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Regiospecific Hydration of *N*-(Diphenylphosphinoyl)propargyl Amines: Synthesis of β-Amino Ketones by Au(III) Catalysis

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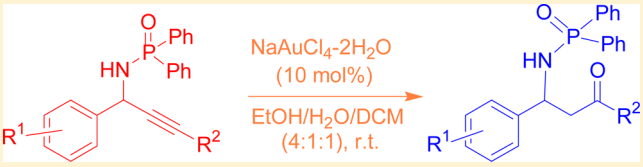
Supporting Information

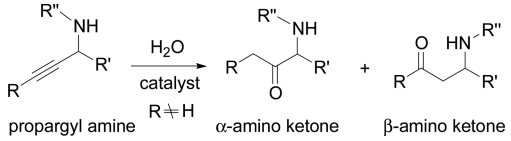
ABSTRACT: A Au(III)-catalyzed regiospecific hydration of *N*-(diphenylphosphinoyl)propargyl amines has been developed to produce various β-amino ketones. These reactions are conducted in the presence of $NaAuCl_4 \cdot 2H_2O$ (10 mol %) in a mixed solvent of $EtOH/H_2O/CH_2Cl_2$ (4:1:1) at room temperature to give the products in 45−71% yield. The high enantiomeric purity of a chiral *N*-(diphenylphosphinoyl)-propargyl amine (85% ee) is maintained after hydration, which makes this method useful for the asymmetric synthesis of chiral β-amino ketones. Reduction of a β-amino ketone product with $Zn(BH_4)_2$ gives a 1,3-amino alcohol with modest diastereoselectivity.



INTRODUCTION

Propargylic amines are versatile synthetic precursors to nitrogen-containing pharmaceuticals, natural products, and other biologically active compounds.[1] For example, the alkyne unit of a propargylic amine can be converted to a carbonyl group by catalytic hydration.[2] As shown in Scheme 1, hydration

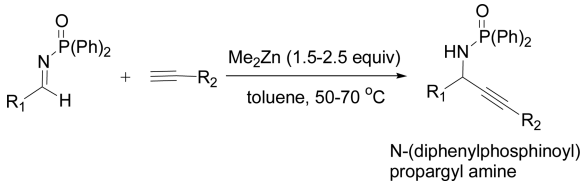
Scheme 1. Hydration of the Propargylic Amine Triple Bond



of an internal alkyne unit of a propargylic amine in the presence of a metal catalyst can generate both α- and β-amino ketones. Although both α- and β-amino ketones are very useful for the synthesis of many functional organic compounds, such as amino alcohols and diamines, there are only limited reports on the regioselective formation of these compounds from hydration of propargylic amines. In several reports, Hg(II) complexes were used, and the observed regioselective formation of the β-amino ketones could be attributed to the aryl group (R = aryl in Scheme 1) on the alkyne carbon of the propargyl amines.[3,4] There was one example on the hydration of an alkyl-substituted propargyl amine (R = alkyl in Scheme 1) catalyzed by using a mixture of $AuClPPh_3$ and AgOTf as the catalyst, which gave a β-amino ketone in good yield.[5] The propargyl amine used in this reaction contains an arylsulfonyl group on the nitrogen.

Propargylic amines can be synthesized by nucleophilic addition of alkynes to imines via deprotonation of terminal alkynes.[1] Among many propargylic amines investigated as synthetic precursors, *N*-(diphenylphosphinoyl)propargyl amines are particularly interesting. These types of compounds can be readily synthesized from the reaction of *N*-(diphenylphosphinoyl)imines with terminal alkynes, as shown in Scheme 2.[6] In this reaction, the *N*-(diphenylphosphinoyl) group[7] can

Scheme 2. Synthesis of *N*-(Diphenylphosphinoyl)propargyl Amines



not only increase the electrophilicity of the imine carbon but also activate $ZnMe_2$ to deprotonate the terminal alkynes for the nucleophilic addition. Several chiral catalysts have also been developed for this reaction for the asymmetric synthesis of propargylic amines.[8] The *N*-(diphenylphosphinoyl) group employed in this reaction can be readily removed from the product in the presence of aqueous hydrogen chloride at room temperature. We propose to explore the use of the *N*-(diphenylphosphinoyl) group of these propagylic amines to direct the regioselective hydration of the alkyne unit. Herein, we report the first example for the regiospecific hydration of *N*-(diphenylphosphinoyl)propargyl amines to generate β-amino ketones by using a Au(III) catalyst at room temperature. We have also demonstrated that when an enantiomerically enriched substrate is used, the high enantiomeric purity of the propargyl amine is maintained in the hydration product.

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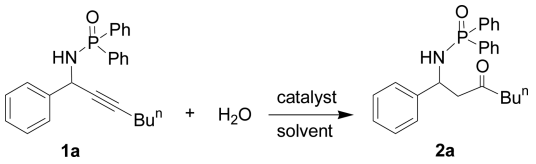
Table 1. Screening of Catalysts and Reaction Conditions for the Hydration of 1a



1a 2a

entry[a]	catalyst	solvent	temp (°C)	time (h)	yield (%)
1	$AgNO_3$	MeOH/H_2O (4:1)	rt	20	nr
2	$Cu(OAc)_2$	MeOH/H_2O (4:1)	rt	20	nr
3	$Hg(OAc)_2$	CH_3CN/H_2O/DCM (4:1:1)	rt	20	trace
4	Zeise's dimer	MeOH/H_2O (3:1)	rt	20	nr
5	Zeise's dimer	MeOH/H_2O (3:1)	50	20	complicated mixture
6	Zeise's dimer	MeOH/H_2O (3:1)	85	12	complicated mixture
7	$NaAuCl_4{\cdot}2H_2O$	EtOH/H_2O (4:1)	rt	20	50
8	$NaAuCl_4{\cdot}2H_2O$	EtOH/H_2O/DCM (4:1:1)	rt	20	62
9	$NaAuCl_4{\cdot}2H_2O$[b]	EtOH/H_2O/DCM (4:1:1)	rt	20	54
10	$NaAuCl_4{\cdot}2H_2O$[c]	EtOH/H_2O/DCM (4:1:1)	rt	20	10
11	Ph_3PAuCl	EtOH/H_2O/DCM (4:1:1)	rt	20	nr
12	$Ph_3PAuCl/AgSbF_6$	EtOH/H_2O/DCM (4:1:1)	rt	20	nr

[a]Alkyne (0.1 mmol), EtOH/H_2O/CH_2Cl_2 (4:1:1, 3 mL); 10 mol % of the catalyst was used unless indicated otherwise. [b]5 mol % of the catalyst was used. [c]1 mol % of the catalyst was used.

