Bicyclo[3.2.0]heptane-Based Enamides by Ru/PNNP-Catalyzed Enantioselective Ficini Reactions: Scope and Application in Ligand Design

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Received 9 December 2011

Abstract: Double chloride abstraction from $[RuCl_2(PNNP)]$ [PNNP = (*S*,*S*)-*N*,*N*′-bis[*o*-(diphenylphosphino)benzylidene]cyclohexane-1,2-diamine] gives the elusive dicationic adduct $[Ru(OEt)_2(PNNP)]^{2+}$ which catalyzes the [2+2] cycloaddition of cyclic alkylidene β-keto esters with a variety of ynamides to produce bicyclo[3.2.0]heptane-based enamides with high yields and enantioselectivity. The structural features of these products are discussed and selected examples are converted into highly modular diene, phosphite-alkene, and diphosphite derivatives, which were tested as bidentate ligands with Rh(I), Ir(I), and Pd(II).

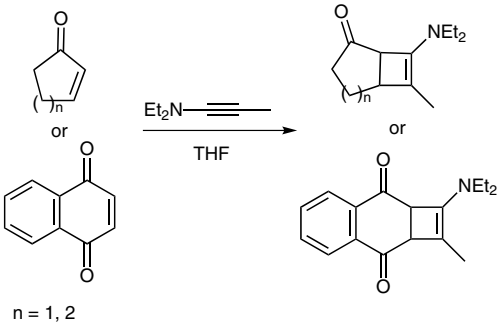
Key words: asymmetric catalysis, biaryls, cycloaddition, bicyclic compounds, ligands, phosphorus, ruthenium

Introduction

Heteroatom-substituted alkynes probably represent the most versatile subgroup within the vast field of alkyne chemistry. Ynamines, bearing a nitrogen-atom-substituted triple bond, have found broad application after their discovery more than 50 years ago and have witnessed a revival in the form of the less electron-rich ynamides in the last 20 years.[1] Ynamides still feature relatively strong polarization of the triple bond, but their electron density is reduced by the delocalization of the nitrogen lone pair onto the electron-withdrawing group. This renders ynamides more stable, usually even toward aqueous workup and chromatography on silica gel.

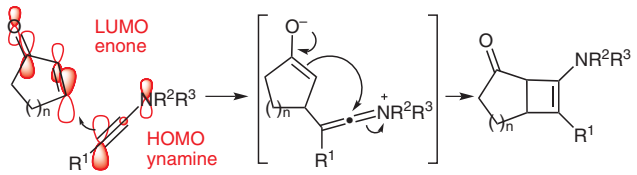
A second important factor for the recent popularity of ynamides is the relatively new discovery of their simple and inexpensive preparation by copper-catalyzed amidation of alkynyl bromides.[2a] Recently, the range of starting materials for ynamides has been extended to terminal alkynes,[2b] geminal dibromides,[2c] alkynyl carboxylic acids,[2d] and alkynyltrifluoroborates.[2e]

The polarization of ynamides provides predictable regioselectivity, which was exploited by Jacqueline Ficini and co-workers to perform their [2+2] cycloaddition on cyclic unsaturated ketones (enones) or quinones (Scheme 1).[3] The resulting highly strained bicyclic products are thermally stable, as the energy required for the conrotatory ring opening of the cyclobutene is not available under the reaction conditions.[4]



Scheme 1 Original version of the Ficini reaction

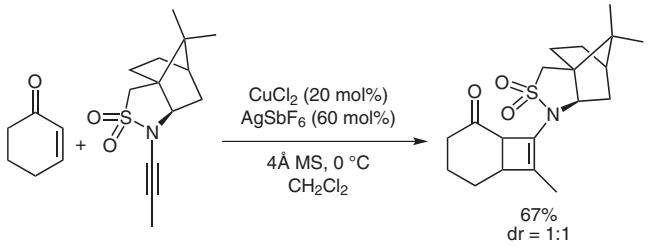
Although formally a [2+2] cycloaddition, the reaction between the ynamide and the enone is likely to occur stepwise via nucleophilic attack of the β-C-atom of the ynamine onto the electrophilic position of the enone (Scheme 2).[4,5] The resulting dipolar intermediate is likely to undergo rapid intramolecular ring closure by attack of the enolate onto the iminium ion. A rationale for this assumption is provided by the fact that the HOMO frontier molecular orbital of the ynamide should have no, or very little, electron density in the α-position to the nitrogen atom, and is thus not well suited for a concerted addition.[4,5]



Scheme 2 Proposed mechanism of the Ficini reaction

After 13 years of development, Hsung recently extended the Ficini [2+2] cycloaddition to *N*-sulfonyl ynamides, which were found to react with cyclohexenone in the presence of high catalyst loadings of $CuCl_2$ (20 mol%) and $AgSbF_6$ (60 mol%) to the corresponding cyclobutenamides in 21–77% yield.[6] The substitution pattern on the ynamide is relatively general, as various combinations of alkyl and sulfonyl substituents on the nitrogen moiety were shown to be reactive. However, only cyclohexenone was tested as the enone, and no diastereoselection was observed when a chiral sultam group was attached to the alkyne moiety of the ynamide (Scheme 3). This may be due to the fact that the chiral information is relatively remote from the reactive center.

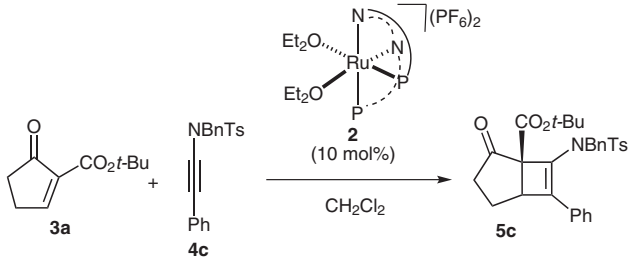
SYNTHESIS 2012, 44, 513–526
Advanced online publication: 30.01.2012
DOI: 10.1055/s-0031-1289679; Art ID: Z114111SS



Scheme 3 First Ficini reaction with *N*-sulfonyl ynamides

Enantioselective Ficini Reaction

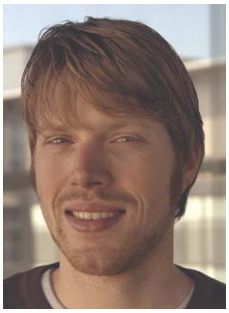
Ynamides are much less reactive than ynamines, which makes them more attractive for enantioselective cycloaddition reactions, as the noncatalyzed reaction can be easily suppressed. However, to the best of our knowledge, no enantioselective [2+2] cycloaddition of ynamides has been reported prior to our communication that describes the use of a chiral Ru/PNNP-derived Lewis acid as catalyst for Ficini reactions.[5] Complex $[RuCl_2(PNNP)]$ (**1**)[7] in dichloromethane was activated by double chloride abstraction with triethyloxonium hexafluorophosphate (2 equiv) to form the elusive dicationic complex $[Ru(OEt_2)(PNNP)](PF_6)_2$ (**2**), which efficiently catalyzes a number of asymmetric transformations of β-keto esters such as electrophilic fluorination,[8] hydroxylation,[9] and Michael addition,[10] as well as Diels–Alder reactions with their alkylidene analogues.[11]



Scheme 4 The first enantioselective Ficini reactions

In analogy to the protocol for the latter reaction class,[11] unsaturated β-keto ester **3a** and ynamide **4c** (1.1 equiv) were added to catalyst **2** (10 mol%), and the mixture was stirred at room temperature overnight (Scheme 4). As TLC analysis revealed that substrate **3a** had been only

Biographical Sketches



Christoph Schotes was born in Mönchengladbach (Germany) in 1982. He studied chemistry at the Technical University of Munich, where he obtained his Bachelor's degree in chemistry (with distinction) in 2006. He carried out his Master study and Ph.D. thesis at the ETH Zurich under the supervision of Prof. Antonio Mezzetti and received his Ph.D. in September 2011. His Ph.D. thesis has been nominated for the medal of the ETH Zurich.

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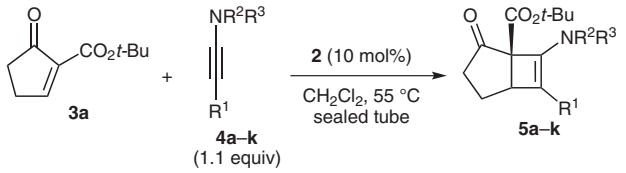
partially converted, the mixture was heated to 55 °C and stirred overnight once again, after which full conversion of **3a** was observed. The corresponding cycloaddition product **5c** was isolated by flash column chromatography on silica gel.

In the optimized reaction, the reaction mixture is heated to 55 °C directly after addition of ynamide **4c**. TLC analysis after 24 hours showed full conversion of the unsaturated β-keto ester **3a**, and the corresponding cyclobutenamide **5c** was isolated in 72% yield. The enantioselectivity was determined to be 90% ee by chiral HPLC analysis (Table 1, entry 3).

Table 1 Ficini Reaction Results[a]



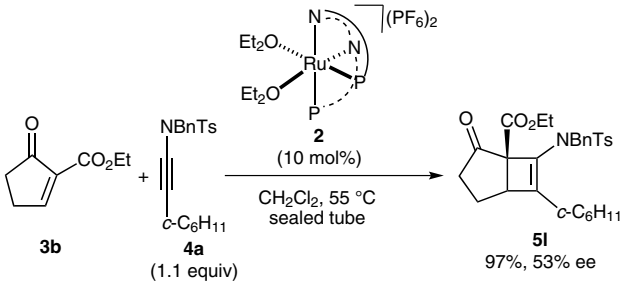
Entry	Product	R^1	R^2	R^3	Yield (%)	ee (%)
1	**5a**	*c*-C_6H_{11}	Bn	Ts	97[b]	90[b]
2	**5b**	*c*-C_6H_{11}	Me	Ts	88	92
3	**5c**	Ph	Bn	Ts	72	90
4[c]	**5c**	Ph	Bn	Ts	66	92
5	**5d**	Ph	Me	Ts	64	87
6	**5e**	Ph	Me	Ms	69	83
7	**5f**	Ph	Me	Mbs	75	61
8	**5f**	*n*-C_6H_{13}	Bn	Ts	99	78
9	**5h**	*n*-C_6H_{13}	Me	Ms	94	70
10	**5i**	*n*-C_6H_{13}	Me	Mbs	99	78
11	**5j**	CH_2OBn	Me	Mbs	60	70
12	**5k**	$(CH_2)_2OTBDMS$	Bn	Ts	86	76

[a] Reaction conditions: see experimental section; Mbs = 4-methoxyphenylsulfonyl.
[b] 75% yield, >99.5 ee after a single recrystallization (hexane).
[c] At r.t., 5 d.

To study the effect of the temperature on the yield and enantioselectivity, the reaction of **3a** with **4c** was run at room temperature for five days for comparison. The enantioselectivity slightly increased to 92%, but at the cost of a lower yield (66%) even after the prolonged reaction time of 5 days (entry 4), whereas the reaction at 55 °C gave 72% yield after 24 hours. Thus, a reaction temperature of 55 °C was used for all further reactions.[5] An advantage of this protocol is that nearly stoichiometric amounts of the ynamides **4** (1.1 equiv) are sufficient to obtain high yields, which is notable for a reaction that forms an all-carbon stereocenter at the bridgehead position of a highly strained unsaturated [3.2.0]bicycle. The results summarized in Table 1 show that the substituent at the β-position of the ynamide is pivotal for the outcome of the reaction. By and large, *n*-hexyl- and cyclohexyl-substituted ynamides give high yields (entries 1, 2, and 8–10). High enantioselectivity is achieved when R^1 is a phenyl or cyclohexyl group (entries 1–7). Thus, the donor character of the alkyl substituents is crucial for high chemical yields, whereas the steric bulk of the cyclic residues is necessary in order to obtain high enantioselectivity. Accordingly, the cyclohexyl-substituted ynamides **4a** and **4b** give the best combination of very high yields and enantioselectivities of up to 92% ee (entries 1 and 2). The crude Ficini product **5a** (90% ee) was obtained as a single enantiomer after recrystallization from hexane (entry 1).

When the sterically even more bulky *tert*-butyl analogue of ynamide **4a** was used, no reaction occurred. Considering the highly crowded situation in the bicyclic products **5**, this limit to the steric bulk tolerated by the system hardly surprises. On the other hand, the Ru/PNNP system is mild enough to tolerate functionalizable moieties (entries 11 and 12), which are intrinsically less stable than their alkyl and aryl analogues.

