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DOI
10.1021/acs.joc.5b00438

Publication date
2015

Document Version
Final published version

Published in
Journal of Organic Chemistry

JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

Enantioselective Synthesis of Tunable Chiral Clickphine P,N-Ligands and Their Application in Ir-Catalyzed Asymmetric Hydrogenation

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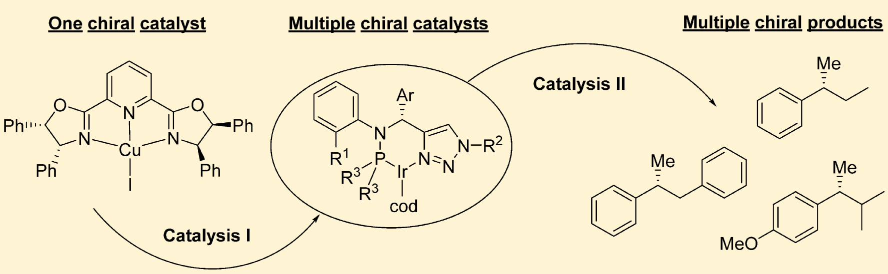
Supporting Information



ABSTRACT: A small library of highly tunable chiral Clickphine P,N-ligands has been prepared in an enantioselective fashion by Cu^{I}-catalyzed asymmetric propargylic amination using a single chiral complex and a subsequent in situ cycloaddition click reaction. The scope of the propargylic amination to yield optically active triazolyl amines is described. The amines are transformed in a one-pot procedure to the corresponding Ir−Clickphine complexes, which serve as catalysts for the asymmetric hydrogenation of di-, tri-, and tetrasubstituted unfunctionalized alkenes. Enantioselectivities of up to 90% ee were obtained in these hydrogenations, which are among the best reported in the case of the tetrasubstituted substrate 2-(4′-methoxyphenyl)-3-methylbut-2-ene (**9**) (87% ee). This is a demonstration of the effective use of the chiral pool, as from one chiral catalyst a library of chiral Ir complexes has been synthesized that can hydrogenate various alkenes with high selectivity.

■ INTRODUCTION

Asymmetric catalysis is increasingly important for the preparation of chiral compounds for the pharmaceutical, agrochemical, and fine chemical industries.[1] Typically, a metal complex based on a chiral ligand is used for asymmetric transformations, and often several chiral ligands need to be explored before a sufficiently selective complex can be identified. The preparation of chiral ligands is mostly based on the use of the available pool of chiral building blocks (i.e., sugars, amino acids), which are built in the ligand or used to prepare the chiral ligand.[2] Remarkably, the use of asymmetric catalysis to prepare chiral ligands for direct use in a certain asymmetric conversion has hardly been explored. Several contributions deal with the asymmetric synthesis of chiral ligands, mainly chiral phosphines, but typically no further catalysis is performed with the synthesized ligands.[3] We wondered whether it would be possible to use one chiral complex to prepare a library of bidentate ligands with a chiral backbone that in turn could be used in the exploration of a certain desired asymmetric transformation. This would result in the catalytic expansion of the chiral pool. In order to validate this concept, we studied the chiral synthesis of P,N-ligands for the iridium-catalyzed asymmetric hydrogenation of alkenes. Asymmetric hydrogenation of alkenes provides a means to rapidly access a vast range of chiral compounds relevant to pharmaceutical and agrochemical use.[1,2] Whereas rhodium-based catalysts are used extensively for functionalized alkenes, iridium provides the catalysts of choice for unfunctionalized substrates.[4] Recently, however, Ir catalysts have also been found to be applicable for increasingly functionalized substrates[4b] such as phosphorus-containing alkenes,[5−7] furans,[8] pyridine derivatives,[9] imines,[10−18] vinyl boronates,[19] and *α*,*β*-unsaturated esters.[20−22] With this increasing number of potential substrates, there is a demand for highly tunable chiral iridium catalysts that are able to convert these substrates with high enantioselectivity. Since the discovery of the high activity and selectivity of Ir−PHOX catalysts in the hydrogenation of imines and unfunctionalized alkenes by Pfaltz and co-workers,[10b,23,24] P,N-ligands have been used frequently in Ir-catalyzed hydro-

Received: February 25, 2015
Published: March 6, 2015

Scheme 1. Retrosynthesis of Chiral Clickphine P,N-Ligands Using Asymmetric Catalysis

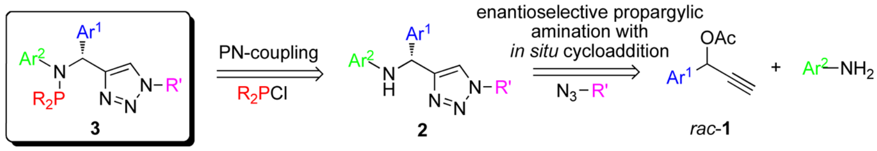
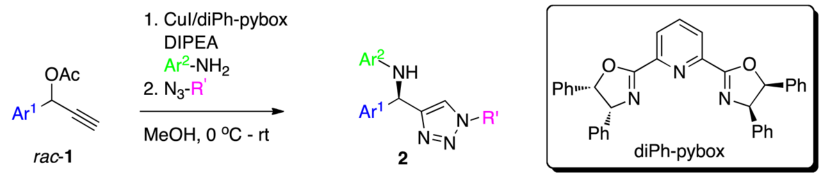


Table 1. Preparation of Optically Pure Triazolyl Amines 2[a]



entry	Ar^1	Ar^2	R′	product	yield (%) (ee (%))	yield (%) recryst.	ee (%) recryst.
1	Ph	2-OMe-Ph	Ph	(*S*)-**2a**	91 (84)	63	>99
2	4-OMe-Ph	2-OMe-Ph	Ph	(*R*)-**2b**	75 (82)	23	>99
3	Ph	Ph	Bn	(*S*)-**2c**	75 (85)	17	99
4	Ph	2-OMe-Ph	Bn	(*R*)-**2d**	–	49	>99
5	Ph	Ph	4-CF_3-Ph	(*S*)-**2e**	90 (84)	68	94
6	2-naphthyl	2-OMe-Ph	Ph	(*R*)-**2f**	–	48	98

[a]Reaction conditions: **1** (1.0 equiv), $ArNH_2$ (2.0 equiv), DIPEA (4 equiv), CuI (0.05–0.10 equiv), and the ligand (0.06–0.12 equiv) were stirred in methanol at 0 °C. After full conversion (as determined by TLC), the azide (1.0 equiv) was added. For entries 1, 3, and 5, bis(4*S*,5*R*)-diPh-pybox was used, and for entries 2, 4, and 6, bis(4*R*,5*S*)-diPh-pybox was used.

genation and seem to be privileged for this transformation.[25] The majority of these ligands rely on chiral oxazolines and pyridines as the nitrogen atom donors. On the other hand, chiral triazole-containing P,N-ligands have not been used to date in Ir-catalyzed hydrogenations or successfully applied in any other asymmetric transformation.[26] The use of achiral triazole-containing P,N-ligands for highly regioselective allylic substitution reactions has been demonstrated by us.[27,28] We anticipated the facile preparation of chiral P,N-ligands via Cu^I-catalyzed cycloaddition, allowing for easy derivatization and fine-tuning of the chiral pocket provided by the ligand. Importantly, asymmetric propargylic amination catalyzed by a Pybox−Cu^I complex potentially gives propargylic amines in enantiomerically pure form,[29,30] which is the basis of our chiral ligand synthesis. In principle, a single chiral catalyst can be used to generate a library of chiral P,N-ligands, as azide ligation to these propargylic amines would furnish triazolyl imines **2**, which can be further decorated with a phosphine to give chiral P,N-ligands **3** (Scheme 1). As Cu^I is already present in the reaction mixture after propargylic amination, we envisioned that addition of the azide to this mixture would result in a one-pot three-component reaction, giving enantiomerically enriched triazolyl amines in only one step. This synthetic strategy would allow the incorporation of four different substituents in only two reaction steps. Therefore, these ligands would be highly tunable, allowing the facile construction of ligand libraries to find suitable catalysts for a range of substrates in Ir-catalyzed hydrogenation. Furthermore, complexation to iridium would result in the formation of a six-membered cyclic chelate, which was found to be a prerequisite for most successful ligands in Ir-catalyzed asymmetric hydrogenations. We anticipate that the chiral center, which resides in the backbone of the ligand, controls the chiral pocket around the metal and thus effects efficient enantioface discrimination.

Here we report a detailed study of the scope and limitations of the asymmetric Cu^I-catalyzed propargylic amination with in situ cycloaddition to furnish chiral triazolyl amines **2**, which are transformed into chiral P,N-ligands **3**. The corresponding Ir complexes are evaluated in the asymmetric hydrogenation of di-, tri-, and tetrasubstituted largely unfunctionalized alkenes.