RESULTS AND DISCUSSION

In order to conduct the hydration of the alkyne unit of *N*-(diphenylphosphinoyl)propargyl amines, we investigated the reaction of compound **1a** with water in the presence of various Lewis acid catalysts, and the results are summarized in Table 1. In general, in order to maintain the *N*-(diphenylphosphinoyl) group, we avoided the strongly acidic conditions often employed in hydration. It shows that when $AgNO_3$ or $Cu(OAc)_2$ was used, no reaction occurred (entries 1 and 2). The reaction in the presence of $Hg(OAc)_2$ at room temperature gave only a trace amount of product (entry 3). Previously, we reported that the Pt(II)-based Zeise's dimer was very effective for the regiospecific hydration of γ-hydroxy-α,β-acetylenic esters.[9] When **1a** was treated with Zeise's dimer at room temperature, no reaction was observed (entry 4). Increasing the temperature to 50 °C or refluxing at 85 °C led to complicated product mixtures (entries 5 and 6). The gold complex $NaAuCl_4$ was previously reported to be effective for the hydration of alkynes.[10] We were delighted to find that this gold complex also catalyzed the hydration of **1a** to generate the β-amino ketone product **2a** in 50% yield at room temperature in a mixed solvent of ethanol and water (4:1) (entry 7). The yield in entry 5 was increased to 62% when methylene chloride was added to improve the solubility of **1a** (entry 8). In this reaction, only the β-amino ketone product was obtained with no observation of the α-amino ketone isomer. This conversion represents the first example for the regiospecific hydration of *N*-(diphenylphosphinoyl)propargyl amine to generate a β-amino ketone. When the amount of $NaAuCl_4$ was reduced to 5 or 1 mol %, the product yield was reduced (entries 9 and 10). We also tested the use of a Au(I) catalyst, Ph_3PAuCl, as well as its combination with $AgSbF_6$, but neither showed catalytic activity under our reaction conditions (entries 11 and 12).[11]

We prepared a series of *N*-(diphenylphosphinoyl)amines, **1a**–**1k**, as shown in Figure 1, using Bolm's method[6] from the reaction of terminal alkynes with *N*-(diphenylphosphinoyl)-imines in the presence of $ZnMe_2$. These compounds were subjected to the gold catalytic hydration conditions of entry 8 in Table 1 to generate β-amino ketones, and the results are summarized in Scheme 3. It shows that the electron-donating Me-substituted propargylic amine **1b** gives a yield higher than that of compound **1c** that contains an electron-withdrawing Br substituent. The hydration of compounds **1d**–**1f** containing a linear alkyl group on the triple bond proceeds in good yields. The reaction of the chlorine-substituted propargylic amine **1g** gave the desired product **2g** in moderate yield (45%), which could be attributed to side reactions of the alkyl chloride under the reaction conditions. Compounds **1h**–**1j** containing a carbocycle on the triple bond and compound **1k** containing a vinyl group on the triple also gave good yields. We also tested the hydration of a substrate with an aryl substituent on the alkyne carbon (R^1 = H and R^2 = Ph), but no reaction was observed.

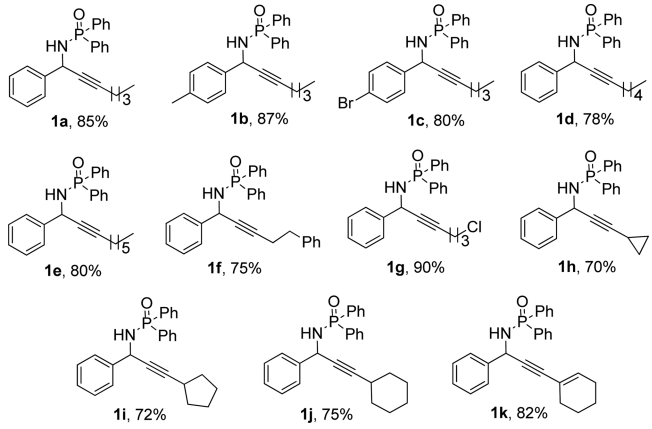


Figure 1. *N*-(Diphenylphosphinoyl)propargyl amines **1a**–**1k** prepared from the reaction of alkynes with *N*-(diphenylphosphinoyl)imines.

Previously, Hammond reported that 3-alkynoates such as **3** undergo a highly regioselective hydration in the presence of $NaAuCl_4$ to give the γ-ketone ester **4** in good yield (Scheme 4).[10b,12] In this reaction, a Au(III)-promoted 5-*endo*-*dig* cyclization intermediate **5** was proposed to account for the observed regioselectivity.

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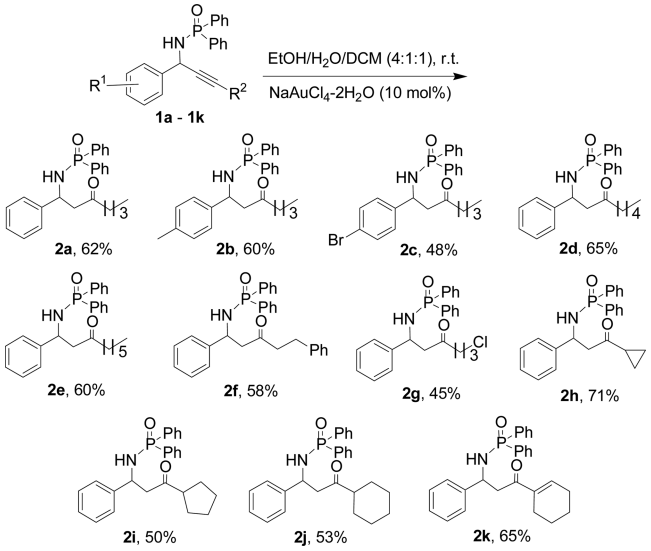
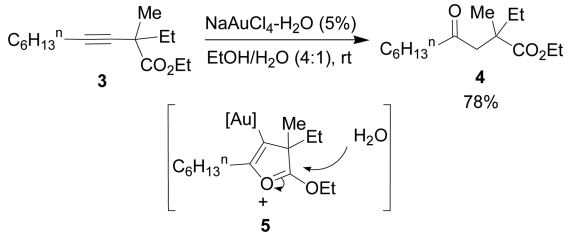
Scheme 3. Gold-Catalyzed Hydration of *N*-(Diphenylphosphinoyl)propargyl Amines 1a−1k



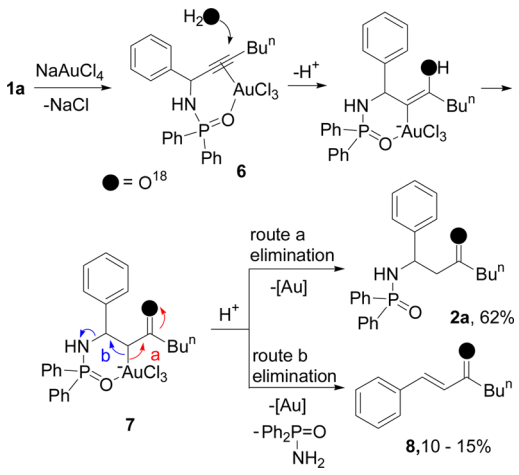
Scheme 4. Regioselective Hydration of 3-Alkynoate 3



In order to gain a better understanding of our Au(III)-catalyzed reaction, we conducted the hydration of **1a** in the presence of $H_2{}^{18}O$. The ^{13}C and ^{31}P NMR spectra of the resulting product **2a** demonstrate that the ^{18}O was incorporated into the ketone group but not in the phosphinoyl group, as an upfield shift of the ^{13}C NMR signal for the carbonyl carbon of **2a** from δ 210.279 to δ 210.228 was observed, but with no shift for the ^{31}P NMR signal. The high-resolution mass spectrum of the product isolated from the hydrolysis in the presence of $H_2{}^{18}O$ gave the molecular ion for **2a** + H^+ at m/z = 408.1967 (calcd for $C_{25}H_{29}NP^{16}O^{18}O$ + H^+ 408.1978), indicating the incorporation of one ^{18}O atom. In the mass spectrum, the base peak is observed for the fragment **2a** − $CH_2C(^{18}O)C_4H_9$ at m/z = 306.1042 (calcd for $C_{19}H_{17}N^{16}OP$ 306.1048) with insignificant ^{18}O incorporation. Thus, the mass spectroscopic study confirms that observed by ^{31}P and ^{13}C NMR analyses, and the carbonyl oxygen of the ketone product is derived from water.

