80% ee; entries 13 and 14, Table 2) compared to the other ligands assessed in this study (Table 2). Interestingly, the sense of stereoinduction in the desymmetrization of **1c** mediated by L13 and L14 is mainly dictated by the stereocenters of the ligand backbone, as the (*S,S*)- and (*R,R*)-TADDOL-containing ligands (L13 and L14, respectively) led to product **2c** having the same absolute configuration.

With an optimal catalyst for desymmetrizing **1c** in hand, the desymmetrization of **1a** and **1b** with the optimal TADDOL-containing ligand L13 was then studied. The substrate scope of the reaction was also expanded to structurally diverse 1,4-dienes **1d–f** using the optimal ligand L13. The optimized reaction conditions and the best results obtained in this study are listed in Table 3. Substrate **1a** and its *O*-silylated analogue **1b** were

Table 3. Substrate Scope for the Desymmetrization of Substrates **1a–f**^{a,b}

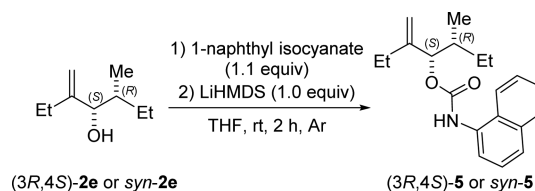


entry	substrate	P (bar)	temp (°C)	time	2:3 ^a	ee of 2 (%) ^{a,c} (config) ^{a,c}
1	1a	1	−40	23 h	>99:1	84 (<i>S</i>)
2 ^d	1b	1	−40	23 h	>99:1	87 (<i>S</i>)
3 ^e	1c	1	−40	23 h	>99:1	80 (<i>S</i>)
4	1d	5	−20	5 d	>98:2	59 (<i>S</i>)
5	1e	5	−20	5 d	>92:8 ^f	70 (<i>3R,4S</i>)
6	1f	1	−40	23 h	>99:1	92 (<i>S</i>)

^aSee footnotes a–d in Table 1. ^bFull conversion was achieved, unless otherwise stated. ^cThe absolute configuration of products **2d–f** was tentatively assigned by analogy with the stereochemical outcome of the reaction leading to **2a**. ^d64% of conversion was obtained. ^eThis result has been shown in Table 2. ^fdr of *syn-2e* > 99:1, as determined by ¹H NMR.¹⁰

efficiently desymmetrized by the Rh catalyst derived from L13 with perfect chemoselectivities (2:3 ratio >99:1) and with high enantioselectivities (84 and 87% ee; entries 1 and 2 in Table 3). Switching from a hydroxyl group (in **1a**) to bulkier silyl ether groups (in **1b** and **1c**) was well tolerated by the catalyst and did not greatly affect the outcome of the reaction in terms of chemo- and enantioselectivity. Substrates **1d** and **1e** were studied in order to assess the influence of substituents at the 2 and 4 positions of the 1,4-diene. The presence of these substituents made necessary the use of higher H₂ pressure (5 bar instead of 1 bar of H₂), higher temperatures (−20 °C instead of −40 °C), and extended reaction times (5 days instead of 23 h). Enantioselectivities of the desymmetrized products **2d** and **2e** were lower (59 and 70% ee, respectively; entries 4 and 5, Table 3) than those observed for the unsubstituted products **1a–c** (compare entries 4 and 5 with

Scheme 2. Derivatization of Product *syn-2e* to **5**¹⁰



entries 1–3 and 6; Table 3). Interestingly, a slight increase in the bulkiness of the substituents at the 2 and 4 positions (from methyl in **1d** to ethyl in **1e**) translated into an increase in the enantioselectivity of up to 11% (from 59 to 70% of ee; compare entries 4 and 5, Table 3). Furthermore, the desymmetrization of **1e** led exclusively to the formation of the *syn-2e* diastereoisomer (dr or *syn:anti* ratio >99:1; entry 5, Table 3).^{10,13} Derivatization of the reaction product *syn-2e* into the 1-naphthylurethane derivative **5** (Scheme 2) was efficiently performed, and the relative stereochemistry of product *syn-2e* was unequivocally established from the crystalline derivative **5** by single-crystal X-ray analysis (Figure 2).¹⁰

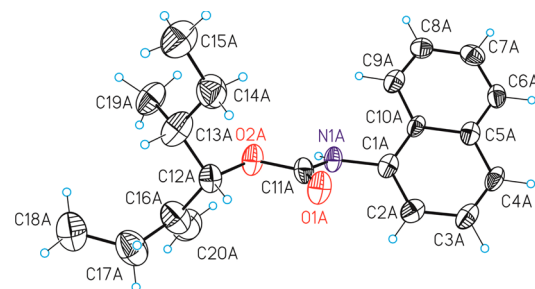


Figure 2. ORTEP Plot (thermal ellipsoids shown at 50% of probability level) of *syn-5*.