As compared to the *tert*-butyl ester analogue **3a** (Table 1), the smaller ethyl ester **3b** gives lower enantioselectivity (53% ee with ynamide **4a**, Scheme 5), which indicates that a bulky ester group is pivotal, as observed in the Diels–Alder reaction[11] and in the previously reported transformations with saturated β-keto esters.[8–10] This general trend is linked to the diastereoselectivity of substrate coordination, which is only high for the *tert*-butyl substrates and has been extensively investigated in a recent report.[11c]

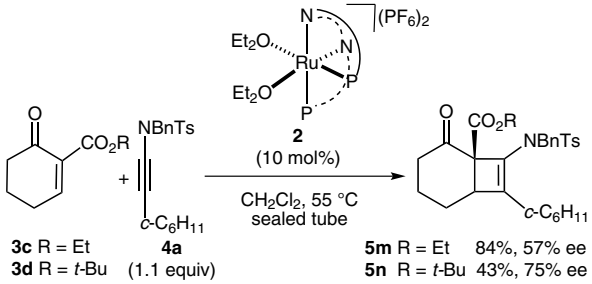


Scheme 5 Ficini reaction with the smaller ethyl derivative **3b**

Preliminary tests with a six-membered-ring substrate, such as ethyl 6-oxocyclohex-1-enecarboxylate (**3c**) (Scheme 6), suggested behavior similar to that of its cyclopentenone analogue **3b**. Thus, we expected an analogous optimization potential for the six-membered-ring *tert*-butyl ester substrate **3d** as for **3a**. However, TLC analysis of the reaction solution shows that **3d** decomposes to a large extent under the reaction conditions.

Due to the limited stability of the alkylidene β-keto esters, partial degradation of the substrate competes with the catalytic cycloaddition reaction, which was not observed for any other alkylidene β-keto esters. Thus, the reaction of *tert*-butyl ester **3d** with **4a** gives low yield and only slightly improved enantioselectivity as compared to the ethyl

analogue **3c** (Scheme 6). Therefore, the cyclohexenone substrates were not studied further.



Scheme 6 Ficini reaction with six-membered-ring derivatives **3c** and **3d**

Stereoselectivity and Structural Aspects

The proposed product structure was confirmed by an X-ray study on a single crystal of enantiomerically pure *tert*-butyl 7-[*N*-benzyl-4-methylphenylsulfonamido]-6-cyclohexyl-2-oxobicyclo[3.2.0]hept-6-ene-1-carboxylate (**5a**) (obtained by recrystallization from hexane) (Figure 1). The value of the Flack parameter indicates the 1*R*,5*S* absolute configuration.

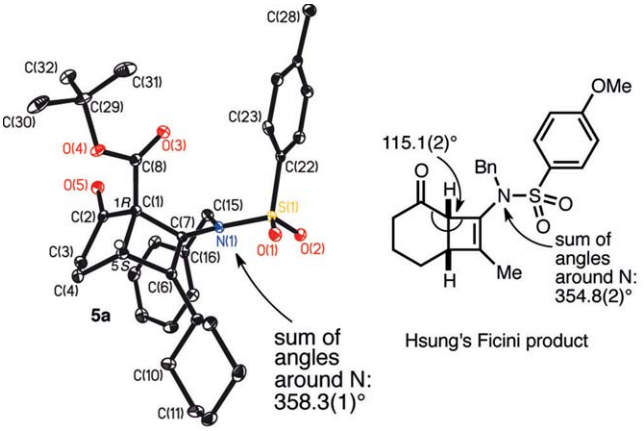
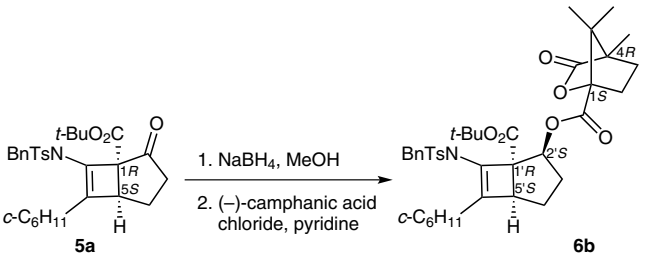


Figure 1 Structural comparison of compound **5a**[5] and Hsung's Ficini product[6]

A comparison to a similar compound reported by Hsung[6] shows that the bond lengths and angles of the cyclobutenamide motif are basically identical, although compound **5a** features a relatively bulky cyclohexyl group on the vinylic C-atom, whereas Hsung's compound only bears a methyl group in this position. This is a clear sign of the extraordinary rigidity of this highly strained bicyclic system. The presence of a quaternary stereocenter at C(1) leads to a significantly contracted C(2)–C(1)–C(7) angle [113.2(1)°] as compared to the corresponding angle in Hsung's Ficini product [115.1(2)°] and to the corresponding angle at the C(5) bridgehead position of **5a** [C(4)–C(5)–C(6): 118.9(1)°].

An interesting effect is observed at the nitrogen atoms in the two molecules. The sum of the angles around N(1) indicates that the geometry at nitrogen is less flattened in Hsung's compound [sum of angles = 354.8(2)°] than in **5a** [sum of angles = 358.3(1)°]. We attribute this fact to the electron-donating *p*-methoxy group in Hsung's compound, which reduces the electron-withdrawing effect of the sulfonyl group. This leads to less delocalization of the lone pair at the nitrogen atom into the sulfonyl group as compared to the corresponding tosyl-substituted compound **5a**.

The assignment of the absolute configuration of **5a** was independently verified by reduction of the ketone function with sodium borohydride, which attacks diastereoselectively from the *exo* face, and esterification of the resulting alcohol **6a** with (–)-camphanic acid chloride (Scheme 7).[5] An X-ray study of a crystal of the camphanic acid ester **6b**, obtained by slow evaporation of a diethyl ether solution confirmed the (1*R*,5*S*)-configuration of **5a** (Figure 2). Thus, the ynamide attacks from the unshielded *re* face of the metal-bound alkylidene β-keto ester, as proposed in our stereochemical model.[5,11c]



Scheme 7 Absolute configuration of Ficini product **5a**

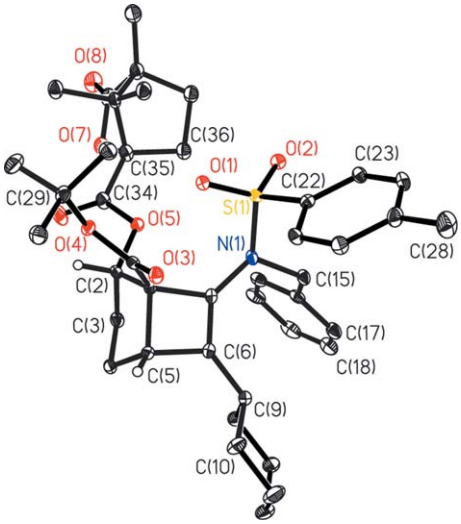


Figure 2 X-ray crystal structure of camphanic acid derivative **6b**[5]

Cyclobutenamides as Ligand Backbone

Toward Diene Ligands

As compound **5a** was obtained in enantiomerically pure form, we envisioned its application as stereogenic backbone for chelating ligands in asymmetric catalysis. In the course of this endeavor, we investigated the behavior of the strained and diversely functionalized bicyclo-[3.2.0]heptene skeleton in standard organic chemistry transformations.

A major advantage of using the Ficini products as a starting point for chiral ligands is the large number of different ligand classes accessible in only a few reaction steps relying on basic organic chemistry. Also, each ligand class would be highly modular as virtually any position of the bicyclo[3.2.0]heptene skeleton is modifiable either by the original Ficini cycloaddition or by simple organic transformations (Figure 3).

We started off by preparing bicyclo[3.2.0]hepta-2,6-diene skeletons where one of the C=C double bonds is part of the enamide moiety generated in the [2+2]-Ficini cycloaddition. Diene ligands are a relatively recent development,[12] but highly efficient systems have already been reported, first and foremost by Hayashi[13] and Carreira (Figure 4).[14]

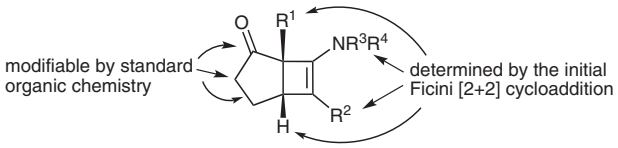


Figure 3 Modularity of Ficini products

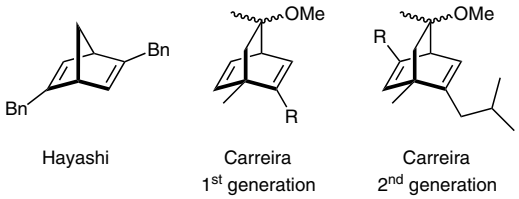
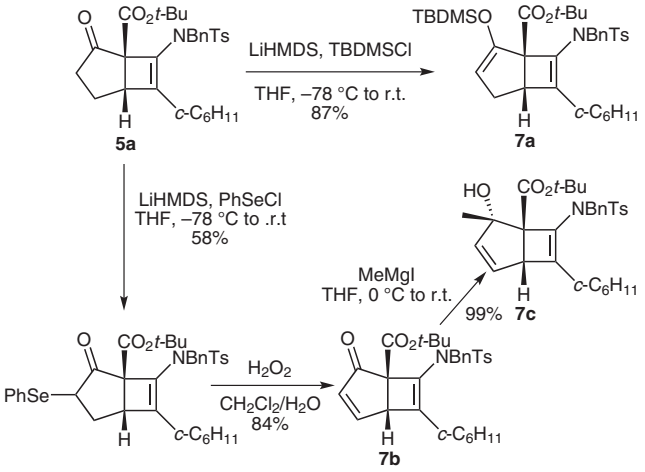


Figure 4 Important diene ligands in the literature

In the course of this project, several structurally different, potential diene ligands were prepared (Scheme 8). The deprotonation of **5a** in the α-position of the ketone with lithium hexamethyldisilazanide, followed by enolate trapping with *tert*-butyldimethylsilyl chloride, gave access to the silyl enol ether **7a** in good yield. The enol ether unit should render this diene rather electron rich. The enone **7b** was prepared because it has a low-lying π*-orbital and should thus be a good acceptor for back-donation from the transition metal.

Diene **7b** was obtained by phenylselanylation and selenoxide elimination with hydrogen peroxide as oxidant in



Scheme 8 Synthesis of diene compounds **7a–c**

49% yield over two steps. The yield increased to 72% by not purifying the phenylselanyl intermediate before the final oxidation/elimination reaction. The 1,2-addition of methylmagnesium iodide occurred stereoselectively onto the *exo* face of **7b** to give a single diastereomer of the allylic alcohol **7c** in excellent yield. The preference for *exo*-attack is probably enhanced by the bulky substituents on the sulfonamide that shield the *endo* face of **7b** or by a directing effect of the ester group.

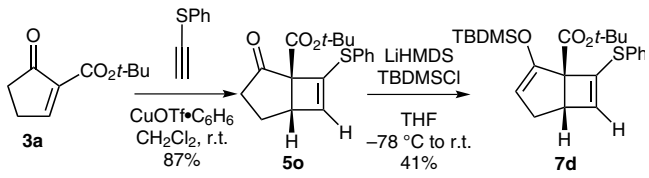
Unfortunately, it was not possible to protect the tertiary alcohol **7c** when using sodium hydride as a base and methyl iodide as an electrophile, a fact that may be accounted for by the steric congestion between the double bonds.[15] However, unprotected alcohol groups are generally not problematic in the coordination of dienes, as Rh(I) and Ir(I) are not particularly oxophilic. This argument is supported by the findings of Hayashi and Rawal.[16]

Preliminary attempts to prepare rhodium(I) complexes of dienes **7a–c** failed. The olefin proton signals in the ^{1}H NMR spectra of deuterochloroform solutions containing **7a–c** and $[Rh(\mu\text{-}Cl)(C_2H_4)_2]_2$ (0.5 equiv) or $[Rh(acac)(C_2H_4)_2]$ (1 equiv) remained unchanged over two hours (see supporting information, Table S2). Changing the solvent to coordinating solvents like tetrahydrofuran or acetonitrile did not accelerate ligand exchange at the transition metal. Likewise, the only reaction observed upon heating the reaction solution to 45 °C or 65 °C was the decomposition of the metal precursors. As iridium(I)–olefin complexes are generally more stable than their rhodium(I) analogues, we studied the reaction of $[Ir(\mu\text{-}Cl)(coe)_2]_2$ (coe = cyclooctene) with **7a** and **7c**. No coordination was observed, though, irrespective of whether coordinating (Et_2O, THF) or non-coordinating ($CDCl_3$) solvents were used.