■ RESULTS AND DISCUSSION

Propargylic Amination with in Situ Cycloaddition. The first step in the synthesis was the preparation of the propargylic amine by application of the enantioselective copper-catalyzed propargylic amination conditions to racemic propargylic acetate **1**. Subsequent triazole formation by the Cu^I-catalyzed azide−alkyne cycloaddition would afford the desired triazolyl amines **2**. Interestingly, most of the reagents required for this "click" reaction were already present in the propargylic amination: copper(I), base, and the acetylene. Since methanol would not disturb the reaction, the addition of the azide should be sufficient for a one-pot procedure. After full consumption of the propargylic acetate, azide addition indeed provided triazole **2** in high yield with retention of the stereochemistry. The absolute configuration of the products can be controlled by using either enantiomer of the diPh-pybox ligand (2,6-bis((4*R*,5*S*)-4,5-diphenyl-4,5-dihydrooxazol-2-yl)pyridine). The products obtained after the reaction were highly crystalline, allowing further enantioenrichment by recrystallization. The first attempt was directly promising: a single recrystallization step gave the single enantiomer in good yield (Table 1, entry 1).

With other compounds we were also able to isolate enantiopure triazolyl amines, although several recrystallization cycles were required for sufficient enantioenrichment, which lowered the yields (entries 2 and 3). Although no single enantiomer was obtained, the 4-trifluoromethylphenyl-substituted triazole **2e** illustrates the ease of ligand variation via this method. In the case of **2d** and **2f**, the products crystallized in high ee from the reaction mixture, and in only one recrystallization step, optically pure product was obtained in moderate yield (entries 4 and 6). The availability of both

DOI: 10.1021/acs.joc.5b00438
J. Org. Chem. 2015, 80, 3634–3642

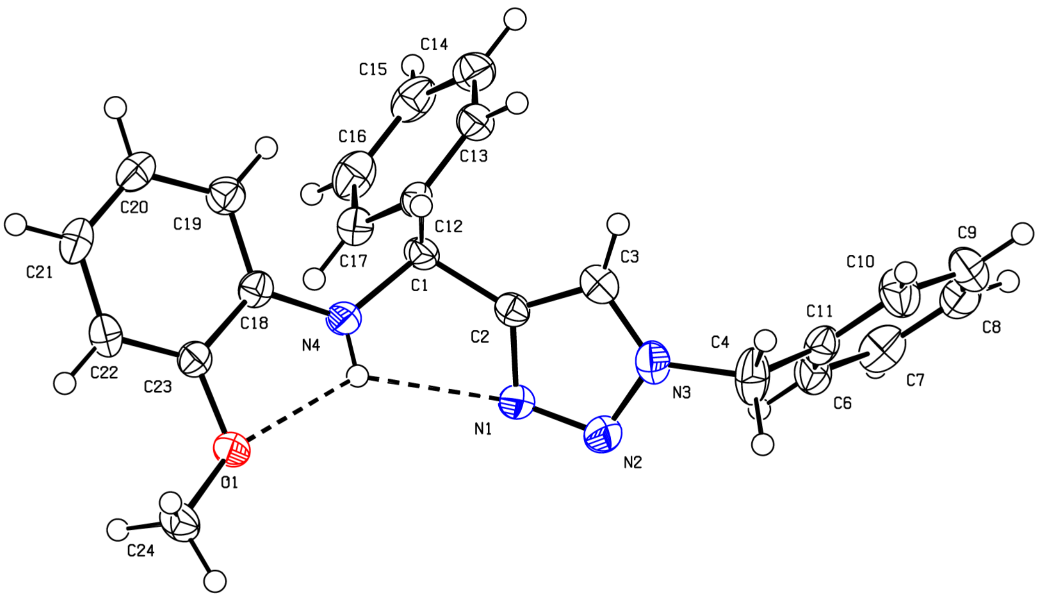
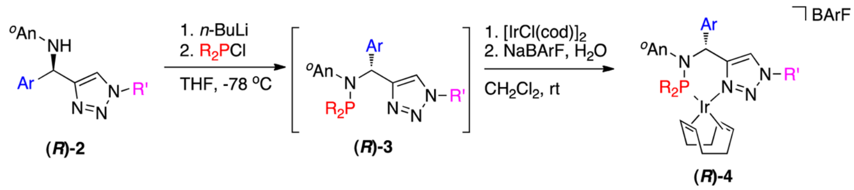


Figure 1. Displacement ellipsoid plot (50% probability level) of triazolyl amine (*R*)-**2d**. The absolute configuration could not be determined crystallographically by anomalous scattering but was assigned according to the enantiopure synthesis. Selected bond lengths (Å) and angles (deg): C_1-N_4 1.448(3), C_1-C_2 1.507(3), C_2-N_1 1.360(3), $O_1\cdots H_{4N}$ 2.22(3), $N_1\cdots H_{4N}$ 2.35(3); $N_4-C_1-C_2$ 107.6(2), $C_1-C_2-N_1$ 121.5(2), $N_4-H_{4N}\cdots O_1$ 108(2), $N_4-H_{4N}\cdots N_1$ 110(2).

Table 2. One-Pot Synthesis of Ir−Clickphine Complexes 4



entry	complex	R	R′	Ar	yield (%)[a]
1	**4a**	Ph	Ph	Ph	53
2	**4b**	Ph	Ph	*p*-MeO-C_6H_4	67
3	**4c**	Ph	Bn	Ph	61
4	**4d**	Ph	Ph	2-naphthyl	70
5	**4e**	^{i}Pr	Ph	Ph	52
6	**4f**	^{i}Pr	Ph	*p*-MeO-C_6H_4	60
7	**4g**	^{i}Pr	Bn	Ph	60
8	**4h**	^{i}Pr	Ph	2-naphthyl	60

[a]Overall yields from triazolyl amine.

enantiomers of the ligand enables the preparation of both (*R*)- and (*S*)-triazolyl amines.

The three-dimensional structure of triazolyl amines **2** was unambiguously confirmed by X-ray crystal structure determination of (*R*)-**2d** (Figure 1). Unfortunately, the configuration of the chiral center at C_1 could not be reliably determined because of twinning of the crystal and the absence of a strong anomalous scatterer. The structure features two intramolecular S(5) hydrogen bonds with the NH group as donor and with the triazole-N_1 and the OMe group as acceptors. These interactions are likely to increase the NH proton's pK_a value, as deprotonation proved difficult. A strong base such as *n*-butyllithium is necessary to remove this proton (vide infra).

The preparation of this type of triazolyl amines **2** is not the first reported. In 2007, similar compounds were synthesized by the group of Botta as potential antimicrobial agents.[31,32] The copper-catalyzed azide−alkyne cycloaddition was performed with enantiopure propargylic amines obtained by kinetic enzymatic resolution of racemic propargylamines.

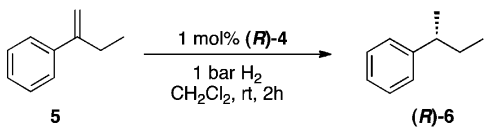
One-Pot Synthesis of Ir−Clickphine Complexes. P−N bond formation is typically achieved by condensation of the amine with a phosphorus chloride in the presence of a weak base such as triethylamine. Application of these conditions to triazolyl amines **2** did not result in any reactivity toward the desired product, which is rationalized by the stabilizing hydrogen-bonding interactions of the NH proton with the triazole and OMe moieties. However, prior deprotonation of the amine with *n*-butyllithium followed by condensation with a phosphorus chloride gave the desired P,N-ligands **3** in almost quantitative conversion (Table 2). Unfortunately, these compounds proved to be highly moisture-sensitive, as they are prone to hydrolysis resulting in P−N bond cleavage, complicating chromatographic isolation. We demonstrated previously that isolation is feasible but with significant loss of

DOI: 10.1021/acs.joc.5b00438
J. Org. Chem. 2015, 80, 3634−3642

material due to decomposition.[29] Therefore, we decided to skip isolation of the ligands **3** and immediately perform complexation with Ir and counteranion exchange to give Ir−BArF complexes **4**. These complexes are insensitive toward air and moisture and can even be purified by flash chromatography with dichloromethane.[31] This results in the rapid one-pot synthesis of Ir complexes **4** from triazolyl amines **2** in good overall yield (50−70%), allowing the construction of a small library of chiral Ir−Clickphine complexes **4a−h** (Table 2).

Asymmetric Hydrogenation. The potential of Ir−Clickphine complexes as catalysts for asymmetric hydrogenation was evaluated in the asymmetric hydrogenation of di-, tri-, and tetrasubstituted largely unfunctionalized alkenes **5**, **7**, and **9**. When standard conditions for the hydrogenation of unfunctionalized alkenes (50 bar H_2) were used in the hydrogenation of the terminal aryl,alkyl-disubstituted substrate **5**, a moderate ee of 47% was obtained with complex **4a** (Table 3, entry 1). It was observed previously that lowering the dihydrogen pressure for this class of substrates can be beneficial for the enantioselectivity.[33] Indeed, when the hydrogenation was conducted at ambient pressure, a good ee of 75% was obtained with complex **4a** (entry 2). Evaluation of the whole library revealed quantitative conversions and ee's of 69−75% for Clickphine complexes **4a−d** containing a diphenylphosphine donor group. However, the use of diisopropylphosphine-functionalized complexes **4e−h** resulted in reduced enantioselectivity (39−44% ee; entries 6−9). The lack of aromatic phosphine substituents may preclude necessary π-stacking interactions required to induce good ee.