On the basis of the above experimental results, a mechanism for the Au(III)-catalyzed hydration of **1a** is proposed in Scheme 5. The chelate coordination of the phosphinoyl group and the alkyne unit to the Au(III) center can generate the intermediate **6**. Nucleophilic addition of water to the activated alkyne unit of **6** followed by an enol-keto tautomerization could give the intermediate **7**. In this step, the water attack at the C3 position should be more favorable than that at the C2 position because the resulting six-membered ring intermediate should be more favorable than a seven-membered ring intermediate. Intermediate **7** has two possible pathways, routes a and b, to eliminate the Au(III) unit. The route a elimination followed by

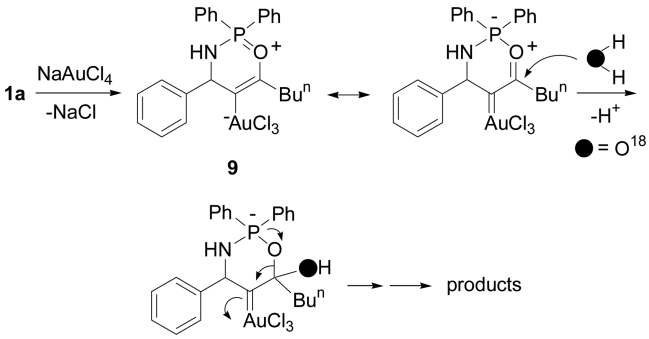
Scheme 5. Proposed Mechanism for the Gold-Catalyzed Hydration of 1a



protonation and tautomerization gave the observed major product, the β-amino ketone **2a**. This mechanism indicates that the phosphinoyl group of the propargylic amines can direct the hydration to occur specifically at the 3-position of the starting propargyl amine. An α,β-unsaturated ketone **8** was also observed as the minor product (10−15% yield) from the gold-catalyzed hydration. Formation of this compound could be attributed to the result of the route b elimination from intermediate **7**.

Although the mechanism proposed in Scheme 5 is reasonable, we also cannot completely rule out another pathway involving the formation of the 6-*endo*-*dig* cyclization intermediate **9** and its subsequent hydrolysis, as shown in Scheme 6. Additional study is necessary in order to distinguish these two mechanisms.

Scheme 6. Another Possible Pathway for the Gold-Catalyzed Hydration of 1a



The regiospecific hydration of the *N*-(diphenylphosphinoyl)-propargyl amines prompted us to study the use of an optically active substrate for this reaction. Recently, we developed an asymmetric addition of aliphatic alkynes to *N*-(diphenylphosphinoyl)imines, affording the *N*-(diphenylphosphinoyl)-propargyl amines with good enantioselectivity.[13] As shown in Scheme 6, (*S*)-**1a** was obtained with 85% ee at room temperature from this asymmetric alkyne addition by using a partially hydrogenated 1,1′-bi-2-naphthol-based catalyst in the presence of $ZnEt_2$ and $Ti(O^iPr)_4$. Applying the conditions for the gold-catalyzed hydration to this optically active propargylic amine led to the formation of the corresponding optically active

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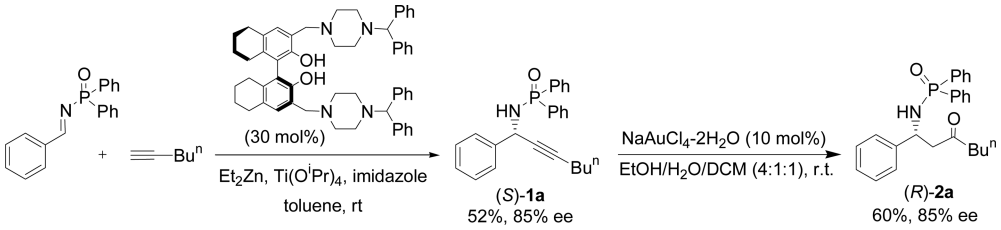
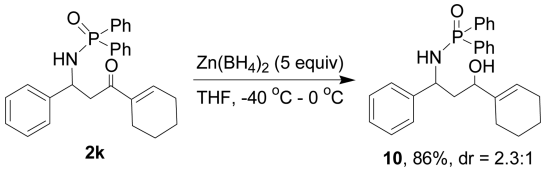
Scheme 7. Preparation of the Optically Active (*S*)-1a and Its Conversion to the *β*-Amino Ketone (*R*)-2a



β-amino ketone (*R*)-**2a** with 85% ee (Scheme 7). This result demonstrates that the gold-catalyzed hydration of the propargylic amines can maintain the enantiomeric purity of the propargylic amine. Thus, this strategy provides an efficient method for the asymmetric synthesis of chiral *β*-amino ketones.

We also tested the reduction of a *β*-amino ketone product obtained from the hydration of a *N*-(diphenylphosphinoyl)-propargyl amine to generate a 1,3-amino alcohol. As shown in Scheme 8, when compound **2k** was treated with $Zn(BH_4)_2$, in situ generated from the reaction of $NaBH_4$ with $ZnCl_2$,[14] the 1,3-amino alcohol product **10** was obtained in 86% yield with a 2.3:1 diastereoselectivity. The modest diastereoselectivity of this reaction can be attributed to the chelate interaction of the carbonyl group and the phosphinoylamine groups of **2k** with the Zn(II) center of the reducing agent. When $NaBH_4$ or $LiBH_4$ was used for the reduction of several of the *β*-*N*-(diphenylphosphinoyl)amino ketones, only a 1:1 mixture of the diastereomeric amino alcohol products was observed. The reaction using $Zn(BH_4)_2$ indicates that it is possible to conduct a diastereoselective reduction of *β*-amino ketones to generate 1,3-amino alcohols. Further enhancement of the diastereoselectivity of this conversion will be explored.

Scheme 8. Reduction of the *β*-Amino Ketone 2k with $Zn(BH_4)_2$



CONCLUSIONS

We have discovered that a simple Au(III) complex can catalyze the regiospecific hydration of *N*-(diphenylphosphinoyl)-propargyl amines to generate *β*-amino ketones under very mild conditions. In this reaction, the *N*-diphenylphosphinoyl group of the substrates should have directed the hydration to occur at the specific alkyne carbon of the propargyl amines. We have also demonstrated that the high enantiomeric purity of a chiral *N*-(diphenylphosphinoyl)propargyl amine can be maintained during the hydration to generate the optically active *β*-amino ketone. This strategy in combination with the asymmetric alkyne addition to *N*-(diphenylphosphinoyl)imines provides a very convenient way for the asymmetric synthesis of chiral *β*-amino ketones that are useful in organic synthesis. Reduction of a *β*-amino ketone with $Zn(BH_4)_2$ gives a 1,3-amino alcohol with modest diastereoselectivity.