There are several possible explanations for the reluctance of ligands **7a–c** to coordinate to d^8 transition metals, such as the pronounced distortion of the bicyclo[3.2.0]hepta-2,6-diene skeleton, which leads to nonparallel double bonds and might hinder efficient back donation from the transition metal into the π*-orbitals. Further possible ex-

planations are the high degree of delocalization and asymmetry of the enamide HOMO (unfavorable both for donation and back donation) or too sterically demanding substituents on the enamide moiety.

In order to exclude some of these possible reasons, the phenylthio derivative **7d** (Scheme 9) was prepared.[17] Compound **7d** should be structurally and electronically different from **7a**, as there is only one substituent on the double bond (decreased steric demand), and the sulfur atom should have a considerably reduced polarizing effect as compared to nitrogen. However, no coordination of **7d** to $[Rh(acac)(C_2H_4)_2]$ was observed after three days in $CDCl_3$ at room temperature. This result suggests that the main reason for the low affinity of the dienes **7a–d** toward Rh(I) and Ir(I) is not the bulkiness of the substituents or the electronic properties of the dienes. Rather, this points to the possibility that the bicyclo[3.2.0]hepta-2,6-diene skeleton is not suitable for chelation, probably due to the twisting of the double bonds or their spatial proximity, which leads to a too small bite angle. However, further investigations are needed in order to verify this hypothesis. Unfortunately, several attempts to crystallize dienes **7a–d** by layering a deuterochloroform solution of the respective compound with pentane or hexane were unsuccessful.



Scheme 9 Synthesis of vinylsulfane compound **7d**

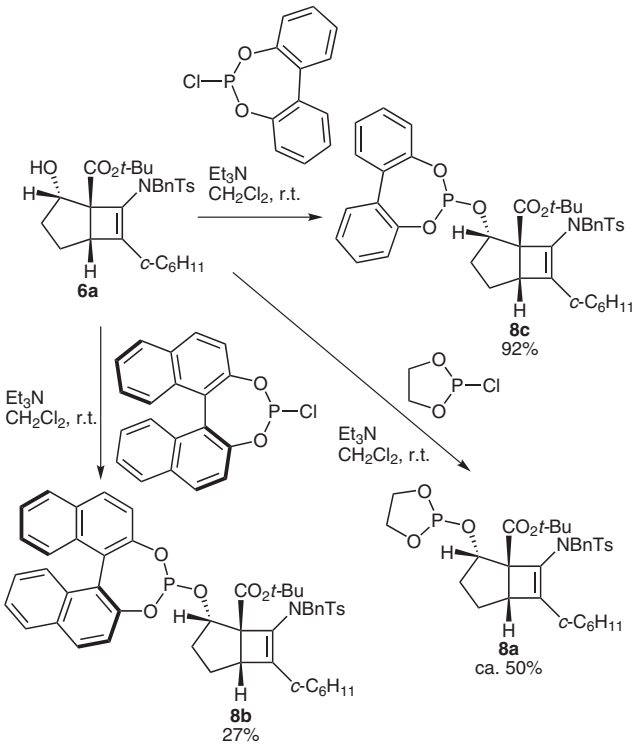
Toward Phosphite-Alkene Ligands

In light of the difficulties encountered in the coordination of diene ligands **7a–d**, we were eager to investigate whether the double bond of an enamide is generally suitable for coordination. Therefore, we envisioned the synthesis of phosphite-alkene complexes that ensure coordination to the transition metal through the phosphite moiety and possibly promote the coordination of the enamide double bond due to the chelate effect.

Since their tumultuous development in the early 1990s, chiral phosphite ligands have found broad application in catalytic reactions such as asymmetric hydrogenation, allylic substitution, and hydroformylation. Thus, the discovery of new binding patterns and chiral backbones for this ligand class is an area of intense research.[18] In addition to simple diphosphite ligands, $P(OR)_3$ donors have been incorporated into bidentate ligands.[19] Hybrid ligands featuring phosphine-,[20] phosphinite-,[21] and phosphoramidite-alkene[22] binding patterns have been reported less frequently. Finally, to the best of our knowledge, hybrid ligands based on a phosphite-alkene combination like **8a–c** are unprecedented. Therefore, we chose glycol-derived **8a** and 2,2′-biphenol-derived **8c** as representative examples of aliphatic and aromatic phosphites with low steric demand on phosphorus. For comparison, we prepared the sterically more demanding (*S*)-BINOL-derived phosphite **8b**. If this compound proved to be a promising ligand, the investigations of matched and mismatched situations would be possible by alternatively using (*R*)-BINOL in the derivatization.

The starting point for these ligands was compound **6a**, the 2-hydroxy derivative of **5a**, which is an intermediate in the synthesis of the camphanic acid derivative **6b** described in Scheme 7.[23] Compound **6a** was isolated in 94% yield from enantiomerically pure **5a**. Derivatization with the phosphorochloridites derived from glycol, 2,2′-biphenol, or (*S*)-BINOL gave the phosphite-alkene ligands **8a–c** (Scheme 10).

The coordination chemistry of the phosphite-alkene hybrid ligands **8a–c** was studied with Rh(I) ($[Rh(acac)(C_2H_4)_2]$, $[Rh(\mu\text{-}Cl)(C_2H_4)_2]_2$) and Ir(I) ($[Ir(\mu\text{-}Cl)(coe)_2]_2$) as metal precursors (see supporting information, Table S3). Ligand **8a** quickly decomposed to unidentified species, most probably hydrolysis products, in the presence of $[Rh(acac)(C_2H_4)_2]$ in deuterochloroform at room temperature, whereas **8b** and **8c** formed several complexes in solution under the same conditions.

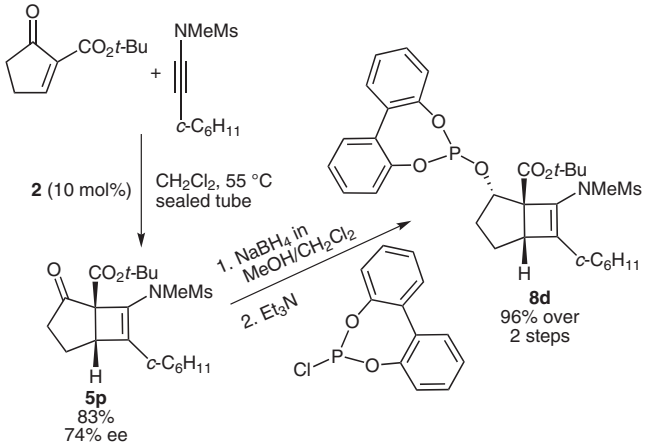


Scheme 10 Synthesis of phosphite-alkene compounds **8a–c**

With **8a–c**, it was not possible to determine unambiguously whether the species formed contain a bidentate ligand or rather two P-coordinated ligands with pendant C=C double bonds. However, ^{13}C NMR spectrum of the reaction solution containing **8c** and $[Ir(\mu\text{-}Cl)(coe)_2]_2$ (0.5 equiv) showed no significant shift of the ^{13}C resonances of the vinylic carbon atoms, which indicates that the alkene

unit does not coordinate. A further possibility that has to be considered when investigating compounds featuring a flexible biphenol (tropos) unit is that atropisomers are formed.[24] The energy barrier for the rotation around the biphenol bond in such complexes is highly dependent on the substitution pattern of the tropos unit, bulkier residues usually resulting in higher barriers.[25]

In order to investigate whether reducing the steric bulk at the enamide moiety would promote its coordination, we prepared the analogous ligand **8d**, which bears a methyl and a mesyl substituent at the nitrogen center (Scheme 11). These groups represent the smallest alkyl-donor/sulfonyl-acceptor combination conceivable. However, the ^{13}C NMR spectrum of the reaction solution of $[Rh(\mu\text{-}Cl)(C_2H_4)_2]_2$ and **8d** in deuterochloroform showed no significant shift of the vinylic carbon signals, and thus indicated that the double bond does not coordinate.



Scheme 11 Synthesis and structure of phosphite-alkene compound **8d**

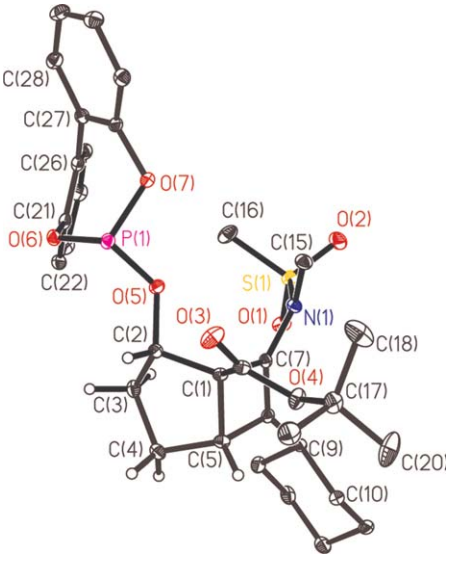
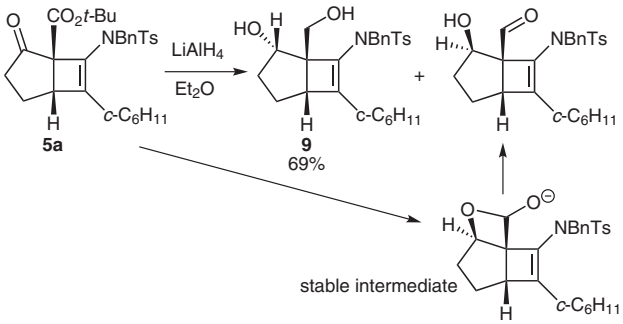


Figure 5 X-ray crystal structure of phosphite-alkene ligand *rac*-**8d**; the (1*R*,2*S*,5*S*)-enantiomer is shown

The crystal structure of **8d** is informative as to the lacking coordinating ability of these ligands (Figure 5).[26] The phosphite substituent on the cyclopentane ring adopts an equatorial position and points away from the enamide unit. Also, there is very little space for the transition metal in the *endo* face of **8d**, which is detrimental to bidentate coordination. However, the crystal structure shows that the phosphite lone pair of **8d** points in the direction of the ester group, which prompted us to investigate whether a chelate ring may be formed by the corresponding diphosphite ligands obtained by reduction of the ester group.

Diphosphite Ligands

The starting material for the synthesis of the cyclobutenamide diphosphite ligands was diol **9**, which was obtained in 69% yield by reduction of **5a** with excess lithium aluminum hydride in diethyl ether (Scheme 12). The *trans*-diol **9** is obtained together with substantial amounts of the corresponding *cis*-aldehyde, which can be separated by flash column chromatography. The reluctance of this compound toward further reduction may be explained by the formation of a stable hemiacetal intermediate, which only releases the corresponding aldehyde after aqueous workup.

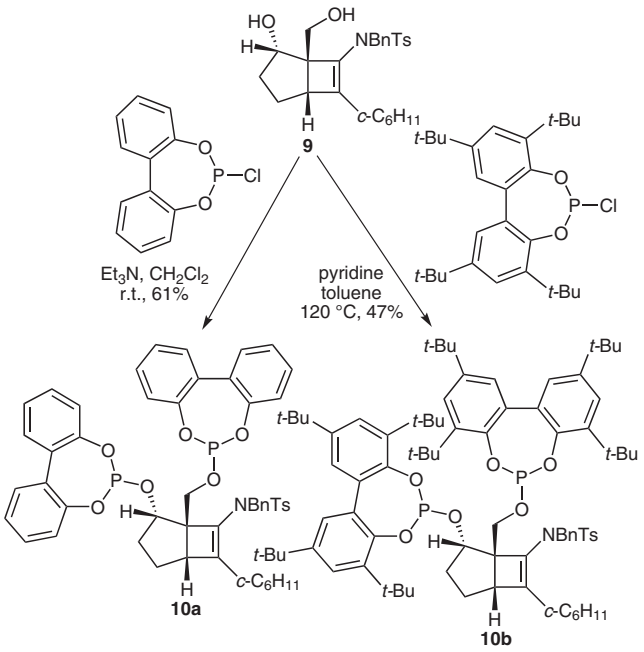


Scheme 12 Reduction of Ficini product **5a** to diol **9**

This conclusion is supported by the fact that a second reduction step (after aqueous workup, without chromatographic separation) with sodium borohydride gives 96% yield of the diol compounds, albeit in a 8:1 *trans*/*cis* ratio. Diphosphite ligands **10a** and **10b** were obtained by derivatization with the corresponding phosphorochloridites in 61% and 47% yield, respectively (Scheme 13).