Table 3. Hydrogenation of α-Ethylstyrene (5) by Ir−Clickphine Complexes 4a−h[a]



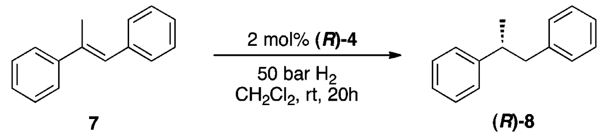
entry	complex	conv. (%)[b]	ee (%)[c]
1[d]	**4a**	>99	47
2	**4a**	>99	75
3	**4b**	>99	73
4	**4c**	>99	71
5	**4d**	>99	69
6	**4e**	>99	44
7	**4f**	>99	41
8	**4g**	>99	39
9	**4h**	>99	40

[a]Reaction conditions: 1.0 mol % **4**, [**4**] = 1 mM, 1 bar H_2, CH_2Cl_2, rt. [b]Conversion determined by GC after 2 h. [c]Enantiomeric excess determined by chiral GC (Supelco β-DEX 225). In all cases the *R* enantiomer was obtained as the major product. [d]Reaction performed at 50 bar.

The enantioselectivity (up to 75% ee) provided by Ir−Clickphine complexes for terminal disubstituted alkenes is lower than that provided by iridium catalysts based on ThrePHOX (up to 94% ee),[33] phosphinite−oxazole (up to 97% ee),[34] and phosphite−oxazoline ligands (up to 99% ee)[35,36] but shows the ability of these complexes to induce significant enantioface discrimination for unfunctionalized alkenes. It should be noted that despite the recent successful examples cited above, many other iridium-based catalysts are completely unselective or unreactive for this substrate.[3,17]

Encouraged by the results obtained in the hydrogenation of disubstituted alkene **5**, we applied our Ir−Clickphine catalysts in the hydrogenation of trisubstituted α-methylstilbene (**7**) (Table 4). Higher pressures (50 bar H_2) and longer reaction times were necessary for the reaction to go to completion compared with those for the disubstituted substrate. Quantitative conversion and an ee of 86% were obtained after 20 h with 1 mol % complex **4a** (entry 1). A higher catalyst loading of 2 mol % improved the ee to 90% and was therefore used for all further hydrogenations of **7** (entry 2). Variation of the substitution pattern on the backbone of the ligand (Ar and R′) led only to slight differences in the enantioselectivity (86−90% ee; entries 3−5) while maintaining quantitative conversion. Similarly as for disubstituted alkene **5**, complexes **4e−h** based on diisopropyl-functionalized phosphines gave lower enantioselectivity (51−72% ee; entries 6−9). α-Methylstilbene (**7**) is frequently used as a benchmark substrate for hydrogenation of unfunctionalized alkenes.[3] The enantioselectivity obtained with Ir−Clickphine complex **4a** (90% ee) is good compared with many known examples but not excellent, as over 99% ee has been reported for this substrate.

Table 4. Hydrogenation of α-Methylstilbene (7) by Ir−Clickphine Complexes 4a−h[a]



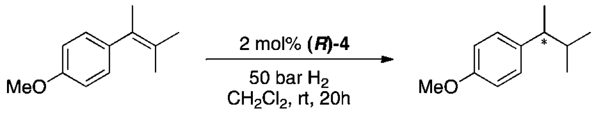
entry	complex	conv. (%)[b]	ee (%)[c]
1[d]	**4a**	>99	86
2	**4a**	>99	90
3	**4b**	>99	86
4	**4c**	>99	87
5	**4d**	>99	83
6	**4e**	>99	71
7	**4f**	>99	72
8	**4g**	>99	59
9	**4h**	>99	51

[a]Reaction conditions: 2.0 mol % **4**, [**4**] = 1 mM, 50 bar H_2, CH_2Cl_2, rt. [b]Conversion determined by GC after 20 h. [c]Enantiomeric excess determined by chiral HPLC (Chiralcel OJ-H). In all cases the *R* enantiomer was obtained as the major product. [d]1.0 mol % **4a**.

Next, we turned to the more challenging tetrasubstituted alkene **9**, which is known to be notoriously unreactive with iridium catalysts.[3] Initial attempts in the hydrogenation of **9** using a 1 mol % loading of Ir−Clickphine complex **4a** and 50 bar H_2 gave only 5% conversion after 20 h but a promising enantioselectivity of 57% ee (Table 5, entry 1). Increasing the catalyst loading to 2 mol % resulted in 51% conversion and 78% ee (entry 2). Under these conditions, all of the Ir−Clickphine complexes were evaluated in the hydrogenation of substrate **9**. For the diphenylphosphine-based complexes, we found a positive influence of the size of the Ar substituent on the conversion and ee (entries 2−5). The *p*-methoxyphenyl-substitueted complex **4b** gave 82% ee at 84% conversion, and the 2-naphthyl derivative afforded 87% ee at 98% conversion. A benzyl substituent on the triazole (R′) resulted in a slightly lower selectivity of 72% ee at 68% conversion. In analogy to the results obtained with substrates **5** and **7**, the diisopropylphos-

DOI: 10.1021/acs.joc.5b00438
J. Org. Chem. 2015, 80, 3634−3642

Table 5. Hydrogenation of 2-(4′-Methoxyphenyl)-3-methylbut-2-ene (9) by Ir−Clickphine Complexes 4a−h[a]



9 → **(−)-10**

entry	complex	conv. (%)[b]	ee (%)[c]
1[d]	**4a**	5	57
2	**4a**	51	78
2	**4b**	84	82
3	**4c**	68	72
4	**4d**	98	87
5	**4e**	98	56
6	**4f**	99	60
7	**4g**	98	43
8	**4h**	84	49

[a]Reaction conditions: 2.0 mol % **4**, [**4**] = 1 mM, 50 bar H_2, CH_2Cl_2, rt. [b]Conversion determined by GC after 20 h. [c]Enantiomeric excess determined by chiral GC (Supelco β-DEX 225). In all cases the (−) enantiomer was obtained as the major product. [d]1.0 mol % **4a**.

phine-based complexes **4e−h** give lower ee's but good conversion (43−60% ee, 84−99% conversion; entries 6−9).

There are only few reports of efficient iridium catalysts for the hydrogenation of tetrasubstituted alkenes. Co and Kim[37] reported 88% ee at 22% conversion after 24 h for the hydrogenation of **9** with an iminophosphoranylferrocene ligand. Pfaltz and co-workers have published several efficient catalysts for this substrate that give up to 92% ee and full conversion at 50 bar.[23,38,39] In the light of these precedents, the performance of Ir−Clickphine catalyst **4d** can be considered among the best reported to date for this substrate.

■ CONCLUSION

We report here for the first time a catalytic strategy to generate libraries of chiral ligands using one chiral parent complex. The strategy is based on Cu^{I}-catalyzed enantioselective propargylic amination, in situ copper-catalyzed cycloaddition, and subsequent condensation with the phosphorus precursor to yield chiral Clickphine P,N-ligands. The scope of the reaction was investigated, and it was found that the protocol allows for substantial variation of the substituents, giving good yields (17−63%) and excellent ee's after crystallization (94−99% ee) for triazolyl amines **2a−f**. Limitations arise only if the enantioselective step does not proceed with sufficient selectivity and the product cannot be further enantiomerically purified by recrystallization. The triazolyl amines were transformed into the corresponding P,N-ligands **3a−h** after deprotonation with *n*-BuLi and reaction with the corresponding phosphorus chloride, and these ligands were reacted immediately to form Ir−Clickphine complexes. This resulted in a one-pot synthesis of a library of Ir−Clickphine complexes **4a−h** in good overall yields (52−67%). Iridium complexes **4a−h** are active catalysts for the asymmetric hydrogenation of di-, tri-, and tetrasubstituted unfunctionalized alkenes, providing enantioselectivities of up to 90% ee. The catalysts are especially suited for notoriously unreactive tetrasubstituted substrates. Up to 87% ee was obtained in the hydrogenation of **9**, which is among the highest selectivities reported for this substrate. Furthermore, the catalyst screening results indicate that complexes based on a diphenylphosphine donor group (**4a−d**, R = Ph) are better suited for these substrates than the diisopropylphosphine-containing derivatives **4e−h** (R = ^{i}Pr). A likely explanation is the lack of π-stacking interactions with the substrate during the enantioface selection in the latter case. The effects of the other substituents (Ar^1, Ar^2, R′) on the enantioselectivity are more subtle and vary for the different substrates, which demonstrates the potential of fine-tuning of the catalyst by variation of these substituents. Most importantly, we report the modular synthesis of chiral Clickphine ligands by generating a small library using an enantioselective propargylic amination step based on one chiral Cu catalyst. The diversity in chirality generated is important because it shows that different efficient iridium catalysts can be made for various challenging unfunctionalized alkenes. We now aim to expand the substrate scope toward other substrates such as phosphinates, furans, and imines with a larger and more diverse library of Clickphine ligands.

■ EXPERIMENTAL SECTION

General Experimental Procedures. All of the reactions were carried out under an atmosphere of argon using standard Schlenk techniques. THF, pentane, hexane, and diethyl ether were distilled from sodium benzophenone ketyl; CH_2Cl_2, isopropanol, and methanol were distilled from CaH_2; and toluene was distilled from sodium under nitrogen. Except for the compounds given below, all of the reagents were purchased from commercial suppliers and used without further purification. The following compounds were synthesized according to published procedures: DiPh-pybox[40] and substrates **5**[41] and **9**.[42] High-resolution mass spectra were recorded on a four-sector mass spectrometer; for FAB-MS, 3-nitrobenzyl alcohol was used as the matrix.