Encouraged by these results, the desymmetrization of substrates leading to enantioenriched dialkyl vinyl tertiary alcohols was pursued. This type of compounds cannot be prepared by asymmetric hydrogenation of carbonyl precursors, and the proposed desymmetrization strategy is an interesting variant to the classical C–C bond forming approach (enantioselective alkylation of a ketone with an organometallic derivative) toward enantioenriched dialkyl vinyl tertiary alcohols.¹⁴ Substrate **1f** was therefore subjected to desymmetrization conditions (entry 6 in Table 3). The desired product **2f** was obtained with complete conversion, perfect chemoselectivity (2f:3f ratio >99:1), and very high enantioselectivity (92% ee; entry 6 in Table 3).

In short, a highly stereoselective catalytic hydrogenative desymmetrization based on Rh complexes derived from phosphine–phosphite ligands has been developed. The lead enantioselective catalyst, derived from the TADDOL-containing ligand L13, has given access to a set of highly enantioenriched secondary and tertiary alcohols (up to 92% ee). The presented results demonstrate the ability of the lead catalyst to differentiate between the two enantiotopic vinyl groups from the substrates. Moreover, the desymmetrization of a substrate containing two pro-stereogenic carbons (**1e**) proceeded with complete diastereoselectivity. Investigations to gain deeper insight in the reaction mechanism are currently underway.

■ ASSOCIATED CONTENT

■ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b01088.

General procedure for catalytic experiments, preparation of substrates, spectral data of known and new compounds, crystallographic data, HPLC data from catalytic experiments (PDF)

X-ray data for *syn*-5 (CIF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: avidal@iciq.es.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank MINECO (CTQ2014-60256-P and Severo Ochoa Excellence Accreditation SEV-2013-0319), the ICIQ Foundation for financial support, Dr. J. Benet-Buchholz and Dr. E. Martin for the X-ray crystallographic analysis of *syn*-5, and B. Balakrishna for his generous gift of ligands L13 and L14. J.-R. L. thanks the ICIQ Foundation for a predoctoral fellowship.