The ^{31}P NMR spectra of both ligands show distinct signals for the two inequivalent phosphite groups.[27] The ^{31}P NMR spectrum of the reaction solution of ligand **10a** with $[Rh(nbd)_2]BF_4$ (1 equiv) in deuterochloroform indicates that the only product is a chelate complex (Figure 6).[28] We attribute the signal broadening to the interconversion of the two *tropos* P donors,[24] which show markedly different dynamic behaviors, in agreement with their different chemical environment.

Both ligands were tested in asymmetric rhodium-catalyzed hydrogenation and in palladium-catalyzed allylic alkylation reactions (Scheme 14), which have both been



Scheme 13 Synthesis of diphosphite compounds **10a** and **10b**

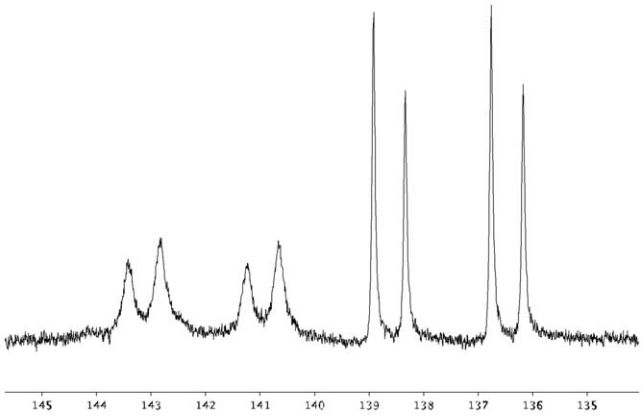
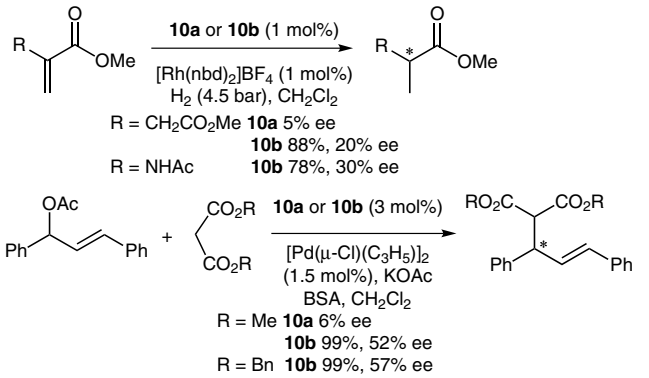


Figure 6 ^{31}P NMR spectrum of the reaction solution of **10a** with $[Rh(nbd)_2]BF_4$ in $CDCl_3$ (122 MHz, δ = 142.0 (dd, $^1J_{Rh,P}$ = 264 Hz, $^2J_{P,P}$ = 72 Hz, ω = 36 Hz), 137.6 (dd, $^1J_{Rh,P}$ = 263 Hz, $^2J_{P,P}$ = 71 Hz, ω = 9 Hz)

reported with diphosphite complexes.[18] In all reactions, the catalyst was prepared in situ.

Ligand **10a** gave essentially racemic products both in the hydrogenation of dimethyl itaconate and in the allylic alkylation reaction of (*E*)-1,3-diphenylallyl acetate with dimethyl malonate (Scheme 14). Therefore, the focus was shifted to ligand **10b**, which bears 3,3′,5,5′-tetra-*tert*-butylbiphenol substituents. The increase of steric bulk has been shown to considerably improve the enantioselectivity of allylic alkylation reactions with furanoside-derived ligands.[29] Indeed, the reaction with ligand **10b** increased the enantioselectivity of the hydrogenation of dimethyl itaconate from 5% to 20% ee, and that of the allylic alkylation of (*E*)-1,3-diphenylallyl acetate from 6% to 52% ee.



Scheme 14 Catalytic hydrogenation and allylic alkylation with diphosphite ligands **10a** and **10b**

The best results for each reaction class were obtained in the hydrogenation of methyl 2-acetamidoacrylate (30% ee) and the allylic alkylation of (*E*)-1,3-diphenylallyl acetate with dibenzyl malonate (57% ee). Though the enantioselectivity remains moderate at best, it is interesting to see the dramatic effect of increasing the steric bulk at the biphenol moiety, which possibly favors the formation of a single atropisomer of the complex (see above), and hence increases the enantioselectivity.

Conclusion and Outlook

In view of the difficulties encountered by Hsung in the non-enantioselective Ficini reaction, the high yields and enantioselectivity obtained with the Ru/PNNP complex **2** are remarkable. Moreover, the coordination of the unsaturated β-keto ester to the chiral, oxophilic Ru/PNNP fragment is a more efficient strategy for enantioselection than introducing a chiral auxiliary at the ynamide nitrogen atom,[6,30] which is remote from the triple bond. Like the earlier reported Diels–Alder reaction,[11] the Ficini reaction has a predictable stereochemistry due to the formation of well-defined catalyst–substrate adducts.[11c,31] Besides using ynamides, the reaction is a further, but still rare example of the use of an unsaturated β-keto ester as substrate for an enantioselective cycloaddition reaction.[5,11]

The dienes and phosphite-alkenes prepared in the course of the exploration of the chemistry of the bicyclic products turned out to be unsuitable as ligands for Rh(I) and Ir(I), as no coordination of the enamide double bond was observed by NMR spectroscopy with these metals. A possibility to eventually achieve coordination of the double bond might include the use of nosyl as a protecting group on the nitrogen to replace the very stable tosyl group. Since the nosyl group is easily cleavable, deprotection would give an enamine, which should be a better ligand than an enamide. We deem that the coordination of such ligands containing an electron-rich enamine might be possible. Also, the expansion of the five-membered ring might enable coordination by changing the relative orientation of the double bonds to each other (Figure 7, **A**).

The diphosphite ligands show some potential in asymmetric catalysis, as ligand **10b** achieved 57% ee in the asymmetric allylic alkylation of (*E*)-1,3-diphenylallyl acetate. Thus, further studies aimed at the optimization of the ligand may prove fruitful. First and foremost, the rigidity of the ligand backbone should be increased. Diol **B** might be prepared by selective oxidation of the primary alcohol group in **9** (Scheme 12) and stereoselective Grignard addition, whereas the diphenyl-substituted compound **C** should easily be accessible by reacting the β-hydroxy ester **6a** with an excess of phenylmagnesium iodide. Both modifications should restrict the possible conformations as opposed to the primary alcohol group in **9**.

A further possible target molecule is the diphosphine ligand **D**, which would probably form considerably more rigid structures after coordination to transition metals, due to the decreased ring size resulting from the elimination of the oxygen spacers from the ligand. This compound may be accessible by bistriflation of **9** with triflic acid anhydride, followed by double S_N2 substitution of the triflate moieties with diphenylphosphine.

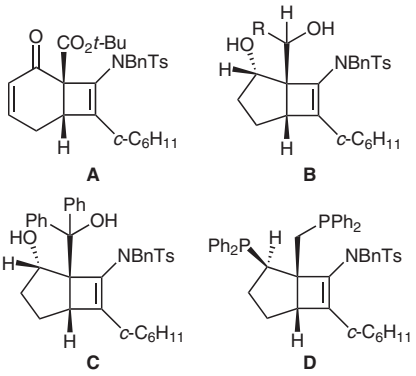


Figure 7 Potential developments of the ligand system

In summary, as shown by the application as a ligand backbone for late-transition-metal chemistry, the Ficini products **5** may prove to be interesting synthons in view of their high degree of modularity and functionalization possibilities.

Unless otherwise stated, all reactions were performed under an argon atmosphere using Schlenk techniques. Et_3N and pyridine were dried with CaH_2 and distilled under an argon atmosphere. PCl_3 was distilled under argon and used directly. All solvents were of puriss. p.a. quality and were distilled under argon atmosphere with standard drying agents (CH_2Cl_2, MeCN, MeOH, toluene: CaH_2; Et_2O, THF, toluene: Na/benzophenone; pentane: Na/benzophenone/diglyme; hexane: Na/benzophenone/tetraglyme). All solvents were freshly distilled prior to use. NMR spectra were measured on the following instruments (frequencies in MHz): Bruker Avance DPX 250 (^{1}H, 250.1; ^{13}C{^{1}H}, 62.5; ^{31}P{^{1}H}, 101.3), DPX 300 (^{1}H, 300.1; ^{13}C{^{1}H}, 75.5; ^{31}P{^{1}H}, 121.5), DPX 400 (^{1}H, 400.1; ^{13}C{^{1}H}, 100.6; ^{31}P{^{1}H}, 162.0), and DPX 700 (^{1}H, 700.1; ^{13}C{^{1}H}, 176.0; ^{31}P{^{1}H}, 283.5). The internal standard is the residual ^{1}H peak of the deuterated solvent used (^{1}H NMR: $CDCl_3$ δ = 7.26; ^{13}C NMR: $CDCl_3$ δ = 77.16). TLC was performed on Merck Silica Gel 60 F254 TLC plates; UV-light (366 or 254 nm), $KMnO_4$, or anisaldehyde was used for detection. Mass spectra were measured by the MS service of the Laboratorium für Organische Chemie (ETH Zurich). Enantiomeric excesses were determined by HPLC using Agilent HPLC 1100 Series system or by chiral gas chromatography. Complex [$RuCl_2$(PNNP)] (**1**) [PNNP = (*S*,*S*)-*N*,*N*′-bis[*o*-(diphenylphosphino)benzylidene]cyclohexane-1,2-diamine],[7] alkylidene β-keto esters **3**,[32] ynamides **4**,[2a] Ficini products **5a**–**n**,[5] and compounds **6a**,**b**[5] that were used to determine the absolute configuration of **5a**, were prepared by published procedures.

***N*-(Cyclohexylethynyl)-*N*-methylmethanesulfonamide**

Prepared according to a literature procedure.[2a] *N*-Methylmethanesulfonamide[33] (390.0 mg, 3.6 mmol, 1 equiv) was added as an emulsion in toluene (7.2 mL) to (bromoethynyl)cyclohexane (735.3 mg, 3.9 mmol, 1.1 equiv). K_2CO_3 (987.7 mg, 7.1 mmol, 2 equiv), $CuSO_4 \cdot 5\ H_2O$ (89.2 mg, 357.3 μmol, 0.1 equiv), and 1,10-phenanthroline (128.8 mg, 714.6 μmol, 0.200 equiv) were added and the soln was heated to 65 °C overnight. After the addition of $CHCl_3$, the soln was filtered and concentrated. The crude oil was purified by flash column chromatography (silica gel, hexane–EtOAc, 10:1); yield: 617.0 mg (2.9 mmol, 80%).

^{1}H NMR (400 MHz, 300 K, $CDCl_3$): δ = 3.03 (s, 3 H, SO_2CH_3), 2.92 (s, 3 H, NCH_3), 2.44–2.32 (m, 1 H, C≡CCH), 1.76–1.62 (m, 2 H), 1.62–1.52 (m, 2 H), 1.45–1.27 (m, 3 H), 1.27–1.19 (m, 3 H).

^{13}C NMR (101 MHz, 300 K, $CDCl_3$): δ = 74.6 (NC≡*C*), 72.6 (N*C*≡C), 39.1 (SO_2CH_3), 35.3 (NCH_3), 32.6, 28.4, 25.6, 24.5.

***tert*-Butyl 2-Oxo-7-(phenylthio)bicyclo[3.2.0]hept-6-ene-1-carboxylate (5o)**

Compound **5o** was prepared according to a literature procedure.[5] *tert*-Butyl 5-oxocyclopent-1-enecarboxylate (**3a**, 100.0 mg, 549 μmol, 1 equiv) in CH_2Cl_2 (5.5 mL) and CuOTf·0.5 C_6H_6 (1.3 mg, 5.5 μmol, 0.01 equiv) were added to ethynyl(phenyl)sulfane[34] (103.1 mg, 768 μmol, 1.4 equiv). The solvent was evaporated after stirring for 10 h at r.t. and the crude product was purified by flash column chromatography (silica gel, hexane–EtOAc, 10:1), to obtain **5o** as a colorless oil; yield: 151.5 mg (479 μmol, 87%).