General Procedure A: Cu-Catalyzed Propargylic Amination with in Situ Cycloaddition. Copper iodide (0.05 equiv) and 2,6-bis((4*R*,5*S*)-4,5-diphenyl-4,5-dihydrooxazol-2-yl)pyridine (DiPh-pybox) (0.055 equiv) were suspended in methanol. The mixture was stirred for 20 min before addition of a solution of the propargylic acetate (1 equiv) in methanol. At the indicated temperature (between −20 and 0 °C), a solution of nucleophile (2 equiv) and DIPEA (4 equiv) in methanol was added. The suspension was stirred until TLC analysis indicated complete conversion of the propargylic acetate. When the reaction was finished, a solution of azide (1 equiv) in methanol was added to the mixture. After full consumption of the acetylene, filtration or evaporation gave the crude product. Silica gel chromatography (typically a small percentage of MeOH in CH_2Cl_2) gave the pure product.

*(S)-2-Methoxy-N-(phenyl(1-phenyl-1H-1,2,3-triazol-4-yl)methyl)-aniline (**2a**).* General procedure A was followed with the enantiomer of the ligand. 1-Phenylprop-2-ynyl acetate (**1a**) (35 mg, 0.20 mmol) was added to the catalyst suspension, which was cooled to 0 °C before the mixture of *o*-anisidine (45 μL, 0.4 mmol) and DIPEA was added. After 5 h of stirring, phenyl azide (24 μL, 0.22 mmol) was added at room temperature. The mixture was stirred for an additional 22 h. The residue obtained after filtration contained the product and some ligand. Silica gel chromatography (EtOAc/PE 1:1) afforded product **2a** as a white solid (65 mg, 91% yield, 84% ee). Recrystallization from EtOAc gave white crystals (45 mg, 63% yield, >99.5% ee). $[\alpha]_D^{20}$ +2 (*c* 0.5, $CHCl_3$). HPLC conditions: Chiralcel AD (4.6 mm × 250 mm), 85:15 heptane/HO*i*-Pr, 1.0 mL/min, λ = 254 nm. ^{1}H NMR (400 MHz; $CDCl_3$): δ (ppm) = 7.73 (d, *J* = 0.3 Hz, 1H), 7.68 (d, *J* = 7.3 Hz, 2H), 7.56−7.31 (m, 8H), 6.83−6.70 (m, 3H), 6.53 (d, *J* = 7.7 Hz, 1H), 5.82 (d, *J* = 3.7 Hz, 1H), 5.27 (d, *J* = 3.6 Hz, 1H), 3.88 (s, 1H). $^{13}C\{^1H\}$ NMR (101 MHz; $CDCl_3$): δ (ppm) = 151.4, 147.1, 141.7, 137.1, 137.0, 129.7, 129.0, 128.8, 127.9, 127.2, 121.1, 120.5, 120.0, 117.5, 111.4, 109.4, 55.6, 55.5. FTIR (film, cm^{-1}): 3428 (m), 3143 (w), 3064 (m), 2835 (w), 1600 (s), 1509 (s), 1458 (s), 1424 (m), 1343 (m), 1224 (s), 1128 (m), 1039 (m), 910 (m). Anal. Calcd for $C_{22}H_{20}N_4O$: C, 74.14; H, 5.66; N, 15.72. Found: C, 74.07; H, 5.71; N,

DOI: 10.1021/acs.joc.5b00438
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15.64. HRMS (FAB+) m/z: $[M + H]^+$ calcd for $C_{22}H_{21}N_4O$ 357.1715; found 357.1716.

*(R)-2-Methoxy-N-((4-methoxyphenyl)(1-phenyl-1H-1,2,3-triazol-4-yl)methyl)aniline (**2b**).* General procedure A was followed. The starting material was 1-(4-methoxyphenyl)prop-2-ynyl acetate (612 mg, 3.0 mmol), and the total amount of MeOH was 25 mL. As the nucleophile, *o*-anisidine (680 μL, 6.0 mmol) was used. After 7 h, slowly warming from −18 to 0 °C, phenyl azide (357 mg, 3.0 mmol) was added, and the mixture was stirred for 17 h before the filtration was performed. Silica gel column chromatography (gradient: 0.5 to 2.0% MeOH in CH_2Cl_2) gave **2b** in good yield (863 mg, 75% yield, 82% ee). Two recrystallization steps from EtOAc gave the enantiopure product (270 mg, 23% yield, >99.5% ee). $[\alpha]_D^{20}$ −26 (*c* 0.5, $CHCl_3$); mp (single enantiomer) 160−162 °C. HPLC conditions: Chiralcel AD (4.6 mm × 250 mm), 80:20 heptane/HO*i*-Pr, 1.0 mL/min, λ = 254 nm, 20 min (major isomer), 48 min (minor isomer). ^{1}H NMR (400 MHz; $CDCl_3$): δ (ppm) = 7.72−7.67 (m, 3H), 7.50−7.46 (m, 2H), 7.43−7.40 (m, 3H), 6.92−6.89 (m, 2H), 6.81−6.69 (m, 3H), 6.53−6.50 (m, 1H), 5.73 (s, 1H), 5.2 (br s, 1H), 3.87 (s, 3H), 3.80 (s, 3H). $^{13}C\{^1H\}$ NMR (101 MHz; $CDCl_3$): δ (ppm) = 159.2 (C_q), 151.7 (C_q), 147.1 (C_q), 137.1 (C_q), 137.0 (C_q), 133.7 (C_q), 129.7, 128.7, 128.4, 121.1, 120.5, 120.0, 117.4, 114.4, 111.4, 109.4, 55.5, 55.3, 55.0. HRMS (FAB+) m/z: $[M + H]^+$ calcd for $C_{23}H_{23}N_4O_2$ 387.1821; found 387.1817.

*(S)-N-((1-Benzyl-1H-1,2,3-triazol-4-yl)(phenyl)methyl)aniline (**2c**).* General procedure A was followed with the enantiomer of the ligand. The starting material was 1-phenylprop-2-ynyl acetate (348 mg, 2.0 mmol), and the total amount of MeOH was 25 mL. As the nucleophile, aniline (365 μL, 4.0 mmol) was used. After 6 h, slowly warming from −18 to 10 °C, benzyl azide (251 μL, 2.0 mmol) was added, and the mixture was stirred for 17 h before the solvent was evaporated. Silica gel column chromatography (gradient: 0.8% MeOH in CH_2Cl_2) gave **2c** in good yield (512 mg, 75% yield, 85% ee). Recrystallization from EtOAc (two portions, 406 mg, 89% ee) and stirring in CH_2Cl_2/*c*-hexane (3:1) and, after filtration, again in CH_2Cl_2/*c*-hexane (1:1) gave the almost enantiopure product (115 mg, 17% yield, 99% ee). $[\alpha]_D^{20}$ −1 (*c* 0.25, $CHCl_3$); mp (single enantiomer) 175−178 °C. HPLC conditions: Chiralcel AD (4.6 mm × 250 mm), 80:20 heptane/HO*i*-Pr, 0.8 mL/min, λ = 254 nm, 28 min (minor isomer), 31 min (major isomer). ^{1}H NMR (400 MHz; $CDCl_3$): δ (ppm) = 7.44 (d, *J* = 8.5 Hz, 2H), 7.37−7.19 (m, 8H), 7.16 (s, 1H), 7.13−7.09 (m, 2H), 6.70 (t, *J* = 7.3 Hz, 1H), 6.58 (d, *J* = 7.7 Hz, 2H), 5.69 (d, *J* = 4.0 Hz, 1H), 5.49 (A of AB, d, *J* = 15.0 Hz, 1H), 5.42 (B of AB, d, *J* = 15.0 Hz, 1H), 4.80 (d, *J* = 3.6 Hz, 1H). $^{13}C\{^1H\}$ NMR (101 MHz; $CDCl_3$): δ (ppm) = 150.8 (C_q), 147.1 (C_q), 141.8 (C_q), 134.7 (C_q), 129.2 (4C), 129.0, 128.8, 128.0, 127.8, 127.1, 121.7, 118.1, 113.9, 55.7, 54.3. HRMS (FAB+) m/z: $[M + H]^+$ calcd for $C_{22}H_{21}N_4$ 341.1766, found 341.1765.