EXPERIMENTAL SECTION

General Data. Reactions were carried out under nitrogen. All commercial chemicals were used without further purification unless otherwise noted. Zinc reagents and catalysts were purchased and stored under dry nitrogen atmosphere. Toluene and tetrahydrofuran were distilled over sodium and benzophenone under nitrogen. Dichloromethane was dried by passing through activated alumina columns under nitrogen. All the NMR spectra were obtained in $CDCl_3$ unless indicated otherwise.

General Procedure for the Syntheses of the *N*-(Diphenylphosphinoyl)propargyl Amines 1. Under nitrogen, an alkyne (2 equiv) was added into a dry 100 mL flask and dissolved in toluene (30 mL). Me_2Zn (1.67 mL, 1.2 M in toluene, 2 equiv) was then added, and the mixture was stirred at room temperature for 30 min. Then, a solution of *N*-(diphenylphosphinoyl)imine (1 mmol, 1 equiv) in toluene (5 mL) was added, and the reaction temperature was increased to 70 °C and stirred for 18 h. The reaction was quenched with the addition of water (20 mL) and extracted with dichloromethane (3 × 20 mL). The organic phase was washed with brine (20 mL) and dried with anhydrous Na_2SO_4, filtered, and concentrated by rotary evaporation. The crude mixture was purified by flash column chromatography on silica gel eluted with hexanes/ethyl acetate (1/1) to give *N*-(diphenylphosphinoyl)propargyl amine products **1** in 70−90% yield.

Characterization of the Propargylic *N*-(Diphenylphosphinoyl)amines 1. *P,P-Diphenyl-N-(1-phenylhept-2-yn-1-yl)-phosphinic Amide,* ***1a:*** White solid, mp 116−118 °C, 329 mg (prepared from 1 mmol imine), 85% yield; ^{1}H NMR (600 MHz, $CDCl_3$) *δ* 8.03 (m, 2H), 7.82 (m, 2H), 7.60 (d, 2H, *J* = 7.8 Hz), 7.52 (t, 1H, *J* = 7.2 Hz), 7.46 (m, 3H), 7.37 (m, 2H), 7.32 (t, 2H, *J* = 7.2 Hz), 7.25 (t, 1H, *J* = 6.6 Hz), 5.13 (t, 1H, *J* = 10.2 Hz), 3.41 (t, 1H, *J* = 9 Hz), 2.21 (t, 2H, *J* = 7.2 Hz), 1.48 (m, 2H), 1.41 (m, 2H), 0.91 (t, 3H, *J* = 7.8 Hz); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) *δ* 141.0 (d, *J* = 4.7 Hz), 132.7 (d, *J* = 9.8 Hz), 131.9, 131.8, 128.5, 128.4 (d, *J* = 11.9 Hz), 127.7, 127.2, 86.2, 79.7 (d, *J* = 6.2 Hz), 46.8, 30.7, 22.0, 18.5, 13.6. These data are consistent with those reported.[8d]

P,P-Diphenyl-N-(1-(p-tolyl)hept-2-yn-1-yl)phosphinic Amide, ***1b:*** White solid, mp 138−140 °C, 153 mg (prepared from 0.44 mmol imine), 87% yield; ^{1}H NMR (600 MHz, $CDCl_3$) *δ* 8.02 (m, 2H), 7.82 (m, 2H), 7.52 (m, 1H), 7.47 (m, 5H), 7.38 (m, 2H), 7.12 (d, 2H, *J* = 7.8 Hz), 5.09 (t, 1H, *J* = 9.6 Hz), 3.37 (t, 1H, *J* = 9 Hz), 2.31 (s, 3H), 2.19 (t, 2H, *J* = 7.2 Hz), 1.47 (m, 2H), 1.40 (m, 2H), 0.91 (t, 3H, *J* = 7.2 Hz); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) *δ* 138.2 (d, *J* = 4.7 Hz), 137.4, 132.7 (d, *J* = 9.8 Hz), 131.9, 131.8, 129.1, 128.4 (d, *J* = 12.6 Hz), 127.1, 86.0, 79.8 (d, *J* = 6 Hz), 46.6, 30.7, 22.0, 21.1, 18.5, 13.6; HRMS [ESI(TOF)] calcd for $C_{26}H_{29}NOP$ [M + H$^+$] 402.1987; found 402.1985.

N-(1-(4-Bromophenyl)hept-2-yn-1-yl)-P,P-diphenylphosphinic Amide, ***1c:*** White solid, mp 140−143 °C, 145.4 mg (prepared from 0.39 mmol imine), 80% yield; ^{1}H NMR (600 MHz, $CDCl_3$) *δ* 8.01 (m, 2H), 7.79 (m, 2H), 7.53 (m, 1H), 7.48 (m, 5H), 7.43 (m, 2H), 7.38 (m, 2H), 5.08 (t, 1H, *J* = 9 Hz), 3.44 (t, 1H, *J* = 7.8 Hz), 2.21 (m, 2H), 1.48 (m, 2H), 1.40 (m, 2H), 0.91 (t, 3H, *J* = 7.2 Hz); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) *δ* 140.1 (d, *J* = 3.8 Hz), 132.6 (d, *J* = 9.9 Hz), 132.0 (d, *J* = 10.5 Hz), 131.7 (d, *J* = 9.8 Hz), 131.5, 129.1, 128.4 (d, *J* = 12.9 Hz), 121.7, 86.6, 79.1 (d, *J* = 6.9 Hz), 46.4, 30.6, 22.0, 18.4, 13.6; HRMS [ESI(TOF)] calcd for $C_{25}H_{26}NOPBr$ [M + H$^+$] 466.0935; found 466.0932.

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P,P-Diphenyl-N-(1-phenyloct-2-yn-1-yl)phosphinic Amide, ***1d:*** White solid, mp 120−122 °C, 313 mg (prepared from 1 mmol imine), 78% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.03 (m, 2H), 7.82 (m, 2H), 7.60 (d, 2H, J = 7.8 Hz), 7.51 (m, 1H), 7.45 (m, 3H), 7.37 (m, 2H), 7.32 (t, 2H, J = 7.2 Hz), 7.24 (m, 1H), 5.13 (t, 1H, J = 9.6 Hz), 3.43 (t, 1H, J = 9 Hz), 2.20 (m, 2H), 1.50 (m, 2H), 1.35 (m, 4H), 0.90 (t, 3H, J = 6.6 Hz); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 141.0 (d, J = 4.5 Hz), 132.7 (d, J = 9.8 Hz), 131.9 (d, J = 7.5 Hz), 131.85 (d, J = 9.8 Hz), 128.45 (d, J = 3.6 Hz), 128.4, 127.7, 127.2, 86.3, 79.7 (d, J = 6.2 Hz), 46.8, 31.1, 28.3, 22.2, 18.8, 14.0; HRMS [ESI(TOF)] calcd for $C_{26}H_{29}NOP$ [M + H$^+$] 402.1987; found 402.1971.