^{1}H NMR (400 MHz, 300 K, $CDCl_3$): δ = 7.51–7.46 (m, 2 H, $SCCH_{arom}$), 7.39–7.28 (m, 3 H, H_{arom}), 5.79 (s, 1 H, H_{olef}), 3.60 (d, *J* = 6.9 Hz, 1 H), 2.96 (ddd, *J* = 18.2, 12.0, 9.1 Hz, 1 H), 2.33 (dd, *J* = 18.2, 8.3 Hz, 1 H), 2.14–2.00 (m, 1 H), 1.94 (dd, *J* = 13.4, 9.1 Hz, 1 H), 1.47 [s, 9 H, $OC(CH_3)_3$].

Enantioselective Ficini Reaction; General Procedure

[$RuCl_2$(PNNP)] (**1**) (10 mg, 0.012 mmol, 0.1 equiv) and $(Et_3O)PF_6$ (6 mg, 0.024 mmol, 0.20 equiv) were stirred in CH_2Cl_2 (1 mL) in a Young Schlenk tube at r.t. overnight. A color change from red to brown indicated the formation of the catalytically active complex. The respective unsaturated β-keto ester **3a–d** (0.12 mmol, 21.9 mg, 1 equiv) was added as a solution in CH_2Cl_2 (1 mL). After 10 min, the ynamide **4a–k** (0.13 mmol, 1.1 equiv) was added. The Young Schlenk was closed and the mixture was heated to 55 °C. After 24 h, the solvent was evaporated under reduced pressure, and the oily residue was subject to flash chromatography on silica gel. See the literature[5] for compound characterization data.

***tert*-Butyl 6-Cyclohexyl-7-(*N*-methylmethylsulfonamido)-2-oxobicyclo[3.2.0]hept-6-ene-1-carboxylate (5p)**

Compound **5p** was prepared according to the general procedure on a 1.14 mmol scale of **3a**. Yield: 379 mg, 953.4 μmol (83%); 74% ee [HPLC (Chiralcel AD-H hexane–*i*-PrOH, 80:20, flow rate 0.5 mL/min, λ = 230.4 nm): t_R = 9.4 (minor), 10.7 min (major)].

^{1}H NMR (400 MHz , 300 K, $CDCl_3$): δ = 3.31–3.27 (m, 1 H, CO-C*H*H), 3.07 (s, 3 H, SO_2CH_3), 3.05–2.97 (m, 1 H, COCH*H*), 2.93 (s, 3 H, NCH_3), 2.42–2.32 (m, 1 H), 2.28–2.20 (m, 1 H), 2.03–1.95

(m, 2 H), 1.94–1.82 (m, 2 H), 1.77–1.69 (m, 2 H), 1.68–1.61 (m, 1 H), 1.43 [s, 9 H, $OC(CH_3)_3$], 1.40–1.10 (m, 5 H).

^{13}C NMR (101 MHz, 300 K, $CDCl_3$): δ = 210.8 (C=O), 167.8 (CO_2t-Bu), 155.5 (NC=*C*), 129.6 (N*C*=C), 82.1 [O*C*$(CH_3)_3$], 67.3 (CCO_2t-Bu), 45.4 (SO_2CH_3), 38.9, 37.5, 36.9, 35.1, 29.9, 28.1 [OC(*C*$H_3)_3$], 26.0, 25.9, 21.3.

HRMS (ESI): *m*/*z* [*rac*-M + NH_4]$^+$ calcd for $C_{20}H_{35}N_2O_5S$: 415.2261; found: 415.2244.

tert-Butyl (1*R*,2*S*,5*S*)-7-(*N*-Benzyl-4-methylphenylsulfonamido)-6-cyclohexyl-2-hydroxybicyclo[3.2.0]hept-6-ene-1-carboxylate (6a)

Compound **5a** (60.0 mg, 109 μmol, 1 equiv) in CH_2Cl_2 (0.4 mL) was added to a stirred soln of $NaBH_4$ (5.8 mg, 153 μmol, 1.4 equiv) in MeOH (0.6 mL) at 0 °C. After 30 min, the reaction was quenched by addition of H_2O, brine, and CH_2Cl_2. The soln was extracted with CH_2Cl_2 (3 ×). The combined organic phases were washed with sat. $NaHCO_3$, H_2O, and brine. Each of the aqueous solns was extracted once with CH_2Cl_2. The combined organic phases were dried ($MgSO_4$), filtered, and concentrated. The crude oil was purified by flash column chromatography (silica gel, hexane–EtOAc, 10:1) to give a clear oil; yield: 56.5 mg (102 μmol, 94%).

^1H NMR (400 MHz, 300 K, $CDCl_3$): δ = 7.84 (d, *J* = 8.2 Hz, 2 H, SO_2CCH), 7.35 (d, *J* = 8.2 Hz, 2 H, SO_2CCHCH), 7.30–7.18 (m, 5 H, H_{arom}), 4.57 (d, *J* = 15.7 Hz, 1 H, PhC*H*HN), 4.52 (d, *J* = 15.7 Hz, 1 H, PhCH*H*N), 4.41–4.31 (m, 1 H, C*H*OH), 3.37 (d, *J* = 8.1 Hz, 1 H, bridgehead), 2.80 (d, *J* = 6.4 Hz, 1 H, CHO*H*), 2.41 (s, 3 H, $ArCH_3$), 2.01–1.82 [m, 2 H, CH(OH)CH_2], 1.61–1.46 (m, 6 H), 1.43 [s, 9 H, $OC(CH_3)_3$], 1.24 (d, *J* = 11.4 Hz, 1 H), 1.14 (d, *J* = 11.4 Hz, 1 H), 1.07–0.77 (m, 5 H).

^{13}C NMR (101 MHz, 300 K, $CDCl_3$): δ = 172.7 (CO_2t-Bu), 153.3 (NC=*C*), 143.9 (N*C*=C), 136.9 (2 C), 129.7, 128.7, 128.3, 128.1, 127.6, 125.1, 81.0 [O*C*$(CH_3)_3$], 73.7 (CHOH), 64.8 (CCO_2t-Bu), 52.6 (Ph*C*H_2N), 46.7 [CH(OH)*C*H_2], 37.8, 30.6, 30.3, 28.1 [OC$(CH_3)_3$], 25.9, 25.8, 22.8, 21.6.

N-Benzyl-*N*-[(1*S*,4*S*,5*S*)-7-cyclohexyl-4-hydroxy-5-(hydroxymethyl)bicyclo[3.2.0]hept-6-en-6-yl]-4-methylbenzenesulfonamide (9)

Compound **5a** (240.0 mg, 437 μmol, 1 equiv) in Et_2O (20 mL) was added to a soln of $LiAlH_4$ (99.4 mg, 2.6 mmol, 6 equiv) in Et_2O (20 mL) at 0 °C. The cooling bath was removed after 30 min and the mixture was stirred for 2 h at r.t. The reaction was quenched by the addition of H_2O (4 mL), 10% KOH (4 mL), and H_2O (8 mL) and filtered through a pad of Celite with EtOAc. The solvent was evaporated and the crude product was purified by flash column chromatography (silica gel, hexane–EtOAc, 3:2) yielding a white solid. A single diastereomer was observed by NMR. A mixture of aldehydes was isolated as a separate fraction by flash column chromatography; yield: 145.0 mg (301 μmol, 69%).

^1H NMR (400 MHz, 300 K, $CDCl_3$): δ = 7.81 (d, *J* = 7.8 Hz, 2 H, SO_2CCH), 7.37–7.22 (m, 7 H, H_{arom}), 4.75 (d, *J* = 14.9 Hz, 1 H, PhC*H*HN), 4.63 (d, *J* = 14.9 Hz, 1 H, PhCH*H*N), 3.84–3.74 (m, 1 H, C*H*OH), 3.73–3.63 (m, 2 H, CH_2OH), 3.16 (br s, 1 H, OH), 2.79 (br s, 1 H, OH), 2.43 (s, 3 H, $ArCH_3$), 2.40 (d, *J* = 7.2 Hz, 1 H, bridgehead), 1.90–1.80 (m, 2 H, CHOHCH_2), 1.58–1.38 (m, 5 H), 1.34–1.22 (m, 2 H), 1.07–0.67 (m, 6 H).

^{13}C NMR (101 MHz, 300 K, $CDCl_3$): δ = 156.5 (NC=*C*), 144.0 (N*C*=C), 137.2, 136.9, 129.8, 129.0, 128.5, 128.0, 128.0, 127.8, 75.1 (CHOH), 66.2 (CH_2OH), 62.5 (*C*CH_2OH), 53.4 (Ph*C*H_2N), 42.0 [CH(OH)*C*H_2], 38.0, 30.8, 30.4, 26.1, 23.9, 22.3, 21.7.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{28}H_{36}NO_4S$: 417.2418; found: 417.2415.

Diene Ligands

tert-Butyl (1*R*,5*S*)-7-(*N*-Benzyl-4-methylphenylsulfonamido)-2-[(*tert*-butyldimethylsilyl)oxy]-6-cyclohexylbicyclo[3.2.0]hepta-2,6-diene-1-carboxylate (7a)

A 1.6 M BuLi in hexane soln (109 μL, 175 μmol, 1.6 equiv) was added to a stirred soln of HMDS (41 μL, 197 μmol, 1.8 equiv) in THF (3 mL) at 0 °C. After 30 min, the soln was cooled to –78 °C and **5a** (60.0 mg, 109.2 μmol, 1 equiv) was added. After 40 min, TBDMSCl (24.7 mg, 164 μmol, 1.5 equiv) was added in THF (4 mL). After 30 min, the cooling bath was removed and the soln was stirred for 30 min at r.t. The reaction was quenched by the addition of Et_2O and sat. NH_4Cl. The soln was extracted with Et_2O (3 ×). The combined organic phases were dried ($MgSO_4$), filtered, and concentrated. The crude product was purified by flash column chromatography (silica gel, hexane–EtOAc, 5:1); yield: 63.0 mg (94.9 μmol, 87%).

^1H NMR (400 MHz, 300 K, $CDCl_3$): δ = 7.70 (d, *J* = 8.4 Hz, 2 H, SO_2CCH), 7.31 (d, *J* = 8.4 Hz, 2 H, SO_2CCHCH), 7.25–7.15 (m, 5 H, H_{arom}), 4.65 (s, 2 H, $PhCH_2N$), 4.53 (s, 1 H, H_{olef}), 3.01 (d, *J* = 8.4 Hz, 1 H), 2.45–2.39 (m, 1 H), 2.38 (s, 3 H, $ArCH_3$), 2.19–2.08 (m, 2 H), 1.65 (d, *J* = 10.2 Hz, 2 H), 1.60–1.50 (m, 2 H), 1.32 [s, 9 H, $OC(CH_3)_3$], 1.28–0.92 (m, 6 H), 0.85 [s, 9 H, $SiC(CH_3)_3$], 0.19 (s, 3 H, $SiCH_3$), 0.11 (s, 3 H, $SiCH_3$).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{38}H_{53}NNaO_5SSi$: 686.3311; found: 686.3306.

tert-Butyl (1*R*,5*S*)-7-(*N*-Benzyl-4-methylphenylsulfonamido)-6-cyclohexyl-2-oxobicyclo[3.2.0]hepta-3,6-diene-1-carboxylate (7b)

A 1.6 M BuLi in hexane soln (239 μL, 382 μmol, 1.4 equiv) was added to a stirred soln of HMDS (85 μL, 409 μmol, 1.5 equiv) in THF (2.4 mL) at 0 °C. After 30 min, the soln was cooled to –78 °C and **5a** (150.0 mg, 272.9 μmol, 1 equiv) was added in THF (0.65 mL). After 30 min, PhSeCl (78.4 mg, 409 μmol, 1.5 equiv) was added. After 1 h, the cooling bath was removed and the soln was stirred for 30 min at r.t. The reaction was quenched by the addition of Et_2O and sat. NH_4Cl. The soln was extracted with Et_2O (3 ×). The combined organic phases were dried ($MgSO_4$), filtered, and concentrated. The crude oil was purified by flash column chromatography (silica gel, hexane–EtOAc, 10:1) to give *tert*-butyl (1*R*,5*S*)-7-(*N*-benzyl-4-methylphenylsulfonamido)-6-cyclohexyl-2-oxo-3-(phenylselanyl)bicyclo[3.2.0]hept-6-ene-1-carboxylate as an off-white solid that decomposes at –20 °C under air within days; yield: 111.6 mg (158.3 μmol, 58%).