*(R)-2-Methoxy-N-((1-benzyl-1H-1,2,3-triazol-4-yl)(phenyl)methyl)aniline (**2d**).* General procedure A was followed. The starting material was 1-phenylprop-2-ynyl acetate (1.0 g, 5.7 mmol), and the total amount of MeOH was 50 mL. As the nucleophile, *o*-anisidine (1.3 mL, 11.5 mmol) was used. After 16 h, slowly warming from −18 to 10 °C, benzyl azide (717 μL, 5.7 mmol) was added, and the mixture was stirred for 17 h. The resulting suspension was concentrated to a volume of ca. 15 mL and cooled to 0 °C. Filtration of the suspension gave an off-white solid, which was recrystallized from EtOAc to yield a white crystalline solid (1.05 g, 49% yield, >99.5% ee). $[\alpha]_D^{20}$ +5 (*c* 1.0, $CHCl_3$); mp (single enantiomer) 155 °C. HPLC conditions: Chiralcel AD (4.6 mm × 250 mm), 80:20 heptane/HO*i*-Pr, 1.0 mL/min, λ = 254 nm, 17 min (major isomer), 32 min (minor isomer). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.45 (d, *J* = 7.5 Hz, 2H), 7.39−7.34 (m, 5H), 7.31 (d, *J* = 7.6 Hz, 1H), 7.26−7.17 (m, 3H), 6.79 (dd, *J* = 7.6, 1.7 Hz, 1H), 6.71 (m, 2H), 6.45 (dd, *J* = 7.6, 1.7 Hz, 1H), 5.71 (d, *J* = 4.1 Hz, 1H), 5.52 (A of AB, d, *J* = 15.0 Hz, 1H), 5.46 (B of AB, d, *J* = 15.0 Hz, 1H), 5.19 (d, *J* = 4.2 Hz, 1H), 3.86 (s, 3H). $^{13}C\{^1H\}$ NMR (126 MHz; $CDCl_3$): δ (ppm) = 134.7 (C_q), 129.2, 128.95, 128.80, 128.1, 127.8, 127.3, 121.1, 55.5. HRMS (FAB+) m/z: $[M + H]^+$ calcd for $C_{23}H_{23}N_4O$ 371.1872, found 371.1871.

*(S)-N-(Phenyl(1-(4-(trifluoromethyl)phenyl)-1H-1,2,3-triazol-4-yl)methyl)aniline (**2e**).* General procedure A was followed with the enantiomer of the ligand. The starting material was 1-phenylprop-2-ynyl acetate (174 mg, 1.0 mmol), and the total amount of MeOH was 10 mL. As the nucleophile, aniline (182 μL, 2.0 mmol) was used. After 6 h of stirring at 0 °C, 1-azido-4-(trifluoromethyl)benzene (187 mg, 1.0 mmol) was added, and the mixture was stirred for 22 h before the solvent was evaporated. Silica gel column chromatography (EtOAc/PE (1:4) with 10−20% CH_2Cl_2 to prevent crystallization) gave **2e** in good yield (353 mg, 90% yield, 84% ee). Recrystallization from EtOAc/*c*-hexane for one night gave the enantioenriched product (266 mg, 68% yield, 94% ee). $[\alpha]_D^{20}$ +10 (*c* 1.0, $CHCl_3$); mp (single enantiomer) 162 °C. HPLC conditions: Chiralcel AD (4.6 mm × 250 mm), 80:20 heptane/HO*i*-Pr, 1.0 mL/min, λ = 254 nm, 29.4 min (minor isomer), 34.6 min (major isomer). ^{1}H NMR (400 MHz; $CDCl_3$): δ (ppm) = 7.84 (d, *J* = 8.7 Hz, 2H), 7.77−7.75 (m, 3H), 7.52 (d, *J* = 8.7 Hz, 2H) 7.41−7.30 (m, 3H), 7.17−7.13 (m, 2H), 6.74 (t, *J* = 7.3 Hz, 1H), 6.65 (d, *J* = 7.9 Hz, 2H), 5.80 (d, *J* = 2.8 Hz, 1H), 4.77 (br s, 1H). $^{13}C\{^1H\}$ NMR (101 MHz; $CDCl_3$): δ (ppm) = 151.7, 146.9, 141.3, 139.4, 130.8 (q, J_{CF} = 33.2 Hz), 129.3, 129.2, 128.2, 127.3, 127.2 (q, J_{CF} = 3.7 Hz), 123.6 (q, J_{CF} = 272.3 Hz), 120.5, 119.9, 118.5, 113.9, 55.8. HRMS (FAB+) m/z: $[M + H]^+$ calcd for $C_{22}H_{18}F_3N_4$ 395.1484, found 395.1485.

*(R)-2-Methoxy-N-(2-naphthyl(1-phenyl-1H-1,2,3-triazol-4-yl)methyl)aniline (**2f**).* General procedure A was followed. The starting material was 1-(2-naphthyl)prop-2-ynyl acetate (300 mg, 1.3 mmol), and the total amount of MeOH was 20 mL. As the nucleophile, *o*-anisidine (302 μL, 2.7 mmol) was used. After 16 h, slowly warming from −18 to 0 °C, phenyl azide (160 mg, 1.3 mmol) was added, and the mixture was stirred for 17 h before the filtration was performed. The crude product was washed with cold MeOH and recrystallized from EtOAc to give enantiomerically pure white crystals (260 mg, 48% yield, 98% ee). $[\alpha]_D^{20}$ −23 (*c* 1.0, $CHCl_3$); mp (single enantiomer) 187−191 °C. HPLC conditions: Chiralcel AD (4.6 mm × 250 mm), 80:20 heptane/HO*i*-Pr, 1.0 mL/min, λ = 254 nm. ^{1}H NMR (400 MHz; $CDCl_3$): δ (ppm) = 8.02 (s, 1H), 7.87 (m, 3H), 7.75−7.62 (m, 4H), 7.58−7.46 (m, 4H), 7.43 (d, *J* = 7.3 Hz, 1H), 6.83 (dd, *J* = 7.5, 1.8 Hz, 1H), 6.80−6.66 (m, 2H), 6.56 (dd, *J* = 7.3, 1.8 Hz, 1H), 5.96 (d, *J* = 3.7 Hz, 1H), 5.36 (d, *J* = 3.6 Hz, 1H), 3.92 (s, 3H). $^{13}C\{^1H\}$ NMR (126 MHz; $CDCl_3$): δ (ppm) = 133.6 (C_q), 133.3 (C_q), 129.8, 129.0, 128.8, 128.2, 127.8, 126.40, 126.25, 126.17, 125.3, 121.2, 120.7, 55.6. HRMS (FAB+) m/z: $[M + H]^+$ calcd for $C_{26}H_{23}N_4O$ 407.1872, found 407.1878.

General Procedure B: Synthesis of Phosphinotriazole Ligands 3. To a solution of triazolyl amine (*R*)-**2** (1 equiv) in THF (50 mM) at −78 °C was added *n*-BuLi (2.5 M in hexanes, 1.05 equiv), and the resulting yellow solution was stirred for 15 min. The corresponding phosphorus chloride (1.05 equiv, Ph_2PCl for **3a**−**d** and $^iPr_2PCl$ for **3e**−**f**) was added, and the solution was stirred for 1 h while being allowed to warm to rt. Formation of the phosphinotriazole was checked by unlocked ^{31}P NMR spectroscopy, which showed resonances at 56−60 and 135−138 ppm for **3a**−**d** and **3e**−**f**, respectively. Evaporation of the solvent in vacuo yielded a white foam, which was directly used without further purification for complexation with iridium.

General Procedure C: Synthesis of Iridium Complexes 4. The corresponding phosphinotriazole (1 equiv) and $[IrCl(cod)]_2$ (0.5 equiv) were stirred in dichloromethane at rt for 1.5 h. NaBArF (1.25 equiv) and H_2O (10 mL) were added, and the heterogeneous mixture was stirred vigorously for 10 min. The aqueous phase was removed and extracted with dichloromethane (2 × 10 mL). The combined organic phases were washed with H_2O (10 mL), dried over $MgSO_4$, and filtered, and the solvent was removed in vacuo. Purification by flash SiO_2 chromatography (CH_2Cl_2) gave the product as a brown or red solid.

*Complex **4a**.* According to general procedure C, ligand (*R*)-**3a** (144 mg, 0.26 mmol), $[IrCl(cod)]_2$ (87 mg, 0.13 mmol), NaBArF (292 mg, 0.33 mmol), and 15 mL of CH_2Cl_2 were used to give the complex as an orange-red solid (233 mg, 53% yield). $[\alpha]_D^{20}$ +51 (*c* 0.5, $CHCl_3$). ^{1}H NMR (400 MHz; $CDCl_3$): δ (ppm) = 8.07 (s, 1H), 7.88 (br s, 2H),