P,P-Diphenyl-N-(1-phenylnon-2-yn-1-yl)phosphinic Amide, ***1e:*** White solid, mp 110−112 °C, 332 mg (prepared from 1 mmol imine), 80% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.03 (m, 2H), 7.82 (m, 2H), 7.60 (d, 2H, J = 8.4 Hz), 7.52 (m, 1H), 7.46 (m, 3H), 7.37 (m, 2H), 7.32 (t, 2H, J = 7.2 Hz), 7.25 (m, 1H), 5.13 (t, 1H, J = 9.6 Hz), 3.41 (t, 1H, J = 9 Hz), 2.20 (m, 2H), 1.49 (m, 2H), 1.38 (m, 2H), 1.29 (m, 4H), 0.88 (t, 3H, J = 7.2 Hz); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 141.0 (d, J = 4.7 Hz), 132.7 (d, J = 9.9 Hz), 131.9 (d, J = 7.4 Hz), 131.8 (d, J = 9.6 Hz), 128.5, 128.4 (d, J = 12.8 Hz), 127.7, 127.2, 86.3, 79.7 (d, J = 6.2 Hz), 46.8, 31.3, 28.6, 28.5, 22.5, 18.8, 14.0; HRMS [ESI(TOF)] calcd for $C_{27}H_{31}NOP$ [M + H$^+$] 416.2143; found 416.2141.

N-(1,5-Diphenylpent-2-yn-1-yl)-P,P-diphenylphosphinic Amide, ***1f:*** White solid, mp 148−150 °C, 326 mg (prepared from 1 mmol imine), 75% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.99 (m, 2H), 7.81 (m, 2H), 7.51 (m, 3H), 7.45 (m, 3H), 7.38 (m, 2H), 7.27 (m, 5H), 7.20 (m, 3H), 5.10 (t, 1H, J = 9.6 Hz), 3.39 (t, 1H, J = 9 Hz), 2.80 (m, 2H), 2.51 (m, 2H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 140.8 (d, J = 4.8 Hz), 140.6, 132.6 (d, J = 9.8 Hz), 131.92 (d, J = 7.7 Hz), 131.88 (d, J = 9.6 Hz), 128.5 (d, J = 1.7 Hz), 128.46, 128.38, 128.36, 127.7, 127.2, 126.3, 85.4, 80.5 (d, J = 6 Hz), 46.8, 34.8, 20.9; HRMS [ESI(TOF)] calcd for $C_{29}H_{27}NOP$ [M + H$^+$] 436.1830; found 436.1818.

N-(6-Chloro-1-phenylhex-2-yn-1-yl)-P,P-diphenylphosphinic Amide, ***1g:*** White solid, mp 107−109 °C, 366 mg (prepared from 1 mmol imine), 90% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.00 (m, 2H), 7.82 (m, 2H), 7.56 (d, 2H, J = 7.8 Hz), 7.52 (m, 1H), 7.47 (m, 3H), 7.39 (m, 2H), 7.33 (t, 2H, J = 7.8 Hz), 7.26 (t, 1H, J = 7.2 Hz), 5.14 (t, 1H, J = 9.6 Hz), 3.61 (t, 2H, J = 6.6 Hz), 3.42 (t, 1H, J = 8.4 Hz), 2.39 (m, 2H), 1.92 (m, 2H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 140.7 (d, J = 4.8 Hz), 132.5 (d, J = 9.8 Hz), 132.0 (d, J = 6.9 Hz), 131.8 (d, J = 9.8 Hz), 128.6, 128.4 (d, J = 12.6 Hz), 127.9, 127.1, 84.1, 80.8 (d, J = 5.6 Hz), 46.7, 43.7, 31.2, 16.2; HRMS [ESI(TOF)] calcd for $C_{24}H_{24}NOPCl$ [M + H$^+$] 408.1284; found 408.1280.

N-(3-Cyclopropyl-1-phenylprop-2-yn-1-yl)-P,P-diphenylphosphinic Amide, ***1h:*** White solid, mp 178−180 °C, 260 mg (prepared from 1 mmol imine), 70% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.01 (m, 2H), 7.80 (m, 2H), 7.56 (d, 2H, J = 7.8 Hz), 7.53 (t, 1H, J = 7.2 Hz), 7.47 (m, 3H), 7.38 (m, 2H), 7.31 (t, 2H, J = 7.8 Hz), 7.25 (t, 1H, J = 5.4 Hz), 5.10 (t, 1H, J = 9.6 Hz), 3.38 (t, 1H, J = 8.4 Hz), 1.24 (m, 1H), 0.74 (m, 2H), 0.63 (m, 2H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 140.9 (d, J = 4.7 Hz), 132.7 (d, J = 9.8 Hz), 131.9 (d, J = 8.7 Hz), 131.8 (d, J = 9.8 Hz), 128.5, 128.4 (d, J = 12.6 Hz), 127.7, 127.2, 89.2, 74.8 (d, J = 6 Hz), 46.8, 8.1, −0.5. These data are consistent with those reported.[8d]

N-(3-Cyclopentyl-1-phenylprop-2-yn-1-yl)-P,P-diphenylphosphinic Amide, ***1i:*** White solid, mp 128−130 °C, 287 mg (prepared from 1 mmol imine), 72% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.04 (m, 2H), 7.80 (m, 2H), 7.60 (d, 2H, J = 7.8 Hz), 7.52 (m, 1H), 7.45 (m, 3H), 7.37 (m, 2H), 7.32 (t, 2H, J = 7.2 Hz), 7.24 (m, 1H), 5.15 (t, 1H, J = 9.6 Hz), 3.42 (t, 1H, J = 9 Hz), 2.64 (m, 1H), 1.88 (m, 2H), 1.71 (m, 2H), 1.57 (m, 4H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 141.0 (d, J = 4.4 Hz), 132.7 (d, J = 9.9 Hz), 131.9 (d, J = 9.8 Hz), 131.7 (d, J = 9.9 Hz), 128.4, 128.3 (d, J = 11.9 Hz), 127.6, 127.3, 90.4, 79.2 (d, J = 6 Hz), 46.8, 33.7 (d, J = 1.2 Hz), 30.2, 24.9; HRMS [ESI(TOF)] calcd for $C_{26}H_{27}NOP$ [M + H$^+$] 400.1830; found 400.1828.