^1H NMR (250 MHz, 300 K, $CDCl_3$): δ = 7.81 (d, *J* = 8.1 Hz, 2 H, SO_2CCH), 7.52–7.44 (m, 2 H, $SeCCH_{arom}$), 7.38–7.14 (m, 10 H, H_{arom}), 4.59 (d, *J* = 15.0 Hz, 1 H, PhC*H*HN), 4.44 (d, *J* = 15.0 Hz, 1 H, PhCH*H*N), 4.31 (dd, *J* = 12.8, 8.3 Hz, 1 H, COCH), 3.17 (d, *J* = 7.1 Hz, 1 H, bridgehead), 2.43 (s, 3 H, $ArCH_3$), 2.34–2.23 (m, 1 H), 2.05–1.88 (m, 2 H), 1.67–1.57 (m, 2 H), 1.40 [s, 9 H, $OC(CH_3)_3$], 1.30–0.77 (m, 8 H).

A 30% aq H_2O_2 soln (146 μL, 1.4 mmol, 10 equiv) was added to a soln of the selenide compound (100.0 mg, 141.9 μmol, 1 equiv) in CH_2Cl_2 (1 mL) and stirred for 3 h. The soln was extracted with CH_2Cl_2 (3 ×) The combined organic phases were dried ($MgSO_4$), filtered, and concentrated. The crude product was purified by flash column chromatography (silica gel, hexane–EtOAc, 10:1) to give a white solid; yield: 65.0 mg (119 μmol, 84%). A total yield of 72% was obtained when *tert*-butyl (1*R*,5*S*)-7-(*N*-benzyl-4-methylphenylsulfonamido)-6-cyclohexyl-2-oxo-3-(phenylselanyl)bicyclo[3.2.0]hepta-6-ene-1carboxylate was used directly and not purified by flash column chromatography.

^1H NMR (400 MHz, 300 K, $CDCl_3$): δ = 7.81 (d, *J* = 8.3 Hz, 2 H, SO_2CCH), 7.49 (dd, *J* = 5.8, 2.6 Hz, 1 H, COCHC*H*), 7.31–7.17 (m, 7 H, H_{arom}), 5.89 (d, *J* = 5.8 Hz, 1 H, COCH), 4.70 (d, *J* = 15.7 Hz,

1 H, PhC*H*HN), 4.62 (d, *J* = 15.7 Hz, 1 H, PhCH*H*N), 3.73 (d, *J* = 2.6 Hz, 1 H, bridgehead), 2.43 (s, 3 H, $ArCH_3$), 2.30–2.20 (m, 1 H, H_{allyl}), 1.71–1.60 (m, 3 H), 1.54–1.45 (m, 1 H), 1.39 (s, 9 H, $OC(CH_3)_3$], 1.34–0.98 (m, 5 H), 0.92–0.78 (m, 1 H).

tert-Butyl (1*R*,2*S*,5*S*)-7-(*N*-Benzyl-4-methylphenylsulfonamido)-6-cyclohexyl-2-hydroxy-2-methylbicyclo[3.2.0]hepta-3,6-diene-1-carboxylate (7c)

A 3 M MeMgI in Et_2O soln (33 μL, 98 μmol, 1.05 equiv) was added to a stirred soln of **7b** (51.1 mg, 93 μmol, 1 equiv) in THF (2 mL) at 0 °C. After 15 min, the cooling bath was removed and the mixture was stirred for 1 h at r.t. The reaction was quenched by the addition of H_2O and brine. The soln was extracted with Et_2O (4 ×). The combined organic phases were dried ($MgSO_4$), filtered, and concentrated. The crude oil was purified by flash column chromatography (silica gel, hexane–EtOAc, 15:1) to give a white solid; yield: 52.5 mg (93.1 μmol, >99%).

^{1}H NMR (400 MHz, 300 K, $CDCl_3$): δ = 8.11 (d, *J* = 8.0 Hz, 2 H, SO_2CCH), 7.39–7.23 (m, 7 H, H_{arom}), 5.79 [dd, *J* = 5.7, 2.4 Hz, 1 H, CMe(OH)CHC*H*], 5.46 [d, *J* = 5.7 Hz, 1 H, CMe(OH)C*H*CH], 4.35 (d, *J* = 14.9 Hz, 1 H, PhC*H*HN), 4.27 (d, *J* = 14.9 Hz, 1 H, PhCH*H*N), 3.53 (d, *J* = 2.4 Hz, 1 H, bridgehead), 2.43 (s, 3 H, $ArCH_3$), 1.72–1.60 (m, 1 H), 1.58 [s, 9 H, $OC(CH_3)_3$], 1.56–1.50 (m, 2 H), 1.26 [s, 3 H, $C(CH_3)OH$], 1.15–0.70 (m, 7 H), 0.61–0.51 (m, 1 H).

tert-Butyl 2-[(*tert*-Butyldimethylsilyl)oxy]-7-(phenylthio)bicyclo[3.2.0]hepta-2,6-diene-1-carboxylate (7d)

A 1.6 M BuLi in hexane soln (168 μL, 269 μmol, 1.7 equiv) was added to a stirred soln of HMDS (63 μL, 300 μmol, 1.9 equiv) in THF (3 mL) at 0 °C. After 30 min, the soln was cooled to –78 °C and **5o** (50.0 mg, 158.0 μmol, 1 equiv) was added. After 45 min, TBDMSCl (35.7 mg, 237 μmol, 1.5 equiv) was added. After 45 min, the cooling bath was removed and the soln was stirred for 1.5 h at r.t. The reaction was quenched by the addition of Et_2O and sat. NH_4Cl. The soln was extracted with Et_2O (3 ×). The combined organic phases were dried ($MgSO_4$), filtered, and concentrated. The crude oil was purified by flash column chromatography (silica gel, hexane–EtOAc, 15:1); yield: 28.2 mg (65.5 μmol, 41%).

^{1}H NMR (400 MHz, 300 K, $CDCl_3$): δ = 7.54 (d, *J* = 7.5 Hz, 2 H, $SCCH_{arom}$), 7.40–7.23 (m, 3 H, H_{arom}), 5.71 (s, 1 H, H_{olef}), 4.58 (s, 1 H, H_{olef}), 3.31 (d, *J* = 9.2 Hz, 1 H, bridgehead), 2.52 (dd, *J* = 15.9, 9.2 Hz, 1 H, H_{allyl}), 2.07 (d, *J* = 15.9 Hz, 1 H, H_{allyl}), 1.50 [s, 9 H, $OC(CH_3)_3$], 0.96 [s, 9 H, $SiC(CH_3)_3$], 0.25 (s, 3 H, $SiCH_3$), 0.22 (s, 3 H, $SiCH_3$).

Monophosphite Ligands

tert-Butyl (1*R*,2*S*,5*S*)-7-(*N*-Benzyl-4-methylphenylsulfonamido)-6-cyclohexyl-2-[(1,3,2-dioxaphospholan-2-yl)oxy]bicyclo[3.2.0]hept-6-ene-1-carboxylate (8a)

Et_3N (23 μL, 163 μmol, 3 equiv) and 79.1 mM 2-chloro-1,3,2-dioxaphospholane in CH_2Cl_2 (1.0 mL, 82 μmol, 1.5 equiv) were added to a stirred soln of **6a** (30.0 mg, 54.4 μmol, 1 equiv) in CH_2Cl_2 (0.8 mL). The solvent was evaporated after 2.5 h and the solid residue was washed with Et_2O (4 × 3 mL). The combined organic phases were dried in vacuo yielding a white, air-sensitive solid. The purity was determined by NMR to be about 85%. It was not possible to further purify the product by recrystallization or flash column chromatography; yield: 20.5 mg (ca. 27 mmol, ca. 50%).

^{1}H NMR (250 MHz, 300 K, $CDCl_3$): δ = 7.70 (d, *J* = 8.3 Hz, 2 H, SO_2CCH), 7.32–7.13 (m, 7 H, H_{arom}), 4.68–4.52 [m, 2 H, $CHOP(OR)_2$ + PhC*H*HN], 4.43 (d, *J* = 16.3 Hz, 1 H, PhCH*H*N), 4.26–4.13 [m, 2 H, $P(OCH_2CH_2O)$], 4.07–3.85 [m, 2 H, $P(OCH_2CH_2O)$], 2.77 (d, *J* = 6.1 Hz, 1 H, bridgehead), 2.37 (s, 3 H, $ArCH_3$), 2.17–2.01 (m, 1 H, H_{allyl}), 1.67–1.40 (m, 4 H), 1.29 [s, 9 H, $OC(CH_3)_3$], 1.24–0.70 (m, 10 H).

^{31}P NMR (162 MHz, 300 K, $CDCl_3$): δ = 136.9.

tert-Butyl (1*R*,2*S*,5*S*)-7-(*N*-Benzyl-4-methylphenylsulfonamido)-6-cyclohexyl-2-[(dinaphtho[2,1-*d*:1′,2′-*f*][1,3,2]dioxaphosphepin-4-yl)oxy]bicyclo[3.2.0]hept-6-ene-1-carboxylate (8b)

Et_3N (23 μL, 163 μmol, 3 equiv) and 4-chlorodinaphtho[2,1-*d*:1′,2′-*f*][1,3,2]dioxaphosphepine[35] (35.8 mg, 80%, 82 μmol, 1.5 equiv) in CH_2Cl_2 (0.6 mL) were added to a stirred soln of **6a** (30.0 mg, 54 μmol, 1 equiv) in CH_2Cl_2 (0.8 mL). The solvent was evaporated after 84 h and the crude product was purified by flash column chromatography (silica gel, hexane–EtOAc, 10:1) to give a white solid; yield: 12.6 mg (14.6 μmol, 27%).

^{1}H NMR (400 MHz, 300 K, $CDCl_3$): δ = 8.02 (d, *J* = 8.9 Hz, 1 H, H_{arom}), 7.95 (d, *J* = 8.4 Hz, 1 H, H_{arom}), 7.89 (d, *J* = 8.7 Hz, 1 H, H_{arom}), 7.81 (d, *J* = 8.1 Hz, 1 H, H_{arom}), 7.62–7.54 (m, 3 H, H_{arom}), 7.50–7.16 (m, 7 H, H_{arom}), 7.05–6.98 (m, 1 H, H_{arom}), 6.96–6.89 (m, 4 H, H_{arom}), 6.84 (d, *J* = 7.4 Hz, 2 H, H_{arom}), 4.95–4.86 [m, 1 H, $CHOP(OR)_2$], 4.29 (d, *J* = 15.8 Hz, 1 H, PhC*H*HN), 4.21 (d, *J* = 15.8 Hz, 1 H, PhCH*H*N), 2.93 (d, *J* = 6.3 Hz, 1 H, bridgehead), 2.19 (s, 3 H, $ArCH_3$), 2.11–1.99 [m, 2 H, H_{allyl} + $CHOP(OR)_2CHH$], 1.98–1.85 [m, 1 H, $CHOP(OR)_2CHH$], 1.70–1.46 (m, 6 H), 1.42 [s, 9 H, $OC(CH_3)_3$], 1.35–0.72 (m, 6 H).

^{31}P NMR (162 MHz, 300 K, $CDCl_3$): δ = 155.2.

tert-Butyl (1*R*,2*S*,5*S*)-7-(*N*-Benzyl-4-methylphenylsulfonamido)-6-cyclohexyl-2-[(dibenzo[*d*,*f*][1,3,2]dioxaphosphepin-6-yl)oxy]bicyclo[3.2.0]hept-6-ene-1-carboxylate (8c)

Et_3N (92 μL, 680 μmol, 7.5 equiv) and 6-chlorodibenzo[*d*,*f*][1,3,2]dioxaphosphepine[36] (102.2 mg, 408 μmol, 4.5 equiv) were added to a stirred soln of **6a** (50.0 mg, 91 μmol, 1 equiv) in CH_2Cl_2 (2.4 mL). The solvent was evaporated after 2 h and the crude product was purified by flash column chromatography (silica gel, hexane–EtOAc–Et_3N, 18:1:1) to give a white solid; yield: 63.8 mg (83.3 μmol, 92%).