DOI: 10.1021/acs.joc.5b00438
J. Org. Chem. 2015, 80, 3634−3642

7.78−7.70 (br m, 10H), 7.57−7.49 (br m), 7.46−7.38 (m, 2H), 7.38−7.30 (m, 2H), 7.29−7.22 (m, 2H), 7.22−7.15 (m, 2H), 7.14 (t, *J* = 7.6 Hz, 1H), 6.95−6.78 (m, 3H), 6.71 (br t, *J* = 7.3 Hz, 1H), 6.45 (d, *J* = 8.1 Hz, 1H), 6.24 (br s, 1H), 5.78 (br d, J_{HP} = 22.3 Hz, 1H), 5.18 (br s, 1H), 3.27 (br s, 1H), 2.75 (s, 3H), 2.60−2.47 (m, 1H), 2.47−2.36 (m, 2H), 2.36−2.23 (m, 2H), 2.22−1.98 (m, 3H), 1.93−1.76 (m, 1H). $^{13}C\{^1H\}$ NMR (101 MHz; $CDCl_3$): δ (ppm) = 162.0 (q, J_{CB} = 49.9 Hz, 4C, C_q), 156.3 (C_q), 148.6 (d, J_{CP} = 5.4 Hz, C_q), 135.6 (C_q), 135.3, 135.1 (br, 8C), 134.1 (C_q), 132.4, 132.3, 132.0, 131.8 (C_q), 131.5, 131.4, 131.2 (C_q), 131.0 (C_q), 130.8, 130.4 (C_q), 129.8 (d, J_{CP} = 2.6 Hz), 129.5, 129.2 (qq, J_{CF} = 31.5 Hz, J_{CB} = 2.7 Hz, C_q), 128.4, 128.3 (d, J_{CP} = 11.0 Hz), 128.0 (d, J_{CP} = 11.3 Hz), 124.8 (q, J_{CF} = 273 Hz, C_q), 121.8, 121.2, 120.8, 117.6 (q, J_{CB} = 3.5 Hz, 4C), 112.3, 97.3 (d, J_{CP} = 10.5 Hz), 92.7 (br), 69.1 (br), 65.5 (br), 65.5 (d, J_{CP} = 13.6 Hz), 54.5, 33.2, 31.9, 30.0, 29.2. $^{31}P\{^1H\}$ NMR (162 MHz; $CDCl_3$): δ (ppm) = 55.9 (s). HRMS (FAB+) *m*/*z*: $[M - BArF]^+$ calcd for $C_{42}H_{41}IrN_4OP$ 841.2647, found 841.2651.

*Complex **4b**.* According to general procedure C, ligand (*R*)-**3b** (128 mg, 0.22 mmol), $[IrCl(cod)]_2$ (74 mg, 0.11 mmol), NaBArF (244 mg, 0.28 mmol), and 15 mL of CH_2Cl_2 were used to give the complex as a red solid (254 mg, 67% yield). $[\alpha]_D^{20}$ +13 (*c* 1.0, $CHCl_3$); decomp. 100−105 °C. ^1H NMR (500 MHz; $CDCl_3$): δ (ppm) = 8.02 (s, 1H), 7.78 (br s, 2H), 7.70 (s, 10H), 7.55−7.53 (m, 3H), 7.49 (s, 5H), 7.42−7.34 (m, 5H), 7.28 (d, *J* = 6.3 Hz, 2H), 7.17 (br s, 2H), 7.11 (t, *J* = 7.3 Hz, 1H), 7.04 (d, *J* = 8.3 Hz, 2H), 6.92−6.90 (m, 3H), 6.70−6.69 (m, 1H), 6.42 (d, *J* = 8.3 Hz, 1H), 6.21 (br s, 1H), 5.72 (br s, 1H), 5.13 (br s, 1H), 3.89 (s, 3H), 3.26 (br s, 1H), 2.72 (s, 3H), 2.42−2.37 (m, 2H), 2.31−2.28 (m, 2H), 2.15−2.05 (m, 4H), 1.84 (br s, 1H). $^{13}C\{^1H\}$ NMR (126 MHz; $CDCl_3$): δ (ppm) = 161.9 (q, J_{CB} = 49.9 Hz, C_q), 160.6 (C_q), 135.45 (C_q), 134.9, 132.0, 131.5, 131.3, 130.7, 129.7, 129.0 (qq, J_{CF} = 31.5 Hz, J_{CB} = 2.7 Hz, C_q), 128.3 (d, J_{CP} = 10.5 Hz), 127.9 (C_q), 125.8 (C_q), 123.6 (C_q), 121.4 (C_q), 121.1, 120.7, 117.6 (septuplet, J_{CF} = 4.0 Hz), 114.6, 112.1 (br), 97.1 (br), 64.7 (d, J_{CP} = 13.7 Hz), 55.7, 54.4, 29.9, 29.3. $^{31}P\{^1H\}$ NMR (202 MHz; $CDCl_3$): δ (ppm) = 56.5 (s). HRMS (FAB+) *m*/*z*: $[M - BArF]^+$ calcd for $C_{43}H_{43}IrN_4O_2P$ 871.2882, found 871.2879.

*Complex **4c**.* According to general procedure C, ligand (*R*)-**3c** (162 mg, 0.29 mmol), $[IrCl(cod)]_2$ (97 mg, 0.15 mmol), NaBArF (319 mg, 0.36 mmol), and 15 mL of CH_2Cl_2 were used to give the complex as an orange solid (303 mg, 61% yield). $[\alpha]_D^{20}$ +19 (*c* 1.0, $CHCl_3$); decomp. 85−90 °C. ^1H NMR (500 MHz; $CDCl_3$): δ (ppm) = 7.83 (s, 10H), 7.59 (s, 4H), 7.57 (s, 1H), 7.55 (d, *J* = 6.9 Hz, 3H), 7.43−7.40 (m, 4H), 7.39 (br s, 1H), 7.35 (m, 4H), 7.29 (td, *J* = 7.7, 2.6 Hz, 2H), 7.21 (t, *J* = 6.7 Hz, 2H), 7.11 (t, *J* = 7.5 Hz, 1H), 6.91 (br s, 3H), 6.71 (t, *J* = 7.5 Hz, 1H), 6.40 (d, *J* = 8.2 Hz, 1H), 6.23 (br s, 1H), 5.75 (A of AB, d, *J* = 14.5 Hz, 1H), 5.62 (br m, 1H, CH), 5.49 (B of AB, d, *J* = 14.5 Hz, 1H), 5.13 (br s, 1H), 3.25 (br s, 1H), 2.50 (br s, 1H), 2.44 (s, 3H), 2.42−2.32 (m, 4H), 2.19−2.18 (m, 1H), 2.06 (m, 2H), 1.84−1.82 (m, 1H). $^{13}C\{^1H\}$ NMR (126 MHz; $CDCl_3$): δ (ppm) = 161.9 (q, J_{CB} = 50.0 Hz, C_q), 156.1 (C_q), 135.0, 132.2 (C_q), 131.9 (d, J_{CP} = 2.5 Hz), 131.7 (C_q), 131.3 (d, J_{CP} = 1.6 Hz), 131.2 (C_q), 130.3, 129.9, 129.6 (d, J_{CP} = 2.7 Hz), 129.3, 129.0 (qq, J_{CF} = 31.4 Hz, J_{CB} = 2.8 Hz, C_q), 128.4, 128.3, 128.2, 128.0 (C_q), 127.8 (d, J_{CP} = 12.0 Hz), 125.8 (C_q), 123.6 (C_q), 121.5 (C_q), 121.0, 117.6 (septuplet, J_{CF} = 4.0 Hz), 112.0, 97.1 (d, J_{CP} = 10.3 Hz), 68.5 (br), 65.2 (br), 65.0 (d, J_{CP} = 13.5 Hz), 56.3, 53.9, 33.3, 31.6, 30.2, 29.1. $^{31}P\{^1H\}$ NMR (202 MHz; $CDCl_3$): δ (ppm) = 57.10 (s). HRMS (FAB+) *m*/*z*: $[M - BArF]^+$ calcd for $C_{43}H_{43}IrN_4OP$ 855.2933, found 855.2924.

*Complex **4d**.* According to general procedure C, ligand (*R*)-**3d** (83 mg, 0.14 mmol), $[IrCl(cod)]_2$ (47 mg, 0.07 mmol), NaBArF (160 mg, 0.18 mmol), and 10 mL of CH_2Cl_2 were used to give the complex as an orange solid (173 mg, 70% yield). $[\alpha]_D^{20}$ +6 (*c* 1.0, $CHCl_3$); decomp. 98−106 °C. ^1H NMR (500 MHz; $CDCl_3$): δ (ppm) = 8.10 (s, 1H), 8.09−8.07 (m, 2H), 7.99 (d, *J* = 8.3 Hz, 1H), 7.94 (s, 1H), 7.84 (d, *J* = 7.9 Hz, 1H), 7.75−7.71 (m, 11H), 7.64 (t, *J* = 7.2 Hz, 1H), 7.60 (t, *J* = 6.8 Hz, 1H), 7.55 (m, 3H), 7.49 (s, 4H), 7.42 (d, *J* = 7.5 Hz, 1H), 7.40 (d, *J* = 7.7 Hz, 1H), 7.36−7.30 (m, 2H), 7.21−7.15 (m, 4H), 6.99−6.94 (m, 3H), 6.75 (t, *J* = 7.5 Hz, 1H), 6.48 (d, *J* = 8.1 Hz, 1H), 6.31 (br s, 1H), 5.92 (d, J_{HP} = 23.1 Hz, 1H), 5.21 (br s, 1H), 3.21 (br s, 1H), 2.74 (s, 3H), 2.47−2.35 (m, 3H), 2.28−2.22 (m, 2H), 2.12−2.09 (m, 1H), 2.06−2.01 (m, 1H), 1.86−1.83 (m, 1H), 1.77 (m, 1H). $^{13}C\{^1H\}$ NMR (126 MHz; $CDCl_3$): δ (ppm) = 161.9 (q, J_{CB} = 49.8 Hz, C_q), 156.2 (C_q), 148.6 (C_q), 135.4 (C_q), 134.9, 133.4 (C_q), 133.0 (C_q), 132.2 (br), 132.0 (d, J_{CP} = 2.1 Hz), 131.6, 131.5 (C_q), 131.3 (d, J_{CP} = 1.9 Hz), 131.2 (C_q), 130.7, 130.6 (C_q), 130.0 (C_q), 129.8, 129.6, 129.0 (qq, J_{CF} = 31.5 Hz, J_{CB} = 2.8 Hz, C_q), 128.3, 128.2 (d, J_{CP} = 1.5 Hz), 128.02, 127.98, 127.94 (C_q), 127.89, 127.7 (d, J_{CP} = 6.1 Hz), 127.2 (br), 126.2, 125.8 (C_q), 123.6 (C_q), 121.8, 121.4 (C_q), 121.2, 120.7, 117.6 (septuplet, J_{CF} = 4.0 Hz), 112.3, 97.4 (d, J_{CP} = 10.0 Hz), 91.8 (br), 69.3, 65.7, 65.1 (d, J_{CP} = 13.9 Hz), 54.4, 32.7, 32.1, 29.8, 29.5. $^{31}P\{^1H\}$ NMR (202 MHz; $CDCl_3$): δ (ppm) = 57.79 (s). HRMS (FAB+) *m*/*z*: $[M - BArF]^+$ calcd for $C_{46}H_{43}IrN_4OP$ 891.2933, found 891.26931.