N-(3-Cyclohexyl-1-phenylprop-2-yn-1-yl)-P,P-diphenylphosphinic Amide, ***1j:*** White solid, mp 155−157 °C, 310 mg (prepared from 1 mmol imine), 75% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.05 (m, 2H), 7.81 (m, 2H), 7.62 (d, 2H, J = 7.8 Hz), 7.52 (m, 1H), 7.47 (m, 3H), 7.38 (m, 2H), 7.32 (t, 2H, J = 7.2 Hz), 7.25 (m, 1H), 5.15 (t, 1H, J = 9.6 Hz), 3.39 (t, 1H, J = 9 Hz), 2.42 (m, 1H), 1.79 (m, 2H), 1.70 (m, 2H), 1.51 (m, 1H), 1.43 (m, 2H), 1.31 (m, 3H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 141.0 (d, J = 4.2 Hz), 132.8 (d, J = 9.9 Hz), 131.9 (d, J = 10.1 Hz), 131.7 (d, J = 9.8 Hz), 128.4, 128.3, 127.6, 127.3, 90.3, 79.6 (d, J = 6.3 Hz), 46.8, 32.5, 29.1, 25.9, 24.8; HRMS [ESI(TOF)] calcd for $C_{27}H_{29}NOP$ [M + H$^+$] 414.1987; found 414.1982.

N-(3-(Cyclohex-1-en-1-yl)-1-phenylprop-2-yn-1-yl)-P,P-diphenylphosphinic Amide, ***1k:*** White solid, mp 154−156 °C, 337 mg (prepared from 1 mmol imine), 82% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.04 (m, 2H), 7.81 (m, 2H), 7.61 (d, 2H, J = 7.2 Hz), 7.52 (m, 1H), 7.46 (m, 3H), 7.37 (m, 2H), 7.32 (d, 2H, J = 7.8 Hz), 7.25 (m, 1H), 6.09 (s, 1H), 5.26 (t, 1H, J = 9.6 Hz), 3.46 (t, 1H, J = 9 Hz), 2.09 (d, 4H, J = 6 Hz), 1.62 (m, 4H); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 140.7 (d, J = 4.4 Hz), 135.1, 132.8 (d, J = 9.8 Hz), 131.9 (d, J = 7.8 Hz), 131.8 (d, J = 9.8 Hz), 128.5, 128.4 (d, J = 12.8 Hz), 127.8, 127.3, 120.2, 87.4, 86.0 (d, J = 6.3 Hz), 47.1, 29.1, 25.6, 22.2, 21.5; HRMS [ESI(TOF)] calcd for $C_{27}H_{27}NOP$ [M + H$^+$] 412.1830; found 412.1829.

General Procedure for the Gold-Catalyzed Hydration of *N*-(Diphenylphosphinoyl)propargyl Amines 1. Under nitrogen, $NaAuCl_4{\cdot}2H_2O$ (10 mol %) was added to a flask. A solution of the *N*-(diphenylphosphinoyl)propargyl amine **1** (1 equiv) in EtOH/H_2O/CH_2Cl_2 (4:1:1, 3 mL) was then added, and the reaction mixture was stirred at room temperature for 20 h. Water (3 mL) was added, and methylene chloride (3 × 5 mL) was used for extraction. The combined organic layer was dried with anhydrous Na_2SO_4, filtered, and concentrated by rotary evaporation. The crude mixture was purified by flash column chromatography on silica gel eluted with hexanes/ethyl acetate (1:1 to 1:5) to give the β-amino ketone products **2** in 45−71% yield.

Characterization of the Racemic β-Amino Ketone Products 2. *N-(3-Oxo-1-phenylheptyl)-P,P-diphenylphosphinic Amide,* ***2a:*** White solid, mp 155−157 °C, 116.3 mg (prepared from 0.465 mmol amine), 62% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.80 (m, 4H), 7.43 (m, 4H), 7.27 (m, 7H), 4.58 (m, 1H), 4.47 (s, 1H), 3.14 (m, 2H), 2.24 (m, 1H), 2.19 (m, 1H), 1.36 (m, 2H), 1.13 (m, 2H), 0.78 (t, 3H, J = 7.2 Hz); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 210.2, 142.4 (d, J = 7.2 Hz), 132.5 (d, J = 9.6 Hz), 131.8 (dd, J = 6.3, 2.6 Hz), 131.6 (d, J = 9.5 Hz), 128.5 (dd, J = 12.5, 9.3 Hz), 128.4, 127.1, 126.4, 51.8, 50.1, 43.5, 25.3, 22.0, 13.7; HRMS [ESI(TOF)] calcd for $C_{25}H_{29}NO_2P$ [M + H$^+$] 406.1936; found 406.1932.

N-(3-Oxo-1-(p-tolyl)heptyl)-P,P-diphenylphosphinic Amide, ***2b:*** White solid, mp 151−153 °C, 141 mg (prepared from 0.563 mmol amine), 60% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.81 (m, 4H), 7.43 (m, 4H), 7.34 (m, 2H), 7.15 (d, 2H, J = 7.8 Hz), 7.08 (d, 2H, J = 7.8 Hz), 4.55 (m, 1H), 4.31 (m, 1H), 3.13 (d, 2H, J = 5.4 Hz), 2.30 (s, 3H), 2.25 (m, 1H), 2.18 (m, 1H), 1.37 (m, 2H), 1.14 (m, 2H), 0.79 (t, 3H, J = 7.2 Hz); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 210.2, 139.4 (d, J = 7.4 Hz), 136.7, 132.5 (d, J = 9.5 Hz), 131.8 (dd, J = 4.4, 2.6 Hz), 131.6 (d, J = 9.5 Hz), 129.1, 128.4 (dd, J = 12.6, 5.3 Hz), 126.2, 51.5, 50.2 (d, J = 2 Hz), 43.5, 25.3, 22.1, 21.0, 13.7; HRMS [ESI(TOF)] calcd for $C_{26}H_{31}NO_2P$ [M + H$^+$] 420.2092; found 420.2086.

N-(1-(4-Bromophenyl)-3-oxoheptyl)-P,P-diphenylphosphinic Amide, ***2c:*** White solid, mp 163−165 °C, 114 mg (prepared from 0.491 mmol amine), 48% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.81 (m, 2H), 7.75 (m, 2H), 7.43 (m, 6H), 7.34 (m, 2H), 7.15 (d, 2H, J = 8.4 Hz), 4.51 (m, 1H), 4.46 (m, 1H), 3.12 (m, 2H), 2.27 (m, 1H), 2.19 (m, 1H), 1.38 (m, 2H), 1.15 (m, 2H), 0.80 (t, 3H, J = 7.2 Hz); ^{13}C{^{1}H} NMR (150 MHz, $CDCl_3$) δ 210.1, 141.5 (d, J = 6.9 Hz), 132.3 (d, J = 9.6 Hz), 131.9 (dd, J = 5.6, 2.7 Hz), 131.6 (d, J = 9.5 Hz), 131.5, 128.5 (dd, J = 12.6, 7.5 Hz), 128.2, 121.0, 51.2, 49.7 (d, J = 2.3 Hz), 43.5, 25.3, 22.1, 13.7; HRMS [ESI(TOF)] calcd for $C_{25}H_{28}NO_2PBr$ [M + H$^+$] 484.1041; found 484.1028.