^{1}H NMR (400 MHz, 300 K, $CDCl_3$): δ = 7.75, (d, *J* = 8.0 Hz, 2 H, SO_2CCH), 7.59–7.44 (m, 2 H, H_{arom}), 7.41–7.34 (m, 2 H, H_{arom}), 7.32–7.20 (m, 4 H, H_{arom}), 7.16–7.07 (m, 7 H, H_{arom}), 4.94–4.85 [m, 1 H, $CHOP(OR)_2$], 4.41 (d, *J* = 16.2 Hz, 1 H, PhC*H*HN), 4.37 (d, *J* = 16.2 Hz, 1 H, PhCH*H*N), 2.89 (d, *J* = 6.2 Hz, 1 H, bridgehead), 2.33 (s, 3 H, $ArCH_3$), 2.18–2.04 (m, 1 H, H_{allyl}), 1.94–1.85 (m, 1 H), 1.84–1.72 (m, 1 H), 1.70–1.63 (m, 1 H), 1.62–1.43 (m, 4 H), 1.41 [s, 9 H, $OC(CH_3)_3$], 1.35–0.75 (m, 7 H).

^{13}C NMR (101 MHz, 300 K, $CDCl_3$): δ = 171.4 (CO_2t-Bu), 154.0 (NC=*C*), 149.7 (CO, arom), 149.6 (CO, arom), 142.9 (N*C*=C), 138.0–122.2 (22 C, arom), 81.6 [O*C*$(CH_3)_3$], 74.5 (d, *J* = 20 Hz, CHOH), 64.6 (CCO_2t-Bu), 51.6 (PhCH_2N), 45.1 {CH[OP$(OR)_2$]CH_2}, 37.9, 30.3, 30.2, 28.1 [OC(CH_3)$_3$], 26.1, 26.0, 22.3, 21.6.

^{31}P NMR (162 MHz, 300 K, $CDCl_3$): δ = 153.4.

tert-Butyl (1*R*,2*S*,5*S*)-6-Cyclohexyl-2-[(dibenzo[*d*,*f*][1,3,2]dioxaphosphepin-6-yl)oxy]-7-(*N*-methylmethylsulfonamido)bicyclo[3.2.0]hept-6-ene-1-carboxylate (8d)

Compound **5p** (210.0 mg, 528 μmol, 1 equiv) in CH_2Cl_2 (1.5 mL) was added to a stirred soln of $NaBH_4$ (28.0 mg, 740 μmol, 1.4 equiv) in MeOH (4 mL) at 0 °C. After 1 h, the reaction was quenched by addition of H_2O, brine, and CH_2Cl_2. The soln was extracted with CH_2Cl_2 (3 ×). The combined organic phases were dried ($MgSO_4$), filtered, and concentrated. The crude oil was purified by flash column chromatography (silica gel, hexane–EtOAc, 4:1) to give a clear oil; yield: 211.0 mg (528 μmol, >99%).

^{1}H NMR (400 MHz, 300 K, $CDCl_3$): δ = 4.40–4.32 (m, 1 H, C*H*OH), 3.45 (s, 1 H, OH), 3.13 (s, 3 H, SO_2CH_3), 3.08 [m, 1 H, CH(OH)C*H*H], 3.02 (s, 3 H, NCH_3), 2.82 (d, *J* = 6.8 Hz, 1 H, bridgehead), 2.49–2.38 (m, 1 H, H_{allyl}), 2.09–1.53 (m, 7 H), 1.46 [s, 9 H, $OC(CH_3)_3$], 1.44–1.11 (m, 6 H).

^{13}C NMR (101 MHz, 300 K, $CDCl_3$): δ = 172.8 (*C*O_2*t*-Bu), 146.1 (NC=*C*), 127.1 (N*C*=C), 81.1 [O*C*(CH_3)$_3$], 72.6 (CHOH), 63.9 (*C*CO_2*t*-Bu), 47.1 (SO_2CH_3), 38.1, 37.5, 36.5, 31.0, 30.4, 28.1 [OC(*C*H_3)$_3$], 26.2, 25.9, 22.6.

Et_3N (154 μL, 1.1 mmol, 9 equiv) and 6-chlorodibenzo[*d*,*f*][1,3,2]dioxaphosphepine[35] (184.4 mg, 736 μmol, 6 equiv) were added to a stirred soln of *tert*-butyl (1*R*,2*S*,5*S*)-6-cyclohexyl-2-hydroxy-7-(*N*-methylmethylsulfonamido)bicyclo[3.2.0]hept-6-ene-1-carboxylate (49.0 mg, 123 μmol, 1 equiv) in CH_2Cl_2 (3 mL). The solvent was evaporated after 1.5 h and the crude product was purified by flash column chromatography (silica gel, hexane–EtOAc–Et_3N, 28:5:2) to give a clear oil; yield: 72.4 mg (118 μmol, 96%).

^{1}H NMR (400 MHz, 300 K, $CDCl_3$): δ = 7.48–7.39 (m, 2 H, H_{arom}), 7.37–7.31 (m, 2 H, H_{arom}), 7.30–7.21 (m, 2 H, H_{arom}), 7.18 (d, *J* = 7.7 Hz, 1 H, H_{arom}), 7.09 (d, *J* = 7.9 Hz, 1 H, H_{arom}), 5.07–4.98 [m, 1 H, CHOP(OR)$_2$], 2.84 (d, *J* = 2.85, 1 H, bridgehead), 2.80 (s, 3 H, SO_2CH_3), 2.64–2.54 (m, 1 H, H_{allyl}), 2.24 (s, 3 H, NCH_3), 2.21–2.06 {m, 2 H, CH[OP(OR)$_2$]CH_2}, 1.85–1.75 (m, 2 H), 1.71–1.58 (m, 4 H), 1.53 [s, 9 H, OC(CH_3)$_3$], 1.42–1.14 (m, 6 H).

^{13}C NMR (101 MHz, 300 K, $CDCl_3$): δ = 172.0 (*C*O_2*t*-Bu), 149.6 (CO, arom), 149.1 (CO, arom), 148.6 (NC=*C*), 131.5, 131.1, 129.9, 129.3, 126.2 (N*C*=C), 125.8, 125.5, 125.2, 122.3, 122.2, 122.0, 81.5 [O*C*(CH_3)$_3$], 74.3 (d, *J* = 24 Hz, CHOH), 62.6 (*C*CO_2*t*-Bu), 45.7 (SO_2CH_3), 37.7, 37.0, 34.1, 30.1, 30.0, 28.2 [OC(*C*H_3)$_3$], 26.3, 25.8, 22.4.

^{31}P NMR (162 MHz, 300 K, $CDCl_3$): δ = 157.4.

HRMS (ESI): *m*/*z* [M – $C_{12}H_8O_3P$ + NH_4]$^+$ calcd for $C_{20}H_{37}N_2O_5S$: 417.2418; found: 417.2415.

X-ray Structure of 8d

CCDC Deposition number: CCDC-856610.[26] Although the starting Ficini product **5p** was enantiomerically enriched, recrystallization of **8d** (74% ee) from hot hexane gave colorless X-ray quality crystals of the $P2_1/c$ space group that contained racemic **8d**. Crystal data for $C_{32}H_{40}NO_7PS$: prism (0.30 × 0.21 × 0.14 mm), monoclinic, $P2_1/c$, cell dimensions (100 K) *a* = 10.5931(15), *b* = 20.825(3), *c* = 15.4905(15) Å, *β* =113.258(7)°, and *V* = 3 139(7) Å^3 with *Z* = 4, D_c = 1.298 Mg/m^3, μ = 0.202 mm^{-1} (MoK*α*, graphite monochromated), λ = 0.71073 Å, *F*(000) = 1 304. The data were collected at 100 K on a Bruker AXS SMART APEX platform in the range 1.73–28.53°. The structure was solved with SHELXTL using direct methods. Of the 31,460 measured reflections with index ranges $-14 \le h \le 14$, $-27 \le k \le 27$, $-20 \le l \le 20$, 7,940 independent reflections (R_{int} = 0.0891) were used in the refinement (full-matrix least squares on F^2) with anisotropic displacement parameters for all non-H atoms. Hydrogen atoms at calculated positions and refined with the riding model and individual isotropic thermal parameters for each group. Final residuals were *R*1 = 0.0389 [for 5,014 reflections with $I > 2\sigma(I)$] and w*R*2 = 0.0811 (all data), GOF = 0.849. Max and min difference peaks were +0.37 and –0.43 eÅ^{-3}, the largest and mean Δ/σ = –0.002 and 0.000. Selected bond lengths and angles are given in Table S1 (see Supporting Information); the numbering scheme is given in Figure 5 (ellipsoids at 30% probability).

Diphosphite Ligands

N-Benzyl-*N*-[(1*S*,4*S*,5*S*)-7-cyclohexyl-4-[(dibenzo[*d*,*f*][1,3,2]dioxaphosphepin-6-yl)oxy]-5-{[(dibenzo[*d*,*f*][1,3,2]dioxaphosphepin-6-yl)oxy]methyl}bicyclo[3.2.0]hept-6-en-6-yl]-4-methylbenzenesulfonamide (10a)

Et_3N (468 μL, 3.4 mmol, 12 equiv) and 6-chlorodibenzo[*d*,*f*][1,3,2]dioxaphosphepine[36] (421.5 mg, 1.7 mmol, 6 equiv) were added to a stirred soln of **9** in CH_2Cl_2 (6.5 mL). The solvent was evaporated after 9 h and the crude product was purified by flash column chromatography (silica gel, hexane–EtOAc–Et_3N, 35:3:2) yielding a white solid; yield: 156.0 mg (171 μmol, 61%). When a mixture of diastereomers of *N*-benzyl-*N*-[(1*S*,5*S*)-7-cyclohexyl-4-hydroxy-5-(hydroxymethyl)bicyclo[3.2.0]hept-6-en-6-yl]4-methylbenzenesulfonamide (4*R*/*S*)-**9** was used as reagent, the product was obtained as an inseparable mixture of diastereomeric diphosphites in similar yield.

^{1}H NMR (400 MHz, 300 K, $CDCl_3$): δ = 7.54 (t, *J* = 6.7 Hz, 2 H, H_{arom}), 7.48 (t, *J* = 6.1 Hz, 2 H, H_{arom}), 7.44–7.16 (m, 17 H, H_{arom}), 7.13 (d, *J* = 7.9 Hz, 2 H, H_{arom}), 6.89 (d, *J* = 7.9 Hz, 2 H, H_{arom}), 4.72–4.63 [m, 1 H, CHOP(OR)$_2$], 4.47 (d, *J* = 15.1 Hz, 1 H, PhC*H*HN), 4.27 (d, *J* = 15.1 Hz, 1 H, PhCH*H*N), 3.80–3.68 [m, 2 H, CH_2OP(OR)$_2$], 2.56 (d, *J* = 6.9 Hz, 1 H, bridgehead), 2.14 (s, 3 H, ArCH_3), 2.01–1.81 (m, 2 H), 1.72–1.62 (m, 1 H), 1.61–1.48 (m, 2 H), 1.48–1.37 (m, 1 H), 1.37–1.24 (m, 2 H), 1.22–1.09 (m, 2 H), 1.08–0.94 (m, 2 H), 0.93–0.75 (m, 2 H), 0.55–0.42 (m, 1 H).

^{13}C NMR (101 MHz, 300 K, $CDCl_3$): δ = 157.5 (NC=*C*), 151.2–149.2 [4 C, CO (arom)], 142.8 (N*C*=C), 138.4–121.9 (32 C, arom), 72.3 [d, *J* = 16 Hz, 1 C, CHOP(OR)$_2$], 65.2 [CH_2OP(OR)$_2$], 61.5 [*C*CH_2OP(OR)$_2$], 51.9 (Ph*C*H_2N), 43.1 [CH(OP(OR)$_2$*C*H_2], 37.5, 30.2, 30.1, 26.1, 25.9, 22.3, 21.4.

^{31}P NMR (162 MHz, 300 K, $CDCl_3$): δ = 150.1, 139.0.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{52}H_{50}NO_8P_2S$: 910.2727; found: 910.2722.