*Complex **4e**.* According to general procedure C, ligand (*R*)-**3e** (103 mg, 0.22 mmol), $[IrCl(cod)]_2$ (73 mg, 0.11 mmol), NaBArF (248 mg, 0.28 mmol), and 10 mL of CH_2Cl_2 were used to give the complex as a brown solid (186 mg, 52% yield). $[\alpha]_D^{20}$ −6 (*c* 1.0, $CHCl_3$); decomp. 90−95 °C. ^1H NMR (500 MHz; $CDCl_3$): δ (ppm) = 8.13 (s, 1H), 7.70 (m, 10H), 7.61−7.52 (m, 6H), 7.49 (d, *J* = 16.1 Hz, 4H), 7.32−7.28 (m, 2H), 6.98−6.95 (m, 2H), 6.86 (q, *J* = 7.7 Hz, 1H), 6.76 (d, *J* = 7.1 Hz, 1H), 5.93 (br s, 1H), 5.14 (d, J_{HP} = 20.1 Hz, 1H), 5.03 (br s, 1H), 4.68 (br s, 1H), 4.57 (br s, 1H), 3.81 (s, 3H), 3.55−3.49 (m, 1H), 3.23−3.18 (m, 1H), 2.90−2.71 (m, 4H), 2.64−2.61 (m, 1H), 2.38−2.35 (m, 1H), 2.13−2.01 (m, 4H), 1.86−1.75 (m, 1H), 1.11 (dd, *J* = 19.4, 6.7 Hz, 3H), 0.72−0.67 (dd, *J* = 17.1, 6.6 Hz, 3H), 0.51−0.42 (m, 3H). $^{13}C\{^1H\}$ NMR (126 MHz; $CDCl_3$): δ (ppm) = 161.8 (q, J_{CB} = 49.9 Hz, C_q), 140.2 (C_q), 138.0, 136.0 (C_q), 134.9, 131.1 (d, J_{CP} = 6.7 Hz), 130.8, 130.7, 130.5 (d, J_{CP} = 5.0 Hz), 130.4, 129.0 (qq, J_{CF} = 31.5 Hz, J_{CB} = 2.8 Hz, C_q), 128.4 (d, J_{CP} = 7.6 Hz), 127.9 (C_q), 126.7, 125.8 (C_q), 125.0, 123.6 (C_q), 121.4 (C_q), 120.7 (d, J_{CP} = 8.3 Hz), 120.5, 117.6 (septuplet, J_{CF} = 4.0 Hz), 101.5 (d, J_{CP} = 9.9 Hz), 94.5, 91.8 (d, J_{CP} = 13.9 Hz), 91.3, 85.0 (d, J_{CP} = 23.9 Hz), 54.6, 34.3, 30.3 (d, J_{CP} = 38.8 Hz), 27.9, 27.4, 22.5, 18.7, 16.7 (d, J_{CP} = 37.2 Hz), 14.2. $^{31}P\{^1H\}$ NMR (202 MHz; $CDCl_3$): δ (ppm) = 58.37 (s). HRMS (FAB+) *m*/*z*: $[M - BArF]^+$ calcd for $C_{36}H_{45}IrN_4OP$ 773.3088, found 773.3082.

*Complex **4f**.* According to general procedure C, ligand (*R*)-**3f** (100 mg, 0.20 mmol), $[IrCl(cod)]_2$ (67 mg, 0.10 mmol), NaBArF (222 mg, 0.25 mmol), and 10 mL of CH_2Cl_2 were used to give the complex as a brown solid (200 mg, 60% yield). $[\alpha]_D^{20}$ +9 (*c* 1.0, $CHCl_3$); decomp. 90−94 °C. ^1H NMR (500 MHz; $CDCl_3$): δ (ppm) = 8.10 (s, 1H), 7.70 (s, 8H), 7.60−7.52 (m, 4H), 7.51 (s, 4H), 7.28 (d, *J* = 8.7 Hz, 1H), 7.12 (br s, 1H), 6.97 (d, *J* = 7.8 Hz, 1H), 6.92−6.85 (m, 3H), 6.79 (d, *J* = 8.5 Hz, 1H), 6.75−6.67 (m, 1H), 6.49 (d, *J* = 8.2 Hz, 1H), 5.87 (br s, 1H), 5.11 (d, J_{HP} = 19.7 Hz, 1H), 5.02 (br s, 1H), 4.67 (br s, 1H), 4.57 (br s, 1H), 3.82−3.66 (m, 8H), 3.57−3.53 (m, 1H), 3.24−3.19 (m, 1H), 2.90−2.62 (m, 4H), 2.12−2.01 (m, 3H), 1.79−1.78 (m, 1H), 1.12 (dd, *J* = 18.8, 6.7 Hz, 3H), 0.89−0.84 (m, 1H), 0.77 (dd, *J* = 17.3, 6.5 Hz, 3H), 0.50−0.42 (m, 3H). $^{13}C\{^1H\}$ NMR (126 MHz; $CDCl_3$): δ (ppm) = 161.8 (q, J_{CB} = 50.0 Hz, C_q), 158.9 (C_q), 136.0 (C_q), 134.9, 133.4 (C_q), 131.1, 130.8, 130.5 (d, J_{CP} = 5.3 Hz), 129.0 (qq, J_{CF} = 31.5 Hz, J_{CB} = 2.8 Hz, C_q), 127.9 (C_q), 127.2, 125.8 (C_q), 125.0, 123.6 (C_q), 121.4 (C_q), 120.5, 117.6 (septuplet, J_{CF} = 4.0 Hz), 112.6, 108.4, 101.4, 94.5, 91.7 (d, J_{CP} = 13.7 Hz), 91.3, 55.3, 54.6 (2C missing, probably of the cod ligand). $^{31}P\{^1H\}$ NMR (202 MHz; $CDCl_3$): δ (ppm) = 58.18 (s). HRMS (FAB+) *m*/*z*: $[M - BArF]^+$ calcd for $C_{37}H_{47}IrN_4O_2P$ 803.3194, found 803.3194.

*Complex **4g**.* According to general procedure C, ligand (*R*)-**3g** (143 mg, 0.29 mmol), $[IrCl(cod)]_2$ (97 mg, 0.15 mmol), NaBArF (319 mg, 0.36 mmol), and 15 mL of CH_2Cl_2 were used to give the complex as a brown solid (286 mg, 60% yield). $[\alpha]_D^{20}$ −5 (*c* 1.0, $CHCl_3$); decomp. 80−84 °C. ^1H NMR (500 MHz; $CDCl_3$): δ (ppm) = 7.71 (m, 10H), 7.57 (s, 1H), 7.52−7.51 (m, 5H), 7.43 (t, *J* = 3.0 Hz, 2H), 7.36−7.35 (m, 2H), 7.21 (t, *J* = 8.0 Hz, 1H), 6.95−6.90 (m, 2H), 6.85 (d, *J* = 7.9 Hz, 2H), 6.81 (t, *J* = 7.7 Hz, 1H), 6.70−6.68 (m, 1H), 5.87−5.85 (m, 1H), 5.80 (A of AB, d, *J* = 14.4 Hz, 1H), 5.47 (B of AB, d, *J* = 14.4 Hz, 1H), 5.00 (br s, 1H), 4.95 (d, J_{HP} = 20.2 Hz, 1H), 4.61 (m, 1H), 4.49−4.45 (m, 1H), 3.36 (s, 3H), 3.15−3.13 (m, 1H), 2.85−2.70 (m, 4H), 2.58−2.55 (m, 1H), 2.07−1.99 (m, 2H), 1.74−1.72 (m, 1H), 1.08 (dd, *J* = 19.1, 6.6 Hz, 3H), 0.89−0.86 (m, 1H), 0.65 (dd, *J* = 17.1, 6.5 Hz,