N-(3-Oxo-1-phenyloctyl)-P,P-diphenylphosphinic Amide, ***2d:*** White solid, mp 157−158 °C, 158 mg (prepared from 0.581 mmol amine), 65% yield; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.83 (m, 2H), 7.78 (m, 2H), 7.46 (m, 1H), 7.40 (m, 3H), 7.32 (m, 2H), 7.27 (d, 4H, J =

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4.8 Hz), 7.20 (m, 1H), 4.58 (m, 1H), 4.45 (m, 1H), 3.13 (d, 2H, J = 5.4 Hz), 2.24 (m, 1H), 2.16 (m, 1H), 1.38 (m, 2H), 1.17 (m, 2H), 1.07 (m, 2H), 0.79 (t, 3H, J = 7.2 Hz); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 210.3, 142.4 (d, J = 7.2 Hz), 132.5 (d, J = 9.5 Hz), 131.8 (dd, J = 6.3, 2.6 Hz), 131.6 (d, J = 9.5 Hz), 128.5 (dd, J = 12.5, 9 Hz), 128.4, 127.1, 126.4, 51.7, 50.0 (d, J = 2.1 Hz), 43.8, 31.1, 22.9, 22.3, 13.8; HRMS [ESI(TOF)] calcd for $C_{26}H_{31}NO_2P$ [M + H^+] 420.2092; found 420.2087.

N-(3-Oxo-1-phenylnonyl)-P,P-diphenylphosphinic Amide, ***2e:*** White solid, mp 143−145 °C, 140.3 mg (prepared from 0.54 mmol amine), 60% yield; ^1H NMR (600 MHz, CDCl3) δ 7.83 (m, 2H), 7.78 (m, 2H), 7.46 (m, 1H), 7.40 (m, 3H), 7.33 (m, 2H), 7.26 (d, 4H, J = 4.2 Hz), 7.20 (m, 1H), 4.57 (m, 1H), 4.48 (s, 1H), 3.13 (d, 2H, J = 5.4 Hz), 2.23 (m, 1H), 2.18 (m, 1H), 1.37 (m, 2H), 1.19 (m, 2H), 1.11 (m, 4H), 0.81 (t, 3H, J = 7.2 Hz); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 210.3, 142.4 (d, J = 7.2 Hz), 132.5 (d, J = 9.6 Hz), 131.8 (dd, J = 6.3, 2.6 Hz), 131.6 (d, J = 9.5 Hz), 128.5 (dd, J = 12.3, 9.2 Hz), 128.4, 127.1, 126.4, 51.8, 50.1 (d, J = 2.1 Hz), 43.8, 31.5, 28.6, 23.2, 22.4, 14.0; HRMS [ESI(TOF)] calcd for $C_{27}H_{33}NO_2P$ [M + H^+] 434.2249; found 434.2250.

N-(3-Oxo-1,5-diphenylpentyl)-P,P-diphenylphosphinic Amide, ***2f:*** White solid, mp 147−149 °C, 149 mg (prepared from 0.568 mmol amine), 58% yield; ^1H NMR (600 MHz, $CDCl_3$) δ 7.82 (m, 4H), 7.48 (t, 1H, J = 7.2 Hz), 7.41 (m, 3H), 7.34 (m, 2H), 7.23 (m, 7H), 7.14 (t, 1H, J = 7.2 Hz), 7.02 (d, 2H, J = 7.8 Hz), 4.59 (m, 1H), 4.38 (s, 1H), 3.15 (d, 2H, J = 4.8 Hz), 2.73 (t, 2H, J = 7.2 Hz), 2.61 (m, 1H), 2.52 (m, 1H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 208.9, 142.3 (d, J = 7.1 Hz), 140.6, 132.5 (d, J = 9.5 Hz), 131.9 (dd, J = 5.9, 2.6 Hz), 131.6 (d, J = 9.5 Hz), 128.56 (d, J = 12.5 Hz), 128.50, 128.4, 128.2, 127.2, 126.4, 126.0, 51.7, 50.4, 45.2, 29.2; HRMS [ESI(TOF)] calcd for $C_{29}H_{29}NO_2P$ [M + H^+] 454.1936; found 454.1925.

N-(6-Chloro-3-oxo-1-phenylhexyl)-P,P-diphenylphosphinic Amide, ***2g:*** White solid, mp 137−140 °C, 172 mg (prepared from 0.744 mmol amine), 45% yield; ^1H NMR (600 MHz, $CDCl_3$) δ 7.82 (m, 2H), 7.78 (m, 2H), 7.43 (m, 4H), 7.34 (m, 2H), 7.27 (m, 4H), 7.22 (m, 1H), 4.59 (m, 1H), 4.31 (s, 1H), 3.39 (dt, 2H, J = 6.0, 1.8 Hz), 3.16 (d, 2H, J = 6.0 Hz), 2.47 (m, 1H), 2.39 (m, 1H), 1.87 (m, 2H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 208.5, 142.2 (d, J = 7.1 Hz), 132.5 (d, J = 9.6 Hz), 131.9 (dd, J = 6.5, 2.6 Hz), 131.6 (d, J = 9.3 Hz), 128.55, 128.51 (dd, J = 8.9, 3.8 Hz), 127.3, 126.3, 51.7, 50.5 (d, J = 2.1 Hz), 44.1, 40.4, 25.9; HRMS [ESI(TOF)] calcd for $C_{24}H_{26}NO_2PCl$ [M + H^+] 426.1390; found 426.1388.

N-(3-Cyclopropyl-3-oxo-1-phenylpropyl)-P,P-diphenylphosphinic Amide, ***2h:*** White solid, mp 174−176 °C, 163 mg (prepared from 0.59 mmol amine), 71% yield; ^1H NMR (600 MHz, $CDCl_3$) δ 7.83 (m, 2H), 7.78 (m, 2H), 7.46 (m, 1H), 7.40 (m, 3H), 7.32 (m, 2H), 7.27 (m, 4H), 7.20 (m, 1H), 4.60 (m, 1H), 4.45 (s, 1H), 3.30 (d, 2H, J = 5.4 Hz), 1.76 (m, 1H), 0.89 (m, 1H), 0.76 (m, 3H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 209.6, 142.5 (d, J = 6.9 Hz), 132.4 (d, J = 9.6 Hz), 131.8 (dd, J = 7.5, 2.7 Hz), 131.6 (d, J = 9.5 Hz), 128.5 (d, J = 11 Hz), 128.4, 127.1, 126.4, 51.8, 50.7 (d, J = 2.1 Hz), 21.5, 11.0; HRMS [ESI(TOF)] calcd for $C_{24}H_{25}NO_2P$ [M + H^+] 390.1623; found 390.1623 (identical to the calcd).

N-(3-Cyclopentyl-3-oxo-1-phenylpropyl)-P,P-diphenylphosphinic Amide, ***2i:*** White solid, mp 174−177 °C, 114 mg (prepared from 0.549 mmol amine), 50% yield; ^1H NMR (600 MHz, $CDCl_3$) δ 7.84 (m, 2H), 7.78 (m, 2H), 7.47 (m, 1H), 7.41 (m, 3H), 7.33 (m, 2H), 7.27 (d, 4H, J = 4.2 Hz), 7.20 (m, 1H), 4.59 (m, 2H), 3.18 (m, 2H), 2.66 (m, 1H), 1.51 (m, 8H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 212.3, 142.5 (d, J = 7.2 Hz), 132.5 (d, J = 9.6 Hz), 131.8 (dd, J = 6.6, 2.6 Hz), 131.6 (d, J = 9.5 Hz), 128.5 (dd, J = 12.5, 9.3 Hz), 128.4, 127.1, 126.3, 52.1, 51.9, 49.1, 28.1 (d, J = 17.4 Hz), 25.8 (d, J = 11.7 Hz); HRMS [ESI(TOF)] calcd for $C_{26}H_{29}NO_2P$ [M + H^+] 418.1936; found 418.1937.