■ REFERENCES

- (1) For selected reviews on this topic, see: (a) Willis, M. C. *J. Chem. Soc., Perkin Trans. 1* **1999**, 1765–1784. (b) Rovis, T. In *New Frontiers in Asymmetric Catalysis*; Mikami, K., Lautens, M., Eds.; John Wiley & Sons, Inc., 2007; p 275. (c) Fernández-Pérez, H.; Etayo, P.; Lao, J. R.; Núñez-Rico, J. L.; Vidal-Ferran, A. *Chem. Commun.* **2013**, 49, 10666–10675 and references cited therein.
- (2) For example, see: (a) *Comprehensive Chirality*; Carreira, E. M., Yamamoto, H., Eds.; Elsevier Science: Oxford, 2012; Vols. 1–9. (b) Rachwalski, M.; Vermue, N.; Rutjes, F. P. J. T. *Chem. Soc. Rev.* **2013**, 42, 9268–9282.
- (3) For a representative book about the classical synthetic methodologies for preparing of enantioenriched all-carbon quaternary centers and their applicability, see: *Quaternary Stereocenters: Challenges and Solutions for Organic Synthesis*; Christoffers, J., Baro, A., Eds.; Wiley-VCH: Weinheim, 2006.
- (4) For selected understudied examples of catalytic reductive desymmetrizations, see ref 1c and references cited therein.
- (5) Nguyen, B.; Brown, J. M. *Adv. Synth. Catal.* **2009**, 351, 1333–1343.
- (6) For the efficient application of P–OP ligands in Rh- and Ir-mediated asymmetric hydrogenations, see: (a) Donald, S. M. A.; Vidal-Ferran, A.; Maseras, F. *Can. J. Chem.* **2009**, 87, 1273–1279. (b) Fernández-Pérez, H.; Donald, S. M. A.; Munslow, I. J.; Benet-Buchholz, J.; Maseras, F.; Vidal-Ferran, A. *Chem.–Eur. J.* **2010**, 16, 6495–6508. (c) Núñez-Rico, J. L.; Fernández-Pérez, H.; Benet-Buchholz, J.; Vidal-Ferran, A. *Organometallics* **2010**, 29, 6627–6631. (d) Etayo, P.; Núñez-Rico, J. L.; Fernández-Pérez, H.; Vidal-Ferran, A. *Chem.–Eur. J.* **2011**, 17, 13978–13982. (e) Núñez-Rico, J. L.; Etayo, P.; Fernández-Pérez, H.; Vidal-Ferran, A. *Adv. Synth. Catal.* **2012**, 354, 3025–3035. (f) Núñez-Rico, J. L.; Vidal-Ferran, A. *Org. Lett.* **2013**, 15, 2066–2069. (g) Fernández-Pérez, H.; Benet-Buchholz, J.; Vidal-Ferran, A. *Org. Lett.* **2013**, 15, 3634–3637. (h) Núñez-Rico, J. L.; Fernández-Pérez, H.; Vidal-Ferran, A. *Green Chem.* **2014**, 16, 1153–1157. (i) Lao, J. R.; Benet-Buchholz, J.; Vidal-Ferran, A. *Organometallics* **2014**, 33, 2960–2963. (j) Fernández-Pérez, H.; Benet-Buchholz, J.; Vidal-Ferran, A. *Chem.–Eur. J.* **2014**, 20, 15375–15384. (k) Lao, J. R.; Fernández-Pérez, H.; Vidal-Ferran, A. *Org. Lett.* **2015**, 17, 4114–4117.
- (7) Ligand L1 was selected for the initial studies due to its high catalytic performance in Rh-mediated asymmetric hydrogenations; see ref 6b,e.
- (8) Determination of the enantiomeric excess of products 2 by chiral GC or HPLC analysis proved to be difficult. For this reason, products 2 were transformed into their benzoate esters 4 to facilitate the analysis (see the Supporting Information for details).
- (9) The P–OP ligands presented in Figure 1 can be categorized in two principal groups: (i) geminal ligands L2–L8 (phosphine and phosphite groups bound to the same carbon) incorporating a stereogenic axis and further stereogenic carbon or phosphorus centers (the Rh complexes derived from these ligands present strained asymmetric environments around the metal center; P–Rh–PO angle of ca. 80°; see ref 6g,i); (ii) vicinal ligands L1 and L9–L14 (phosphine and phosphite groups bound to vicinal carbons) containing two consecutive stereogenic C-atoms (these ligands also incorporate enantiopure BINOL- or TADDOL-derived phosphites).
- (10) See the Supporting Information for further details.
- (11) For selected examples on the efficient application of P–OP ligands bearing the TADDOL-derived phosphite in asymmetric catalysis, see: (a) Falk, A.; Fiebig, L.; Neudorfl, J.-M.; Adler, A.; Schmalz, H.-G. *Adv. Synth. Catal.* **2011**, 353, 3357–3362. (b) Naemi, Q.; Dindaroglu, M.; Kranz, D. P.; Velder, J.; Schmalz, H.-G. *Eur. J. Org. Chem.* **2012**, 2012, 1179–1185. (c) Dindaroglu, M.; Akyol, S.; Simsir, H.; Neudorfl, J.-M.; Burke, A.; Schmalz, H.-G. *Tetrahedron: Asymmetry* **2013**, 24, 657–662. (d) Falk, A.; Goederz, A.-L.; Schmalz, H.-G. *Angew. Chem., Int. Ed.* **2013**, 52, 1576–1580. (e) Falk, A.; Cavalieri, A.; Nichol, G. S.; Vogt, D.; Schmalz, H.-G. *Adv. Synth. Catal.* **2015**, 357, 3317–3320.
- (12) For the preparation of ligands L13 and L14, see: Balakrishna, B.; Bauzá, A.; Frontera, A.; Vidal-Ferran, A. *Chem.–Eur. J.* **2016**, DOI: 10.1002/chem.201601464. A practical method for the preparation of Rh-complexes derived from L13 suitable for this chemistry has recently been reported in: Balakrishna, B.; Vidal-Ferran, A. *Synthesis* **2016**, 48, 997–1001.
- (13) The *anti*-diastereoisomer was not detected by ¹H NMR analysis of the reaction crude.
- (14) For reviews regarding this topic, see: (a) Betancort, J. M.; García, C.; Walsh, P. J. *Synlett* **2004**, 5, 749–760. (b) Kanai, M. C–C Bond Formation (1,2-Alkenylation). In *Comprehensive Chirality*; Carreira, E. M., Yamamoto, H., Eds.; Elsevier Science: Oxford, 2012; Vol. 4, pp 343–354. (c) Madduri, A. V. R.; Harutyunyan, S. R.; Minnaard, A. J. *Drug Discovery Today: Technol.* **2013**, 10, e21–e27. (d) Rong, J.; Pellegrini, T.; Harutyunyan, S. R. *Chem.–Eur. J.* **2016**, 22, 3558–3570. For selected examples, see: (e) García, C.; LaRochelle, L. K.; Walsh, P. J. *J. Am. Chem. Soc.* **2002**, 124, 10970–10971. (f) Li, H.; Walsh, P. J. *J. Am. Chem. Soc.* **2005**, 127, 8355–8361. (g) Jeon, S.-J.; Li, H.; Garcia, C.; LaRochelle, L. K.; Walsh, P. J. *J. Org. Chem.* **2005**, 70, 448–455.