DOI: 10.1021/acs.joc.5b00438
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3H), 0.34 (ddd, J = 21.4, 14.6, 6.9 Hz, 6H). $^{13}C\{^1H\}$ NMR (126 MHz; $CDCl_3$): δ (ppm) = 161.9 (q, J_{CB} = 49.9 Hz, C_q), 155.5 (C_q), 140.2 (C_q), 137.9, 134.9, 133.4 (C_q), 132.9 (C_q), 130.2, 129.9, 129.8 (d, J_{CP} = 1.6 Hz), 129.0 (qq, J_{CF} = 31.5 Hz, J_{CB} = 2.8 Hz, C_q), 128.7, 128.5, 128.34, 128.30, 128.2, 128.1, 128.0 (C_q), 126.6, 125.8 (C_q), 124.9, 123.6 (C_q), 122.9 (d, J_{CP} = 4.6 Hz), 121.5 (C_q), 121.4, 117.6 (septuplet, J_{CF} = 4.0 Hz), 112.4, 101.0 (d, J_{CP} = 10.3 Hz), 94.4, 91.4 (d, J_{CP} = 14.1 Hz), 91.0, 84.7 (d, J_{CP} = 15.0 Hz), 69.5 (d, J = 9.5 Hz), 56.4, 54.0, 38.0, 31.7, 30.2 (d, J_{CP} = 38.8 Hz), 27.7, 27.5 (d, J_{CP} = 34.6 Hz), 27.3, 18.6, 16.8 (d, J_{CP} = 7.6 Hz), 16.5 (d, J_{CP} = 3.8 Hz), 15.7. $^{31}P\{^1H\}$ NMR (202 MHz; $CDCl_3$): δ (ppm) = 57.90 (s). HRMS (FAB+) m/z: $[M - BArF]^+$ calcd for $C_{37}H_{47}IrN_4OP$ 787.3245, found 787.3232.

Complex 4h. According to general procedure C, ligand (R)-**3h** (72 mg, 0.14 mmol), $[IrCl(cod)]_2$ (47 mg, 0.07 mmol), NaBArF (160 mg, 0.18 mmol), and 8 mL of CH_2Cl_2 were used to give the complex as a brown solid (140 mg, 60% yield). $[\alpha]_D^{20}$ −8 (c 1.0, $CHCl_3$); decomp. 97−100 °C. ^1H NMR (500 MHz; $CDCl_3$): δ (ppm) = 8.18 (s, 1H), 8.00 (s, 1H), 7.80−7.67 (m, 10H), 7.66−7.52 (m, 4H), 7.50−7.45 (m, 6H), 7.44−7.37 (m, 3H), 7.31−7.28 (m, 2H), 7.00 (d, J = 8.8 Hz, 2H), 6.86 (d, J = 7.6 Hz, 1H), 6.84 (d, J = 8.8 Hz, 1H), 6.74 (d, J = 7.8 Hz, 1H), 6.13−6.08 (m, 1H), 5.34 (d, J_{HP} = 19.9 Hz, 1H), 5.08−5.05 (m, 1H), 4.73−4.70 (m, 1H), 4.64−4.57 (m, 1H), 3.84 (s, 3H), 3.31−3.18 (m, 2H), 2.92−2.76 (m, 4H), 2.22−1.94 (m, 3H), 1.88−1.73 (m, 1H), 1.14 (dd, J = 19.5, 6.7 Hz, 3H), 0.69 (dd, J = 17.2, 6.6 Hz, 3H), 0.52 (dd, J = 16.5, 7.0 Hz, 3H), 0.46 (dd, J = 13.2, 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (126 MHz; $CDCl_3$): δ (ppm) = 161.8 (q, J_{CB} = 49.8 Hz, C_q), 156.0 (C_q), 137.8 (C_q), 137.5, 136.9, 134.9, 133.9 (C_q), 133.3 (C_q), 132.2 (C_q), 131.11 (d, J_{CP} = 9.7 Hz), 130.8, 130.5 (d, J_{CP} = 5.1 Hz), 129.0 (qq, J_{CF} = 31.5 Hz, J_{CB} = 2.8 Hz, C_q), 128.3 (d, J_{CP} = 4.0 Hz), 128.2, 127.9 (C_q), 127.3, 126.8, 126.4, 125.8 (C_q), 125.7, 124.4, 124.1, 123.6 (C_q), 122.9, 121.5, 121.4 (C_q), 120.72, 120.66, 120.56, 117.6 (septuplet, J_{CF} = 4.0 Hz), 112.8, 112.6 (d, J_{CP} = 26.8 Hz), 94.3, 91.4, 87.7, 85.0 (d, J_{CP} = 24.0 Hz), 54.7, 35.6, 35.3, 29.9, 27.4, 19.1, 16.6, 15.9. $^{31}P\{^1H\}$ NMR (202 MHz; $CDCl_3$): δ (ppm) = 59.04 (s). HRMS (FAB+) m/z: $[M - BArF]^+$ calcd for $C_{40}H_{47}IrN_4OP$ 823.3245, found 823.3253.

General Procedure for Hydrogenation Experiments at High Pressure. The hydrogenation experiments were carried out in a Chemspeed Technologies Accelerator SLT workstation under inert conditions. For a typical screening experiment, stock solutions of complexes (R)-**4a−h** and the substrates were prepared and subsequently mixed by the automated liquid handler. This procedure resulted in catalyst and substrate concentrations of 1.0 and 50−100 mM, respectively, in the reactor. The hydrogenations were carried out at a dihydrogen pressure of 50 bar at room temperature for 20 h. Product samples were prepared directly after completion of the program and analyzed by chiral GC or HPLC.

Hydrogenation of Alkene 5. 2-Phenylbutane. The ee was determined by chiral GC analysis (Supelco β-DEX 225, isothermal at 55 °C): t_R = 35.9 min (R), t_R = 36.5 min (S).

Hydrogenation of Alkene 7. 1,2-Diphenylpropane. The ee was determined by chiral HPLC analysis (Chiralcel OJ-H, 0.8 mL min^{-1}, n-hexane/iPrOH 99.5:0.5 v/v): t_R = 8.9 min (R), t_R = 11.9 min (S).

Hydrogenation of Alkene 9. 2-(4-Methoxyphenyl)-3-methylbutane. The ee was determined by chiral GC analysis (Supelco β-DEX 225, 50 °C, 1 °C min^{-1}, 130 °C): t_R = 66.4 min (major), t_R = 67.1 min (minor), t_R = 72.6 min (substrate).

General Procedure for Hydrogenation Experiments at Ambient Pressure. A solution of 0.25 mmol of substrate and 1 mol % iridium complex (R)-**4** (0.0025 mmol) in 2.5 mL of dry dichloromethane was prepared under argon in a 10 mL Schlenk flask. The reaction mixture was stirred for 120 min at rt with slow bubbling of hydrogen gas through the solution, introduced through a stainless-steel needle. After completion of the reaction, samples were taken and analyzed by chiral GC (see above).

X-ray Crystal Structure Determination of (*R*)-2d. $C_{23}H_{22}N_4O$, FW = 370.45, colorless needle, 0.54 mm × 0.12 mm × 0.06 mm, monoclinic, $P2_1$ (No. 4), a = 10.7827(4) Å, b = 5.5491(3) Å, c = 15.8189(8) Å, β = 92.612(2)°, V = 945.53(8) Å^3, Z = 2, D_{calc} = 1.301 g/cm^3, μ = 0.08 mm^{-1}. X-ray intensities were measured on a diffractometer with a rotating anode (graphite monochromator, λ = 0.71073 Å) at a temperature of 150(2) K. The crystal appeared to be twinned with a twofold rotation about hkl = $(\bar{1}01)$ as the twin operation. This twin relationship was taken into account during the integration with Eval15[43] and absorption correction with the TWINABS[44] software (0.62−0.75 correction range). 16104 Reflections were obtained up to a resolution of $((\sin \theta)/\lambda)_{max}$ = 0.61 Å^{-1}. Because of the absence of strong anomalous scatterers, the absolute structure could not be determined reliably, and it was decided to merge the Friedel pairs, resulting in 1994 unique reflections (R_{int} = 0.052), of which 1785 were observed $[I > 2\sigma(I)]$. The structure was solved with direct methods using SIR-97.[45] Least-squares refinement was performed with SHELXL-97[46] on F^2 for all reflections using an HKLF5 reflection file.[47] The absolute configuration was assigned according to the enantiopure synthesis. Non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms were introduced in calculated positions. The N−H hydrogen atom was refined freely with isotropic displacement parameters; all other hydrogen atoms were refined as rigid groups. 259 parameters were refined with 1 restraint. R_1/wR_2 $[I > 2\sigma(I)]$: 0.0354/0.0784. R_1/wR_2 [all reflns]: 0.0429/0.0821. S = 1.048. Twin fraction = 0.124(3). $\Delta\rho_{min/max}$ = −0.16/0.13 e/Å^3. Drawings, structure calculations, and checking for higher symmetry were performed with the PLATON software.[48]

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of NMR spectral data of new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

NRSC-C and NWO-CW are gratefully acknowledged for financial support. We thank J. W. H. Peeters for measuring high-resolution mass spectra.

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DOI: 10.1021/acs.joc.5b00438
J. Org. Chem. 2015, 80, 3634−3642