N-(3-Cyclohexyl-3-oxo-1-phenylpropyl)-P,P-diphenylphosphinic Amide, ***2j:*** White solid, mp 159−162 °C, 141 mg (prepared from 0.617 mmol amine), 53% yield; ^1H NMR (600 MHz, $CDCl_3$) δ 7.83 (m, 2H), 7.78 (m, 2H), 7.46 (m, 1H), 7.41 (m, 3H), 7.32 (m, 2H), 7.26 (d, 4H, J = 4.8 Hz), 7.19 (m, 1H), 4.56 (m, 2H), 3.18 (m, 2H), 2.10 (m, 1H), 1.65 (m, 3H), 1.56 (m, 2H), 1.10 (m, 5H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 213.2, 142.5 (d, J = 7.1 Hz), 132.5 (d, J = 9.6 Hz), 131.8 (dd, J = 6.2, 2.7 Hz), 131.6 (d, J = 9.6 Hz), 128.5 (dd, J = 12.5, 9 Hz), 128.3, 127.0, 126.4, 51.8, 51.4, 48.0, 27.7 (d, J = 10.2 Hz), 25.7, 25.4; HRMS [ESI(TOF)] calcd for $C_{27}H_{31}NO_2P$ [M + H^+] 432.2092; found 432.2089.

N-(3-(Cyclohex-1-en-1-yl)-3-oxo-1-phenylpropyl)-P,P-diphenylphosphinic Amide, ***2k:*** White solid, mp 115−118 °C, 172 mg (prepared from 0.616 mmol amine), 65% yield; ^1H NMR (600 MHz, $CDCl_3$) δ 7.84 (m, 2H), 7.80 (m, 2H), 7.45 (m, 1H), 7.39 (m, 3H), 7.32 (m, 2H), 7.28 (m, 2H), 7.26 (m, 2H), 7.18 (t, 1H, J = 7.2 Hz), 6.77 (s, 1H), 4.62 (m, 1H), 4.54 (m, 1H), 3.43 (dd, 1H, J = 16.8, 4.2 Hz), 3.34 (dd, 1H, J = 15.6, 6 Hz), 2.12 (m, 2H), 2.04 (m, 2H), 1.50 (m, 4H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 199.7, 142.7 (d, J = 6.9 Hz), 141.1, 139.3, 132.4 (d, J = 9.5 Hz), 131.8 (d, J = 2.7 Hz), 131.7 (d, J = 9.6 Hz), 128.4 (dd, J = 12.5, 6.8 Hz), 128.3, 126.9, 126.5, 52.3, 44.7 (d, J = 2.3 Hz), 26.0, 22.7, 21.7, 21.3; HRMS [ESI(TOF)] calcd for $C_{27}H_{29}NO_2P$ [M + H^+] 430.1936; found 430.1938.

Characterization of the Chiral β-Amino Ketone Products (*R*)-2a. *(R)-N-(3-Oxo-1-phenylheptyl)-P,P-diphenylphosphinic Amide, (R)-***2a:** White solid, mp 155−157 °C, 125.6 mg (prepared from 0.517 mmol amine), 60% yield; 85% ee determined by HPLC analysis, CHIRALCEL OD-H column, 90:10 hexanes/^{i}PrOH, flow rate = 1.0 mL/min, λ = 230 nm; retention time, t_{major} = 7.9 min, t_{minor} = 14.4 min; $[\alpha]_D^{23}$ = −66.8 (c = 1.45, $CHCl_3$); ^1H NMR (600 MHz, $CDCl_3$) δ 7.80 (m, 4H), 7.43 (m, 4H), 7.27 (m, 7H), 4.58 (m, 1H), 4.47 (s, 1H), 3.14 (m, 2H), 2.24 (m, 1H), 2.19 (m, 1H), 1.36 (m, 2H), 1.13 (m, 2H), 0.78 (t, 3H, J = 7.2 Hz); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 210.2, 142.4 (d, J = 7.2 Hz), 132.5 (d, J = 9.6 Hz), 131.8 (dd, J = 6.3, 2.6 Hz), 131.6 (d, J = 9.5 Hz), 128.5 (dd, J = 12.5, 9.3 Hz), 128.4, 127.1, 126.4, 51.8, 50.1, 43.5, 25.3, 22.0, 13.7; HRMS [ESI(TOF)] calcd for $C_{25}H_{29}NO_2P$ [M + H^+] 406.1936; found 406.1932.

Reduction of the β-Amino Ketone 2k with $Zn(BH_4)_2$. Under nitrogen, the β-amino ketone **2k** (0.152 mmol, 65.1 mg, 1 equiv) was dissolved in THF (2.0 mL) and cooled to −40 °C. $Zn(BH_4)_2$ (0.76 mmol, 0.3 M in THF, 2.5 mL, 5 equiv) was added dropwise, and the reaction mixture was stirred for 1 h at −40 °C. Then, the reaction mixture was warmed to 0 °C and stirred for another hour. Water (2.0 mL) was added to quench the reaction at 0 °C, and methylene chloride (3 × 4 mL) was then used for extraction. The organic phase was dried with anhydrous Na_2SO_4, filtered, and concentrated by rotary evaporation. The crude mixture was purified by flash column chromatography on silica gel eluted with hexanes/ethyl acetate (1:1) to give the 1,3-amino alcohol **10** as a colorless oil in 86% yield (56.3 mg). ^1H NMR analysis showed a 2.3:1 diastereomeric ratio: ^1H NMR (600 MHz, $CDCl_3$) δ 7.85 (m, 2H), 7.70 (m, 2H), 7.50 (t, 1H, J = 7.8 Hz), 7.42 (m, 3H), 7.27 (m, 5H), 7.13 (d, 2H, J = 7.2 Hz), 5.67 (s, 1H), 4.42 (m, 1H), 4.33 (d, 1H, J = 10.2 Hz), 3.45 (t, 1H, J = 9.6 Hz), 1.97 (m, 5H), 1.77 (m, 1H), 1.53 (m, 5H); $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 144.3 (d, J = 6.2 Hz), 139.5, 132.8 (d, J = 9.9 Hz), 132.0 (dd, J = 30.2, 2.4 Hz), 131.5 (d, J = 9.8 Hz), 128.5, 128.4 (dd, J = 52.1, 12.5 Hz), 126.9, 126.0, 121.7, 70.8, 52.3, 45.5, 24.9, 24.6, 22.7, 22.6; HRMS [ESI(TOF)] calcd for $C_{27}H_{30}NO_2PNa$ [M + Na^+] 454.1912; found 454.1906.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01111.

NMR spectra and HPLC plots of the compounds and details of the ^{18}O labeling experiment (PDF)

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Notes

The authors declare no competing financial interest.

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