N-Benzyl-*N*-[(1*S*,4*S*,5*S*)-7-cyclohexyl-4-[(2,4,8,10-tetra-*tert*-butyldibenzo[*d*,*f*][1,3,2]-dioxaphosphepin-6-yl)oxy]-5-{[(2,4,8,10-tetra-*tert*-butyldibenzo[*d*,*f*][1,3,2]dioxaphosphepin-6-yl)oxy]-methyl}bicyclo[3.2.0]hept-6-en-6-yl]-4-methylbenzenesulfonamide (10b)

Pyridine (292 μL, 3.6 mmol, 13 equiv) and 2,4,8,10-tetra-*tert*-butyl-6-chlorodibenzo[*d*,*f*][1,3,2]dioxaphosphepine[37] (528.3 mg, 1.1 mmol, 4 equiv) were added to a stirred soln of a mixture of diastereomers (4*R*/*S*)-**9** (130.0 mg, 8:1 mixture of diastereomers, 278.0 μmol, 1 equiv) in toluene (8 mL) in a Schlenk tube fitted with a Young valve and heated to 120 °C overnight. The solvent was evaporated and the crude product was purified by flash column chromatography (silica gel, hexane–Et_3N, 99:1) yielding a white solid. Even though a mixture of diastereomers (4*R*/*S*)-**9** was used as reagent, the product was obtained as a single diastereomer as determined by NMR; yield: 178.0 mg (131 μmol, 47%, 53% based on **9** used).

^{1}H NMR (400 MHz, 300 K, $CDCl_3$): δ = 7.65 (d, *J* = 8.1 Hz, 2 H, SO_2CCH), 7.46–7.43 (m, 3 H, H_{arom}), 7.38 (d, *J* = 2.4 Hz, 1 H, H_{arom}), 7.23–7.19 (m, 2 H, H_{arom}), 7.15 (d, *J* = 8.1 Hz, 2 H, SO_2CCHC*H*), 7.08–7.04 (m, 3 H, H_{arom}), 7.02–6.95 (m, 4 H, H_{arom}), 4.78–4.70 [m, 1 H, CHOP(OR)$_2$], 4.24–4.07 [m, 3 H, CH_2OP(OR)$_2$ + PhC*H*HN], 3.69 (d, *J* = 15.5 Hz, 1 H, PhCH*H*N), 2.48 (d, *J* = 6.4 Hz, 1 H, bridgehead), 2.38 (s, 3 H, ArCH_3), 1.91–1.73 (m, 2 H), 1.70–1.61 (m, 1 H), 1.58–1.11 [m, 75 H, 8 C(CH_3)$_3$ + 3 H], 1.10–1.06 (m, 1 H), 0.98–0.71 (m, 6 H), 0.62–0.48 (m, 2 H).

^{13}C NMR (101 MHz, 300 K, $CDCl_3$): δ = 157.8 (NC=*C*), 146.6–145.7 [4 C, CO (arom)], 143.1 (N*C*=C), 140.4–123.8 (32 C, arom), 73.4 [d, *J* = 29 Hz, 1 C, CHOP(OR)$_2$], 65.3 {d, *J* = 15 Hz, 1 C, [CH_2OP(OR)$_2$]}, 61.7 [*C*CH_2OP(OR)$_2$], 50.4 (Ph*C*H_2N), 43.5 [CH(OP(OR)$_2$*C*H_2], 37.7, 35.7–34.6 [8 C, *C*(CH_3)$_3$], 32.2–31.1 [24 C, C(CH_3)$_3$], 30.3, 29.8, 26.3, 25.9, 22.3, 21.6.

^{31}P NMR (162 MHz, 300 K, $CDCl_3$): δ = 159.2, 144.7.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{84}H_{114}NO_8P_2S$: 1358.7735; found: 1358.7732.

Dimethyl 2-Methylsuccinate; Typical Procedure by Asymmetric Hydrogenation of Dimethyl 2-Methylenesuccinate

*Using ligand **10a**:* Bis(norbornadiene)rhodium(I) tetrafluoroborate (1.2 mg, 3.2 μmol, 0.01 equiv) and **10a** (2.9 mg, 3.2 μmol, 0.01

equiv) were stirred in CH_2Cl_2 (0.8 mL) for 5 min. Dimethyl 2-methylenesuccinate (50.0 mg, 316 μmol, 1 equiv) was added and the soln was transferred into an autoclave with CH_2Cl_2 (0.5 mL). After stirring for 5.5 h at with H_2 (4.5 bar), the pressure was released and the crude mixture was filtered through a pad of Celite with Et_2O.; yield: not determined; 5% ee [HPLC (Chiralcel OD-H, hexane–*i*-PrOH, 98:2, flow rate 0.8 mL/min, λ = 210.8 nm): t_R = 9.9 (minor), 17.3 min (major)].

^{1}H NMR (400 MHz, 300 K, $CDCl_3$): δ = 3.69 (s, 3 H, CO_2CH_3), 3.68 (s, 3 H, CO_2CH_3), 2.92 (dqd, *J* = 8.1, 7.2, 6.0 Hz, 1 H, C*H*MeCO$_2$Me), 2.74 (dd, *J* = 16.6, 8.1 Hz, 1 H, C*H*HCO$_2$CH$_3$), 2.41 (dd, *J* = 16.6, 6.0 Hz, 1 H, CH*H*CO$_2$CH$_3$), 1.22 (d, *J* = 7.2 Hz, 3 H, CH_3).

*Using ligand **10b**:* yield: 44.8 mg (280 μmol, 88%); 20% ee (HPLC: conditions as above).

Methyl 2-(Acetylamino)propanoate by Asymmetric Hydrogenation of Methyl Acetamidoacrylate

Following the typical procedure using methyl acetamidoacrylate ligand **10b** for 10 h with H_2 4.7 (bar). The crude product was filtered through a pad of silica gel with EtOAc; yield: 39.5 mg (272 μmol, 78%); 30% ee [GC (Supelco a-dex column, 30 m × 0.25 mm, 0.25 μ film, isotherm at 110 °C): t_R = 12.08 (major), 12.20 min (minor)].

^{1}H NMR (400 MHz, 300 K, $CDCl_3$): δ = 6.22 (br s, 1 H, NH), 4.62–4.52 [m, 1 H, C*H*(NHAc)(CO$_2$CH$_3$)], 3.72 (s, 3 H, CO_2CH_3), 1.99 [s, 3 H, NHC(=O)C*H*$_3$], 1.37 (d, *J* = 7.2 Hz, 3 H, CH_3).

Dimethyl (*E*)-2-(1,3-Diphenylallyl)malonate; Typical Procedure by Asymmetric Allylic Alkylation of Dimethyl Malonate

*Using ligand **10a**:* [Pd(μ-Cl)(allyl)]$_2$ (1.1 mg, 3.0 μmol, 0.015 equiv) and **10a** (5.5 mg, 6.0 μmol, 0.03 equiv) were stirred in CH_2Cl_2 (0.4 mL) for 20 min. (*E*)-1,3-Diphenylallyl acetate[38] (50.4 mg, 200 μmol, 1 equiv) in CH_2Cl_2 (0.6 mL), dimethyl malonate (68 μL, 600 μmol, 3 equiv), BSA (147 μL, 600 μmol, 3 equiv), and KOAc (1.0 mg, 10 μmol, 0.05 equiv) were added and the soln was stirred for 12 h at r.t. The reaction was quenched by the addition H_2O and CH_2Cl_2. The soln was extracted with CH_2Cl_2 (4 ×). The combined organic phases were dried ($MgSO_4$), filtered, and concentrated. The crude oil was purified by flash column chromatography (silica gel, hexane–EtOAc, 9:1) to give an off-white solid; yield: not determined; 6% ee [HPLC (Chiralcel OD-H, hexane–*i*-PrOH, 99:1, flow rate 0.4 mL/min, λ = 280.2 nm): t_R = 30.2 (minor), 32.5 min (major)].

^{1}H NMR (400 MHz, 300 K, $CDCl_3$): δ = 7.38–7.18 (m, 10 H, H_{arom}), 6.50 (d, *J* = 15.7 Hz, 1 H, PhC*H*=CH), 6.35 (dd, *J* = 15.7, 8.5 Hz, 1 H, PhCH=C*H*), 4.37 (dd, *J* = 10.8, 8.5 Hz, 1 H, H_{allyl}), 3.97 [d, *J* = 10.8 Hz, 1 H, C*H*(CO$_2$Me)$_2$], 3.70 (s, 3 H, CO_2CH_3), 3.52 (s, 3 H, CO_2CH_3).

*Using ligand **10b**:* yield: 64.1 mg (197.6 μmol, 99%); 52% ee (HPLC: conditions as above).

Dibenzyl (*E*)-2-(1,3-Diphenylallyl)malonate by Asymmetric Allylic Alkylation of Dibenzyl Malonate

Following the typical procedure using dibenzyl malonate and ligand **10b**. The crude oil was purified by flash column chromatography (silica gel, hexane–EtOAc, 12:1) to give a clear oil. The product was contaminated with inseparable dibenzyl malonate. The purity was determined by comparison of intensities of characteristic NMR signals; yield: 94.2 mg (197.7 μmol, 99%); 57% ee [HPLC (Chiralcel AD-H, hexane–*i*-PrOH, 90:10, flow rate 0.5 mL/min, λ = 254.4 nm): t_R = 49.4 (minor), 61.0 min (major).

^{1}H NMR (400 MHz, 300 K, $CDCl_3$): δ = 7.28–7.18 (m, 18 H, H_{arom}), 7.06–7.02 (m, 2 H, H_{arom}), 6.42 (d, *J* = 15.8 Hz, 1 H, PhC*H*=CH), 6.32 (dd, *J* = 15.8, 8.2 Hz, 1 H, PhCH=C*H*), 5.12 (d, *J* = 12.3 Hz, 1 H, CO$_2$C*H*HPh), 5.08 (d, *J* = 12.3 Hz, 1 H, CO$_2$CH*H*Ph), 4.94 (d, *J* = 12.4 Hz, 1 H, CO$_2$C*H*HPh), 4.90 (d, *J* = 12.4 Hz, 1 H, CO$_2$CH*H*Ph), 4.32 (dd, *J* = 10.9, 8.2 Hz, 1 H), 4.06 [d, *J* = 10.9 Hz, 1 H, C*H*(CO$_2$Bn)$_2$].

Coordination Studies

Coordination of Dienes; General Procedure

Diene ligand **7a–d** (20.0 mg, 1 equiv) and metal precursor [Rh(μ-Cl)(C$_2$H$_4$)$_2$]$_2$, [Ir(μ-Cl)(coe)$_2$]$_2$, or [Rh(acac)(C$_2$H$_4$)$_2$] (1 equiv) were dissolved in $CDCl_3$, MeCN, THF, or Et_2O (0.5 mL) and transferred into a Young NMR tube under argon. For MeCN, THF and Et_2O, the ^{1}H NMR spectra were measured after evaporating the solvent in vacuo and dissolving the residue in $CDCl_3$. The results are summarized in Table S2 (see Supporting Information).

Coordination of Phosphite–Alkenes; General Procedure

Phosphite-alkene ligands **8a–d** (20.0 mg, 1 equiv) and metal precursor [Rh(μ-Cl)(C$_2$H$_4$)$_2$]$_2$, [Ir(μ-Cl)(coe)$_2$]$_2$, or [Rh(acac)(C$_2$H$_4$)$_2$] (1 equiv) were dissolved in $CDCl_3$, MeCN, THF, or Et_2O (0.5 mL) and transferred into a Young NMR tube under argon. For experiments under H_2 atmosphere, 1 mL of solvent was used and H_2 was bubbled through the soln until the solvent was reduced to ca. 0.5 mL. The ^{31}P chemical shifts (162 MHz, 300 K) and coupling constants of the observed complexes are summarized in Table S3 (see Supporting Information).

Coordination of Diphosphites; General Procedure

Diphosphite ligand **10a** or **10b** (20.0 mg, 1 equiv) and metal precursor [Rh(nbd)$_2$]$_2$ BF$_4$ or [Rh(acac)(C$_2$H$_4$)$_2$] (1 equiv) were dissolved in $CDCl_3$ (0.5 mL) and transferred into a Young NMR tube under argon.

Supporting Information

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synthesis.

Acknowledgment

We thank Mr. Raphael Aardoom for the X-ray crystal structure determinations.

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